A randomized clinical trial was conducted in Emory Healthcare breast imaging centers to identify women at increased risk of hereditary breast/ovarian cancer (HBOC) and to determine the most effective means of referral to maximize uptake of genetic counseling (GC) services. Increased risk was determined using the Breast Cancer Genetics Referral Screening Tool (B-RST™), a validated electronic family history screener designed to identify persons at risk for HBOC. Despite successful identification of more than 600 at-risk individuals, initial GC uptake was low in all three referral groups: 1) self-referral, 2) electronic health record message to ordering provider, and 3) direct patient contact by study staff. To understand barriers to uptake in this setting, and to maximize the number of patients who ultimately received cancer genetic services, we emailed a follow-up survey to 239 qualifying participants who had not scheduled a genetic counseling appointment within three months of their positive B-RST result (group 1) or their last contact with the study (groups 2 & 3). The survey’s purpose was twofold: to remind and educate participants about the benefits of GC, and to identify GC barriers among individuals at increased risk of HBOC. The survey explored numerous psychosocial measures, e.g., cancer worry, risk perception, HBOC knowledge, perceived barriers, benefits of, and attitudes about genetic counseling. The most commonly reported barriers to scheduling were lack of physician recommendation (71%), health insurance concerns (67%) and indecision about GC (66%). However, 52% reported interest in future GC contact. A majority (52%) also indicated they were somewhat or very likely to receive genetic counseling within the next six months. Of 97 survey participants (response rate 40.4%), 15 individuals (15.5%) completed GC following the survey, most within three months. This rate is more than double that of those who did not complete the survey (7.3%), suggesting that the additional point of contact was effective in increasing GC uptake.
Family history information is often collected from women while undergoing a screening mammogram. A computer software algorithm was implemented within a mammography platform that identifies individuals at-risk for Lynch syndrome based on Amsterdam and revised Bethesda criteria, and generates a risk notification letter. This study aimed to describe how individuals interpret the risk notification letter and determine factors that influenced the decision whether or not to pursue genetic counseling and/or genetic testing after receipt of a risk notification letter. Of 40,277 individuals who had a mammogram over 8 months, 376 were identified at-risk for Lynch syndrome (0.93%) and those who had not previously undergone genetic counseling were sent a risk notification letter (N=365). A survey with closed and open-ended questions was developed and sent to those who received a risk notification letter. A total of 57/365 completed the survey for a 15.6% response rate. Only 4 (7.0%) reported they had genetic counseling following receipt of the risk notification letter. Commonly identified barriers to pursuing a genetic counseling appointment included lack of perceived benefit, lack of awareness and fear of risk, cost and insurance discrimination concerns, lack of referral, and external factors (time, illness, etc.). When presented options for what might have made them respond to the risk notification letter, the most commonly selected response was adding information to the letter about benefits to genetic testing (93% highly or somewhat likely), followed by adding information about hereditary cancer syndromes and including personal information about their family history of cancer. This study provides insight to increase genetic counseling uptake in this population.

Information Seeking and Scanning Behaviors in Individuals Scheduled for Cancer Genetics Consultations

Platform Presentations: Cancer
Submitter: Sabrina Nichole DiMaso, MS, DuPage Medical Group

Presenting Author: Sabrina Nichole DiMaso, MS, DuPage Medical Group

Primary Author: Sabrina Nichole DiMaso, The Ohio State University

Author 2: Shelly Hovick, PhD, The Ohio State University

Author 3: Alexandra Ilacqua, MS, LGC, Mount Carmel Health System
Information seeking (actively searching for information) and scanning (exposure to information in the absence of actual intention to receive it) have been studied in the context of health behaviors, but there are very little data about the impact of information behaviors on the perceptions of individuals presenting for genetic counseling. To investigate, we conducted a cross-sectional survey of patients scheduled for cancer genetic counseling appointments (N=111). The electronic survey instrument was built using constructions of the Planned Risk Information Seeking Model (PRISM), which states that intent to seek information is the result of one’s perceptions of their own knowledge insufficiency, risk perceptions, and attitudes and beliefs toward information seeking. The survey collected information about primary topics of interest and sources of information seeking and scanning, as well as relationships between information behaviors and risk perceptions, perceived knowledge, perceived control, cancer-related worry, and understanding of the genetic counseling process. The majority of participants (84.7%) report information scanning. More than half (54.1%) report information seeking. Those without a personal history of cancer were more likely to seek information than those with a personal history of cancer. The most likely source of information seeking was the Internet. Information seeking was found to be associated with higher perceived knowledge, higher personal control over cancer risk, and better understanding of the genetic counseling process (ps < .05). This data sparks discussion over the effects of information behaviors as well as how information behaviors may be leveraged by genetic counselors in their clinics. Understanding information seeking and scanning behaviors of genetic counseling clients is the first step in understanding client information needs in order to tailor genetic counseling information interventions. This study serves as a pilot for future projects about information behaviors in the context of genetic counseling.

Identification of cancer risk during prenatal genetic counseling sessions: Evaluation of current practice protocols

Platform Presentations: Cancer
Submitter: Jennifer Cech, UC Irvine
Presenting Author: Jennifer Cech, UC Irvine
Primary Author: JENNIFER CECH, PhD, University of California, Irvine
Author 2: MAUREEN BOCIAN, MD, MS, University of California, Irvine
Author 3: KATHRYN SINGH, MPH, MS, LCGC, University of California, Irvine
Author 4: KATHRYN STEINHAUS FRENCH, MS, LCGC, University of California, Irvine

At our center, 59% of three-generation pedigrees taken during a prenatal genetic counseling session in 2016 included an incidental finding of any cancer, a 19% increase from 2010. Due to this high prevalence of reported family histories of cancer, prenatal genetic counselors are in a position to identify and refer at-risk patients for comprehensive cancer genetic risk assessment and testing. The aim of this study was to assess current practice protocols of prenatal genetic counselors to understand if
there is uniformity in how they evaluate and respond to families with reported cancer history. An online survey of 104 prenatal genetic counselors revealed that the majority of counselors ask about age of diagnosis when cancer is discussed, but only 61% ask about cancer every time they take a three-generation pedigree or use a questionnaire that includes cancer. When presented with sample pedigrees, prenatal counselors responded differently to a high risk of cancer in a maternal vs. a paternal lineage; 24% elected to refer to cancer genetic counseling for a paternal high-risk family compared to 62% for a maternal high-risk pedigree. Counselors with only prenatal experience were more likely to discuss the option of cancer genetic counseling for a low-risk history, whereas those with prior cancer experience were more likely to tell the patient the history was not suggestive of a hereditary cancer predisposition syndrome. This study also determined that practice protocols of prenatal genetic counselors have changed in the last eight years; there was an 11% increase in how often they took a three-generation family history that included cancer in 2010 vs. those same counselors’ responses in 2016. This study highlights the need for a standard practice protocol to guide prenatal genetic counselors on how to evaluate, respond, and relay information regarding cancer genetic risk assessment to prenatal patients.

Uveal Melanoma Prognostic Genetic Testing: An Emerging Role for Genetic Counselors

Platform Presentations: Cancer
Submitter: Honey Nagakura, MS, CGC,

Presenting Author: Honey Nagakura, MS, CGC,

Primary Author: Honey Nagakura, MS, CGC, Integrated Genetics

Author 2: Amy Cronister,

Author 3: Jaime Jessen,

Uveal Melanoma (UM) Prognostic Genetic Testing, performed on UM tumor cells, is used to predict the chance of metastatic disease. Genetic tumor results are combined with tumor histology and patient demographics to produce a personalized survivorship prediction. Here we present two cases with different results to illustrate the underlying counseling issues. Both patients were diagnosed with uveal melanoma and had prognostic genetic testing. Patient 1 is a 55-year-old male whose tumor had a largest basal diameter (LBD) of 8mm. Tumor genetic testing revealed disomy 3.GNAQ exon 5 sequencing showed the p.Q209 mutation, confirming that tumor tissue was sampled. Based on this and individual clinical and histomorphological data provided by the referring physician, the patient was given a survivorship prediction of 92-95% in 10 years, compared to the control group of 91%. Patient 2, by comparison, is a 53-year-old female whose tumor had an LBD of 19mm and monosomy 3. Her survivorship prediction was 22-31% in 10 years, compared to the control group of 95%. For both patients, the counseling process included a review of the testing technologies performed, factors incorporated into the survivorship prediction, and disclosure and discussion of the patient’s survivorship prediction for years 3, 5, and 10, compared to controls. The objective for each session was to help the
patient understand the implications of the patient’s individualized results, and importantly, to address individual psychosocial needs and concerns.

Genetic counselors have the expertise to disclose UM prognostic genetic testing results and address psychosocial issues. As the applications of tumor testing continue to advance, genetic counselors have a unique opportunity to collaborate with oncologists and other cancer care providers to facilitate patient understanding regarding the results and implications of genetic tumor testing.

Identifying Individuals with Mutations Prior to Cancer Diagnoses using NCCN Criteria: Successful or Not?

**Platform Presentations: Cancer Guidelines and Risk Assessment**

*Submitter: Brian Reys, MS, CGC, UT Southwestern*

*Primary Author: Brian Reys, MS, CGC, UT Southwestern*

*Presenting Author: Brian Reys, MS, CGC, UT Southwestern*

*Author 2: Caitlin Mauer, UT Southwestern Medical Center*

*Author 3: Sara Pirzadeh-Miller, UT Southwestern Medical Center*

*Author 4: Theo Ross, UT Southwestern Medical Center*

**Introduction:** Early detection and prevention are cornerstones in the efforts to reduce cancer morbidity and mortality. Current guideline goals are to identify high-risk individuals before they develop cancer. NCCN BRCA1/2 genetic testing criteria are widely recognized standards for offering BRCA1/2 testing. This study aims to evaluate the effectiveness of current NCCN criteria in identifying high-risk patients before their cancer diagnoses. <br />

**Methods:** A retrospective chart review was performed for 650 patients with a personal history of cancer (breast, ovarian, pancreatic, and prostate) seen at UT Southwestern and affiliate hospitals between 2009-2018. All patients tested positive (pathogenic/likely pathogenic) for a breast cancer-associated mutation (ATM, BARD1, BRCA1, BRCA2, BRIP1, CDH1, CHEK2, MRE11A, NBN, NF1, PALB2, PTEN, RAD50, RAD51C, RAD51D, TP53). Review determined if patients met NCCN (v1.2018) BRCA1/2 testing criteria before and after their personal diagnosis of cancer. Patients who met testing criteria for other syndromes were excluded. The study controlled for known mutations in families, past iterations of NCCN guidelines and instances of limited family history. <br />

**Results:** Of patients with BRCA1/BRCA2 mutations, 86/243 (35%) and 60/186 (32%), respectively, met NCCN testing criteria only after their personal diagnosis of cancer. These rates were higher in patients positive for mutations in moderate risk genes: ATM (22/55, 40%), CHEK2 (36/63, 57%) and PALB2 (18/40, 45%). 10 (2%) patients never met NCCN criteria despite their cancer diagnosis, 5 of those being positive for a BRCA1/2 mutation. Overall, 245/650 (38%) of patients did not meet NCCN criteria until after their cancer diagnosis. <br />

**Conclusion:** 38% of patients with known cancer risk-causing mutations would not have met NCCN criteria prior to their diagnosis of cancer. As the field debates the merits of population based testing, this study suggests the current criteria for identifying high-risk patients are not successful at preventing cancers.
Moderate Penetrance Breast Cancer Genes: Surgical Decisions and Bilateral Breast Cancer Risk

**Platform Presentations: Cancer Guidelines and Risk Assessment**

*Submitter: Jordan Berg, UT Southwestern*

*Presenting Author: Jordan Berg, UT Southwestern*

*Primary Author: Jordan Berg, UT Southwestern*

*Author 2: Caitlin Mauer, UT Southwestern*

*Author 3: Brian Reys, UT Southwestern*

*Author 4: Sara Pirzadeh-Miller, UT Southwestern*

*Author 5: Theodora Ross, UT Southwestern*

With the onset of panel testing in cancer genetics, more and more patients are diagnosed with mutations in moderate risk breast cancer (BC) genes including ATM, CHEK2, and PALB2. A paucity of data regarding bilateral BC risk exists for these genes and the implications for surgical decisions. Here we determined prevalence of bilateral BC among ATM, CHEK2, and PALB2 carriers and surgical decisions following BC diagnosis and positive genetic testing. Retrospective chart review was performed for women with a personal history of BC who tested positive for a pathogenic mutation in ATM, CHEK2, or PALB2 within the UT Southwestern cancer genetics program between 2013-2017. Cancer diagnoses and treatment plans were analyzed for those that met inclusion criteria. A total of 14,593 patients underwent genetic counseling/testing. Of 136 patients who met inclusion criteria, 47 ATM, 55 CHEK2, and 38 PALB2 mutations were identified. Nine women (6.6%) had two mutations and four of these were a combination of ATM, CHEK2, or PALB2 mutations. Rates of bilateral BC at time of genetic diagnosis were 12.8% (6/47) for ATM, 16.4% (9/55) for CHEK2, and 13.2% (5/38) for PALB2, as compared to 7.6% (277/3661) among internal control population. Of those with unilateral BC, 86.7% (104/120) had not chosen to undergo prophylactic mastectomy of the remaining breast prior to genetic diagnosis. Of these, 37.8% (14/37) of ATM, 39.5% (15/38) of CHEK2, and 48.3% (14/29) of PALB2 carriers chose prophylactic surgery following genetic diagnosis. This study shows that prevalence of bilateral BC in ATM, CHEK2, and PALB2 carriers is higher than expected. Despite NCCN guidelines not formally recommending prophylactic bilateral mastectomy based on ATM, CHEK2, and PALB2 mutations alone, 37.8% of BC patients in the cohort elected bilateral mastectomy following positive genetic testing. While further studies are needed to clarify incidence of bilateral BC among ATM, CHEK2, and PALB2 carriers, these data suggest genetic counselors need to be prepared to discuss risks of second primary cancers and surgical planning.

Triple Negative Breast Cancer – an Indication for Testing Beyond BRCA1/BRCA2

**Platform Presentations: Cancer Guidelines and Risk Assessment**

*Submitter: Katherine Skora,*
Background: Triple negative breast cancer (TNBC) is a feature of BRCA1-related breast cancer (BC) and the National Comprehensive Cancer Network (NCCN) recommends BRCA1/BRCA2 (BRCA) testing for women with TNBC diagnosed ≤60, regardless of family history of breast, ovarian, pancreatic or prostate cancer (FHx). It is unclear if this indication is also appropriate for cancer panels. We assessed yield and proportions of BRCA variants between patients meeting only this criterion (TNBC 46-60, no FHx) and those meeting other criteria.<br />

Methods: We retrospectively reviewed personal and family histories of patients referred for cancer panel testing. Individuals had testing for at least ATM, BRCA, CDH1, CHEK2, PALB2, PTEN and TP53, and were excluded if they were male, <18, of Ashkenazi Jewish ancestry or had ovarian or pancreatic cancer. Chi-square and Fisher’s exact tests were used to compare yields.<br />

Results: Among BC patients, 10.4% (n=24,381) carried at least one pathogenic/likely pathogenic variant (PV), 35.6% of which were in BRCA. Among women with TNBC 46-60 and no FHx (n=426), 7.0% had a PV; 51.6% of PVs were in non-BRCA genes. We compared yields and BRCA proportions to other groups meeting NCCN criteria. For women with BC ≤45, no FHx (n=2,403), 8.6% had a PV (58.6% in non-BRCA). Women with BC ≤50 and a second primary BC, no FHx (n=335), had a 14.3% yield (59.2% in non-BRCA). Finally, women with BC ≤50 with FHx (n=9844), had a 12.7% yield (61.8% in non-BRCA). There was a significant difference in yield between TNBC 46-60 (no FHx) and women with BC≤50 with a second BC (7.0% vs 14.3%, p=0.0011) as well as in comparison to BC≤50 with FHx (7.0% vs 12.7%, p<0.001). The difference between TNBC 46-60 and BC≤45 was not significant (7.0% vs 8.6%, p=0.34).<br />

Conclusions: Per current guidelines, TNBC ≤60 is an indication for only BRCA testing. Guidelines for testing of other genes in these individuals are not available. In women who only met this criterion, over 50% of PVs were in non-BRCA genes. These data support testing women with TNBC ≤60 for a broader spectrum of cancer genes.

Adult-onset neurologic disease risks in carriers of recessive conditions: Current knowledge, practices, and attitudes of genetic counselors providing carrier screening.

Platform Presentations: Counseling/Psychosocial
Submitter: Tara A Jones, MS, Cedars Sinai
Carriers of certain autosomal recessive and X-linked recessive conditions are also at risk to develop adult-onset conditions. With the increasing use of expanded universal carrier screening, patients at risk for adult-onset conditions will be identified in the preconception/prenatal period. The current practices and attitudes of preconception/prenatal genetic counselors (PPGCs) regarding risk discussions for adult-onset conditions during pre- and/or post-test counseling sessions are unknown. To address this gap, PPGCs were surveyed regarding their attitudes and practices on counseling patients for adult-onset neurological conditions, using a well-published link in fragile X premutation carriers with a risk to develop tremor/ataxia (FXTAS) and a newer link in affected patients and carriers of Gaucher disease with a risk to develop Parkinson disease (GBA-PD), as proxies. Between November 10 to December 22, 2017, PPGCs who were members of NSGC and counseled about carrier screening within the past three years were invited to take an online survey. One hundred twenty genetic counselors completed the survey. A majority of counselors reported awareness of the GBA-PD link (n = 78; 65%), though few reported discussing it in preconception/prenatal settings (n = 30; 38.5%). Contrastingly, nearly 100% of respondents reported discussing FXTAS (n = 117) in the same settings. The GBA-PD link was discussed more consistently when disclosing positive GBA results or when the patient/family approached the topic. Main reasons for not discussing the GBA-PD link included: not knowing enough about the link and the lack of professional guidelines. The main reasons for discussing either link included: the presence of peer-reviewed literature regarding the link, respecting a patient’s right-to-know, and, in the case of FXTAS, the presence of guidelines from professional organizations. These results highlight an inconsistency in PPGCs discussions of adult-onset risks with carriers and a need to develop guidelines to help standardize the care and education of these patients.

Effect of Providing Education about Carrier Results via Web versus Genetic Counselor on the Subsequent Therapeutic Relationship

Platform Presentations: Counseling/Psychosocial
Submitter: Lori A. Hamby Erby, National Human Genome Research Institute/Johns Hopkins Bloomberg School of Public Health GCTP

Primary Author: Lori A. Hamby Erby, National Human Genome Research Institute/Johns Hopkins Bloomberg School of Public Health GCTP
The expertise of genetic counselors should be targeted to contexts in which clients are most likely to benefit. One possible delivery model involves education via a web platform with follow-up genetic counseling to assist with adaptation to the information. A prior study of carrier results delivery to healthy adults beyond childbearing years examined post-session outcomes and demonstrated noninferiority of web-based results delivery when compared to delivery by a genetic counselor (GC). The counseling tasks in genetic counseling rely on the development of a therapeutic relationship. Psychotherapy research demonstrates that a therapeutic relationship grows stronger when the counselor and client meet multiple times. We examined whether the therapeutic relationship as assessed by an observer was higher in post-carrier results follow-up genetic counseling sessions when results were previously delivered by the same genetic counselor than when results were delivered via the web. Participants were part of the NIH ClinSeq study. They were first randomized to receive education about their results via a web platform or via a GC and were then further randomized to receive follow-up genetic counseling or not. We rated audio recordings of 73 follow-up genetic counseling sessions using the observer version of the Working Alliance Inventory (WAI-O). Eleven sessions were rated by a second coder, with an inter-rater reliability of 81.1%. T-tests were used to consider differences in WAI-O scores between the two groups who received follow-up counseling. Participants had a mean age of 63 years and were primarily white (93%) and well-educated. The mean therapeutic alliance scores did not differ significantly between the two study arms (education by GC 5.34/7; education by web 5.24/7; t=0.72, p=0.24). Results suggest that the use of a web platform in this specific context did not adversely affect the subsequent therapeutic relationship, but it would be important to consider this in future studies with higher impact genetic test results.

Preimplantation genetic diagnosis in inherited heart diseases: A qualitative study

Platform Presentations: Counseling/Psychosocial
Submitter: Laura Yeates, Centenary Institute and Royal Prince Alfred Hospital

Primary Author: Laura Yeates, Centenary Institute and Royal Prince Alfred Hospital

Presenting Author: Laura Yeates, Centenary Institute and Royal Prince Alfred Hospital

Author 2: Kristie McDonald, Centenary Institute

Author 3: Charlotte Burns, Centenary Institute and Royal Prince Alfred Hospital
Introduction: Preimplantation genetic diagnosis (PGD) is a reproductive technique that ensures a pathogenic variant is not passed to the next generation. PGD is known to cause significant emotional burden. Inherited heart diseases show variable penetrance and clinical heterogeneity, ranging from asymptomatic individuals to heart failure and sudden cardiac death. Here we explore the experiences of PGD in the setting of inherited heart diseases.

Method: Participants were recruited from a specialised multidisciplinary cardiac genetic clinic. Purposive sampling was used. Patients and partners who had previously considered and/or undertaken PGD were invited to participate. A semi-structured interview schedule was developed to explore overall experiences and reasons for PGD uptake. Broad topics included experience of disease, reproductive history, psychosocial and financial considerations. Interviews were recorded, transcribed verbatim and thematic analysis performed.

Results: 14 participants were recruited (12 with an inherited cardiomyopathy, 1 with an inherited arrhythmia and 1 partner). Two broad themes emerged: 1. Past experience influencing now: encompassing patients experience of disease, reproductive history and personal beliefs, and 2. Deliberating the decision: including uncertainty for self and future generations, judgement from others, isolation and financial considerations. Amongst those who chose to undergo PGD (7/14), past experience of a significant cardiac event, such as family history of sudden cardiac death, was an important factor in the decision process.

Conclusion: The decision to undergo PGD in inherited heart disease is complex and influenced by individual experience of disease. We highlight key areas where genetic counselling intervention may assist in PGD decision processes.

Rare Disease Caregiving in America: What Genetic Counselors Need to Know

Platform Presentations: Counseling/Psychosocial
Submitter: Erica Ramos, MS, LCGC,
Presenting Author: Erica Ramos, MS, LCGC,
Primary Author: Erica Ramos,
Author 2: C. Grace Whiting, National Alliance for Caregiving
Author 3: Lisa Weber-Raley, Greenwald & Associates
Author 4: Nicole Boice, Global Genes

An estimated 25-30 million Americans have a rare disease or condition. As the genetic underpinnings of rare disease are elucidated and genetic testing becomes more accessible, more individuals are likely to engage with genetic counselors. Understanding the needs of these patients, families and caregivers is paramount.

In fall 2017, the National Alliance for Caregiving, in partnership with Global Genes, conducted a national online quantitative study of 1,406 unpaid caregivers age >=18 living in the United States who provide care to a child or adult with a rare disease or condition. 71% of rare caregivers provide care to someone whose rare disease or condition is genetic. 400 unique rare
diseases and conditions were captured with cystic fibrosis (9%), pulmonary arterial hypertension (4%), atypical hemolytic uremic syndrome, Ehlers-Danlos syndrome, and Fabry disease (2% each) among the most often mentioned. 73% of these rare caregivers report that their care recipient consulted with a genetic counselor. Most rare caregivers are immediate relatives, with 59% caring for their own child under 18, 17% caring for their own adult child, and 14% caring for a spouse/partner. 22% cared for multiple individuals with rare disease. Rare caregivers say providing care is emotionally stressful (67%), twice as high as that of general caregivers. 41% report having fair or poor emotional or mental health. 74% of rare caregivers struggle with a sense of loss for what their care recipient’s life would be like without their condition. Only 44% feel their role as a rare caregiver has had a positive impact on their family. 31% of rare caregivers turn to a genetic specialist/counselor for information. Among all rare caregivers, 11% indicate that a genetic counselor is needed and difficult to find. This research suggests rare disease has a broad and lasting impact on caregivers, in both daily life and long-term well-being. As these caregivers are often family, genetic counselors are well-positioned to contribute to the rare caregiving community by recognizing and addressing their needs.

Psychometric properties of the Genetic Counselling Outcome Scale (GCOS): A Rasch analysis

Platform Presentations: Counseling/Psychosocial
Submitter: Jehannine C. Austin, PhD, MSc, CGC, CCGC, University of British Columbia

Primary Author: Kennedy Borle,
Author 2: Jehannine Austin,
Author 3: Skye Barbic,
Presenting Author: Kennedy Borle,

Background: In genetic counseling research, the Genetic Counseling Outcome Scale (GCOS) is becoming widely used to measure empowerment. Although the GCOS was developed and validated in a clinical genetics setting, there is little psychometric data about the instrument and Rasch Measurement Theory (RMT) has not been applied. The measurement model underpinning RMT has potential to support the clinical relevance of GCOS scores, thereby advancing an evidence-based approach to measuring empowerment in genetic counseling. Purpose: To use RMT to explore how the scales psychometric properties of the GCOS could be fine-tuned for measuring empowerment in genetic counseling.

Methods: We used retrospective data from a clinic in which the GCOS was routinely administered before (T1) and one-month after (T2) a psychiatric genetic counseling appointment. We tested the psychometric quality of the items using methods guided by RMT. Specifically, we tested the ordering of response option thresholds, fit, spread of the item locations, residual correlations, person separation index (PSI), and stability across time. Results: 235 participants (avg age: 39.4 years (SD=12.1), 82% female) completed the GCOS at T1 and T2. The original 24 items showed poor overall fit to the Rasch model, with 23/24 items showing statistical and graphical evidence of misfit. Fit was improved by
collapsing response scale to three categories and removing eight items. The final 16-items showed excellent overall fit to the Rasch model ($\chi^2=119.9$, df=112, $p=0.29$), high reliability ($r_p=0.85$), an ordered response scale structure, and no item bias for gender, age, or ethnicity. The set of items showed strong evidence for picking up genetic counseling related change (mean =0.91 logits).<br />Conclusions: These data support a set of 16 items to measure a uni-dimensional construct of empowerment in this context. Collectively, the 16-items demonstrated high sensitivity to pick up change over time. Opportunity exists to revisit the original 24-item set to address the anomalies revealed by the RMT analysis and refine the GCOS.

**Closing the Disparity Gap: Alternative Service Delivery Models as an Opportunity to Increase Access to Genetic Testing in Underrepresented Groups**

**Platform Presentations: Diversity and Access**

*Submitter: Lauren Ryan, MS, LCGC, Color Genomics*

*Presenting Author: Lauren Ryan, MS, LCGC, Color Genomics*

*Primary Author: Lauren Ryan, MS, LCGC, Color Genomics*

*Author 2: Anjali Zimmer, Ph.D., Color Genomics*

*Author 3: Cynthia L. Neben, Ph.D., Color Genomics*

*Author 4: Alicia Y. Zhou, Ph.D., Color Genomics*

**Introduction:** Traditionally, access to genetic counseling and testing has been largely restricted to affluent and urban populations. However, as demand for these services grows, the field is developing alternative service models to accommodate broader populations. Here, we describe the model of testing at one clinical laboratory, Color Genomics, that includes testing through a traditional model, ordered by the client’s own healthcare provider (traditional), and testing of two unique populations: people who received testing as an employee benefit (benefits) and people who self-initiated with an independent provider (independent). **Methods:** We analyzed 52,752 individuals who underwent testing with a 30-gene NGS panel for hereditary cancer risk. All tests were ordered by a healthcare provider and included access to complimentary, telephone-based genetic counseling. **Results:** The average age in the benefits cohort was lower compared to independent or traditional cohorts (40.0 vs. 48.6 vs. 51.7 years), as were the rates of personal diagnoses of cancer (3.9% vs. 19.6% vs. 44.8%), highlighting the opportunity to provide genetic information when there is the greatest potential for risk reduction. Benefits had a higher proportion of males (49.3%) compared to independent (19.2%) or traditional (15.9%) cohorts, despite most genes on the panel affecting risk for both sexes. The benefits cohort was more ethnically diverse (43.9% non-Caucasian) compared to independent (25.3%) or traditional (33.9%) cohorts. Positive rates were lower in benefits (5.8%) but similar in independent (10.2%) and traditional (11.7%). Rates of variants of uncertain significance (VUS) were similar (22.0% benefits, 18.3% independent, 20.3% traditional). **Conclusions:** Taken together, these data support the likelihood of high clinical benefit to broader populations. By adding alternative service delivery models, clinical
laboratories such as Color enable self-selection of genetic testing uptake and present opportunities to increase access and diversity in the testing population across age, sex, and ethnicity.

UNDERSTANDING BARRIERS TO GENETIC TESTING FOR SICKLE CELL TRAIT: THE AFRICAN-AMERICAN MALE PERSPECTIVE

Platform Presentations: Diversity and Access
Submitter: Shandrea Da'chelle Foster,
Primary Author: Shandrea Da'chelle Foster,
Author 2: Debera Zvejnieks, USC Genetic Counseling Program
Author 3: Yvonne Donald, James R. Clark Memorial Sickle Cell Foundation
Author 4: Christopher Mazoue, USC Orthopedic Surgery
Presenting Author: Shandrea Da'chelle Foster,

Research has shown a reluctance in African-American males to pursue testing for sickle cell trait. Few studies have tried to discern what barriers are contributing to this issue within the African-American male community. Research suggests a lack of knowledge may be the biggest contributing factor. This study hypothesized there would be a significant difference in knowledge of sickle cell trait based on educational level, age, and health beliefs. African-American male participants (N=116), ages 18 and over, completed a questionnaire assessing knowledge, risk perception, health beliefs, barriers, and motivating factors within the context of sickle cell trait. One-way and two-way analysis of variance identified age as an influential factor. Results showed a significant interaction between age and knowledge of sickle cell trait and sickle cell disease (p = .009). Factors including perceived discrimination, perceived risk of sickle cell trait based on parent report, and sentiments on playing sports with sickle cell trait were all influenced by age (all p < 0.05). Health beliefs such as having tattoos or piercings and getting annual check-ups with a primary care physician were also influenced by age (both p < 0.02). The most significant barrier identified was a lack of information about testing options from primary care physicians, while the largest motivating factor for testing was for personal health reasons. Findings from this study could aid genetic counselors with strategies to increase sickle cell trait testing in African-American men. Thereby, increasing awareness of sickle cell trait in the community for informative health and reproductive outlook.

Meeting the needs of Low Health Literacy patients in the Era of Precision Medicine: A Pilot Intervention to Improve Patient-Provider Communication in Cancer Genetic Counseling

Platform Presentations: Diversity and Access
Submitter: Galen Joseph, University of California, San Francisco
Presenting Author: Galen Joseph, University of California, San Francisco
Genomic literacy is necessary to realize the promise of Genomic Medicine, particularly in the context of efforts to increase participation of diverse populations in genomics research and clinical practice. We present results of a pilot intervention to improve oral communication between genetic counselors (GCs) and their low health literacy (LHL) patients. The intervention consisted of: communication workshop curriculum development and evaluation; 2-month post-workshop interviews with participating GCs (n=9) about their efforts to apply LHL communication strategies in practice; observations of counseling sessions (n=24) with 2 GC workshop participants and post-counseling patient interviews (n=9). The 4.5-hour workshop presented evidenced-based strategies for effective communication with LHL patients (e.g. Plain Language, Teach-back), and exercises to practice adapting them to the counseling context. GCs reported appreciating the opportunity to refine their communication skills; however, they found techniques like plain talk and teach-back challenging to adopt given their training and communication habits. GCs also raised concerns about achieving informed consent and providing scientifically accurate information when using plain language, but were pleased that reducing the quantity of information they conveyed allowed more time for psychosocial counseling. Observations and patient interviews showed positive outcomes for patients who clearly understood the implications of the test and the next steps, and who expressed satisfaction with the counseling. These findings are the starting point for a RCT that will compare “traditional” genetic counseling with a “modified” protocol incorporating LHL strategies for returning exome sequencing results to diverse patients as part of the CSER2 (Clinical Sequencing Evidence-Generating Research) consortium. If proven beneficial, we will work with GC training programs and practicing GCs to adopt these modified practices to ensure that the benefits of genomics reach all populations and do not exacerbate existing health disparities.

Attitudes and Beliefs of the Amish and Mennonite Communities Towards Medical Photography in the Context of Facial Dysmorphology Novel Analysis

Platform Presentations: Diversity and Access
Submitter: Jillian Lineburg, Arcadia University

Presenting Author: Jillian Lineburg, Arcadia University

Primary Author: Jillian Lineburg, Arcadia University
Recent advances in medical photography pose new ethical questions for the field. Among such advances is Face2Gene, a suite of phenotyping applications using facial recognition analysis to supply possible diagnoses. The primary aim of this study was to assess attitudes toward medical photography in the Old Order Amish and Mennonite (Plain) communities of Lancaster County within the context of use for phenotyping software. The Plain communities often eschew portrait photography in accordance with their cultural practices of humility and emphasis on community. The secondary aim of this study was to obtain photographs for use in training Face2Gene on two conditions with distinctive physical features. Interviews were conducted with parents of individuals with Cortical Dysplasia- Focal Epilepsy Syndrome (CDFE) and Polyhydramnios, Megalencephaly and Symptomatic Epilepsy (PMSE). Both conditions are found in Plain communities and in the general population. Thirteen individuals participated in a face-to-face interview that explored preferences, comfort, and attitudes about medical photography. Eleven participants consented to medical photography. Responses were recorded, transcribed, and coded for common themes. Four themes emerged: trust, confidentiality, relevance, and values. Trust in medical providers influenced participant preference for methods of medical photography. Participants felt a desire to uphold the privacy of the individual and security of their photographs. Furthermore, there was greater acceptance of photography if it was directly relevant to the patient’s care. Though it competes with other cultural values that speak against photography, altruism emerged as an important motivator for participation in medical photography. Further research about medical photography in the digital age is needed to elucidate preferences, attitudes, and beliefs in other cultures. However, this study contributes to the foundation for future research that would make possible the creation of ethical guidelines and best practices for medical photography.

Geometric Inclusivity: An assessment of current practices in pedigree nomenclature for patients identifying as transgender and gender nonconforming

Platform Presentations: Diversity and Access
Submitter: Liz Sheehan,
Presenting Author: Liz Sheehan,
Primary Author: Liz Sheehan, Brandeis University
Author 2: Gayun Chan-Smutko, Brandeis University
Author 3: Robin Bennett, University of Washington
Author 4: Miles Harris, Mount Sinai Center for Transgender Medicine and Surgery

The healthcare community is attempting to expand its knowledge of lesbian, gay, bisexual, and transgender health; however, much of existing literature and research concentrates on fluidity in sexual orientation rather than gender identity. Both NSGC and the National Comprehensive Cancer Network
(NCCN) have differing guidelines for acceptable pedigree symbols to represent transgender patients and minimal recommendations for gender nonconforming (GNC) patients. A key advantage to standardized pedigree nomenclature is consistency in interpretation of the family structure by providers. One potential barrier to uniform representation and consistent care for patients who identify as transgender or GNC is the inconsistency of accepted pedigree symbols to represent them. We assess the variability of current pedigree symbol practice among genetic counselors and students as well as self-reported confidence in addressing their transgender and GNC patients’ psychosocial needs through a survey distributed through NSGC. Participants felt symbols more closely associated with recommendations set forth by NSGC (41.1%) and NCCN (29.7%) for transgender patients would be most appropriate and emphasized a desire to be affirming of their patient’s gender identity. We found a greater degree of variability in symbols representing a GNC patient, with 19.2% of participants selecting “other” and explaining they were unsure of the best choice. Overall confidence in addressing psychosocial needs was low. Fewer than 10% reported feeling “very confident” meeting psychosocial needs and this was positively correlated with prior education on transgender and GNC healthcare (p<.002). A high interest (99%) in further education demonstrates a recognition of self-education as an effective strategy for increasing awareness and improving competency. Renewed engagement with transgender and GNC communities on educational content as well as affirming approaches to pedigree nomenclature with an eye towards standardization is necessary for appropriate and consistent care.

Challenges to Informed Consent for Exome Sequencing: A Best Worst Scaling Experiment

Platform Presentations: ELSI
Submitter: Rachel Gore, ScM, University of Maryland School of Medicine

Presenting Author: Rachel Gore, ScM, University of Maryland School of Medicine

Primary Author: Rachel Gore, ScM, National Human Genome Research Institute, SBRB Branch

Author 2: John F. P. Bridges, PhD, The Ohio State University, Dept. of Biomedical Informatics

Author 3: Julie S. Cohen, ScM, CGC, Kennedy Krieger Institute

Author 4: Barbara B. Biesecker, MS, PhD, CGC, RTI, International

As exome sequencing expands as a diagnostic tool, patients and providers have voiced concerns about the breadth and scope of potential results. Genetic counselors report perceived challenges to prioritizing complex information during consent sessions. This study aimed to understand how genetic counselors approach the consent process and weigh the relative importance of its components. Best-worst scaling was used to characterize how genetic counselors prioritize essential elements of informed consent specific to exome sequencing. The development of a best-worst scaling experiment was informed by a systematic literature review and two focus groups. Choice sets were created using a balanced incomplete block design, where participants selected the most and least important element of informed consent in each set. Mediation analyses was used to assess whether responses were associated with previous experience ordering exome sequencing, perceived efficacy in consenting patients, and
counselors’ tolerance for ambiguity. An online survey was distributed to all full members of the National Society of Genetic Counselors and completed by 342 recipients in a variety of practice specialties. Data were analyzed using mean best-worst scores to summarize how often each object was selected as most and least important. Ranking of best-worst scores suggests that genetic counselors prioritize collaborative decision-making, assessing patient understanding, and managing expectations for results, with the least emphasis placed on discussing technological complexities. Stratified analyses by paired t-tests found that counselors with more experience ordering exome sequencing, and those reporting higher perceptions of patients’ ability to manage information were significantly more likely to prioritize discussion of variants of uncertain significance (p<0.05). Results convey counselors’ prioritization of individual patient needs for obtaining informed consent for exome sequencing, and that professional characteristics and attitudes may influence preemptive discussion of uncertain results.

Ethical Implications of Laboratory-Sponsored Items and Events for Genetic Counselors: An Exploratory Study

Platform Presentations: ELSI
Submitter: Arielle Flynn,
Primary Author: Arielle Flynn,
Author 2: Alexandria Meyer, Ambry Genetics
Author 3: Taylor Berninger, Augustana-Sanford Genetic Counseling GradProgram; USCDHealth
Author 4: Kate Partynski, St. Joseph Health
Presenting Author: Arielle Flynn, Augustana-Sanford Genetic Counseling Graduate Program

In this exploratory study, we sought to record and analyze the opinions of training and practicing genetic counselors from all specialties with regards to the gift-giving practices of genetics laboratories. In a 28-question survey sent through the NSGC listserv, 704 completed responses were received. Quantitative data was analyzed using descriptive statistics and comparisons with Chi-Square analysis. Respondent demographics appear to reflect NSGC reported demographics. Responses showed a diverse range of opinion and a concerning lack of knowledge regarding rules about accepting gifts within their own institutions and awareness of laws and regulations at any level. Participant knowledge of laws surrounding gift-giving varied; 16.8% reported knowing of laws, 26.4% reported no knowledge of laws, and 56.8% reported being unsure if there are any laws. Factors associated with reported knowledge of the existence of laws include current genetics laboratory employment, whether or not there is a requirement to report gifts, age, years working as a genetic counselor, and opinion on the need for maximum gift values. When asked their perception of gift-giving as a conflict of interest (COI), 56.8% of respondents view gift-giving as a COI and 43.2% do not. Several factors associated with individual opinion regarding this practice as a COI include opinions on the need for maximum gift values and need to report gifts, being required to report gifts, age, gender, and primary practice location. Based on an analysis of responses, we suggest an increase in education events and discussions to promote knowledge regarding legal, employer, and graduate program regulations involving laboratory gifts. We
also suggest implementation of education regarding the history of gift-giving in the medical sphere to give context to discussions surrounding gift-giving from laboratories to genetic counselors.

Outcomes of return of secondary findings among a multi-site study

Platform Presentations: ELSI
Submitter: Barbara Bowles Biesecker, PhD, Senior Health Policy Analyst, Research Triangle Institute, International

Presenting Author: Barbara Bowles Biesecker, PhD, Senior Health Policy Analyst, Research Triangle Institute, International

Primary Author: Barbara Biesecker, Research Triangle Institute, International

Author 2: Ragan Hart, University of Washington

Author 3: Leslie Biesecker, NHGRI, NIH

Author 4: Robert Green, Harvard University

Author 5: David Veenstra, University of Washington

Author 6: Jonathan Berg, University of North Carolina

Author 7: Lucia Hindorff, NHGRI, NIH

Return of secondary findings (SF) from genome sequencing, as recommended by the ACMG, offers patients the opportunity to manage elevated risks from identification of medically actionable variants. The clinical benefits of receiving these results depend on compliance with recommended health care. Genetic counselors consent participants to receipt of SF and help to evaluate those found to have them. Within the NIH Clinical Sequencing Exploratory Research consortium, 18 participants consented to be interviewed, comprising 10 adults and 8 parents of children who underwent sequencing across 9 institutes. An IRB-approved structured interview guide framed assessment of psychological reactions, clinical follow up and communication of results to at-risk relatives. For 15 interviewees, the secondary finding was unexpected. The importance of life context in which the SF was learned proved to be a key theme, notably among parents of an affected child. No participant voiced regret over learning of their SF. Thirteen interviewees pursued follow up with a health care provider; 7 with their primary care provider, and 6 met with a specialist as recommended. All 18 reported their SF to one or more first degree relatives. Eleven responded that no relative underwent testing related to the SF. None of the 18 interviewees reported pursuit of health care services beyond recommendations based on their SF. Rather, there was under compliance with recommended care. Together these findings provide early data that research participants manage secondary findings well, although further studies are needed. Genetic counselors will be essential to ensuring appropriate follow up care and counseling.

Adolescents share their views: a qualitative analysis of adolescents’ preferences for learning genomic sequencing results
Purpose: The American College of Medical Genetics (ACMG) recommendations for the return of secondary results conflict with long standing recommendations to defer predictive testing for adult onset conditions for minors until the age of majority. The ACMG recommendations do support parents’ choices to opt in or out of secondary analysis for their child for 59 genes; yet there is no consideration of soliciting adolescents’ preferences and choices in these decisions. This study aimed to (1) explore the reasons adolescents choose to learn, or not learn, sequencing results for conditions that are or are not preventable, treatable, have adult-onset, and carrier-status and (2) describe the involvement adolescents want when making testing decisions.

Methods: After independently choosing the type of genomic research results they wanted to learn, adolescents and one of their parents were interviewed to explore the reasoning behind their choices. Interviews were audio-recorded and transcribed. Transcripts were analyzed using a constant comparative method, and deductive and inductive codes were used for thematic analysis. Results: Among 64 adolescents, aged 13-17, the most commonly excluded conditions were those not treatable (n=22, 71%) and not preventable (n=18, 58%). Three major themes emerged from adolescent discussions about why they made their choices: (1) actionability of information, (2) knowledge seeking, and (3) consideration of psychological impact. Reasons expressed among adolescents were similar, but adolescents who chose to exclude results placed greater emphasis on risk; whereas adolescents who chose to learn results paced greater emphasis on benefits. Nearly all adolescents (98%) wanted to be involved in the decision making process, and over half (n=34) wanted to make testing choices independently. Conclusions: Our research contributes empirical evidence to support professional guidelines about adolescents’ engagement and preferences in genetic testing decisions. Key words: adolescents, genomic sequencing results, preferences, predictive testing, qualitative

Moral Distress in Genetic Counseling

Purpose: The American College of Medical Genetics (ACMG) recommendations for the return of secondary results conflict with long standing recommendations to defer predictive testing for adult onset conditions for minors until the age of majority. The ACMG recommendations do support parents’ choices to opt in or out of secondary analysis for their child for 59 genes; yet there is no consideration of soliciting adolescents’ preferences and choices in these decisions. This study aimed to (1) explore the reasons adolescents choose to learn, or not learn, sequencing results for conditions that are or are not preventable, treatable, have adult-onset, and carrier-status and (2) describe the involvement adolescents want when making testing decisions.

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Moral distress is the phenomenon whereby health care providers experience the inability to take action or act in morally appropriate ways when encountering a morally compromising situation. The identified correlation of moral distress to burnout and resignation in nursing and other health care fields has led to increasing attention and concern among health care professionals to identify the sources of moral distress, as well as find ways to alleviate it. An online mix-method survey was sent to NSGC members and used to gain information on (1) sources of moral distress, (2) emotions involved, (3) coping strategies, and (4) suggestions to alleviate it. The ProQOL 5 scale was included to measure genetic counselor compassion satisfaction, burnout, and secondary traumatic stress. Two hundred and thirteen genetic counselors completed the survey. Forty-eight percent of respondents experienced moral distress and fourteen sources were identified. The greatest sources were situations involving genetic testing, pregnancy termination, and finances. Those more likely to experience moral distress worked in a prenatal setting (35%), were over the age of 50 (26%) and worked for more than 21 years (24%). Genetic counselors were more likely to talk to a co-worker for support, and seek social support, address the source of the problem, and sustain self through working with patients as coping strategies. Most genetic counselors (16.7%) recommended talking to another genetic counselor to alleviate moral distress. Moral distress did not correlate with genetic counselor burnout, but did correlate with higher levels of secondary traumatic stress (P<.01). Thirty-two percent of genetic counselors considered leaving their specialty and 23% considered leaving their profession based on their experience(s) with moral distress. Our study establishes the existence of moral distress in the genetic counseling field and supports the need for coping strategies and recommendations in order to alleviate future genetic counselor moral distress.

**Discovery of Y chromosome SNPs on DTC testing leads to a 46, XY disorder of sexual differentiation diagnosis in a 32-year-old woman**

*Platform Presentations: Incidental and Unexpected Findings*
*Submitter: Brooke Moriarty Nightingale, The Ohio State University*

*Presenting Author: Brooke Moriarty Nightingale, The Ohio State University*

*Author 2: Judith A. Westman, MD, The Ohio State University*

*Author 3: Dawn C. Allain, MS, CGC, The Ohio State University*

*Primary Author: Brooke M. Nightingale, MS, The Ohio State University*

A 32-year-old woman was referred for genetic evaluation and counseling by her PCP because testing performed by a direct to consumer (DTC) genetic testing company identified Y chromosome SNPs. Patient reported lack of menstrual periods, painful/failed gynecologic and sexual encounters. Physical examination revealed fatty breast tissue rather than true mammary development, axillary hair, normal external female genitalia, and pubic hair in a gynecoid pattern. FSH and LSH were consistent with post-
menopausal levels and TSH level was normal. Family history was negative for features of an inherited disorder of sexual differentiation (DSD). Transabdominal ultrasound revealed an atrophic uterus and possible atrophic gonads. Cytogenetic analysis was ordered revealing a normal, male karyotype (20/20 cells). NGS panel was ordered and identified a likely pathogenic exon 7 deletion in NR5A1. Pathogenic variants in this gene have been associated with hypospadias, ambiguous genitalia, and rarely full sex reversal in 46,XY individuals. Early menopause has been associated with female carriers, which was consistent with our patient’s maternal family history. The case was complicated by various psychosocial aspects. The patient had a history of anxiety and major depressive disorder. She initiated DTC testing to learn more about her mental health, ancestry, and unique genetic traits. She was unprepared for a DSD diagnosis. She had unstable housing and transportation, limited telephone access, and significant mental health issues which interfered with result disclosure, understanding and coping with results, and subsequent scheduled surgeries. While the DSD diagnosis was beneficial to our patient’s physical health (risk-reducing surgery), it impacted her mental health and gender identity. As the availability of DTC testing grows, more incidental findings will be identified. This case illustrates the role of genetic professionals in confirming DTC testing results, creating a diagnostic plan, and providing psychosocial counseling.

A Pilot Study of CLIA-compliant Secondary Findings in Research Sequencing: Outcomes Amongst Recipients of Positive and Negative Reports

Platform Presentations: Incidental and Unexpected Findings
Submitter: Julie Chevalier Sapp, National Human Genome Research Institute

Presenting Author: Julie Chevalier Sapp, National Human Genome Research Institute

Author 2: Jennifer J. Johnston, Medical Genomics and Metabolic Genetics Branch, NHGRI

Author 3: Kate Driscoll, Medical Genomics and Metabolic Genetics Branch, NHGRI

Author 4: Alexis Heidlebaugh, Social and Behavioral Research Branch, NHGRI

Author 5: Ane Sargardia, Social and Behavioral Research Branch, NHGRI

Author 6: D. Nadine Dogbe, Social and Behavioral Research Branch, NHGRI

Primary Author: Julie C. Sapp, Medical Genomics and Metabolic Genetics Branch, NHGRI

Author 7: Kendall Umstead, Social and Behavioral Research Branch, NHGRI

Author 8: Erin Turbitt, Social and Behavioral Research Branch, NHGRI

Author 9: Katie Lewis, Medical Genomics and Metabolic Genetics Branch, NHGRI

Author 10: Barbara B. Biesecker, Social and Behavioral Research Branch, NHGRI

Author 11: Leslie G. Biesecker, MD, Medical Genomics and Metabolic Genetics Branch, NHGRI
Debate about the return of secondary findings from research exome/genome sequencing remains despite consensus in the clinical realm. This study piloted a process for returning CLIA-validated secondary findings to participants and described the outcomes of receiving such results. We developed a novel, research-clinical translational genomics process for CLIA-validated secondary findings analysis of research exome data and results return by a genetic counselor. Eleven intramural principal investigators at the National Institutes of Health implemented this process in their protocols over a two-year period. Nearly 1,200 individuals were sequenced, 14 positive secondary findings were validated and returned to 18 participants by one of two genetic counselors not involved in the primary protocols. Disclosures were performed primarily by phone, took an average of 55 minutes, and included obtaining a targeted family history and provision of specific referrals to genetic counselors in specialty clinics in the participants' local area. Follow-up interviews were performed with 13 participants after receipt of a positive report. There were no indicators of significant distress from the secondary findings. Eleven participants communicated their results to family members and 9 reported accessing recommended health care services. Further, a sample of 107 participants who received a negative secondary findings report returned via postal mail were surveyed four months after their result. Most demonstrated accurate understanding of the result and expressed reassurance (64%). However, a sizable minority (up to 17%) expressed some confusion regarding the distinction of primary from secondary findings. These findings contradict the assumption that participants will experience psychologic distress and pursue excessive health care utilization after receipt of secondary findings. These outcomes also demonstrate a tractable coupling of clinical and research genomic sequencing and provide evidence for how genetic counselors may play an integral role in large-scale genomics research.

Proactive Genetic Screening in a primary care setting reveals surprising results

Platform Presentations: Incidental and Unexpected Findings
Submitter: Allison Janson Hazell, Genetic Counsellor, Medcan Clinic

Primary Author: Allison Janson Hazell, Genetic Counsellor, Medcan Clinic

Author 2: Jessica Gu, Medcan

Author 3: Monica Zarb, Medcan

Author 4: Jill Furnival, Medcan

Author 5: Lea Velsher, Medcan & North York General Hospital

Author 6: James Aw, Medcan

Presenting Author: Allison Hazell, Medcan

Introduction: Advances in genomic research and DNA sequencing technologies have revolutionized our ability to offer large gene panels at reasonable costs. Limited data exist on the true prevalence and penetrance of “rare” actionable genetic conditions in the unselected (or “healthy”) population. Initial studies, largely based on the 2013 ACMG recommendations for the return of incidental findings, suggest that 1 to 9% of individuals harbor pathogenic or likely pathogenic mutations in medically actionable
genes. Additionally, evidence continues to support the clinical utility of genetic testing in determining appropriate medical management for these “healthy” individuals. Purpose: Report on our experience with elective genetic screening and our results to date, including: family history, specific mutations identified, actionable findings, cascade screening, challenges in determining penetrance and screening protocols. Methods: Medcan, a preventive health and wellness clinic in Toronto, Canada, serves over 20,000 patients annually. In September 2017, we began offering a proactive 139-gene panel (based on ACMG59 with additional actionable genes) through Invitae. The laboratory reports only pathogenic and likely pathogenic variants. Medcan clients are offered our “Proactive Genetic Screening (PGS)” service during their annual health assessment for an additional fee, and meet with a genetic counselor for pre- and post-test counseling. Results: As of May 8, 2018, 590 clients have undergone PGS and 97 are positive for a health-related risk; an additional 400 clients are anticipated by November 2018. Our positive rate is higher than expected at 16%, and has resulted in changes to screening recommendations for 80% of positive clients. Of the positive cancer- and cardiac-related results, 34% and 25% reported relevant family history, respectively. Conclusion: Our experience with elective genetic testing in a high volume primary care setting provides insight into expectations and recommendations for the future of genomic screening in the “healthy” population.

A Comprehensive Look at the Neurodevelopmental Outcomes and the Effects of Early Hormonal Therapy (EHT) in a Large, Prenatally Diagnosed Population of Boys with 47,XXY (Klinefelter syndrome)

Platform Presentations: Incidental and Unexpected Findings
Submitter: Carole Samango-Sprouse, Ed.D., The Focus Foundation
Primary Author: Carole Samango-Sprouse, Ed.D., The Focus Foundation
Presenting Author: Carole Samango-Sprouse, Ed.D., The Focus Foundation
Author 2: Selena Chea, The Focus Foundation
Author 3: Teresa Sadeghin, The Focus Foundation
Author 4: Dr. Andrea Gropman, Children’s National Health System

There have been significant advances in procedures for early detection and innovations for the care of boys with 47,XXY. This occurs 1:660 and presents with language-based learning disorders, intact spatial cognition, and executive dysfunction. There have been several prospective studies involving large, prenatally diagnosed 47,XXY cohorts from the 1970-80s, but an updated and comprehensive study on these boys is necessary to provide information on the early childhood trajectory and potential effects of EHT. 171 prenatally identified boys with 47,XXY were referred for neurodevelopmental evaluations between 0-3 years of age. This cohort was segregated by EHT status: EHT (n=65) and non-EHT (n=106), and compared across scales of neurodevelopmental domains: Preschool Language Scales (PLS)’s auditory comprehension (AC) & expressive communication (EC); Bayley Scales of Infant Development (BSID)’s mental development index (MDI) & psychomotor development index (PDI); Early Language Milestone Scale (ELM)’s expressive (EL) & receptive (RL) language; and Expressive One Word
The EHT group showed significant differences on the PLS’ AC & EC (P<.0001) when compared to the non-EHT. On BSID, treated boys had significantly higher MDIs & PDIs (P<.0001) than untreated. The EHT group also showed significantly improved EL (P=.0017) & RL (P=.015) on the ELM, and EOWPVT (P=.037). The number of families who receive a fetal, neonatal, or early childhood diagnosis of 47,XXY is increasing due in large part to the greater use of noninvasive prenatal testing (NIPT). It is critical that providers have a knowledge base that will enhance delivery of current, accurate information. This study provides further support that EHT has potentially positive effects on the neurodevelopment in boys with 47,XXY. Early and targeted interventions are key aspects of counseling that will have the potential to alter the long-term prognosis of boys with 47,XXY. Future study is warranted to elucidate the optimal timing and dosage for treatment during early childhood years.

Counseling Conundrum: Sex Discordance Identification Following Preimplantation Genetic Testing for Aneuploidy (PGT-A) or Noninvasive Prenatal Testing (NIPT) Using SNP-Based Methodologies

**Platform Presentations: Incidental and Unexpected Findings**

*Submitter: Katherine L. Howard, Natera*

*Primary Author: Katherine L. Howard, Natera*

*Presenting Author: Katherine L. Howard, Natera*

*Author 2: Melissa Maisenbacher, Natera, Inc.*

*Author 3: Katrina Merrion, Natera, Inc.*

*Author 4: Wendy DiNonno, Natera, Inc.*

**INTRODUCTION:** PGT-A and NIPT determine fetal sex with high accuracy before/during pregnancy. If additional prenatal screening or clinical presentation at birth suggests sex discrepancy, medical follow-up is needed to rule out a disorder of sexual differentiation.

**OBJECTIVE:** Describe reported cases and etiologies of sex discrepancy after PGT-A or NIPT.

**METHODS:** Provider reported cases of possible sex discrepancy after PGT-A or NIPT at a single lab were retrospectively reviewed. For PGT-A, genotyping was performed using Illumina Cyto12 SNP-based microarray with informatics. For NIPT, cell-free DNA was isolated and amplified by massively-multiplexed PCR targeting 13,392 SNPs covering chromosomes 13, 18, 21, X and Y. Only cases with complete evaluation to identify a cause for discrepancy were included.

**RESULTS:** Four of 23,297 (0.02%) PGT-A cases and 49 of 1,081,541 (0.005%) NIPT cases had discrepant sex suspected pre/post-delivery. For PGT-A, 2 (50%) resulted from incorrect embryo transfers (biological parental match but not the intended embryo) and 2 (50%) resulted from natural conception around the time of embryo transfer. For NIPT, phlebotomy labeling errors comprised 6 (12.2%); confined placental mosaicism, 10 (20.4%); ultrasound errors, 13 (26.6%); and disorders of sexual development (DSD), 20 (40.8%). DSDs diagnosed include: 5 cases of ovotesticular (chimeric/gonadal dysgenesis), 4 cases of 46,XX (male/ambiguous genitalia; 1 congenital adrenal hyperplasia) and 11 46,XY (female/ambiguous genitalia; 6 with androgen insensitivity syndrome). No
discrepancies were due to lab error for PGT-A/NIPT cases.<br />

**CONCLUSIONS:** A SNP-based methodology can eliminate sample swap, natural conception around the time of embryo transfer and vanished twin as causes of discordant sex after PGT-A or NIPT. Other causes of discordant sex can include ultrasound errors, PGT/NIPT result errors, embryo mosaicism, confined placental mosaicism and various DSDs. A thorough investigation can provide reassurance and guide appropriate medical management and counseling about cause and recurrence risk.

**Genetic testing of patients with cerebral palsy reveals one-third of cases have a monogenetic cause and a significant recurrence risk**

**Platform Presentations: Neuromuscular/Pysciatric**

*Submitter: Claire Teigen, GeneDx*

*Primary Author: Claire Teigen, GeneDx*

*Presenting Author: Claire Teigen, GeneDx*

*Author 2: Houda Zghal Elloumi, GeneDx*

*Author 3: Francisca Millan Zamora, GeneDx*

*Author 4: Julie Scuffins, GeneDx*

*Author 5: Dianalee McKnight, GeneDx*

Cerebral palsy (CP) is a broad diagnostic term encompassing disorders impacting movement and posture caused by changes in the fetal or infantile brain (Rosenbaum et al., 2007). CP is a common clinical diagnosis, with an incidence of 1 in 500 births, and therefore is often found in a family history (Oskoui et al., 2013). However, CP may not be addressed in genetic counseling as it is commonly attributed to complications at birth rather than to a genetic etiology (MacLennan et al., 2018). We aimed to establish the contribution of genetic causes to CP. Results from exome sequencing (ES) of 1346 patients with CP were retrospectively reviewed. Overall, ES yielded a positive result indicating a genetic etiology in 32.7% of cases (440/1346). Testing of a proband concurrently with parents (ES-trio) had a significantly higher diagnostic yield (35.3%) compared to proband-only testing (23.3%; p<0.005). Positive findings were reported in 225 different genes, indicating the tremendous genetic heterogeneity of CP. Among the positive results, in 65.2% the causative variants were autosomal dominant, 20.7% autosomal recessive, and 13.4% X-linked. ES-trio testing revealed that the majority of patients diagnosed with an AD or XL disorder (71.4%) had de novo variants. These finds indicate a significant recurrence risk in 32% (139/440) of positive cases: 21% (91/440) of probands had biallelic variants, 3% (15/440) had maternally inherited X-linked variants, and 4% (23/440) had an inherited autosomal dominant variant. Overall, a trio-based comprehensive approach to genetic testing for CP can help to identify a genetic etiology in approximately one-third of cases. Such findings can be informative for genetic counseling for families by not only providing an accurate recurrence risk but also information on prognosis, adjusted therapies, and management options. <br />

Rosenbaum et al. (2007) Dev Med Child Neurol Suppl 109 :8-14 (PMID:
Open Communication of Duchenne Muscular Dystrophy Facilitates Disclosure Process by Parents to Unaffected Siblings

**Platform Presentations: Neuromuscular/Pysiatric**

**Submitter: Laura Anne Goodell,**

**Presenting Author: Laura Anne Goodell,**

**Primary Author: Laura Anne Goodell, University of Maryland School of Medicine**

**Author 2: Katharine Bisordi, University of Maryland School of Medicine**

**Author 3: Elizabeth Ulm, Cincinnati Children’s Hospital Medical Center**

**Author 4: Rachel Nusbaum, University of Maryland School of Medicine**

Duchenne muscular dystrophy (DMD) is a progressive childhood onset neuromuscular disease with no known cure. There is extensive literature about the impact of a diagnosis on the psychosocial well-being of unaffected siblings, with a need for additional research to provide information about optimal ways to disclose this information to unaffected children. We sought to explore the parental experience disclosing a sibling’s diagnosis of DMD to unaffected children who were age 8-17 years old either at the time of their sibling’s diagnosis or presently. Parents were recruited through Maryland Muscular Dystrophy Association, Parent Project Muscular Dystrophy, and Cincinnati Children’s Hospital Medical Center Neuromuscular Center. An existing interview guide, rooted in family communication, was modified to incorporate themes and topics found in literature specific to DMD and disclosure to unaffected siblings. We qualitatively explored these experiences through semi-structured interviews and performed thematic analysis using a coding system to identify overarching themes and subthemes. Several main themes regarding challenges to the disclosure process emerged. We identified the following themes in procedural aspects of disclosure: lack of provider support, importance of the DMD community, and open and gradual timeline of disclosure. Under emotional experiences, we identified these themes: overwhelming nature, elements of surprise disclosure, and balancing parental and sibling needs. Most questions from unaffected siblings related to procedural elements of care such as treatments and equipment. Additional unanticipated themes emerged that may contribute to the knowledge of family culture surrounding DMD: the complex role of Facebook as a family resource, deferring carrier testing for siblings, and inclusion of DMD in school projects. While the process of disclosure is complicated by a variety of factors such as lack of provider support and overwhelming emotional burden, families highlight the importance of open communication in discussion with unaffected children.

Survey Validation for Screening of Hypermobile Ehlers-Danlos Syndrome

**Platform Presentations: Neuromuscular/Pysiatric**

**Submitter: Megan Quinlan, Cleveland Clinic**
Presenting Author: Megan Quinlan, Cleveland Clinic

Primary Author: Megan Quinlan,

Author 2: Lisa Martin, Cincinnati Children's Hospital Medical Center

Author 3: Lisa Berry, Cincinnati Children's Hospital Medical Center

Author 4: Jodie Johnson, Cincinnati Children’s Hospital Medical Center

Author 5: Derek Neilson, Cincinnati Children’s Hospital Medical Center

Introduction: Hypermobile Ehlers-Danlos Syndrome (hEDS) is the most common inherited connective tissue condition and individuals with the condition experience systemic effects. Although it often runs in families, there is no known genetic etiology for hEDS. Unfortunately, diagnosis for hEDS is based on clinical evaluation making family history studies difficult. To clarify the etiology of hEDS, development and validation of self-administered tools are needed. <br />

Methods: We developed a self-administered survey comprised of photographs and questions capturing the criteria for the 2017 International Classification for hEDS. We invited patients with clinically diagnosed hEDS and their family members to fill out our survey. To validate our survey, we compared our survey estimates of hEDS diagnosis status to retrospective clinical diagnoses by medical record review. Specifically, we compared Beighton scores individual diagnostic features, and overall diagnosis status for individuals with or without hEDS. <br />

Results: Sixty-two participants filled out the survey including 30 patients. Our survey-estimated Beighton scores were consistent with clinical scoring, generally being 1-point lower. The features that were best predictors of hEDS were 2017 Classification Criterion 1 and Criterion 2 Feature C. Specifically, participants with hEDS were more likely to have chronic pain and a positive 5-point questionnaire (p=0.0003; p=0.0001 respectively). Overall, our survey correctly classified 85% (22/26) of participants. <br />

Conclusions: With modifications, our survey tool could be used as a screening tool for larger studies assessing relatives’ diagnosis status. Similarly, the survey could be used in a clinical setting to determine which individuals are most likely to meet criteria for a diagnosis of hEDS. <br />

Keywords: Hypermobility Ehlers-Danlos Syndrome, Ehlers-Danlos Syndrome Hypermobility Type, hypermobility, survey, screening, inheritance

The role of MTHFR C677T variants in postpartum psychopathology: A prospective study of at-risk women to inform prenatal genetic counseling practice

Platform Presentations: Neuromuscular/Psychiatric

Submitter: Emily Morris, University of British Columbia / Provincial Health Service Authority

Primary Author: Emily Morris, University of British Columbia / Provincial Health Service Authority

Presenting Author: Emily Morris, University of British Columbia / Provincial Health Service Authority

Author 2: Catriona Hippman, University of British Columbia

Author 3: Caitlin Slomp, University of British Columbia
Background: Postpartum mental illnesses (PPMI) are urgent health concerns, but their etiology is not well understood. Low red blood cell (RBC) folate has been associated with psychiatric disorders, and one study suggested that perinatal folic acid supplementation can improve maternal long-term depression symptomatology. The MTHFR C677T variant influences folate metabolism, and some studies have implicated it in psychiatric disorders, making it a strong candidate gene for PPMI. Objective: To explore the relationship between MTHFR C677T genotype, RBC folate levels, and PPMI (depression, mania, and psychosis) in women with a history of mood or psychotic disorders. Hypothesis: In the first three months postpartum TT homozygous women would have increased symptoms of depression, mania, and psychosis, compared to CC homozygotes. Methods: We recruited a prospective cohort (N=365) of pregnant women (psychiatric history confirmed by the Structured Clinical Interview for the DSM-IV (SCID-IV)). At 3 times postpartum, we administered the Edinburgh Postnatal Depression Scale (EPDS), Clinician-Administered Rating Scale for Mania (CARS-M) and the Positive and Negative Symptom Scale (PANSS)- for psychosis and obtained blood samples to measure RBC folate and determine genotype. We investigated the interaction between RBC folate and genotype on the highest EPDS, and CARS-M scores with linear regression, and the proportion of PANSS above cut-off with logistic regression. Results: There was no significant interaction between RBC folate and MTHFR genotype on highest EPDS (p=0.19), CARS-M (p=0.09), or PANSS (p=0.14). There was also no difference between genotypes for EPDS CARS-M or PANSS (all p>0.05) controlling for RBC folate, and no relationship between RBC folate and any of the scales on its own (all p>0.05). Conclusion: Our data do not support a relationship between MTHFR, folate, and risk for postpartum psychopathology in at-risk women, at least in the context of food fortification/supplement use. These data can inform genetic counseling practice.

CYP2C19 genotype is associated with tolerability and response outcomes in escitalopram-treated youth with anxiety and/or depressive disorders

Platform Presentations: Neuromuscular/Psychiatric
Submitter: Stacey Aldrich, MS, Washington University in St. Louis
Presenting Author: Stacey Aldrich, MS, Washington University in St. Louis
Primary Author: Stacey Aldrich, University of Cincinnati
In children and adolescents, antidepressants are commonly used to treat anxiety and depressive disorders, but most pharmacogenetic studies to date have focused on adults when investigating the association between CYP2C19 genotype and treatment outcomes with escitalopram and citalopram (es/citalopram). CYP2C19 encodes the main enzyme responsible for metabolizing the two antidepressants into therapeutically inert metabolites. DNA sequence variants directly impact the enzyme’s efficacy, with variants categorized as no function, normal function or increased function alleles. In adults, slower CYP2C19 metabolizers have higher blood concentrations of es/citalopram at an equivalent dose, while faster CYP2C19 metabolizers have lower blood concentrations. As a result, slower metabolizers may be at higher risk for side effects and faster metabolizers at higher risk for treatment failure. Our retrospective study analyzed electronic medical record data from 263 youth <19 years with anxiety and/or depressive disorders who were prescribed es/citalopram (n=263). Slower CYP2C19 metabolizers experienced more side effects than faster metabolizers during es/citalopram treatment (p<0.01), and a higher percentage of slower metabolizers discontinued es/citalopram compared with normal metabolizers (p<0.01). Meanwhile, faster metabolizers responded more quickly to es/citalopram (p<0.01) and trended toward fewer days spent in inpatient hospitalization (p=0.06). The results highlight a disparity in es/citalopram treatment outcomes when a standardized dosing approach is used without consideration of CYP2C19 genotype in pediatric patients with anxiety and/or depressive disorders. Larger studies are needed to confirm these findings and to assess whether personalizing the dose of es/citalopram based on CYP2C19 genotype enhances treatment outcomes. These results may aid genetic counselors when advising clinicians and families on the implications of CYP2C19 test results in this setting, especially as many pediatric genetic disorders have higher rates of anxiety and depressive disorders.

A Novel Automated Service Delivery Model for Negative NIPT Results in the Era of Technology Enabled Healthcare

Platform Presentations: Service Delivery
Submitter: Cassidi Dailey Kalejta, Metis Genetics

Primary Author: Cassidi Dailey Kalejta, Metis Genetics

Presenting Author: Cassidi Dailey Kalejta, Metis Genetics

Author 2: Sonja Eubanks Higgins, MS, LCGC, Metis Genetics

Author 3: Hilary Kershberg, MS, LCGC, Southern California Permanente Medical Group
Introduction: As the demand for genetic counselors (GCs) increases, alternatives to traditional service delivery models are needed. Recent studies show, patients increasingly prefer technology enabled healthcare. Patients are relying less on healthcare providers (HCPs) and instead are using various sources to obtain healthcare information, including non-clinical and online content. We propose an automated method of delivering post-test education and disclosure of negative Non-Invasive Prenatal Testing (NIPT) results to ensure appropriate patient support with clinically accurate information.

Methods: Pregnant women defined as high-risk registered with Genetics Maven (Maven), a proprietary HIPAA-compliant web-based portal, to receive their negative NIPT result through our automated process. When the negative test result was available, patients watched a 2-minute educational video, answered three comprehension questions, and consented to downloading their result only if they wanted to learn the predicted sex of the fetus.

Results: From 04/2017 – 04/2018, 3901 patients viewed the educational video and downloaded their test result. Of these patients, 2 (0.05%) answered 0/3 questions correctly, 32 (0.82%) answered 1/3 questions correctly, 545 (13.97%) answered 2/3 questions correctly, and 3322 (85.16%) answered 3/3 questions correctly. Patients completed the automated process at all hours of the day with 87% downloading their result outside of typical HCP office hours.

Discussion: This data supports the effective communication of negative NIPT results to patients through this automated delivery model. Patients demonstrated a clear understanding of the material presented and, if desired, accessed the educational materials multiple times. Patients engaged at a time of their choosing without an office visit. Further studies could reveal if this automated process of result disclosure combined with clinically accurate video education is equally effective for other genetic tests.

Barriers associated with uptake of genetic counseling and testing in a randomized study of remote genetic services compared to usual care in community practices without genetic providers.

Platform Presentations: Service Delivery
Submitter: Cara Cacioppo, MS, LCGC, University of Pennsylvania Telegenetics Program
Presenting Author: Cara Cacioppo, MS, LCGC, University of Pennsylvania Telegenetics Program

Primary Author: Cara N. Cacioppo, University of Pennsylvania

Author 2: Brian Egleston, Fox Chase Cancer Center

Author 3: Colleen Burke Sands, University of Pennsylvania

Author 4: Syeda Abbas, University of Pennsylvania

Author 5: Linda Patrick-Miller, University of Chicago Medical Center

Author 6: Neeraja Reddy, Mapmygenome

Author 7: Elisabeth McCarty-Wood, University of Pennsylvania

Author 8: Susan M. Domchek, University of Pennsylvania

Author 9: Angela R. Bradbury, University of Pennsylvania

Background: Providing telegenetic services by phone or real-time videoconference (RVC) for patients at community practices without access to genetic providers could increase access to genetic testing. Uptake of genetic services via telegenetics compared to usual care options has not been reported.

Methods: To date, 106 patients at 6 community practices were randomized to remote genetic counseling (35 phone; 31 RVC) and 40 to usual care. Primary outcomes were uptake of genetic counseling and testing at 6 months. We used Fisher's exact tests, T-tests, logistic regressions, and thematic coding for analyses.

Results: To date, 79% (52/66) of participants in the remote services arms had pre-test genetic counseling as compared to 5% (2/40) in the usual care arm (p < 0.001). 56% (37/66) in the remote services arm completed genetic testing and 4 genetic carriers were identified as compared to 12.5% (5/40) and 0 carriers in the usual care arm (p < 0.001 for genetic testing uptake). Three common themes emerged around barriers and challenges to accessing genetic services for participants in the usual care arm who have not received genetic testing at six months: lack of information about how to access genetic counseling/testing (23%; 8/35), concerns about insurance coverage/potential cost (14%; 5/35), and competing priorities, (i.e., limited time due to other medical and treatment appointments) (14%; 5/35).

Conclusions: These data suggest that offering telegenetic services may increase the uptake of genetic counseling and/or testing and identification of genetic carriers in community practices without access to genetic services. Continued evaluation of the access barriers to genetic services in the community setting is critical to understanding uptake of genetic counseling and testing.

Genetic Education: Patient Satisfaction with a Prenatal Video Tool

Platform Presentations: Service Delivery
Submitter: Joan B. OLIVER, Integrated Genetics

Presenting Author: Joan B. OLIVER, Integrated Genetics
In accordance with the NSGC Genetic Counselor Workforce Working Group goal of “identifying and integrating tools that increase efficiency and productivity of genetic counselors in clinical practice,” a team of genetic counselors from Integrated Genetics created genetic education videos targeted to patients without complex genetic risk factors. These videos were intended to augment a patient’s discussion with providers. They included basic elements of genetic screening and testing options: Video 1 covered prenatal screening and diagnosis of chromosome abnormalities; Video 2 covered carrier screening. Testing options were presented without test brand names. Concepts of inheritance and risk, screening versus diagnosis, and patient-based decisions and autonomy were conveyed via graphics and narrated by an on-screen genetic counselor. The videos were piloted (Video 1: N=158 viewings; Video 2: N=33 viewings) in OBGYN or perinatology offices. A Likert scale measured 6 aspects of patient feedback. Responses to Video 1 and Video 2 respectively, found: 99%/100% agreed that “information was at a level I could understand;” 98%/100% agreed that “visual images helped me to understand;” 90%/94% agreed that “information helped me make decisions about testing options.” Viewer comments were elicited and revealed that the graphic depictions of complex genetic terminology and education on understanding risk were most helpful; others wanted a shorter video or wanted an individualized risk assessment. Both videos were subsequently modified based on the feedback. Our pilot demonstrated that videos performed at a high level of patient satisfaction, providing evidence that this tool could increase efficiency of GC services and enhance the patient experience. Areas of further study include evaluation of the lower scores related to patient decision-making to determine if content could be added to better facilitate this process.

Leveraging Scalable Genetic Counseling Tactics to Meet the Needs of a Statewide Genomic Screening Initiative

**Platform Presentations: Service Delivery**

*Submitter: Kelly Moreland East, MS, CGC, HudsonAlpha Institute for Biotechnology*

*Presenting Author: Kelly Moreland East, MS, CGC, HudsonAlpha Institute for Biotechnology*

*Primary Author: Kelly East, MS, CGC, HudsonAlpha Institute for Biotechnology*

*Author 2: Ashley Cannon, PhD, MS, CGC, University of Alabama at Birmingham*

*Author 3: Meagan Cochran, MS, CGC, HudsonAlpha Institute for Biotechnology*

*Author 4: Anna Hurst, MD, MS, FACMG, University of Alabama at Birmingham*

*Author 5: Whitley Kelley, MS, CGC, HudsonAlpha Institute for Biotechnology*

*Author 6: Brandon Shaw, MS, CGC, University of Alabama at Birmingham*
The Alabama Genomic Health Initiative (AGHI) was launched in 2017, and became one of the first statewide, state-funded programs to bring genomic testing to a large, unselected population. Through AGHI, Alabama residents have access to a genotype-based screening test aimed at identifying known pathogenic variants in 59 genes found on the ACMG Secondary Findings v2.0 list. As of April 2018, 1,654 people have consented to be a part of the initiative. AGHI is a collaboration between the University of Alabama at Birmingham and the HudsonAlpha Institute for Biotechnology. A team of genetic counselors from both institutions work together to meet the educational and counseling needs of the program. Participants who receive a positive genotyping result confirmed in a CLIA-certified laboratory receive a personal phone call from an AGHI genetic counselor to discuss the result. To date, 1.1% have received a positive result, indicating the presence of a genetic risk factor. Pathogenic variants have been identified in 9 different genes, including APOB, BRCA1, BRCA2, LDLR, MYBPC3, MLH1, MYH7, PKP2, and RYR1. 50% of positive results have been unexpected – meaning there was little personal or family history associated with the risk factor identified. It is critical to attend to the needs of participants receiving a negative result. We have developed a process for quickly assessing personal and family history to guide follow-up after result disclosure. History is gathered during the enrollment process and reviewed by a genetic counselor. Internally developed criteria are used to flag individuals who may benefit from clinical genetics follow-up regardless of genotyping result. Individualized information about the suspicious family history and recommendations for follow-up are included within the AGHI result report. To date, 44% of all AGHI participants have been labeled with a “strong” personal or family history. In the era of cost-effective genomic testing, it is of increasing importance for genetic counselors to develop, evaluate, and share scalable service delivery models.

Cost-Savings and High Patient Satisfaction with Automated Disclosure of NIPT Results

**Platform Presentations: Service Delivery**

*Submitter: Cassidi Dailey Kalejta, Metis Genetics*

*Primary Author: Cassidi Dailey Kalejta, Metis Genetics*

*Presenting Author: Cassidi Dailey Kalejta, Metis Genetics*
Introduction: Healthcare professionals (HCPs) spend valuable time and resources disclosing Non-Invasive Prenatal Testing (NIPT) results. We developed a novel, automated negative NIPT disclosure process to save HCPs time and provide education and test results to women. <br />

Methods: High-risk, pregnant Southern California Permanente Medical Group (SCPMG) women who opted for NIPT (performed by Illumina) received their negative results through the automated process. HCPs provided patients with registration instructions. Registered women received an email indicating their result was available, watched an educational video explaining the negative NIPT result, and answered three comprehension questions. Women downloaded their result if they elected to learn the predicted chromosomal sex of the fetus. They were invited to complete a survey regarding the efficiency, ease, and satisfaction with the disclosure process. Of note, women with positive results were not included. <br />

Results: 829 women out of 4429 registered women responded to the survey. The following percentage of women strongly agreed/agreed with: ease of account creation and portal navigation (95%); efficient and convenient result disclosure (93%); felt informed after watching the 2-minute video (95%); and preferred downloading results rather than waiting for their next appointment (97%). On average, SCPMG saved 10-12 minutes/patient. Cost savings for SCPMG is approximately $8.00-$9.00/patient, or $88,500/year for the high-risk population and $354,000 if expanded to the general-risk population. <br />

Discussion: Our ongoing study demonstrates high satisfaction and cost-savings with this automated, scalable solution. Women prefer receiving their result electronically versus waiting for their next doctor’s visit. Secure and automated solutions will allow HCPs to focus on women with positive results, which require a higher level of attention and care. Further studies should be performed to validate, confirm, and extend the findings of this study.<br />

Perspectives from the Trenches: An Analysis of How the Workforce is Currently Utilized to Train the Next Generation of Genetic Counselors
The demand for qualified individuals to provide genetic services is rapidly increasing, creating an explosion of jobs within the field of genetic counseling. Training additional genetic counselors would help address the emergent demands for genetic services, but the availability of clinical supervision to train students is a rate-limiting factor. This study aimed to evaluate experiences and the perspectives of genetic counselors on the clinical training of genetic counseling students. Four hundred fifteen patient-facing genetic counselors belonging to either the NSGC or ABGC completed an anonymous online survey. Approximately half of participants provided clinical supervision in 2017 and these participants represented 98% of accredited programs in the United States in Canada. The majority of participants (94.3%) perceived the training of additional students as either extremely important or very important. Approximately 55% of participants indicated that they could train additional students per year, with 34.1% of those participants reporting the ability to train an additional 3-5 students yearly. Participants without a genetic counseling program within 60 miles of their clinic were more likely to report that they could train more students. Workload, patient volume, and number of additional professional responsibilities were not found to be associated with participants’ capacity to train more students. Inclusion of telemedicine cases and expansion of internship opportunities outside direct patient care were ranked as the most effective ways to train additional students. These findings illustrate that patient-facing genetic counselors not only endorse the training of additional genetic counseling students, but also have the ability to provide additional clinical supervision. The utilization of clinical sites located further from existing training programs, potentially using telemedicine or travel stipends, as well as the incorporation of internship experiences in industry, research, and laboratories may allow more students to be trained.

Standardized Patients: Enhancing Genetic Counseling Graduate Training

Platform Presentations: Training and Workforce
Submitter: Lisa Jay Kessler, Arcadia University
Presenting Author: Lisa Jay Kessler, Arcadia University
Primary Author: Lisa Jay Kessler, Arcadia University, Genetic Counseling Program
Author 2: Denise LaMarra, Perelman School of Medicine
Accredited genetic counseling programs teach 22 practice-based competencies (PBCs) in four domains. The purpose of this pilot study was to determine the effectiveness of using standardized patients (SPs) to formatively assess interpersonal competencies (domain II). SPs are individuals trained to portray patients in a consistent, measurable way to teach/assess healthcare trainees, and provide opportunities to practice emotionally and medically challenging cases without a clinical supervisor present. SP methodology has not been studied yet in the context of GC graduate education. Two case scenarios were developed in collaboration with a medical school's SP Program: 1) Whole exome (WES) consenting with a secondary finding result and 2) Huntington disease (HD) testing. Sixteen second-year GC students participated in pre- and post-test sessions for both scenarios. Sessions were video-recorded, monitored by faculty, and evaluated by clinical supervisors. SPs provided verbal feedback and completed communication/interpersonal skills checklists for each trainee. Students completed self-assessments and satisfaction surveys after each session. SPs rated GCs as demonstrating good or very good levels of empathy 100% of the time (WES) and 94% of the time (HD). SPs reported feeling comfortable or very comfortable referring a friend or family member to this counselor 100% of the time in the WES case, and 81% in the HD case. All students indicated the feedback from the SPs was helpful; the average feedback score was 3.38/4 for the WES case and 4/4 for the HD case. Results show that this SP program effectively assessed GC students on their interpersonal and counseling skills. The SPs identified deficiencies that allowed for targeted video review and subsequent tailored feedback from faculty. Preparation with SPs can reduce the dependence on clinical rotations for basic skill development, allowing clinical supervisors time to teach more advanced skills, and increasing their ability to work with additional students to ease the workforce issue.

Exploring the Developmental Process of Genetic Counseling Supervisors

**Platform Presentations: Training and Workforce**

*Submitter: Caitlin Reid,*

*Primary Author: Caitlin Reid,*

*Presenting Author: Caitlin Reid,*

*Author 2: Monica Marvin, University of Michigan*

*Author 3: Beverly Yashar, University of Michigan*

*Author 4: Ian MacFarlane, Elizabethtown College*

With the expansion of genetic counseling (GC) training programs, more counselors are being asked to provide clinical supervision earlier in their career. Formal training opportunities related to this responsibility are limited and the developmental trajectory of novice supervisors’ skills is not well understood. Our goal was to understand novice supervisors’ needs in order to better support their confidence and competence as supervisors. Eligible GC participants were recruited through the American Board of Genetic Counseling, had 1 to 5 years of clinical experience, had supervised at least 2
students and planned to continue supervising. Twenty participants completed semi-structured phone interviews using a novel interview guide that explored preparation for and motivation to supervise, definition and perception of successful supervision, and challenges and related solutions. Transcripts were coded and themes were identified using an inductive approach. All participants were female, less than 34 years old, most worked at a University Medical Hospital (n=13) and had 6 or more supervisors at their site. A variety of clinical specialties were represented. Participants mean self-rated competency as a supervisor was a 6.8 (standard deviation of 1.5) on a scale of 1 to 10 (not at all competent to completely competent). Most described student feedback as a common tool for self-assessment and skill development. Student feedback was received in varied ways and was most often perceived as positive in nature. Many participants defined “successful supervision” as having a successful relationship with the supervisee, although definitions of successful relationships varied. Additionally, most defined confidence in one’s GC skills as an important prerequisite to confidence as a supervisor. Our findings suggest supporting the development of novice supervisors requires fostering self-efficacy in genetic counseling skills, improving formative and summative forms of student feedback, and developing tools that help novice supervisors self-assess their clinical and supervision skills.

Statewide Assessment of the Utah Genetic Counseling Clinical Workforce

Platform Presentations: Training and Workforce

Submitter: Karin M. Dent, University of Utah Health Sciences Center

Primary Author: Karin M. Dent, University of Utah Health Sciences Center

Presenting Author: Karin M. Dent, University of Utah Health Sciences Center

Author 2: Erin E. Baldwin, ARUP Laboratories; Salt Lake City, UT

Author 3: Marjan Champine, Huntsman Cancer Institute, University of Utah; Salt Lake City

Author 4: Katie Dunn, Humana, Inc.; Louisville, KY

Author 5: Michelle Landon, Myriad Genetics Laboratories; Salt Lake City, UT

Author 6: Heather Sarin, Utah Dept of Health; Salt Lake City, UT

Author 7: Lauren Wallace, Division of Reproductive Genetics, Intermountain Healthcare;

Author 8: Nancy C. Rose, Division of Reproductive Genetics, Intermountain Healthcare;

Author 9: Jenna Christensen, Utah Medical Education Council; Salt Lake City, UT

In 2017, the Governor-appointed Utah Medical Education Council (UMEC) surveyed the Utah (UT) genetic counselor (GC) workforce. The goal was to illustrate the composition and distribution of the active GC workforce and to determine if it can sufficiently meet current and future demands of the state. The UMEC and an advisory committee developed a 29-question survey mailed to all genetic counselors holding a Utah GC license. The survey questions were designed to assess factors such as practice setting, specialty, professional responsibilities, and licensee plans to reduce hours, retire, or
otherwise leave the field. Data collection was completed in December 2017 and analyzed by SPSS. The survey response rate was 86%. Of the 147 respondents, 78% practiced in UT. Thirty-seven percent of those lived in and provided services in state; 41% lived outside of UT and provided some services in state. Fifty-seven percent of the workforce living in UT reported counseling patients. Clinical settings in UT experienced a net GC loss of 3.7% over the last two years due to the workforce moving primarily into non-clinical settings. Of the clinically active GCs, one third of those living in UT reported seeing 5-10 patients per week, while 23% of GCs living outside of UT reported counseling more than 20 patients per week. Although it is unclear if all respondents counseled patients full-time, the results suggest 1.2 clinical GCs per 100,000 UT residents. In order to maintain this ratio, 2.0 additional clinical FTEs will be needed per year as the current workforce continues to transition into non-clinical roles, reduce hours, or retire. While these data reflect current trends in the UT clinical GC workforce, they likely mirror national trends supporting the need for expansion of professional training and the creation of strategic initiatives to reduce the gap between GC clinical service demands and availability.

The Current Landscape of Genetic Counseling (GC) Licensure in the United States

Platform Presentations: Training and Workforce
Submitter: Natalie Vena, Celmatix

Primary Author: Natalie Vena, Celmatix

Presenting Author: Natalie Vena, Celmatix

Author 2: Jennifer Helgeson, Celmatix

Author 3: Elaine A. Sugarman, Celmatix

GC service providers must be appropriately licensed and comply with regulations defined by the states in which patients reside. With the growing use of telegenetics, providers offering nationwide GC services must ensure appropriate licensure coverage. The National Society of Genetic Counselors offers guidance in establishing licensure legislation, but the application and renewal requirements vary greatly among states. Here we describe the current requirements for obtaining and maintaining GC licensure in the US. By May 2018, 22 states had active GC licensure legislation. An application (7 online, 15 paper) must be submitted to the state licensing board with initial application and licensing fees ($40-$400). All states require official documentation of American Board of Genetic Counseling certification. Eighteen states require an official transcript from an Accreditation Council for Genetic Counseling accredited program, 5 require multiple professional recommendations and/or employment verification, and 2 require additional training programs. Four states require supplemental information, such as proof of identity, resume, or liability insurance documentation. Additional incurred costs may include passport photos, notarization, and postage. Fourteen states require background checks, and 9 require fingerprinting. Nine states have fees associated with the background check ($5-$70), with added fingerprinting or Criminal Offender Record Information fees not included. Nineteen states require verification of applicants' existing professional out-of-state licenses, and 13 charge a fee for each request ($4-$50). All states require license renewal ($30-$500), but renewal schedules and continuing
education requirements vary. The cost, time, and documentation required to submit, obtain, and maintain individual state licensure places an increasing burden on providing nationwide GC services. While licensure helps establish competences and ensure public protection, opportunities to simplify the process and support counselors pursuing multiple licenses should be explored.

Incorporation of Genetic Testing for Familial Hypercholesterolemia Doubles Diagnosis Rate

Platform Presentations: Variant Interpretation and Diagnostic Utility

Submitter: Emily Brown, MGC, CGC, Johns Hopkins Hospital

Presenting Author: Emily Brown, MGC, CGC, Johns Hopkins Hospital

Primary Author: Emily Brown, Johns Hopkins University

Author 2: Laura Goodell, University of Maryland

Author 3: Rebecca McClellan, Johns Hopkins University

Author 4: Kathleen Byrne, Johns Hopkins University

Author 5: Thorsten Leucker, Johns Hopkins University

Author 6: Steven Jones, Johns Hopkins University

Author 7: Seth Martin, Johns Hopkins University

Introduction

Familial hypercholesterolemia (FH) is a hereditary condition characterized by elevated LDL-C from birth leading to premature coronary artery disease and physical sequelae of lipid deposition in tissues. Early diagnosis is critical since timely treatment can prevent atherosclerosis and coronary heart disease. Nevertheless, less than 10% of prevalent cases of FH in the United States have been diagnosed. Low rates of diagnosis are attributable in part to affected patients not meeting the stringent clinical diagnostic criteria of the Dutch Lipid Clinic Network (DLCN).

Methods

We retrospectively reviewed patients seen in the Advanced Lipids Disorders Clinic at Johns Hopkins Hospital between 2015 and 2018. DLCN criteria were applied to classify each patient, before and after genetic testing, as having Unlikely, Possible, Probable, or Definite FH. Genetic testing included sequencing and deletion duplication analysis of four genes (LDLR, PCSK9, APOB, and LDLRAP1). Variants were classified according to the 2015 ACMG guidelines.

Results

The retrospective review identified 108 adult probands who were seen in our clinic for evaluation for FH. Eighteen individuals (17%) were determined to carry a likely pathogenic or pathogenic variant and have heterozygous FH. Nine of these individuals (50%) met criteria for Definite FH on clinical grounds prior to genetic testing. The clinical and family histories, and physical exam features, of the remaining nine patients were not sufficient to provide a definitive diagnosis. Only after a positive genetic test result did these patients meet criteria for Definite FH.

Conclusions

Incorporating genetic testing for FH doubled our diagnosis rate when compared to classifying solely on clinical grounds. Affected individuals may not have originally met DLCN criteria for a variety of reasons including having a mild...
phenotype or previous treatment which modified their clinical phenotype. Therefore, our data support genetic testing in evaluation for FH, as a diagnosis has important implications for patients and their relatives.

Clinical utility of clinical whole genome sequencing (cWGS): a review of pilot data from 88 cases

Platform Presentations: Variant Interpretation and Diagnostic Utility

Submitter: Carolyn Brown, Genetic Counselor, Illumina

Presenting Author: Carolyn Brown, Genetic Counselor, Illumina

Primary Author: Carolyn M. Brown, Illumina Inc.

Author 2: Alka Malhotra, Illumina Inc.

Author 3: Krista Bluske, Illumina Inc.

Author 4: Aditi Chawla, Illumina Inc.

Author 5: Amanda Clause, Illumina Inc.

Author 6: Maria Laura Cremona, Illumina Inc.

Author 7: Miguel Del Campo, Rady Children's Hospital

Author 8: Carolina Galarreta, Rady Children's Hospital

Author 9: R Tanner Hagelstrom, Illumina Inc.

Author 10: Marilyn C. Jones, Rady Children's Hospital

Author 11: Diane Masser-Frye, Rady Children's Hospital

Author 12: Julia McEachern, Illumina Inc.

Author 13: Denise L. Perry, Illumina Inc.

Author 14: Keisha Robinson, Illumina Inc.

Author 15: Alicia Scocchia, Illumina Inc.

Author 16: Erin Thorpe, Illumina Inc.

Author 17: Kristen Wigby, Rady Children's Hospital

Author 18: John Belmont, Illumina Inc.

Author 19: Ryan J. Taft, Illumina Inc.
Clinical whole genome sequencing (cWGS) is a test that detects many variant types, including single nucleotide, copy number and mitochondrial variants. cWGS is not yet widely available and data addressing its clinical utility, defined as the ability to inform clinical decision making and, ultimately, to improve outcomes, are limited.

To investigate the clinical utility of cWGS, surveys were sent to the ordering providers of 94 probands in Illumina’s iHope program, a philanthropic initiative that provides cWGS to individuals with limited access to genetic testing. 88 surveys have been completed. In 58 (66%) probands, > 1 variant of potential clinical relevance was reported. In 29/58 cases (50%), results prompted changes in management including implementation of condition-specific supportive interventions, specialist referrals, imaging studies or physiological testing. For example, a child with CHRNE-associated congenital myasthenic syndrome was referred to neurology for medication management. In children with Rubenstein-Taybi and Kaufmann syndromes, secondary findings in PMS2 and BRCA2 were identified as affecting future management.

In 30 (34%) probands, no variants were reported. In 3/30 (10%) negative cases, results impacted management by prompting specialist referrals or by facilitating the decision to pursue skin biopsy. In 4/30 (13%) cases, a reduced likelihood of genetic disorders promoted exploration of alternate etiologies.

Diagnostic, prognostic and recurrence information are not typically considered as elements of clinical utility, but were identified as benefits of cWGS; posttest counseling was informed by cWGS in 52/58 (90%) cases with variants reported and in 4/30 (13%) of negative cases.

In summary, pilot data suggest that cWGS contributes to clinical decision making in nearly half of probands and informs genetic counseling in about two thirds. Many of these changes would not have been considered without the information gleaned from cWGS. Ongoing research is needed to understand the effects of these management changes on patient outcomes.

In a Class All By Itself: The Importance of Reclassifying Genes and Variants to Better Guide Patient Care

Platform Presentations: Variant Interpretation and Diagnostic Utility
Submitter: Zoe Powis, Ambry Genetics

Primary Author: Zoe Powis, Ambry Genetics

Presenting Author: Zoe Powis, Ambry Genetics

Author 2: Kelly Radtke, Ambry Genetics

Author 3: Erica Smith, Ambry Genetics

Author 4: Kirsten Blanco, Ambry Genetics

Author 5: Wendy Alcaraz, Ambry Genetics

Author 6: Sha Tang, Ambry Genetics

Author 7: Kelly D.F. Farwell Hagman, Ambry Genetics
Since exome sequencing (ES) became commercially available, technological advancements and the knowledge of benign and disease-causing variation in novel candidate disease genes have greatly increased. Advancements and gene discovery have established need for periodic reanalysis and reclassification of previous cases. Procedures vary and can include proactive reanalysis and/or provider-driven reanalysis. The reanalysis method most likely to lead to diagnosis following has not been studied. Herein we investigate outcomes of reanalysis amongst varying indications for reanalysis patients with previous ES. Since 2011, 636 cases had at least one completed re-analysis and/or reclassification, with 673 total. 417 were provider-initiated, 256 lab-initiated, 228 upgraded, 39 downgraded and 406 were had no changes in reported classification, (some with changes in individual gene and/or alteration reclassification but resulting in no overall change). Provider initiated reanalysis was less likely to result in a reclassification, regardless of whether updated clinical information was provided (Provider request unchanged 399/417 (95.7%), lab initiated changed 248/256 (96.9%), p<0.0001) and lab driven reanalysis was more likely to result in an upgraded result (210/256 (82.1%), p<0.0001)). The primary reasons for reclassifications were upgrades due to new literature describing new gene-disease relationships, and downgraded alterations due to new population frequency databases (p<0.0001, 0.0049 respectively). Our findings suggest that proactive reanalysis with literature surveillance on alterations and new gene-disease discoveries enhances diagnoses. The comprehensive nature of ES makes it uniquely powerful for identifying novel molecular diagnoses at both first analysis and reanalysis. Data sharing with collaborations to publish data on new disease genes is paramount to aid in new diagnoses. These data emphasizes the importance of counseling patients about the likelihood of result reclassification and navigating the complexity of changes in diagnosis.

Outcomes of 94 Patient-Driven Family Studies for Reclassification of Unselected Variants of Uncertain Significance

Platform Presentations: Variant Interpretation and Diagnostic Utility
Submitter: Ginger Jade Tsai, University of Washington
Presenting Author: Ginger Jade Tsai, University of Washington
Primary Author: Ginger Jade Tsai, University of Washington, Department of Laboratory Medicine
Author 2: John Michael O. Rañola, University of Washington, Department of Laboratory Medicine
Author 3: Christina Smith, University of Washington, Department of Laboratory Medicine
Author 4: Lauren Thomas Garrett, University of Washington, Department of Laboratory Medicine
Author 5: Silvia Casadei, University of Washington, Department of Medicine
Author 6: Brian H. Shirts, University of Washington, Department of Laboratory Medicine

Family studies for reclassification of variants of uncertain significance (VUS) are available for select families at many commercial laboratories, but there are few studies that describe outcomes such as reclassification results and patient satisfaction. In light of growing patient demand for VUS
reclassification, we evaluated outcomes of a patient-driven framework that offered familial VUS reclassification analysis to any adult with any clinically ascertained VUS from any laboratory. With guidance from our online tutorial FindMyVariant.org, participants gathered family history information to build pedigrees, coordinated sample collection for relatives, and communicated information between the study and their families. We performed quantitative cosegregation analysis when possible and evaluated variant classifications using Tavtigian’s unified framework, which facilitates combining Bayesian analysis with ACMG/AMP guidelines. 94 families with 114 VUS, predominantly in cancer risk genes, were recruited over two years. Success rates for family member recruitment and VUS reclassification were calculated from the 46 families who had been enrolled for at least one year. A mean of 6.5 relatives per family were invited to participate, and a mean of 4.3 relatives per family returned samples for genotyping. 29 of 56 VUS (52%) in these 46 families were reclassified. In the entire cohort of 94 families, we observed diverse VUS reclassification pathways, including identification of a de novo variant and testing of multiple siblings for a recessive variant in trans with a known pathogenic variant. When quantitative cosegregation analysis was not possible, genotyping of relatives often contributed to reclassification by identifying relatives with phenotypes highly specific for or incompatible with specific classifications. Given access to familial testing and educational materials, motivated families can contribute substantial information to VUS reclassification. Clinical laboratories should consider offering family studies to all patients with VUS.

Variant Interpretation is a Wide-Spread and Valuable Practice Amongst Clinical Genetic Counselors Across Multiple Specialties

Platform Presentations: Variant Interpretation and Diagnostic Utility

Submitter: Karen Wain, Geisinger - Autism & Developmental Medicine Institute

Primary Author: Karen Wain, Geisinger - Autism & Developmental Medicine Institute

Presenting Author: Karen Wain, Geisinger - Autism & Developmental Medicine Institute

Author 2: Danielle R. Azzariti, Laboratory for Molecular Medicine

Author 4: Amy Knight Johnson, University of Chicago

Author 5: Patti Krautscheid, ARUP Laboratories

Author 6: Julianne O'Daniel, University of North Carolina at Chapel Hill

Author 7: Deborah Ritter, Baylor College of Medicine

Author 8: Juliann M. Savatt, Geisinger - Autism & Developmental Medicine Institute

Author 9: Christa Lese Martin, Geisinger - Autism & Developmental Medicine Institute

Author 10: Erin Rooney Riggs, Geisinger - Autism & Developmental Medicine Institute

Author 3: Jenny Goldstein, University of North Carolina at Chapel Hill
Broad-scale genomic technologies are incorporated into clinical care across many specialties, and recent variant interpretation guidelines, databases, and other resources have emerged to address interpretative challenges related to this testing. While variant interpretation (VI) practice has traditionally been the purview of clinical laboratories, clinical genetic counselors (GCs) are increasingly reporting assessing evidence for VI purposes in clinical practice. The aim of this study was to explore the practice of VI by clinical GCs across multiple clinical specialties. An online survey was administered to National Society of Genetic Counselors (NSGC) members via Survey Monkey. GCs providing part- or full-time clinical counseling were eligible. Respondents (n=239, ~9.6% response rate) represented all major clinical specialties. Demographics were generally consistent with the 2018 NSGC Professional Status Survey, though there was a lower rate of prenatal GCs (24.3% vs. 41.%). The majority (68.3%) report reviewing evidence documented by the laboratory in most (>60%) reports received; 45.5% report assessing evidence beyond what is noted in a report. VI is often performed independently (43.8%), and many respondents utilize team discussions (31.3%) or case conferences (30.8%). Most respondents (67.4%) have disagreed with a laboratory interpretation, but this is typically rare or infrequent (96.5%). There were no associations between VI practice and clinical specialty, years practicing, or previous/current laboratory or research roles. Factors that influence the decision to perform VI in clinical practice were 1) when the variant was interpreted as being of uncertain significance (74.9%), 2) the consistency of a reported variant with patient phenotype (70.9%), and 3) the consistency of a variant interpretation with ClinVar/other databases (65.9%). This study confirms that VI activities occur frequently in GC clinical practice across specialties and are an important part of genomic medicine. These results should inform GC educational curricula and scope of practice.
Poster Presentations

A-1 High throughput counseling: meeting the demand for carrier screening results disclosure and patient management.

**Access & Service Delivery**

*Submitter: Aishwarya Arjunan, Counsyl*

*Primary Author: Aishwarya Arjunan, Counsyl*

*Presenting Author: Aishwarya Arjunan, Counsyl*

*Author 2: Rotem Ben-Shachar, Counsyl*

*Author 3: Jamie Kostialik, Counsyl*

*Author 4: Katherine Johansen Taber, Counsyl*

Although professional organizations have recommended carrier screening for conditions like cystic fibrosis for years, advances in technology have allowed for the adoption of expanded carrier screening (ECS), which increases the scope of information available to patients and providers alike. We describe a technology platform designed to facilitate large-scale dissemination of carrier screening information and results. Counsyl has developed a technology platform that provides automated results delivery of carrier screening results, genetic education, and genetic counseling. We performed a retrospective analysis of de-identified individuals whose carrier screening results were delivered through the automated platform. For both screen-positive and screen-negative patients, we analyzed the frequency of genetic consultation requests, elected consultation type (scheduled or on-demand) and duration, and patients’ consultation satisfaction ratings. Over an eight-year period, 278,318 carrier screening results were issued through the system. Of these, 41,050 patients (15%) elected genetic counseling, with some electing multiple consultations, resulting in a total of 43,343 consultations. Half of all consultations were for patients who received negative results. Approximately 32% of all consultations completed were on-demand. Median consultation time was ten minutes (interquartile range: 5-15 minutes) for all results. The median patient satisfaction rating for consultations was 4.9/5.0. Historically, patients with negative test results were not referred for further counseling or education. In this cohort, approximately 50% of patients choosing to schedule a consultation had negative results, demonstrating a desire for post-test genetic counseling irrespective of screening results. Our platform provides an effective means of following medical guidelines on post-genetic testing patient management, which is important for delivering quality care as genetic testing uptake grows among the general population.

A-10 Barriers and facilitators to reaching a diagnosis of monogenic diabetes from the patients’ perspective: A qualitative study

**Access & Service Delivery**

*Submitter: Yue Guan, Emory University*
Background: About 95% monogenic diabetes is misdiagnosed as either type 1 or type 2 diabetes (T1DM/T2DM). Few studies have examined the diagnostic challenges from the patients’ perspective. This qualitative study aimed to investigate patients’ journeys to obtaining a MODY diagnosis by elucidating the range of factors that can act as barriers and facilitators throughout this process.<br /><br />Methods: We recruited participants from the Personalized Diabetes Medicine Program (PDMP) at University of Maryland and used respondent-driven sampling to recruit additional patients. We conducted qualitative phone interviews between October 2016 and June 2017 with nine patients with diagnoses of monogenic diabetes (1 MODY1, 7 MODY2, and 1 MODY3) and one parent of a patient with MODY10. Interview data were audio recorded, transcribed, and analyzed both inductively and deductively using thematic content analysis.<br /><br />Results: All patients were female, with a mean age of 35 (range: 7-67 years). The amount of time these patients were misdiagnosed ranged from a few months to 41 years. Initial analysis identified barriers in four broad themes: 1) patient-related (overlapping symptoms with T1DM or T2DM, perceived test utility, self-efficacy, knowledge, fear of being a “difficult” patient); 2) provider-related (low provider awareness, lack of access to knowledgeable provider); 3) provider-patient relationship and communication (negative provider attitudes toward patients’ beliefs and expectations, rushed discussions of patients’ concerns, few evidence-based responses, lack of empathy when addressing patient’s symptoms), and 4) system-related (imperfect screening tools, cost of testing, limited patient informational and support resources, complexity of healthcare system).<br /><br />Conclusion: Given the thematic range of the identified barriers, the diagnostic process of MODY is highly complex. Genetic counselors are in a prime position to identify at-risk patients while obtaining a family history. Understanding the barriers may result in quicker MODY diagnoses.
Genetic counseling assistants (GCAs) have the potential to address the high demand for genetic counseling services by promoting task-sharing, increasing genetic counselor efficiency, and allowing for higher level duties to be optimized by genetic counselors. However, little research has been published on the role of GCAs in genetic counseling. The present study explored GCAs current tasks, the appropriateness of tasks, their impact on the profession, and how these findings compared between genetic counselors with and without GCAs. Genetic counselors with and without experience working with GCAs were recruited via an online survey. Participants (n=271) reported that GCAs work in most clinical and laboratory settings, and in all primary specialties frequently performing clerical tasks but less often clinically involved tasks such as calling patients with genetic test results. There was no difference in the reported frequency of each task between participants with and without GCAs. Participants without GCAs reported more tasks on average than those with GCAs (p<0.001). Both groups reported clerical tasks as more appropriate than clinically involved tasks (p<0.001). Only one difference in perceived appropriateness of tasks existed, those with GCAs reported calling patients with VUS results as more appropriate (13%) than those without GCAs (4%) (p<0.05). Primary limitations to include more tasks included GCAs' heavy workload and lack of training and experience. Potential benefits of working with GCAs included increases in time available for higher-level duties, patient volumes, and efficiency. A primary concern noted about GCAs’ roles was a poorly defined scope practice for GCAs (n=182). These data provide genetic counselors with a more generalizable understanding of current GCA roles on a national level, across specialties. Additionally, these data may help establish a scope of practice for GCAs and creates a baseline job description for genetic counselors interested in implementing a GCA into their practice to increase patient access to genetic counseling services.

A-16 Implementation of Dedicated Cascade Testing Clinic to Improve Access and Efficiency

**Access & Service Delivery**

*Submitter: Michelle Fay Jacobs, University of Michigan*

*Presenting Author: Michelle Fay Jacobs, University of Michigan*

*Primary Author: Michelle Jacobs, Michigan Medicine*

*Author 2: Erika Koeppe, Michigan Medicine*

*Author 3: Jenae Osborne, Michigan Medicine*

*Author 4: Andrea Murad, Michigan Medicine*

*Author 5: Monica Marvin, Michigan Medicine*

*Author 6: Dianne Samad, Michigan Medicine*
Cascade testing (CT), which involves genetic testing of relatives of individuals with genetic conditions, is currently underutilized. The UM Cancer Genetics Clinic observed one barrier to CT was the 6+ month wait time for our weekly new patient clinic (NPC). Given that individuals being seen for CT generally require shorter appointments and less genetic counselor (GC) time, we sought to determine whether a different triaging and scheduling model could streamline CT appointments with the goals of improving uptake of CT and optimizing genetic counselor time.<br />
In October 2016, we implemented a half-day Cascade Testing Clinic (CTC) 1-2 times per month. CTC consists of 30-minute GC only visits, compared to 75-minute GC/MD slots in NPC. Criteria to be scheduled include: 1) No personal history of cancer, 2) Documentation of familial pathogenic/likely pathogenic variant, and 3) Family history received and reviewed by GC to ensure no genetic testing indicated beyond familial variant. During scheduling, patients are told that fulfilling these criteria allows for an appointment within 2 months rather than first available in NPC.<br />
Data were collected from Oct. 2016-Apr. 2018. Statistical analyses were performed with Chi-squared and t-tests. Average wait time between referral and appointment date for CTC was 58 days compared to over 6 months for NPC (p<0.05). GC only visits and requiring family information in advance allows for efficient use of GC time. Per one full-time effort GC, an average of 5.9 patients were seen in a half-day in CTC compared to 2.6 per half-day in NPC (p<0.05). During this 19-month period, 251 single site analysis tests were ordered compared to 199 in the same time period prior to initiation of CTC (1.3-fold increase). No-show rate in CTC was 4.6% compared to 9.1% in NPC (p=0.08).<br />
Our CTC allows for patients with family histories of an inherited cancer syndrome to be seen more efficiently, saving provider and patient time. Creating this clinic led to an increase in the number of CT patients seen by our clinic with minimal increase in GC time.

A-19 Detecting Unaffected Individuals for Lynch Syndrome (DUAL): An Institutional Experience

Access & Service Delivery
Submitter: Sayoni Lahiri, UT Southwestern
Presenting Author: Sayoni Lahiri, UT Southwestern
Primary Author: Sayoni Lahiri, UT Southwestern Simmons Comprehensive Cancer Center
Author 2: Sara Pirzadeh-Miller, UT Southwestern Simmons Comprehensive Cancer Center
Author 3: Jillian Huang, Humana
Author 4: Theodora Ross, UT Southwestern Simmons Comprehensive Cancer Center
Author 5: Emily Berenson, UT Southwestern Simmons Comprehensive Cancer Center

With an estimated incidence of 1:300, Lynch syndrome (LS) is classified as a tier 1 genomic application by the CDC due to the significant potential for positive impact on public health. Although identifying LS
early can increase one’s cancer-free lifespan by up to 24 years with appropriate follow-up, only 2% of LS patients have been identified, as current testing strategies focus on identifying LS through individuals with an existing cancer diagnosis. Using the following multipronged approach, we screened individuals in the general population for LS and offered them genetic counseling/genetic testing (GC/GT): we incorporated cancer family history (FH) questionnaires into mammography and GI clinics in local hospitals; partnered with the CPRIT-grant funded CSPAN Coalition to distribute educational FH cards to patients undergoing colon cancer (CC) screening; distributed FH cards to 24 Hour Fitness members as part of a LS awareness campaign; formed a coalition of local LS experts to address factors that affect compliance with follow-up care; and used cascade testing to identify at-risk relatives. To overcome barriers to access to GC, we provided phone counseling and mailed saliva kits for tests that assess up to 46 genes associated with hereditary cancer.<br />

In the first 18 months, we screened 73,219 individuals to identify 3,434 (5%) at high risk (HR) for LS, of whom 377 (11%) underwent GC/GT. Of 248 patients who had GT, 32 (13%) tested positive: 11 (34%) had LS, 10 (31%) had mutations in other CC genes, and 11 (34%) had mutations in non-CC genes. Of the 11 LS patients, 10 (91%) were unaffected. We also identified 88/216 (41%) individuals with negative GT results who would be considered HR based on reported FH of CC.<br />

DUAL is an effective way to identify unaffected individuals at increased risk for CC with the potential to reduce the burden of CC on the population as a result. This service delivery model addresses some barriers to GC/GT, and we will continue to refine this processes to improve uptake of phone counseling, test completion, and uptake of cascade testing.<br />

A-22 Beyond the Clinic: A pilot study integrating genetic counseling and mobile health technology

Access & Service Delivery
Submitter: Kestutis Micke, University of Colorado

Presenting Author: Kestutis Micke, University of Colorado

Primary Author: Kestutis Micke, University of Colorado

Author 2: R. Beth Dugan, University of Michigan

Author 3: Beverly Yashar, University of Michigan

Author 4: Shawna J. Lee, University of Michigan

The use of mobile health and text messaging in health care delivery has expanded over recent years with successes in medication adherence, depression treatment, and patient education. Although telemedicine and social media have been successfully integrated into genetic counseling practice, mobile health technologies, such as text messaging, have not been utilized in our field. Mobile health has the potential to expand genetic counseling services, especially as the number of patients continues to outpace available counselors. This study sought to determine the utility of a text message program by sending supportive and educational text messages three times per week to parents whose newborn has
a congenital heart defect. Mental health scores of depression and anxiety scores were measured using the Edinburgh Postpartum Depression Scale (EPDS) and the six-item State Trait Anxiety Inventory (STAI-6), respectively. Participants were also asked to give feedback about the program as a whole. A total of 16 patients and 8 partners have been consented thus far from the University of Michigan Fetal Diagnostic Center. Preliminary data (n=2) suggests that text messaging is positively accepted by families who find value in educational messages about their child’s development and felt the messages helped to cope with stressors and improve mental health. However, our data also suggests limits to the program based on the severity of a diagnosis – families whose child had multiple anomalies may need different forms of support. In addition to examining mental health, we have begun to identify a number of considerations for successful implementation of a text messaging program in terms of message content, frequency, level of personalization, back-and-forth messaging between patient and provider and beyond. Although text messaging programs need to be studied in greater detail with more diverse patient populations in the genetic counseling context, it has the potential to be integrated into the clinical setting, further expanding the reach of the genetic counselor.

A-25 Genetic counseling in an emergent country: Disparity in access to genetic cancer risk assessment for breast cancer within the Mexican population.

Access & Service Delivery
Author 2: Jose Luis Barrera Franco, Centro Oncologico Estatal ISSEMyM
Author 3: Saul Campos Gomez, Centro Oncologico Estatal ISSEMyM
Submitter: Guillermo Pacheco Cuellar, MD MS, Centro Oncologico Estatal ISSEMyM
Primary Author: Guillermo Pacheco Cuellar, MD MS, Centro Oncologico Estatal ISSEMyM

Background: Breast cancer (BC) is the most common malignancy in Mexico. 5-10% of BCs are hereditary. In Mexico the lack of resources, including geneticists/genetic counselors and the cost of genetic testing, are barriers to set up GCRA (Genetic Cancer Risk Assessment) clinics. Besides few public health programs offer GRCA to their beneficiaries; moreover 62% of Mexican population lacks health insurance. Seguro Popular (SP) offers health services to 50 million of low-income Mexicans without health coverage, but SP doesn’t cover GRCA nor testing for BC. COEI offers services to two different populations: COEI Beneficiaries (CB) and SP. GCRA and genetic testing are only covered for CB. Methods: This retrospective study compared clinical and demographic data between these cohorts. From Nov 2016 to Dec 2017, all new BC patients (pts) were referred to GRCA according to NCCN guidelines. SP pts were also invited to participate; we provided them voluntary this service. We collected demographic, familial and medical data. Genetic testing was offered only to some CB pts because of our limited budget. Descriptive and nonparametric statistics were used. Results: We compared the data of 74 cases: 51 were CB and 23 SP pts. The average age at diagnosis was 41.8, 18(24.3%) of tumors were triple negative. SP pts tended to be younger, and with more advanced disease than the CB population but without statistical differences. SP group was less educated than the CB pts (p > 0.001). Conclusions: Except for education level, no
other difference was seen. More research is needed to explore the relationship with the lower degree of education, clinical stage and health care access. Our sample is small, but it reflects the lack of access to GCRA services for low income and less educated pts across the country. GCRA could benefit SP group, to modify habits, start promptly and adapted screening, and have the choice to undergo genetic testing. If we consider the high percent of population who lack of GRCA services, we are missing opportunities to inform, and promote early detection of cancer.

A-28 On second thought...Updates to personal and family history using an interactive online tool

Access & Service Delivery
Submitter: Lauren Ryan, MS, LCGC, Color Genomics

Presenting Author: Lauren Ryan, MS, LCGC, Color Genomics

Primary Author: Lauren Ryan, M.S., L.C.G.C., Color Genomics

Author 2: Scott Topper, Ph.D., FACMG, Color Genomics

Author 3: Will Stedden, Ph.D., Color Genomics

Author 4: Cynthia L. Neben, Ph.D., Color Genomics

Author 5: Anjali Zimmer, Ph.D., Color Genomics

Author 6: Alicia Y. Zhou, Ph.D., Color Genomics

Introduction: A comprehensive pedigree and health history are central to effective genetic counseling. However, traditional methods for collecting this information have limitations, as personal and family histories are usually collected at a single point in time, in conversation with a single person. Methods: The clinical laboratory Color Genomics has implemented an online, interactive family history tool that aims to address some of these limitations through direct interaction with the individual, at their convenience. This tool lets individuals build their own family trees, solicits relevant clinical information, and supports the review and modification of the information at any time and place. It also supports secure and collaborative editing with family members. Here, we report how 36,356 individuals utilized this online, interactive family history tool and how the collected information changed over time. Results: We found that more than 54.0% of individuals returned to their own pedigree to make changes after the initial session (a median of 12 days later). Only 8.8% of individuals made changes to their personal health history. However, 73.4% of individuals made changes to family health history, suggesting that subsequent conversations after the initial session may identify other relevant information. In addition, 406 individuals had family members participate in the development of the family pedigree; the most striking contribution was to the health history of other relatives (54.3%). This is consistent with our understanding that the story of family is collectively held, often in fragments. Conclusion: This analysis did not attempt to answer the question of the impact of these changes on the accuracy of the
information or on the output of risk models. However, the data presented here clearly illustrate that the creative integration of technology can effectively engage individuals in a critical activity and demonstrate the extent to which original pedigree information might be revised upon review and discussion among relatives.

A-31 A Need for Genetic Screening/Counseling Referrals in Breast, Ovarian, Colorectal, and Endometrial Cancer

Access & Service Delivery
Submitter: Kathryn Ann Mraz, MS, CGC, UTHealth

Presenting Author: Kathryn Ann Mraz, MS, CGC, UTHealth

Primary Author: Tiffany Truong, (see biography)

Author 2: Nadia Abelhad, (see biography) of author 1

Author 3: Hiba Ali, see biography of author 1

Author 4: David Fink, see biography of author 1

Author 5: Brittanie Morris, MS, CGC, see institution from bio in author 1

Author 6: Elizabeth Nugent, MD, see bio from author 1

Author 7: Kathryn Mraz, MS, CGC, see institution from bio in author 1

Author 8: Anneliese Gonzalez, MD, see institution from bio in author 1

INTRODUCTION: Patients with genetic predispositions for cancer have significantly increased risk of multiple primary cancer(s) making them candidates for various management changes. Thus, recognizing and offering appropriate genetic screening is an important aspect of oncologic management. As part of a quality-control project to identify areas for improved access to genetic counseling, we retrospectively analyzed four primary cancer groups (breast/ovarian/colorectal/endometrial) to determine how frequently patients meeting NCCN criteria for genetic screening received a counseling referral.

METHODS: Records of all adult patients newly diagnosed with breast/ovarian/colorectal/endometrial cancer at Memorial Hermann Hospital Texas Medical Campus (MHH TMC) in 2016 were reviewed to determine if they met genetic screening criteria per NCCN guidelines and if referral to a genetic counselor was made. RESULTS: Among 128 breast cancer cases, 60 met criteria for screening, 32 were referred. Among 24 ovarian cancer cases, all met criteria, 14 were referred. Among 93 CRC cancer cases, 19 met screening criteria, 6 were referred. Of note, 30 CRC cases did not have immunohistochemical (IHC) analysis performed. Among 41 endometrial cancer cases, 5 patients met screening criteria, 3 were referred. Also, 18 endometrial cases did not have IHC performed. CONCLUSIONS: There is a substantial discrepancy between those who qualify for genetic screening and those referred to a genetic counselor across primary breast/ovarian/colorectal/endometrial cancer cases. At least 50% of each of the
reviewed cancer primaries except CRC who met criteria were referred. Among missed referrals, 61% of breast and 70% of ovarian were established with an MHH-TMC specialist which allows for physician education and patient referral. IHC analysis to pre-screen for Lynch syndrome was universal at MHH-TMC in 2016, but only 68% CRC and 56% endometrial cancer cases underwent IHC analysis. Further pathology communications to determine IHC attempts and sample issues may identify cases that warrant genetic evaluation.

A-4 Health Literacy Effects on Health-Related Needs of Pregnant Women and Their Caregivers

**Access & Service Delivery**

*Submitter: Sarah Rose Carpenter,*

*Presenting Author: Sarah Rose Carpenter,*

*Primary Author: Sarah Rose Carpenter,*

*Author 2: Gretchen Purcell Jackson, M.D., Ph.D, Vanderbilt University Medical Center*

*Author 3: Martha E Dudek, M.S., LC.G.C., Vanderbilt University Medical Center*

*Author 4: Christina Badger Hurst, MS, CGC, Informed DNA*

Introduction: Increased health literacy and fulfillment of informational needs are associated with improved health outcomes. The objective of this study was to further characterize the needs of pregnant women and their caregivers based on their level of health literacy, in order to better understand how to meet these needs.

Methods: This study re-examined data collected from a previous study at Vanderbilt University Medical Center. Pregnant women before 36 gestational weeks seen at Vanderbilt University Medical Center and their caregivers were enrolled. A mixed methodology, cross-sectional study was conducted by collecting information on needs, demographics, and health literacy scores from an interview, questionnaire, and Rapid Estimate of Adult Literacy in Medicine scale (REALM). Data was analysed using a previously validated need taxonomy, Wilcoxon Test and Pearson’s Test, Spearman P2 and redundancy tests, and logistic regression models.

Results: Participants with adequate health literacy were more likely to have their needs met than those of limited or marginal health literacy ($x^2=4.08$ adjusted p-value=0.043) and expressed more needs on average (11.3 v 7.7, p-value=0.04). Although no significant relationship was found between type of need and health literacy, some needs expressed by those with adequate health literacy were not expressed by those with limited or marginal health literacy. Conclusions: Those with lower health literacy have fewer needs and are less likely to have their needs met. To address these needs, health professionals can ensure that information is provided to the level of the patient’s understanding and can provide a discussion of needs that may have not yet been anticipated.
A-7 The Pediatric Cardiovascular Genetic Counseling Service: A Unique Convergence of Clinical Genetics and Cardiovascular Care

**Access & Service Delivery**

*Presenting Author: Samantha L. Freeze, Genetic Counselor, Indiana University School of Medicine/ Riley Hospital for Children*

*Primary Author: Samantha Leslie Freeze, Indiana University*

*Author 2: Stephanie Ware, Indiana University*

*Author 3: Benjamin Helm, Indiana University*

*Submitter: Samantha Freeze, MS, LCGC,*

**Introduction:** Cardiovascular genetic counseling (CVGC) is a relatively new practice sub-specialty. Most GCs in this setting evaluate adults for inherited CV risk and facilitate family screening/testing to reduce risk for catastrophic cardiac events. To date, there have been no studies assessing CVGC practice in the pediatric setting. **Aim:** To describe GC patient encounters in a pediatric CVGC service over a 2.5-year period (August 2015-May-2018). **Results:** GVGCs participated in 669 initial encounters in varied settings including inpatient consults (152/669, 23%) and initial outpatient clinic visits (517/669, 77%). Patients were referred for personal and/or family histories of cardiomyopathies, arrhythmias, congenital heart defects (CHD), aortopathies and sudden cardiac arrest. Most inpatient consults were requested for personal history of CHD (102/152, 67%). Personal and family history of cardiomyopathies (144/517, 28%) and arrhythmias (106/517, 21%) were the most common outpatient indications. While most patients were referred for non-syndromic heart disease, 82/669 (12%) were referred for evaluation of a possible syndromic diagnosis. Over 937 patient encounters, 517 (55%) genetic tests were sent; 106 (21%) returned with a positive result. The most common tests utilized were single site testing (115/517, 22%) and chromosome microarray (CMA) (111/517, 21%). Clinical family screening was recommended for 581/669 (87%) probands with a total of 2060 echocardiograms and 1620 electrocardiograms recommended. **Conclusions:** The pediatric CVGC service is unique in comparison to general pediatric and adult CVGC clinics, requiring additional expertise in congenital and syndromic heart disease as well as use of varied genetic tests including whole exome sequencing and CMA. This service model combines tenants of clinical genetics with those of adult cardiovascular medicine to provide comprehensive genetics care to pediatric patients with or at-risk for heritable heart disease.

B-11 Identifying Genetics Referrals within a Radiology Practice in a Community Based Hospital Setting

**Access & Service Delivery**

*Submitter: Julie Handy, Penn Medicine Virtua Cancer Program*

*Presenting Author: Julie Handy, Penn Medicine Virtua Cancer Program*
Purpose: Studies have demonstrated that referral rates for individuals appropriate for genetic counseling and testing based on National Comprehensive Cancer Network (NCCN) guidelines are as low as 21.7%. Although rates are increasing, genetic counseling services remain underutilized. In order to capture a portion of this missed population, and to increase referral rates to the Cancer Genetics Program within the Penn Medicine Virtua Cancer Program, a family history questionnaire was implemented within the radiology department for women undergoing routine mammography.

Methods: The Cancer Genetics Program functions within a community based hospital setting, serving patients and physicians within the Burlington, Camden and Gloucester counties of Southern New Jersey. The questionnaire assessed for personal and family history of cancer that would indicate eligibility for a genetics referral.

Results: Between May, 2017 and February, 2018, a total of 226 questionnaires were received. Of the individuals who returned questionnaires, 93 (41%) reported a personal and/or family history of cancer that would qualify them for genetic counseling. Of those eligible for genetic counseling, 45 (48%) individuals expressed that they were open to contact from the Genetic Counseling Program in order to schedule an appointment. Three patients, 6% of those who were contacted, were subsequently scheduled for genetic counseling appointments.

Conclusion: While we were able to identify more patients eligible for genetic counseling through implementation of this questionnaire, the percentage of those scheduling genetic counseling visits was still quite low. We are attempting to increase this number through education of radiology clinicians and staff administering this questionnaire, expanding the questionnaire to additional radiology centers and utilizing Virtua’s centralized schedulers to contact and schedule patients eligible for genetics referrals based on questionnaire results.

B-14 “A positive light for our community”: Hmong reactions to receipt of individual and community pharmacogenetic research results

Access & Service Delivery
Submitter: Katherine Holzer,

Primary Author: Katherine Elizabeth Holzer, University of Minnesota

Author 2: Heather A. Zierhut, University of Minnesota

Author 3: Kathleen A. Culhane-Pera, East Side Family Clinic, St. Paul, MN
Introduction: Participants in genomic research have historically lacked racial and ethnic diversity, limiting the application of findings to minority populations and leading to potential health disparities. Recent studies with minority populations, including the Hmong, have gauged interest in genomic research and revealed that participants want to receive their individual results after participating in studies. Research assessing minority participants’ reactions after receiving personal genomic results is needed to return future results in a culturally appropriate manner. The purpose of this study was to recruit Hmong participants for a pharmacogenetic study and describe participants’ reactions to receiving their personal and collective research results. Methods: Using a community-based participatory research (CBPR) approach, we collaborated with a Hmong community advisory board to conduct a qualitative study comprising three focus groups with 24 Hmong adults in Minnesota. We then used a thematic analysis approach to analyze the data. Results: In general, participants responded positively toward the results, including the view that personal results are useful for tailoring medicines by informing what medicines their bodies may “accept” (txais) and what medicines may “fit” or “not fit” (haum/tsis haum) their bodies. Many participants interpreted their results through a cultural lens, expressing the concept that diet and other environmental factors may influence their results through their roj ntsha (flesh and blood), which they inherit from their parents. Also, many acknowledged linguistical, educational, and cultural factors that may limit the utility of results for Hmong individuals. Discussion: Pharmacogenetic results may be useful for Hmong participants, however, genetic counselors and other providers should be cognizant that many Hmong individuals may incorporate these results into their pre-existing concepts of genetics and medicines.
A survey of ALS clinician genetic testing practices identified lack of consensus on the offer of testing and divergent views towards testing as compared to ALS patients

**Access & Service Delivery**

*Submitter: Holly Klepek, The Ohio State University*

*Presenting Author: Holly Klepek, The Ohio State University*

*Primary Author: Holly Klepek, The Ohio State University*

*Author 2: Haikady Nagaraja, PhD, The Ohio State University*

*Author 3: Adam Quick, MD, The Ohio State University*

*Author 4: Stephen Kolb, MD, PhD, The Ohio State University*

*Author 5: Stephen Goutman, MD, University of Michigan*

*Author 6: Jennifer Roggenbuck, LCGC, The Ohio State University*

Recent advances in ALS gene discovery have both empowered and challenged clinicians providing care for persons with ALS. Ten years ago, commercial ALS genetic testing was limited to SOD1 sequencing. In 2018, assays for the C9orf72 expansion, multigene panels, and whole exome sequencing are available, and a genetic etiology may be established in ~70% of fALS and ~15% of sALS (Chia et al, 2018). However, the offer of genetic testing is not yet ‘standard of care’ in practice, particularly for sALS (Byrne et al, 2012; Arthur et al, 2016; Vajda et al, 2017). In 2012, the European Federation of Neurological Societies (EFNS) directed that genetic testing should not be performed in “cases with sporadic ALS with a typical classical ALS phenotype” (Andersen et al, 2012), while US guidelines do not address the issue (Miller et al, 2009). In order to study current genetic testing practices, we surveyed the Northeast ALS Consortium, an international group of specialist ALS clinicians. Responses were received from 80/255 (response rate=31.4%). While 92.3% indicated they offer genetic testing to patients with fALS, 52.3% offer testing to patients with sALS, revealing a lack of consensus with respect to the approach to genetic testing in the typical patient with ALS. Additionally, comparison of clinician and patient attitudes towards genetic testing identified significant differences in how each group values genetic information. Patients were more likely to see value of genetic testing for themselves and for family members, and less likely to strongly value the scientific potential of testing. ALS genetic testing and counseling guidelines, addressing test indication, interpretation, and counseling, may assist clinicians in navigating the challenges of this technology and enable equitable patient access to genetic information.
The state of Texas does not currently license genetic counselors (GCs). A survey of GCs concluded licensure legitimizes genetic counseling as a distinct health profession and increases protection of healthcare consumers. In a 2009 study, 64% of respondents to an NSGC survey reported utilizing the 96040 billing code. Those that did not bill reported it was because of institutional policy barriers, lack of credentialing, or lack of state licensure. We aimed to survey GCs in Texas to determine their billing and credentialing practices, by distributing an electronic survey secured on a platform developed in the Baylor College of Medicine Office of Research IT. Twelve GCs who bill and/or are credentialed were interviewed regarding their institutional processes, and provided examples of applications and documentation required. Seventy six of the 145 GCs contacted via email, completed the survey (response rate 52.4%). The majority of respondents see patients at a University Medical Center (n=39), do not bill (n=48), and are not credentialed by their institution (n=42). Those that do bill are billing third party payers, Medicare/Medicaid, and patients directly, using the 96040, 99241-99255 codes, or incident to a physician. Reported reimbursement ranges from $25-165. Twenty GCs (26%) reported being credentialed as part of their practice at nine institutions within Texas. Notably, 14 GCs did not know if they were credentialed, and 26 have never attempted to obtain credentialing. Respondents felt credentialing increased reimbursement rates and increased patient access to better quality genetic counseling services. They reported a lack of state licensure, institutional requirements, a limited awareness of and low perceived value of genetic counseling as potential barriers to credentialing. Despite a lack of state licensure, some GCs in Texas are credentialed and successfully billing for their services. This data provides other GCs practicing in states without licensure a pathway to seek credentialing or bill at their own institution.
B-20 Looking Deeper: Experiences of a Newly Founded Multidisciplinary Differences of Sexual Development and Endogenetics Clinic at Children's Hospital of Philadelphia (CHOP)

**Access & Service Delivery**

Submitter: Jacqueline M. M. Leonard, MSc, MS CGC, Children's Hospital of Philadelphia

Presenting Author: Jacqueline M. M. Leonard, MSc, MS CGC, Children's Hospital of Philadelphia

Primary Author: Jacqueline Leonard, MSc, MS, CGC, Children's Hospital of Philadelphia

Author 2: Emma Bedoukian, MS CGC, Children's Hospital of Philadelphia

Author 3: Louise Pyle, MD, PhD, Children's Hospital of Philadelphia

Those with Differences of Sexual Development (DSDs) represent a unique patient population that requires coordinated multidisciplinary care addressing complex medical and psychosocial needs, including a critical role for genetic assessment and counseling. This study reports the two-year experience of the DSD and Endogenetics clinic at CHOP, done in collaboration with Endocrinology, Urology, Psychology, and Genetics to provide state of the art integrated team care for this patient population. To date, 61 patients have received comprehensive genetic care through this clinic. Main referral sources include Endocrinology (75%), Genetics (8.8%) and Urology (5%). 92.5% were referred for a full diagnostic work-up, while 7.5% required genetic counseling for previously ordered results. The diagnostic work-up for DSD cases has followed the published recommendations of proceeding with whole exome sequencing (WES) following a non-diagnostic karyotype/microarray analysis, and negative single gene testing. 67.2% of evaluated individuals have completed genetic testing, with an overall diagnostic yield of 52% for a likely or definitive molecular diagnosis. An additional 16% received a variant of uncertain significance from genetic testing. Test types sent include single gene testing (60%), WES (32%), gene panels (22%), and karyotype/microarray (20%). Diagnostic yield varies by test type: 62.5% for single gene test, 44% for gene panels, 15% for WES, 25% for karyotype/microarray. The select presented cases will highlight the complexity of diagnostic workup, including the need for ongoing psychosocial assessment and support for both the proband and their parents. Medical management implications based on genetic test results include determining sex of rearing, surgical interventions, hormonal supplementation, and germ cell neoplasia in situ risk and surveillance guidelines. Our experiences confirm the need of genetic evaluation, testing and counseling in the multidisciplinary care model for individuals with endocrinopathies and DSDs.

B-23 Development of the first dedicated on-call cardiovascular genetic counseling service

**Access & Service Delivery**

Submitter: Tia Gabriela Rill Moscarello, MS, CGC, Stanford Health Care

Presenting Author: Tia Gabriela Rill Moscarello, MS, CGC, Stanford Health Care
Background: Genetics care is increasingly being integrated into cardiology and is typically provided on a referral basis with access limited by the availability of outpatient appointments. We identified a need for immediate genetics evaluations, such as when time-sensitive treatment decisions depend on genetic testing or family history assessment, or when the patient has traveled a long distance for care.

Objective: To describe the development and implementation of a novel on-call cardiovascular genetic counseling service for inpatient and outpatient care.

Methods: Retrospective chart review of all consecutive consults in the initial year and five months (December 1, 2016 to May 7, 2018) of the on-call cardiovascular genetic counseling service.

Results: We developed a genetic counselor role dedicated to providing on-demand cardiovascular genetics care. The service was advertised to providers in cardiology who paged the on-call genetic counselor to provide an urgent consult. In its first year, the on-call service saw 50 new inpatients and 40 new outpatients. Most consults were requested for cardiomyopathies (55/90, 61%). Most inpatients (42/50, 84%) and all outpatients (40/40, 100%) were seen the same day the consult was requested or the following business day. The most frequent reason for requesting an immediate outpatient genetics evaluation was distance the patient traveled to see their cardiologist (20/40, 50%). Time-sensitive consults included genetic testing and DNA banking before withdrawal of life support and family history assessment in cases of unexplained sudden cardiac arrest or arrhythmias of unclear etiology. The volume of consults increased by a mean of 82% per month over the first 6 months. The total number of providers requesting consults increased from 7 in the first three months to 36 by the end of the study period.

Conclusion: Our initial experience with this novel service demonstrates that there is a need for on-demand cardiovascular genetics evaluations and that this need can be met via an on-call cardiovascular genetic counseling service.

B-26 Improving Timely Access to Genetic Counseling for Oncology Patients Through an Integrated Telehealth Genetic Counseling Service

Access & Service Delivery
Submitter: Alison E. Payne, GeneMatters, LLC

Primary Author: Alison E. Payne, GeneMatters, LLC

Author 2: Ann Burch, Methodist Estabrook Cancer Center

Author 3: Darlene Haven, GeneMatters, LLC

Author 4: Kiley Johnson, GeneMatters, LLC
In August of 2017, a cancer center in Omaha, Nebraska (Nebraska Methodist Hospital; Methodist Estabrook Cancer Center), added a telehealth genetic counseling service to their existing clinical model. Prior to using telehealth services, the cancer center had one on-site clinical GC to see all oncology patients referred for genetic counseling, with the availability of this genetic counselor being limited to one day per week. It was hypothesized that utilization of telehealth for genetic counseling services would improve access to care for patients in need of genetic counseling in the oncology setting, particularly in this location, where there was limited access to genetic counselors. Quantitative data collected by the cancer center from the six months prior to using telehealth genetic counseling services was compared to data from six months after the implementation of telehealth genetic counseling services. Qualitative data was also collected using open-ended questions. Areas of improvement in the clinical setting and patient care included: 1) An increase in the number of new patient referrals to the cancer center (an approximate 28% increase per month), 2) A 50% increase in number of patients seen per week for genetic counseling 3) Reduced wait time for returning patients to obtain a second genetic counseling appointment (reduced from approximately two weeks to one week with use of telehealth service, and 4) Increased productivity/decreased work burden for the one on-site clinical GC (turnaround time for completion of GC letters was improved). In conclusion, the addition of a telehealth service, which provided availability for genetic counseling with remote genetic counselors, improved access to care for oncology patients in the clinical/hospital setting. Telehealth genetic counseling could therefore be considered a useful model which can be added in the clinical setting, especially in clinics and hospitals where access to genetic counseling services may be limited.

B-29 Getting Lean: Improving Efficiency in Genetics Clinics
Access & Service Delivery
Submitter: Christine Grey Spaeth, Cincinnati Children’s Hospital Medical Center

Presenting Author: Christine Grey Spaeth, Cincinnati Children's Hospital Medical Center

Primary Author: Christine Spaeth, Cincinnati Children's Hospital Medical Center

Author 2: Anna Butts, Cincinnati Children’s Hospital Medical Center

Author 3: Julianne Hartmann, Cincinnati Children’s Hospital Medical Center

The need for evidence-based service delivery models focused on high-quality and efficient delivery of genetic counseling services is a key feature of NSGC’s 2016-2018 strategic initiative. Lean thinking is a systematic method to create maximum value for patients by reducing waste and wait. The purpose of this project was to utilize the principles of Lean thinking to improve efficiency in genetics clinic, focusing on clinical visits which involved a genetic counselor or nurse and a physician. Project members observed clinic visits to document wait times, time spent with providers and information gathered by different
providers. Based on these observations three primary areas of intervention were identified: 1) standardization of medical assistant roles, 2) redundant questions and documentation across providers and 3) variation in hand-off process. Medical assistant intakes were standardized and documented in the electronic medical record (EMR) to reduce repetition across providers. Elimination of unnecessary or redundant questions resulted in a significant reduction in GC/nurse and physician template length (20% and 50%, respectively). Provider templates were modified to automate transfer of documentation from GC/nurse to physician notes with the goal of improving communication and decreasing physician documentation time. Finally, providers were encouraged to utilize either a standardized hand-off process or a combined GC/nurse and physician visit to decrease patient wait time during hand-offs. Standardized hand-offs decreased patient wait time from 15 to 5 minutes (67% decrease). Combined visits decreased overall encounter time of from 78 to 35 minutes (55% decrease). Decrease in waste and wait times allowed the opportunity to increase value added time to patient encounters, such as time spent in education or counseling. This project is the first demonstration of the successful use of Lean thinking in genetics clinics. Future steps include implementing process changes across all providers and exploring additional opportunities to improve efficiency.

B-32 A Survey of Genetic Counselors’ Current Methods of Implementing Telegenetic Services

Access & Service Delivery
Submitter: Brenda Zuniga, Vanderbilt University

Presenting Author: Brenda Zuniga, Vanderbilt University

Author 2: Kate Shane, MS, LGC, The Ohio State University

Author 3: Dawn C. Allain, MS, LGC, The Ohio State University

Author 4: Lindsey Byrne, MS, LGC, Mount Carmel Health System

Primary Author: Brenda Zuniga, BS, The Ohio State University

Telegenetics allows genetic counselors and other genetics providers to increase access to services by facilitating communication between patients and genetics providers across long distances and underserved populations. The aims of this study were to characterize the logistics of telegenetics appointments and describe the perceived benefits and limitations. Full members of the National Society of Genetic Counselors (NSGC) who currently provide or have previously provided telegenetic services to counsel patients were invited to participate in a web-based survey. Eligible respondents completed 48 items related to the logistics of the delivery of telegenetic services, perceived benefits and limitations, useful resources, and improvement recommendations. One-hundred fifty-nine members of the NSGC responded. Fifty-two percent and 23.4% of respondents reported providing telegenetic services in the cancer and prenatal specialties respectively; the remainder reported providing telegenetic services in a variety of other specialties. Sixty percent of respondents reported providing telegenetic services in one
state and 3.8% in 50 states. Forty-nine percent of respondents reported holding a valid license to practice in one state and 1.9% in 20 states. The most common software platforms used for video and audio access were Vidyo (13.9%), Skype (12.0%), and Cisco WebEx (10.8%) while 43% reported software as a barrier. Thirty-nine percent reported billing 3rd party/HMO and 19.6% reported no charge for telegenetic services. Twenty-two percent reported billing using CPT code 96040. Although this study found an increase in genetic counselors billing for telegenetic services compared to previous studies, billing continues to be reported as the biggest barrier of the use of telegenetics. The results of this study may serve as reference for genetics professionals wishing to incorporate telegenetics into their practice. Results may also contribute to the development of telegenetic practice guidelines by further describing current practices, barriers and limitations of telegenetics.

B-5 EPIC fail! Effect of Electronic Health Record Transition on First Trimester Screening Results Reporting, an illustration of the role of genetic counselors in ensuring patient notification

Access & Service Delivery
Submitter: Martha Shaw Dudek, MS LCGC, Vanderbilt School of Medicine

Presenting Author: Martha Shaw Dudek, MS LCGC, Vanderbilt School of Medicine

Author 3: Martha Dudek, Vanderbilt University

Primary Author: Stephanie Dallas, MD, Vanderbilt University Medical Center

Author 2: Adam Huggins, MD, MMHC, Vanderbilt University Medical Center

In November 2017, our institution transitioned to a new Electronic Health Record (EHR). This was a fundamental change in clinic workflow, laboratory result reporting and communication. Genetic results are not easily integrated into EHRs. Timely results reporting is essential in prenatal genetics to ensure patients have results early, in case termination of pregnancy is considered. We hypothesized that EHR transition to eStar would increase the time to patient notification of first trimester genetic screening results despite extensive clinician education and planning. Retrospective chart review was completed for 319 patients who elected first trimester screening May 2017 - February 2018. The elapsed days from blood draw to provider and patient notification were reported in a REDCap database and data stratified by before and after the EHR transition. Data were analyzed using STATA v. 15.1. Descriptive summary statistics were generated; median and mean data were compared using Mann-Whitney U test of non-parametric data, with a pre-specified alpha level of 0.05. Difference in categorical variables were compared using Fisher’s Exact test. The total time from lab draw to patient notification of results was significantly longer following the change in EHR from StarPanel (median 7 days, interquartile range (IQR) 5-12 days) to eStar (median 14 days, IQR 8 to 25 days), p <0.001. The median time for lab results to be reported was identical across these two eras (median 3 days, IQR 2-4). Time from provider acknowledgment of results to patient reporting was significantly longer in the eStar era (median 5 days, IQR 1-14 compared to median 0 days, IQR 0-1 days, p <0.001). While 12% of patient results were not
scanned into eStar, all charts had documentation from the genetic counselors of the results. This study demonstrates that provider education is not enough to mitigate the logistical challenges when transitioning to new EHR. Genetic counselors serve an important role in ensuring providers are notified of results when results are not consistently scanned into the EHRs.

B-8 Experience of Telehealth Cancer Genetics Practice in a Large Community Healthcare System

Access & Service Delivery
Submitter: Mariah Gleason, MS, CGC, Carolinas HealthCare System is Atrium Health

Primary Author: Mariah Gleason, MS, CGC, Carolinas HealthCare System is Atrium Health

Presenting Author: Mariah Gleason, MS, CGC, Carolinas HealthCare System is Atrium Health

Author 2: Stacy Lenarcic, Levine Cancer Institute, Atrium Health

Author 3: Alexandra Henshaw, Levine Cancer Institute, Atrium Health

Author 4: Lisa Amacker-North, Levine Cancer Institute, Atrium Health

Atrium Health is a large multi-hospital regional medical system, based largely in North and South Carolina but expanding to other areas. Cancer genetic counseling services have been offered to patients in Charlotte since 1996. With the expanding reach of the Levine Cancer Institute, it became a goal to standardize access to cancer genetics across locations. Barriers to cancer genetics included 1) financial and time constraints for patient or provider travel, 2) regional physicians without genetics training, and 3) limitations of timeliness of monthly outreach clinics. The proposed solution was genetic counseling offered by telehealth. Studies have demonstrated telehealth genetic counseling to be an effective alternative to in-person genetic counseling especially when there are geographical barriers. The goal of the telehealth genetics program was to increase referrals of women meeting National Comprehensive Cancer Network guidelines for Hereditary Breast and Ovarian Cancer from a baseline of 35% to 75% by 2015. In 2011, data review indicated that less than 35% of appropriate women were referred. The program began in 2012 with two telehealth sites. By 2015, 100% of women with ovarian cancer and 94% of women with breast cancer were referred. During this pilot project, patients reported satisfaction with their telehealth experience, similar to other reports of patient satisfaction. The program has expanded to offer services at nine regional clinics. In 2017, 68% of women who received genetic counseling were seen at their regional clinic as opposed to the main hospital. 16 patients were seen by telehealth in 2012; 354 patients were seen by telehealth in 2017. This service is estimated to have saved our patients $30,492 and 558.5 hours of travel time in 2017. This expansion of services required support from senior leadership, genetic counseling staff, and regional physicians to provide timely and cost-effective care to our regional patients.
Genetic testing and counseling have become increasingly accessible to patients of diverse backgrounds, including patients whose first language is not English. Professional medical interpreters (PMI) can play a pivotal role in helping patients who are limited-English proficient (LEP) understand genetic information and foster the opportunity for shared-decision making between LEP patients, their families, and providers. Prior data has shown that PMI increase understanding and lead to better patient outcomes. Our study seeks to expand on this data by describing what roles interpreters engage in when working with Spanish-speaking LEP patients in the medical and metabolic genetics clinics. Due to the abstract nature of genetic information, understanding how interpreters alter or accommodate the communication of genetic information is critical to meeting the needs of this patient population. We conducted an exploratory descriptive study to characterize the roles of interpreters and their communication patterns, in genetic counseling sessions when professional interpreters are required for Spanish-speaking LEP patients. We recorded nine patient sessions in the metabolic (n=3) and medical genetics (n=6) clinics at one institution. Transcriptions were back-translated from English and Spanish. Content analysis was used to identify themes of distinct roles of the interpreter and their communication patterns. We found that interpreters serve not only as language translators but also impact the understanding of genetic information, impact the role of the genetics provider and act as patient advocates. We also observed systems challenges to communication for Spanish-speaking LEP patients, including a limited availability of in-person interpreters, the dual use of in-person and iPad interpreters during a patient’s session and limited materials available in the patient’s primary language. Our preliminary data suggest that interpreters can play critical and specific roles in helping Spanish-speaking LEP patients understand genetic information beyond mere interpretation.
C-15 Assessing the Need and Desire for Cancer Genetics Education among Rural Healthcare Providers

Access & Service Delivery

Presenting Author: Bailey Bergt Hulswit, MS, University of Michigan

Primary Author: Bailey Hulswit, MS, Wayne State University

Author 2: Angela Trepanier, MS, CGCD, Wayne State University

Submitter: Bailey Bergt Hulswit, MS,

Patient access to cancer genetic counseling services (CGCS) usually requires a referral from a provider without advanced genetics training. Providers may not know how to identify and refer patients at risk, especially in rural areas with limited access to CGCS. This study aimed to assess cancer genetics knowledge, referral practices, and educational needs of rural healthcare providers in an area with an increased rate of early onset breast cancer and limited access to CGCS. A novel survey was created based on a review of the literature and responses to an informal survey given to board members of a Rural Healthcare Network (RHN) in the target area. Survey drafts were reviewed by subject matter experts and RHN board members. The final survey included 22 questions assessing knowledge, ability to identify and refer appropriate patients and comfort with the related tasks, interest in learning about cancer genetics and learning mode, and demographics. RHN board members distributed the survey via email to an estimated 100 providers; 14 completed the survey (14%). All respondents were female with an average of 8.7 years of clinical experience (SD= 9.4). Respondents accurately identified appropriate indications for cancer genetics referral 83.1% of the time. They felt extremely comfortable taking a family medical history (M= 4.67 on a 5 point scale, SD=0.90), neutral about identifying individuals at increased risk of hereditary cancer (M=3.27, SD= 1.1), and somewhat uncomfortable about making a referral (M=2.75, SD=1.1) or explaining genetic counseling (M=2.17, SD=1.1). Providers wanted to learn about cancer genetics but preferred CME activities that would minimally disrupt their schedule. Barriers to education included beliefs that hereditary cancer is uncommon and that their patients cannot afford genetic testing. To date, no one has taken the free, web-based CME module on cancer genetics that was offered. This study highlights challenges to helping rural healthcare providers improve access to CGCS. Addressing such challenges is critical to reducing health disparities.

C-18 Implementing Next-Generation Sequencing in Post Mortem Cases of Sudden Cardiac Death: A Public Health Laboratory Perspective

Access & Service Delivery

Submitter: Kimberly Anderson, M.S., CGC, University of Wisconsin, Madison

Presenting Author: Kimberly Anderson, M.S., CGC, University of Wisconsin, Madison

Primary Author: Angela M Lager, PhD, FACMG, Wisconsin State Laboratory of Hygiene
Sudden unexplained death is a difficult situation for any family to navigate. When it occurs in the young (<40 years old), these deaths are often cardiac related and many are thought to be due to an underlying genetic condition. Post mortem analysis of sudden cardiac death (SCD) cases is an important component to uncovering the cause of death, but one-third of SCD cases remain unexplained by autopsy. A molecular autopsy (post mortem genetic testing) can provide another chance to identify the cause of death. This gives the family an opportunity for closure, but also allows other family members to be tested for the identified, and often treatable, genetic condition. Unfortunately, one of the biggest obstacles to this service is cost. To address this barrier in the state of Wisconsin, we created a program (NextGenPM) that provides gratis testing for cases of suspected SCD and negative findings on autopsy. To participate in this program, surviving blood relatives are asked to be seen at the Inherited Arrhythmias Clinic at the UW Hospital in Madison, WI. These relatives undergo a baseline cardiac evaluation as well as discuss the family history with a genetic counselor, who then facilitates the testing of the decedent. Since starting the program in fall of 2016, we have completed 5 cases. Next-generation sequencing (NGS) was used to identify sequence variants in genes associated with arrhythmia or cardiomyopathy with heterozygous missense variants identified in 4 of the 5 cases in four different arrhythmia or cardiomyopathy associated genes (PKP2, RYR2, TTN, SNTA1). Of 4 positive cases, three families had at-risk family members undergo targeted testing for the familial variant. The accessibility and utility of NGS is helping to advance the study and diagnosis of complex disorders like arrhythmias and cardiomyopathies. Through the NextGenPM program, families are not only able to access this technology, but also obtain appropriate screening and surveillance measures for surviving blood relatives.

C-21 Who is providing genetic counseling around the world?
Access & Service Delivery
Submitter: Brittney Mary Meays,
Primary Author: Brittney Mary Meays,
Presenting Author: Brittney Mary Meays,
The demand for genetic testing continues to rise, and with it, the need for genetic counseling is increasing. In the U.S., genetic counseling is a standard of care, but the practice is markedly different in countries outside of North America. Professional genetic counselors do not exist in every country of the world, raising questions about who is covering this need in those countries. We aimed to elucidate who provides genetic counseling services around the world. To do so, we surveyed professionals in the field of clinical genetics and genetic counseling from countries outside of North America. Participants (N=219) representing 37 countries, from 6 continents, completed surveys regarding their professional title, educational background, work settings, and laws governing the practice of genetic counseling. Our data reveals a large variety in the practice model of genetic counseling, with medical and non-medical professionals assuming this niche to cover the needs of patients. Grouping participants in eight geographical regions showed a significant correlation between the participants' professional title and their region of practice (p-value <0.05). The variability in the use of the title “genetic counselor” itself highlights an important consideration for future studies that aim to characterize the genetic counseling practice at the global scale; studies should focus on providers of genetic counseling rather than genetic counselors, otherwise, some variation would be neglected if the professional title is used as the only inclusion criteria.

C-24 Genetic Testing Outcomes by Race: Observations from Michigan's Hereditary Cancer Network

Access & Service Delivery
Submitter: Andrea Murad, MS, LCGC, University of Michigan Medicine

Presenting Author: Andrea Murad, MS, LCGC, University of Michigan Medicine

Primary Author: Andrea M. Murad, Michigan Medicine

Author 2: Dianne Samad, Michigan Medicine
Author 3: Jenae Osborne, Michigan Medicine
Author 4: Michelle Jacobs, Michigan Medicine
Author 5: Monica Marvin, Michigan Medicine
Author 6: Erika Koeppe, Michigan Medicine
To date, most large-scale genomic studies have been comprised predominately of non-Hispanic White populations. Barriers to access and underutilization of genetics services have resulted in a paucity of clinical and research data on racial and ethnic minorities, perpetuating health disparities in the field of cancer genetics. Here we report clinical observations on the uptake and outcomes of genetic testing by race, utilizing data from Michigan’s Hereditary Cancer Network (HCN), a partnership between the Michigan Department of Health and Human Services and 22 cancer genetics practices across Michigan.

Clinical partners have contributed data to the HCN database for BRCA-related genetic counseling visits since 1/1/08 and Lynch syndrome-related visits since 1/1/16. As of 12/31/17, data from 24,952 patients was collected. Patients were 83.3% non-Hispanic White, 6.9% Black, 1.8% Asian, and 1.8% Hispanic (6.2% other/not reported), demonstrating a significant under-representation of minorities compared to Michigan’s overall population (75.4% non-Hispanic White, 14.2% Black, 3.1% Asian, 5.0% Hispanic, 2.4% Multiracial). Uptake of genetic testing was lowest among Black individuals compared with other races (59.1% vs 65.5%, p < 0.01). Black individuals who did complete testing had the lowest rate of positive tests compared with other races overall (11% vs 15%, p<0.01). Variants of unknown significance (VUS) were more common in minority populations, particularly Asians (7.6%) and Blacks (5.5%), compared to Whites (3.5%) (p<0.01). The HCN is an excellent surveillance tool that provides a unique opportunity to identify gaps in genetic services for minority populations. This data illustrates the racial/ethnic disparities in individuals presenting for cancer genetic services and pursuing genetic testing in Michigan. Observations from this program demonstrate that multi-faceted efforts are needed to improve racial and ethnic disparities in genetic testing for hereditary cancer syndromes.
Background: Genome.One is the first service in Australia to develop and implement a Patient Data Access Policy, facilitating patient access to their full genomic data. The default practice by most clinical laboratories worldwide has been to not return full genomic data to individuals. However, with increasing public awareness about genomic testing, growing numbers of patients, research participants and consumers are requesting access to their data. Considerations around the legal, ethical and practical implications must be central to the development of a policy for patient data access. Here we aim to provide a summary of these considerations, as well as a record of our personal experience in developing and implementing our policy.<br />Methods:<br />1. Review of literature and current practices<br />2. Review State, National and International guidelines examining access rights<br />3. Legal review of draft policy including recommendations<br />4. Establishment of internal processes for policy implementation<br />5. Data collection and survey of patient satisfaction<br />

Outcome: Individuals tested through Genome.One now have access to their genomic data on an encrypted hard drive including FASTQ, BAM and VCF files. They also receive a PDF copy of their pathology report, and a fact sheet which outlines the contents of the hard drive and provides information about re-analysis, supply of data to third parties, and disclaimers. Piloting of this policy began in January 2018, and of 242 completed samples, we have processed 15 requests (7%) for release of genomic data, half for transfer of data to their treating clinician, and half for access to their data for personal use. Our policy has not yet been actively promoted, therefore we expect that these numbers will increase significantly as we broaden awareness of this service. Survey data is providing insights into the reasons for data access requests and intended plans for use. Facilitating further research has been key to many of our requests to date, however personal utility and feelings of ownership are also crucial elements that have been highlighted.

C-3 Service Delivery Model Interests, Needs, and Barriers Reported by Genetic Counselors

**Access & Service Delivery**

Submitter: Emily Boothe, University of Mississippi Medical Center

Presenting Author: Emily Boothe, University of Mississippi Medical Center

Primary Author: Emily Boothe, MS, CGC, University of Mississippi Medical Center

Author 2: Christine Delaney, MS, CGC, Myriad Genetics, Inc.

Author 3: Stephanie A. Cohen, MS, LCGC, St. Vincent Health

In fall 2017, the Service Delivery Model (SDM) subcommittee surveyed the NSGC membership regarding the use of alternate service delivery models with an online questionnaire. Among 517 usable responses (16% response rate), more than half (54.4%) of respondents indicated their current model of service delivery was not adequate to address the need in their area. Two-thirds (64.8%) indicated they were either in the process of or planning to make changes to their SDM although 40.6% did not have a specific timeline for these changes. Open responses regarding the need for new SDMs and barriers to
implementation were analyzed for themes. Themes identified among genetic counselors (GCs) who felt their current SDM was inadequate included understaffing (GCs, physicians, and support), lack of geographic access, under-identification of patients, lack of physician availability, and issues with billing and licensure. GCs who saw a need for a new or different SDM but were not currently considering implementation identified issues including lack of GCs, physicians, and support staff; lack of support by the administration and/or institution; concerns about quality; billing and licensure issues; and lack of time to implement a new SDM. Almost all these themes were echoed in response to what barriers exist to implement an alternate SDM, with the additional themes of funding, technology issues, physical space limitations, and lack of physician time. Finally, 123 respondents provided ways they believed their SDMs are unique or innovative. Several themes recurred among both the GCs who were planning to implement a new SDM and those who were not, such as the inability to bill and staffing shortages, suggesting these issues are universal to GC practice, regardless of SDM. Based on GC interest in alternate SDMs, there is a need for education and support to implement alternate SDMs and a need for resources to overcome barriers in all SDM types.

C-30 Experience with healthy individuals pursuing genomic screening: providing guidance for genomic counseling via a telemedicine approach

Access & Service Delivery
Submitter: Betsy Swope, Genome Medical

Presenting Author: Betsy Swope, Genome Medical

Primary Author: Betsy J. Swope, MS, LCGC, Genome Medical, Inc

Author 2: Sarah Kalia, MS, LCGC, Genome Medical, Inc

Author 3: Scott M. Weissman, MS, LCGC, Genome Medical, Inc

Author 4: Audrey Fan, MS, LCGC, Genome Medical, Inc

Author 5: Hailey Shabazz, Genome Medical, Inc

Author 6: Erynn G Gordon, MS, LCGC, Genome Medical, Inc

Author 7: Paldeep Atwal, MD, Genome Medical, Inc

Author 8: Robert C. Green, MD, MPH, Genome Medical

Author 9: Steven B. Bleyl, MD, PhD, Genome Medical

Proactive genomic screening is increasingly being explored by healthy individuals. We describe our experience providing access to genomic screening to apparently healthy individuals via assessment, counseling, and test authorization using a telemedicine platform. Patients were referred via physician or self referral, and were scheduled for a 30 minute telemedicine consultation by phone or video.
Family and medical histories were obtained during the visit. The details of proactive genomic testing, including various options ranging from targeted panels to whole genome sequencing, were discussed. Tests were authorized for participants who elected to pursue testing. Follow-up counseling was offered with results disclosure. A total of 73 patients were seen, with the majority of patients (63%) opting for the visit by phone. The average age of the participants was 49.9 (range 27 to 80) and most (83%) were Caucasians. Of 73 patients counseled about proactive screening, 62 (83.7%) of patients went on to request testing. Of completed results to date, 17 patients (23%) were reported as positive (single or bi-allelic pathogenic/likely pathogenic variants for dominant or recessive conditions, respectively) for results that may impact clinical management. These patients were further evaluated for pertinent family history and sub-clinical phenotypes, and referred for further follow-up and surveillance. Our experience with healthy individuals pursuing genomic screening reveals a higher rate of positive results than would be expected. The potential to identify at risk individuals in a motivated population reinforces the need for a patient-centered approach to counseling that provides accurate information of the benefits, limitations, and uncertainties of testing while supporting the individual’s motivation for access to genetic information. We address the challenges and insights gained through this experience and provide guidance for counselors encountering this new frontier of population based, rather than indication based, genomic counseling.

C-6 Accessibility of Pregnancy Termination: A Pilot Study of Genetic Counselors and Abortion Providers Throughout the United States

Access & Service Delivery

Submitter: Lauren Facchini, Sarah Lawrence College

Presenting Author: Lauren Facchini, Sarah Lawrence College

Primary Author: Lauren Facchini, Sarah Lawrence College, Program of Human Genetics

Author 2: Brianne Dingmann, Sarah Lawrence College, Program of Human Genetics

Author 3: Kaitlyn Brown, Sarah Lawrence College, Program of Human Genetics

Author 4: Laura Hercher, Sarah Lawrence College

Author 5: Caitlin Cooney, NYU Langone Health

Author 6: Komal Bajaj, NYC Health + Hospitals & Albert Einstein College of Medicine

Recent literature suggests that availability and accessibility of pregnancy termination services affect patient care and decision-making. This survey of genetic counselors and abortion providers examined circumstances affecting referral for pregnancy termination throughout the United States and analyzed regional differences as they correspond to the number of state laws restricting access to abortion. 116 responses from currently practicing prenatal genetic counselors and 30 responses from abortion providers were analyzed using Survey Monkey and SPSS using Chi-square tests, t-tests, Fisher's exact
tests, and a one-way ANOVA with Tukey’s post hoc analysis. Accessibility of pregnancy termination was assessed as a function of multiple variables including cost to the patient, how quickly it can be obtained, and how far patients must travel. States were characterized in their attitude to abortion using Guttmacher Institute’s Policy Trends in the States 2017, which defines them as supportive, middle-ground, hostile, or extremely hostile, based on the number of abortion restrictions each state has enacted. Overall, our findings show that genetic counselors in hostile states were more likely to refer patients to outside providers for terminations than counselors in supportive states regardless of gestational age, with 89.9% of counselors in hostile states referring to providers more than 4 hours away for referrals over 24 weeks gestation as compared to 56.5% in supportive states. Counselors in hostile states were more likely than counselors in supportive states to report that factors such as insurance coverage, out of pocket costs, wait times, travel, and the availability of appointments had an impact on patient decision-making with regard to termination of pregnancy.

C-9 Changes in Service Delivery Model Use among genetic counselors from 2010 to 2017

Access & Service Delivery

Submitter: Samantha Greenberg, Huntsman Cancer Institute

Primary Author: Samantha Greenberg, Huntsman Cancer Institute

Presenting Author: Samantha Greenberg, Huntsman Cancer Institute

Author 2: Ryan Noss, Cleveland Clinic

Author 3: Stephanie Cohen, St. Vincent Health

In 2010, the NSGC membership was surveyed about their use of service delivery models (SDMs) including in-person, telephone, telegenetic, and group genetic counseling. Since that time, the demand for genetic counseling services has increased. We hypothesized that the usage of alternate SDMs has increased to help address the growing demand. To assess for changes in SDM use and interest in implementing innovative SDMs, the SDM subcommittee sent an electronic survey to the NSGC membership (N=3616), which was open from August 2017-December 2017. Descriptive statistics, Chi-square analysis and independent T-tests were used to compare and identify differences between 2010 and 2017. There were 590 total responses (16.3% response rate) with 517 usable responses, representing multiple specialties. Most (92.7%) reported they used in-person GC always or often, which is significantly less than the 95.7% rate reported in 2010 (p<0.01). Wait times for in-person appointments are longer, with 26.8% stating the third next available appointment is within 1 week and 24.4% within 1-2 weeks, compared to 35% and 30%, respectively in 2010 (p<0.01). Telephone GC was reported by 12.4% as a model used always or often, compared to 8% in 2010, however the difference was not statistically significant. The number of GCs using telegenetics always or often increased from 2.2% to 6.7% (p<0.01), however group GC utilization decreased from 3.2% to 1.4% (p<0.05). Almost all respondents (93%) were interested in implementing a new SDM, however many (74%) identified
barriers to implementation. Given the high demand for GC services, it is not surprising that wait times seem to have gotten longer. It appears that GCs are attempting to compensate by implementing alternate SDMs to improve access for patients. There is strong interest in learning about and implementing innovative SDMs to improve access and efficiency. However, resources need to be developed to help GCs overcome barriers to implement new SDMs to achieve these goals.

A-34 The Complexity of Genetic Counseling for Pulmonary Fibrosis

Adult

Submitter: Nikkola Carmichael, Brigham and Women's Hospital

Presenting Author: Nikkola Carmichael, Brigham and Women’s Hospital

Primary Author: Nikkola Carmichael, MS, CGC, Brigham and Women's Hospital

Author 2: Shannon Gampala-Sagar, Brigham and Women’s Hospital

Author 3: Dominick Leone, MPH, Brigham and Women's Hospital

Author 4: Luisa Quesada Arias, MD, Brigham and Women's Hospital

Author 5: Lisa DiGianni, PhD, Brigham and Women's Hospital

Author 6: Gary M. Hunninghake, MD, Brigham and Women's Hospital

Author 7: Ivan O. Rosas, MD, Brigham and Women's Hospital

Author 8: Benjamin Raby, MD, MPH, Brigham and Women's Hospital

Until ten years ago, idiopathic pulmonary fibrosis (IPF) was considered a predominantly sporadic disease caused by environmental factors such as smoking, radiation, organic and inorganic exposures, heartburn, and autoimmune disease. However, genetics is now estimated to account for approximately 1/3 of the disease risk. Rare variants in telomerase genes cause autosomal dominant Short Telomere Syndrome (STS), characterized by telomere lengths below the 10th percentile, pulmonary and liver disease, bone marrow dysfunction, and premature greying. A common promoter variant in MUC5B (c.-3133G>T) is present in 9% of the general population, and increases the risk for IPF by 6.8 (heterozygous) and 20.8 (homozygous) times over the background rate of approximately 1 in 10,000-30,000 individuals. The combination of environmental factors, monogenic etiologies, and susceptibility variants complicates genetic counseling for this disease.<br/>

We present the case of a 70-year-old woman referred to our Pulmonary Genetics Clinic for evaluation due to IPF and macrocytosis. Although she had no family history suggestive of STS, her telomere lengths were tested and found to be below the 1st percentile. Genetic testing identified two variants of uncertain significance in RTEL1, c.1668-8G>A (intronic) and c.1747T>A (p.Phe583Ile). We evaluated four of her siblings, performing pulmonary function testing, CT imaging of the chest, telomere length analysis, and genetic testing. Of the four siblings, none had short telomeres or the coding RTEL1 variant. However, all four siblings were heterozygous for the MUC5B IPF-
susceptibility variant, and three had evidence of IPF on imaging and functional testing. This case illustrates that testing negative for a known rare cause of IPF segregating in a family does not eliminate the risk of disease attributable to common variants or shared environment. Our experience from this illustrative case and others suggests that relatives of individuals with IPF may benefit from clinical screening for IPF regardless of results of genetic testing.

A-37 Overlapping phenotypes of spondylometaphyseal dysplasia-Kozlowski type and Charcot-Marie-Tooth disease type 2C secondary to a TRPV4 pathogenic variant.

Adult
Submitter: Eden Jessica Faye, University of Wisconsin Madison
Presenting Author: Eden Jessica Faye, University of Wisconsin Madison
Primary Author: Eden Jessica Faye, University of Wisconsin School of Medicine and Public Health
Author 2: Peggy Modaff, University of Wisconsin School of Medicine and Public Health
Author 3: Richard M Pauli, University of Wisconsin School of Medicine and Public Health
Author 4: Janet M Legare, University of Wisconsin School of Medicine and Public Health

TRPV4, a non-selective calcium permeable ion channel, is expressed broadly in many organs including bone and neurons. TRPV4 is versatile and responds to multiple stimuli including heat, mechanical stress, and various chemicals. Pathogenic variants in TRPV4 are known to cause both a spectrum of skeletal dysplasias and a spectrum of neuropathies. Recent publications have documented a few patients who have a combined phenotype of a skeletal dysplasia and a neuropathy secondary to a TRPV4 pathogenic variant. We present an additional patient who has an overlapping neuromuscular and skeletal phenotype secondary to a TRPV4 pathogenic variant. The patient has spondylometaphyseal dysplasia-Kozlowski type and Charcot-Marie-Tooth disease type 2C. This and prior reports illustrate that TRPV4 related skeletal dysplasias and TRPV4 related neuropathies are not distinct disorders secondary to unique sets of pathogenic variants as originally postulated, but rather are two phenotypes on the same spectrum that may be distinct or overlap. This report adds to the knowledge about the TRPV4 spectrum of disorders and recommends that evaluation for patients presenting with any TRPV4 related disorder include assessment for both skeletal and neurological findings.

A-40 Pain and Fatigue Associated with Generalized Joint Hypermobility in Gaucher Disease

Adult
Submitter: Farrah Rachelle Mahan, Cincinnati Children's Hospital Medical Center
Primary Author: Farrah Rachelle Mahan, Cincinnati Children's Hospital Medical Center
Gaucher Disease (GD) is a lysosomal storage disease characterized by hepatosplenomegaly, pulmonary disease, fatigue, and bone pain and crises. While most physicians show primary concern with visceral and hematologic symptoms, patients report interest in decreasing fatigue and pain, which has an effect on quality of life. Generalized joint hypermobility (GJH) is characterized by joint laxity and increased joint range, and has also been seen to affect levels of both pain and fatigue. The relationship in patients with GD between chronic pain, residual fatigue, and GJH was investigated. Participants were those with GD Type 1 who performed a Beighton Score and five-part questionnaire to meet diagnostic criteria for GJH. The Brief Pain Inventory (BPI) and Fatigue Severity Scale (FSS) were used to assess levels of pain and fatigue. Therapeutic goals and the Disease Severity Scoring System (DS3) were used to evaluate treatment goals and disease involvement. 33% of our population (4/12) met GJH criteria. Of those with GJH, 50% expressed moderate pain severity and 25% reported moderate pain interference, compared to 12.5% and 0% of those without GJH. 50% of both groups reported severe fatigue. There was a strong positive correlation between reported values of pain severity, pain interference, and fatigue. Participants were found to meet a median of 96.3% of Gaucher-related therapeutic goals. In those with GJH versus those without GJH, 50% and 57.1%, respectively, were assessed as having “mild disease” involvement. We did not see significant changes in the levels of pain and fatigue between the two groups of participants, but the study did reinforce those who report higher levels of pain severity and interference also report high levels of fatigue, regardless of a GJH diagnosis. Someone with high levels of pain may need to have anticipatory management for fatigue. Our patients were well-managed and met many therapeutic goals, which may account for the levels of pain and fatigue reported. Future studies recommended include larger, more generalizable studies for GD and GJH.
Ehlers Danlos Syndrome, Hypermobility type (hEDS) is an inherited connective tissue disorder characterized primarily by joint hypermobility, soft skin and joint pain. Without proper management, quality of life can be negatively impacted. Prompted by increasing hEDS referrals, limited genetics clinic appointment slots, and minimal research assessing the role of genetic services for hEDS, a chart review of patients referred for hEDS was conducted. Medical records on 212 patients (median age 31, 89% female) seen at Michigan Medicine Medical Genetics clinic in 2014 and 2015 were evaluated. The primary outcome measure was a diagnosis of hEDS. Pearson’s Chi-square test and logistic regression was applied to determine the impact of multiple clinical variables (referral source, institution, and indication, physical stressors, patient reported family history of hEDS, Beighton score, Brighton criteria). Strikingly, 26% of our clinic’s appointments annually were filled by hEDS patients. An hEDS diagnosis was made for most patients (67%). Genetic testing was ordered for 4.7% of patients. Referrals to specialists were made 44% of the time but did not differ between patients with and without hEDS diagnoses. Interestingly, 58% of patients reported one or more physical stressors (e.g. sports involvement or trauma), but this did not significantly impact likelihood of diagnosis (X²=0.53, p=0.47; B=-0.23, p =0.47).

The only significant clinical variables impacting the diagnosis outcome variable were obtained during the appointment: patient reported family history of hEDS (X²=6.66, p=0.01; B=-0.78, p=0.01), Beighton score (X²=81.53, p=<0.001; B=0.66, p=<0.001), and Brighton criteria (X²=144.22, p=<0.001; B=-6.24, p=<0.001). These significant clinical factors could be ascertained by non-geneticists. This change could allow for expedited diagnosis and management of hEDS patients while reserving limited genetics clinic appointments for other clinical indications.

Huntington disease (HD), a progressive neurodegenerative disorder, characterized by chorea, cognitive decline, and behavioral abnormalities has a mean age of onset of 35-44 years. Onset at >60y was historically reported as rare with a fully penetrant allele. An HTT allele with ≥40 CAG repeats is categorized as fully penetrant; while reduced penetrance range is 36-39 repeats. We present the
case of a 75 year old female evaluated for a family history of HD. Her sister was found to have 41 CAG repeats in HTT and was diagnosed at 70y, reportedly with abnormal movements since 60y. The patient denies current medical problems, including history of anxiety, depression, mental illness, abnormal movements, loss of coordination, or cognitive decline. She does not have any signs/symptoms of HD. MRI Brain w/ and w/o contrast did not show changes typically seen with HD; with brain volume within normal limits for her age and no evidence of caudate atrophy. Genetic testing revealed HTT alleles with 17 and 40 CAG repeats, consistent with fully penetrant Huntington disease. <br />

Reports suggest that late onset HD represents 4.4-11.5% of HD diagnoses and that these individuals may be at greater risk of missed diagnosis due to perceived lower risk. Another study defines the 97.5% age boundary for individuals with 40 CAG repeats as 71.7y. Our case highlights the importance of counseling asymptomatic at-risk individuals ≥60y of age about the full age range of symptom onset in preparation for HD testing. It also suggests a need for further research regarding protective factors in families with later onset and expanding the range of reduced penetrance alleles. In this new era, we may find that we need to reconsider diseases previously classified as “fully penetrant” and our approach to counseling older asymptomatic patients. There also appears to be a dearth in the literature regarding current anticipatory guidance offered to older individuals seeking pre-symptomatic HD testing and the role genetic counseling may play in identifying and properly counseling older at risk individuals.<br />

B-38 Assessing the Effects of Renin Angiotensin System Drugs on Lung Function in Patients with Cystic Fibrosis

Adult
Submitter: Stephanie Sue Gerber, Case Western Reserve University

Presenting Author: Stephanie Sue Gerber, Case Western Reserve University

Primary Author: Stephanie Gerber, Case Western Reserve University

Author 2: Anne Matthews, PhD, FACMG, Case Western Reserve University

Author 3: Anna Mitchell, MD, PhD, University Hospitals Cleveland Medical Center

Author 4: Rebecca Darrah, M.S., PhD, Case Western Reserve University

Multiple genome wide association studies have been conducted to search for potential genetic modifiers for cystic fibrosis (CF) and have found an association between the genetic region containing AGTR2, which codes for the angiotensin II type 2 receptor, and pulmonary function in CF patients. AGTR2, which is part of the renin angiotensin system (RAS), is responsible for regulating blood pressure, among other things. Multiple studies have found an association between high angiotensin converting enzyme (ACE) levels, an enzyme in the RAS, and decreased lung function, but few have evaluated the impact of blocking the RAS on lung function in CF patients. The purpose of this study was to determine if the use of RAS drugs associated with differences in pulmonary function in CF patients. It was hypothesized that ACE inhibitors would associate with improved lung function while angiotensin II type
1 receptor blockers (ARBs) would associate with decreased lung function. A retrospective chart review and matched paired t-tests were performed to compare lung function before and after initiation of RAS drugs. Of the 210 adult CF patients in the University Hospitals of Cleveland CF patient database, 26 (12.4\%) had been diagnosed with hypertension and 21 (10\%) were taking a RAS drug. No significant differences were found between the average FEV1% predicted rate of change before and after the initiation of ACE inhibitors (N=7, P=0.485) and between the average of the mean FEV1% predicted before and after the initiation of ACE inhibitors (N=7, P=0.958). In addition, no significant differences were found between the average FEV1% predicted rate of change (N=11, P=0.913) or between the average of the mean FEV1% predicted (N=11, P=0.313) before and after initiation of ARBs. While the hypothesis was not supported by results of this study, the data introduce important questions about the possible influence of RAS drug dosage, age at RAS drug initiation, and ACE genotype on the impact of these drugs on lung function in CF patients that should be further explored in future studies.

**B-41 Healthcare Transitions for People with Thalassemia**

**Adult**

*Submitter: Lauren A Morse,*

*Presenting Author: Lauren A Morse,*

*Primary Author: Lauren Morse, Sarah Lawrence College*

*Author 2: Radhika Sawh, Sarah Lawrence College*

*Author 3: Anne Greb, Sarah Lawrence College*

Thalassemia is a chronic genetic condition that lowers the quality of life of affected individuals. Despite the medical advances that have prolonged life expectancy, people with thalassemia still score lower in health related quality of life (HRQOL) compared to the average North American. One method in which HRQOL may be improved in patients with chronic conditions is to improve the healthcare transition process from pediatric to adult care. We developed an original study in which 105 adults affected by thalassemia completed a questionnaire about their current treatment experiences and their preferences about what to incorporate in a healthcare transition plan for future generations. My goals were to determine if people with thalassemia living in North America are followed by pediatric or adult physicians, what their healthcare experience has been, and what they would like to see included in a transition plan. This study found that nearly one third of adults with thalassemia living in North America are treated by pediatric specialists for their thalassemia, and that they are significantly more satisfied with their care compared to those who see adult physician specialists. In addition, adults with thalassemia prefer that healthcare transition plans involve communication between the pediatric and adult healthcare provider and that the transition program allows the patient to advocate for themselves in their medical treatment. This study illustrates the value of healthcare transition programs for thalassemia and the major components of a transition plan that are fundamental to this patient population.
C-33 Huntington's Disease Diagnosis Without a Known Family History

Adult

Submitter: Tanya Megerian Bardakjian,

Primary Author: Tanya M Bardakjian, University of Pennsylvania Health System

Author 2: Kaylee Faulkner, University of Pennsylvania Health System

Author 3: Rachel Paul, University of Pennsylvania Health System

Author 4: Pedro Gonzalez-Alegre, University of Pennsylvania Health System

Presenting Author: Tanya M Bardakjian, University of Pennsylvania Health System

Introduction: Huntington disease is an autosomal dominant condition. Accurate diagnosis of HD is critical for appropriate clinical management and genetic counseling. The absence of a documented or known family history of HD is often misleading to non-experienced clinicians, who should be cognizant of special counseling considerations in these cases. Objective: To describe the diagnostic challenges and genetic counseling considerations in individuals diagnosed with HD without a documented family history.

Methods: We identified all patients seen in the HD clinic in 2 years (July 2015-July 2017). Charts were reviewed and those without a diagnosis of HD excluded. For the remainder of the patients (HD), we reviewed the chart to determine if there was a known family history of HD at the time of diagnosis. We included those who are the first HD diagnosis in the family. Results: Total of 176 patients were seen at the HD Center in the study period, 129 had a diagnosis of HD. Of these, 32 (25%) were the first known diagnosis in the family. Of those, 10 had evidence a family member that in retrospect, likely had HD, 7 were adopted, 5 had no contact with the parent or family member affected by HD, 9 had an entirely negative history and there was one case of non-paternity. Subjective analysis of the response to the diagnosis for those with out and with a family history will be presented. Conclusion: We have a high rate of first HD diagnosis likely due to referral bias. Obtaining a detailed three generation pedigree of an individual presenting with symptoms suggestive of HD, without a known family history often reveals family members with motor, cognitive or psychiatric symptoms. Reaction to diagnosis differs between those with and without a known HD family history.

C-36 Assessing the Barriers to Cardiac Care in Carriers of Duchenne and Becker Muscular Dystrophy

Adult

Submitter: Lauren Renae Eekhoff,

Presenting Author: Lauren Renae Eekhoff,

Primary Author: Lauren Renae Eekhoff, University of South Carolina
Duchenne and Becker muscular dystrophy (DBMD) are X-linked conditions due to mutations in the dystrophin gene that cause progressive muscle weakness and cardiomyopathy in affected males. Roughly two-thirds of mothers with a son with DBMD are carriers of the condition. Carriers typically do not manifest muscular symptoms but up to 60% are at risk for cardiac abnormalities; one study found 10% of DBMD carriers with dilated cardiomyopathy. The American Academy of Pediatrics (AAP) recommends that carriers of DBMD receive an initial complete cardiac evaluation by a cardiologist that includes an echocardiogram and electrocardiogram (EKG) with re-evaluation every 5 years beginning at age 25-30. As many as 35-54% of carriers are not adhering to the AAP recommendations despite knowing their carrier status. Limited research has been conducted into the barriers that carriers face in accessing recommended cardiac screenings. We surveyed 60 carriers of DBMD recruited through DuchenneConnect to determine their current cardiac care practices. The majority (71.7%, 43/60) reported adherence to appropriate cardiac care while 28.3% (17/60) of carriers surveyed did not receive appropriate care. Semi structured telephone interviews were conducted with 11 carriers who in the last 5 years had not seen a cardiologist, had an echocardiogram, or had an EKG to determine the perceived challenges that carriers face in obtaining appropriate cardiac care. From the participants interviewed (11/17), seven major themes emerged. The primary theme identified was a perceived lack of awareness among healthcare providers regarding cardiac risks in carriers as evidenced by the following quote: “Each cardiologist is like, “I have no idea why you’re here.” And I explain to them...if I’m a carrier that means I may have cardiomyopathy...both of them had no idea what I was talking about.” Increased awareness, health education regarding risks for carriers, and advocacy efforts are needed for healthcare providers and DBMD carriers in order to ensure that this entire population receives appropriate cardiac care.

C-39 Clinical Utility of Whole Exome Sequencing in Adult Medical Genetics Patients: A Case Series

**Adult**

*Submitter: Lauren Elizabeth Hipp, University of Michigan*

*Presenting Author: Lauren Elizabeth Hipp, University of Michigan*

*Primary Author: Lauren E. Hipp, University of Michigan*

*Author 2: Wendy R. Uhlmann, University of Michigan*

*Author 3: Shane Quinonez, University of Michigan*
Introduction: Cases demonstrating the clinical utility of whole exome sequencing (WES) have focused on pediatric patients. We present three adult patients from our Medical Genetics Clinic that document the role of WES in medical management.

Case Reports: Patient A, age 24, presented with ataxia and dystonia. First line WES identified compound heterozygous variants in TH, consistent with a diagnosis of Tyrosine Hydroxylase Deficient Dopa-Responsive Dystonia. Complete and sustained clinical response on levodopa had been previously reported, leading to recommendations for increased dose and duration of levodopa treatment. Results also led to recommendations against serotonin agonists for obesity management.

Patient B, age 33, presented with short stature, learning delay, premature ovarian failure, pancytopenia, and parotid gland carcinoma. Previous evaluation included normal karyotype, microarray, and DNA breakage studies. WES identified compound heterozygous variants in LIG4, consistent with Ligase IV Deficiency. Findings directed recommendations for annual immunodeficiency screening, 3 month follow-up for cytopenias, restrictions on radiation exposure, and high-risk cancer screening, resulting in early diagnosis and treatment of hepatocellular carcinoma.

Patient C, age 31, presented with a clinical diagnosis of Osteogenesis Imperfecta (OI) type 3 and desire to pursue in vitro fertilization with pre-implantation genetic diagnosis. Panel testing for skeletal dysplasias and microarray were non-diagnostic. WES identified compound heterozygous variants of LEPRE1, consistent with a diagnosis of autosomal recessive OI type 8. LEPRE1 sequencing in her partner was negative. The patient pursued natural conception with a successful outcome.

Discussion: Use of WES in adults is evolving. Documenting the utility of WES is critical for its continued implementation, given limitations of insurance coverage in patients >18. These cases provide evidence for the role of WES in adult genetics evaluations and demonstrate its utility for treatment, screening, and family planning.

C-42 Applying Maslow's Hierarchy of Needs to Understand the Socio-Emotional Experiences of Adults with an Intellectual Disability

Adult
Submitter: Erin Nordquist,
Presenting Author: Erin Nordquist,
Primary Author: Erin Nordquist, Providence Health and Services
Author 3: Elizabeth Petty, University of Wisconsin
Author 4: Jane Sheldon, University of Michigan-Dearborn
Author 2: Beverly M. Yashar, University of Michigan

Research on adults with intellectual disabilities (ID) provides little exploration of their socio-emotional experiences, and generally relies on proxy over self-reporters. To better understand the socio-emotional experiences of these individuals from their own perspectives we used the top three tiers of Maslow’s Hierarchy of Needs (love & belonging, self-esteem, self-actualization) to design face-to-face interviews
allowing adults with ID to self-report their socio-emotional experiences and needs. A question format based on Harter’s Self-Perception Profile for Children (n=15 questions with 4-6 questions per tier) generated quantitative and qualitative data. Adults with ID (n=5) were recruited from a non-profit vocational and social skill-building farm. Due to uncertain validity, quantitative data was not analyzed. Using Maslow's hierarchy, thematic analysis of qualitative data identified emerging themes across participants’ responses. We found that love & belonging focused on activities/time spent with others and valuing relationships with family/staff/significant others over friends. Self-esteem focused on positive self-image and was sourced from abilities and social interactions. Self-actualization themes were less reflective of traditional needs and included morality based in rule adherence/following instructions and relying on others for conflict resolution. Participants generally defined their socio-emotional experiences and needs in relation to others rather than as an individual, consistent with a collectivistic cultural framework. This pilot study found that Maslow’s love & belonging and self-esteem tiers are relevant to adults with ID and highlights the value of recognizing their abilities and their focus on interpersonal relationships. The identified need for conflict-resolution skills suggests the importance of providing focused support in this area to adults with ID and their family members. While Maslow’s framework helped identify critical needs, future research should explore needs within a collectivistic framework.

A-46 Cancer Risk Education and Wellness (CREW) Tool: Development and Analysis
Cancer
Submitter: Andrea Dawn Forman,

Primary Author: Zoe Bogus, MS, Arcadia University
Author 2: Lisa Kessler, MS, LCGC, Arcadia University
Author 3: Andrea Forman, MS, LCGC, Fox Chase Cancer Center
Presenting Author: Zoe Bogus, MS, Arcadia University

Introduction: Individuals undergoing cancer risk assessment may be uniquely motivated to learn about modifiable cancer risk factors. Prior research showed that at least 81% of genetic counseling patients rated several modifiable risk factors, e.g. exercise, as very or extremely important to discuss in genetic counseling sessions. Genetic counselors (GCs) shared that they often mention some lifestyle risk factors during visits, but are limited by time and concerns about expertise. 98% of surveyed GCs expressed interest in a tool to help incorporate this information into their practice. This study involved development of the Cancer Risk Education and Wellness (CREW) tool and feedback about the tool from genetic counseling patients and GCs.<br />

Methods: The tool includes information on smoking, alcohol use, body weight, exercise, and UV exposure. Each section has information related to cancer risks, tips to reduce cancer risk by altering lifestyle, and links to additional information and support. Online assessment surveys were sent to patients in a cancer registry who previously underwent cancer genetic counseling and members of the NSGC Cancer SIG. <br />

Results: 137 of 870 patients and 102 of 1200
GCs completed the surveys. Over 80% of both patients and GCs found the tool “very easy to understand” and over 64% of patients and GCs found the tool to be helpful or very helpful. For patients, exercise and body weight were the most useful sections and 68% would make lifestyle changes based on this information. 76% of GCs stated that they would be interested in using this tool with some or most of their patients and 54% of GCs would be interested in a guide to use this tool most effectively. Discussion: Patients and genetic counselors both found the tool to be easy to understand and found the information provided to be helpful. Use of this tool in cancer genetic counseling sessions will help GCs share modifiable risk factor information in an easy to understand and time sensitive way. Future research should involve development of a guide for GCs interested in using this tool.


Cancer

Submitter: Katherine Clayback, Case Western Reserve University

Presenting Author: Katherine Clayback, Case Western Reserve University

Primary Author: Katherine Clayback, Case Western Reserve University

Author 2: Anne Matthews, PhD, FACMG, Case Western Reserve University

Author 3: Goutham Narla, MD, PhD, University Hospitals Cleveland Medical Center

Author 4: Michelle Merrill, MS, LGC, University Hospitals Cleveland Medical Center

Multi-gene panel testing for inherited cancer susceptibility has emerged without corresponding specific clinical guidelines for when this broad testing approach is most appropriate. Commercial laboratories offering this testing provide a wide variety of testing options, ranging from gene panels that include a few clinically actionable genes to larger pan-cancer panels. Many times, if testing is recommended, the choice of the scope of testing is left mainly to the patient with support from a genetic counselor. This study explored what factors influence the scope of testing chosen, if any factors should be considered when genetic counselors discuss a patient’s testing options, and if minorities are more likely to have variants of uncertain significance (VUS) identified. This retrospective chart review examined three years of medical records (n=2205) of patients seen by genetic counselors in cancer genetics at a large academic health center. These data represent 1001 patients who met inclusion criteria. The majority of patients (n=790, 78.9%) chose to undergo testing via a larger gene panel. Logistical regression data demonstrated that patients who were tested before undergoing surgical treatment (n=314, 31.4%) for breast cancer were more likely to select a smaller panel (p=0.002) than those who had a family history of breast cancer (n=800, 79.9%) who were more likely to select a larger panel (p=0.032). Genes with the most pathogenic mutations were BRCA1/2 (n=42), ATM (n=14), and CHEK2 (n=7). Genes with the most VUS were BRCA1/2 (n=33), ATM (n=32), and NBN (n=21). This study also concluded that large multi-gene panels are more likely to have VUS (p=<0.001) by two-tailed independent t-test. Additionally, a one-way
ANOVA analysis determined that African Americans in this cohort (M=0.43, SD=0.783) were more likely than Caucasians (M=0.24, SD=0.520) to have a VUS (p=<0.001). It is anticipated that these study results may help genetic counselors best facilitate their patient’s testing decisions with a more comprehensive assessment of what impacts a patient’s decision.

A-52 Genetic Testing Alters Care for von Hippel-Lindau Syndrome Phenocopy Cancer
Submitter: Morgan Depas, MS, CGC, Medical College of Wisconsin
Presenting Author: Morgan Depas, MS, CGC, Medical College of Wisconsin
Primary Author: Morgan Depas, The Medical College of Wisconsin
Author 2: Carolyn Horton, MS, CGC, Ambry Genetics
Author 3: Amanda Jacquart, MS, CGC, The Medical College of Wisconsin

A diagnosis of von Hippel-Lindau (VHL) can be made with clinical criteria or identification of a pathogenic variant (PV) or a variant likely pathogenic (VLP) in the VHL gene via germline genetic testing. Clinical and analytic sensitivity of germline testing in individuals with clinical diagnosis of VHL approaches 100%, and due to the rare and specific tumor spectrum, phenocopies are rare. Therefore, despite lifelong surveillance recommendations, patients with a long standing clinical diagnosis of VHL may not pursue molecular confirmation due to financial burden or other barriers. Our proband, a 41-year-old male, presented to clinic due to an incidental renal cell mass subsequently diagnosed as clear cell renal cell carcinoma (RCC). His family history was significant for a clinical diagnosis of VHL in his mother due to multiple spinal hemangioblastomas, pancreatic cysts, and RCC. She had declined genetic testing previously due to out of pocket cost. The proband underwent genetic testing primarily to provide information to his sister and her children. A 19 gene next generation sequencing (NGS) panel for hereditary RCC was performed and was negative. Due to the uninformative results, the patient’s mother agreed to testing and underwent the same multigene panel. Her testing revealed a VLP in VHL, c.483_500dup18; NGS metrics were consistent with a germline call. Retesting of the proband’s original peripheral blood sample, new blood specimen, and RCC tumor via Sanger sequencing were all negative for the familial VLP. An opthalmological exam was performed to evaluate for retinal hemangioblastoma and was also normal. This case highlights the role of genetic testing for individuals with long standing hereditary cancer syndromes. Specifically, our patient has been determined to be a phenocopy and without his mother’s molecular result, would continue to undergo unnecessary and costly screening with potentially needless invasive interventions. This also created clarity and peace of mind for his unaffected sister who also tested negative for the family variant.
A-55 What you find when you go looking: A unique CTNNA1 variant in an early onset diffuse gastric cancer

Cancer

Submitter: Dana Farengo Clark, MS, MS, LCGC, Penn Medicine/Abramson Cancer Center

Presenting Author: Dana Farengo Clark, MS, MS, LCGC, Penn Medicine/Abramson Cancer Center

Primary Author: Dana Farengo-Clark, Abramson Cancer Center, University of Pennsylvania

Author 2: Rashmi Tondon MD, University of Pennsylvania, Perelman School of Medicine

Author 3: Bryson W. Katona, MD, PhD, University of Pennsylvania

Gastric cancer is due to a heritable cause in ~10% of cases. Germline mutations in CDH1 are well known to lead to hereditary diffuse gastric cancer (HDGC) syndrome, however only 1-3% patients with diffuse gastric cancer have an identifiable CDH1 mutation. More recently, CTNNA1 has been identified as a potential candidate gastric cancer risk gene, however while there is some data associating CTNNA1 loss-of-function (LOF) mutations with HDGC, CTNNA1 remains a limited evidence gene. Herein, we report a 25 year old female who presented with bone metastases of unclear origin. Biopsy of a metastasis revealed a poorly differentiated carcinoma with signet ring cell features of likely gastrointestinal origin. Subsequent work-up included an upper endoscopy, which revealed diffuse gastric adenocarcinoma with signet ring cells in the cardia and fundus. The patient had no family history of gastrointestinal cancer in any first or second degree relatives. Given her early onset gastric cancer, a 26 gene panel was ordered, which demonstrated normal CDH1, but did reveal a variant of uncertain significance (VUS) in CTNNA1 (c.1351C>T, p. Arg451*). This nonsense mutation has not been reported in the literature, and given the paucity of data on CTNNA1 it was classified as a VUS by the commercial lab. Variant tracking revealed that the patient’s mother and brother both carried the CTNNA1 VUS. Subsequent upper endoscopy in these relatives with Cambridge protocol biopsies of the stomach demonstrated no signet ring cells; however the patient’s mother was found to have fundic gland polyps with low grade dysplasia. Their future continued surveillance strategy remains uncertain. At this time it remains unclear whether the observed CTNNA1 VUS is responsible for the proband’s gastric cancer, or if carrying this CTNNA1 VUS increases risk of DGC, highlighting the difficulties that arise from inclusion of limited evidence genes in multi-gene panel testing.

A-58 Acute Cutaneous Toxicity in Women with Breast Cancer and Heterozygous Mutations in Breast Cancer Genes

Cancer

Submitter: Amber Gemmell, MS, CGC, UT Southwestern Medical Center

Presenting Author: Amber Gemmell, MS, CGC, UT Southwestern Medical Center

Author 4: Nathan Kim, MD, PhD, UT Southwestern Medical Center
Radiosensitivity is a hallmark of several autosomal recessive conditions, such as Ataxia Telangiectasia and Fanconi Anemia. Carriers for these syndromes are at an increased risk for breast cancer. Minimal data exist regarding radiosensitivity in patients with heterozygous mutations in these and other genes causative of breast cancer. This study assessed dermatitis, an acute toxicity, in women with breast cancer who underwent radiation therapy (RT) at an NCI-designated Comprehensive Cancer Center and who had a pathogenic mutation in one of 16 breast cancer risk genes identified between January 2013 and July 2017. A retrospective chart review was performed to assess dermatitis. Dermatitis was scored using Common Terminology Criteria for Adverse Events scale ranging from grades 0-5, with grade 0 being no toxicity, and 4 or 5 representing life threatening consequences and death, respectively. A total of 56 women with breast cancer and a mutation in a breast cancer risk gene underwent RT. The majority (59%) of patients had BRCA1 (19/56) or BRCA2 (14/56) mutations. Additional mutations included PALB2 (8/56), CHEK2 (8/56), ATM (3/56), RAD51D (2/56), RAD51C (1/56), PTEN (1/56). Of the 56 women, dermatitis information was available for 49. One of 49 (2%) women had grade 3 or higher dermatitis after receiving chest wall radiation. This patient has a pathogenic mutation in ATM (c.8494C>T; p.Arg2832Cys). In total, 1/49 (2%) women with breast cancer and a mutation in a breast cancer risk gene showed grade 3 or higher dermatitis. This is compared to 2.2% in a baseline population. Although limited, this study highlights minimal dermatitis in breast cancer patients who carry a mutation in a breast cancer risk gene, suggesting that women with heterozygous mutations in breast cancer risk genes are not at increased risk of acute cutaneous toxicity from therapeutic radiation. Replication in a larger population and analysis of additional acute and late toxicity data are needed to further elucidate risks for these patients and determine potential radiosensitivity.

A-61 An Unexpected Pathogenic SDHC Variant Detected by Germline Cancer Panel Testing

Cancer

Submitter: Carolyn Garby Haskins, MS, CGC, Moffitt Cancer Center
Pathogenic variants (mutations) in the SDHC gene are associated with hereditary paraganglioma/pheochromocytoma (PGL/PCC) syndrome. PGL/PCC is typically characterized by head and neck PGLs that are usually benign but can become malignant; extra-adrenal tumors and PCCs also occur. Most cases are due to variants in the SDHB and SDHD genes. Mutations in SDHC account for 4% to 8% of PGL/PCC cases, and phenotypic outcomes for individuals with SDHC mutations are not well established. Here, we present a case report of a patient who had an unexpected SDHC finding on cancer panel testing.<br />A 69-year-old female of Caucasian ancestry underwent genetic testing through her primary care provider based on her personal and family history of breast cancer. Testing revealed an SDHC mutation, c.397C>T (p.Arg133*), which is a known founder mutation that may account for up to 31% of PGL in the French Canadian population. Functional studies show that the mutation causes loss of heterozygosity and loss of SDHB protein expression. <br />The patient was referred to a genetic counselor and shared the following history. Thyroid cancer (subtype unknown) was diagnosed at age 37 and treated with a total thyroidectomy. Left-sided ductal carcinoma in situ (DCIS) was diagnosed at age 58 and treated with a lumpectomy, radiation, and tamoxifen therapy for 3 years. Two non-melanoma skin cancers were diagnosed in her 60s. Paternal history included multiple myeloma in the patient’s father and 2 second-degree relatives with colon cancer under 50. Maternal history included an aunt with breast cancer diagnosed in her 40s.<br />Through germline testing for hereditary cancer, we identified a mutation in a gene associated with PGL/PCC syndrome, SDHC; however, a medical history revealed a phenotype that differs from a typical PGL/PCC clinical presentation. Thus, testing may help identify atypical cases and improve description of the phenotype associated with SDHC mutations. <br />

Cancer
Submitter: Christine Keywan, Boston Children's Hospital
Presenting Author: Christine Keywan, Boston Children’s Hospital

Primary Author: Christine Keywan, Boston University

Author 2: Zohra Ali Khan Catts, Helen F Graham Cancer Center Research Institute

Author 3: Audrey Squire, Seattle Children’s Hospital

Author 4: Emily Dalton, Ambry Genetics

Background<br>ATM, CHEK2, NBN and PALB2 are moderate risk cancer genes that confer a 17-58% lifetime risk of breast cancer. This study describes the clinical utility of testing these genes in families at elevated risk of breast cancer. <br>Methods <br>Patients in this study carry pathogenic mutations in ATM, CHEK2, NBN, or PALB2. Each pedigree was analyzed to determine what breast cancer risk management options would be recommended based upon personal and family cancer history data alone. This was compared to the recommendation given to the patient following the identification of a pathogenic mutation. Proband were contacted to report what surgical or screening options they pursued and what communication and cascade testing has occurred within their families. <br>Results<br>81.0% of women affected by breast cancer and 47.1% of unaffected women gained access to annual breast MRI due to their mutation. 19% of affected women and 52.9% of unaffected women would have been recommended annual breast MRI based on personal and family history data alone. 29.7% of affected women underwent risk reducing mastectomy and 17.6% of unaffected women underwent prophylactic mastectomy. 69.8% of probands informed all first-degree relatives of their genetic test result, and 22.9% of first-degree relatives pursued genetic testing. 71.7% of first-degree female relatives could increase their breast cancer screening should they test positive for the familial mutation.<br>Conclusions<br>Genetic testing for moderate risk breast cancer genes offers clinical utility because probands and their family members gain access to risk management options that would not be available to them otherwise.

A-67 Ovarian endometrioid adenocarcinoma with focal yolk sac differentiation in a pre-menopausal patient leading to diagnosis of Lynch syndrome

Cancer
Submitter: Brooke Levin, Cooper University Health System

Primary Author: Brooke Levin, MD Anderson Cancer Center at Cooper University Health System

Author 2: Kathleen Kenley, UW Medicine Valley Medical Center

Author 3: Julieta Barroeta, Department of Pathology, Cooper University Health System

Author 4: Lauren Krill, MD Anderson Cancer Center at Cooper University Health System

Author 5: Pallav Mehta, MD Anderson Cancer Center at Cooper University Health System
Author 6: Janhvi Sookram, Cooper University Health System

Presenting Author: Kathleen Kenley,

Introduction: Ovarian endometrioid adenocarcinoma with yolk sac differentiation is a rare tumor with fewer than twenty cases in the literature. Endometrioid adenocarcinoma is the most common epithelial ovarian tumor associated with Lynch syndrome, whereas yolk sac and germ cell tumors are less frequently reported. Presented is the case of a pre-menopausal woman with an ovarian endometrioid adenocarcinoma with focal yolk sac component who was found to have a germline MSH2 mutation confirming a diagnosis of Lynch syndrome. Case Report: A 29 year-old female nulligravid patient presented after imaging for right lower quadrant pain demonstrated a pelvic mass. Prior to surgery, the patient’s CA-125 and HE (human epididymis protein)-4 were elevated at 474 U/mL and 336 pmol/L, respectively, and beta-hCG, inhibin B and alpha fetoprotein (AFP) were within normal range. Lactate dehydrogenase (LDH) was elevated at 645 U/mL. Laparotomy and a fertility-sparing surgery with comprehensive staging were completed. Final pathology revealed a stage IC1 grade 3 endometrioid ovarian carcinoma with focal yolk sac differentiation. Chemotherapy included four cycles of bleomycin, etoposide, and cisplatin (BEP) followed by four cycles of carboplatin and paclitaxel. After chemotherapy, total hysterectomy and left salpingo-oophorectomy were performed with benign pathology. Germline genetic testing revealed a pathogenic mutation in MSH2, c.2038C>T (p.R680X), and a variant of uncertain significance in ATM, c.9002G>A (p.S3001N). Both of the patient’s parents were adopted and the health history of extended biological relatives was unknown. Genetic testing for the patient’s father revealed that he was positive for the MSH2 mutation. Discussion: Though a rare tumor, ovarian endometrioid adenocarcinoma with focal yolk sac differentiation may occur with Lynch syndrome. Genetic testing may be considered for individuals with this rare tumor pathology. Though small family structure can limit risk assessment, ultimately genetic testing may guide future cancer treatment and surveillance.

A-70 Paired germline testing and somatic tumor sequencing for Lynch syndrome: the clinical challenges of uncertain results

Cancer

Submitter: Kimberly Rutledge Matthijssen, Inova Health System

Presenting Author: Kimberly Rutledge Matthijssen, Inova Health System

Primary Author: Kimberly Matthijssen, MS, LCGC, Inova Translational Medicine Institute

Author 2: Amanda Schott, MS, LCGC, Inova Translational Medicine Institute

Author 3: Dina Alaeddin, MGC, Inova Translational Medicine Institute

Author 5: Tiffani DeMarco, MS, LCGC, Inova Translational Medicine Institute

Author 4: Natalie Hauser, MD, Inova Translational Medicine Institute
Paired germline testing and somatic tumor DNA sequencing in cases of suspected Lynch syndrome (LS) has the ability to rule out the condition in patients whose tumor exhibits mismatch repair (MMR) deficiency, yet who may not have an identifiable germline MMR mutation. Currently, up to 69% of discordant tumor IHC and germline testing results are attributable to biallelic somatic MMR mutations. In these cases, patients’ risks of developing additional LS cancers are not increased, and unnecessary screening could be avoided. We present a case of a 46 year old female diagnosed with endometrioid uterine adenocarcinoma. IHC testing indicated a loss of MSH2 and MSH6 protein expression. Her family history was unremarkable for LS cancers. A germline multi-gene panel and paired tumor MMR gene sequencing was ordered. A single pathogenic somatic mutation and three somatic variants of uncertain significance (VUS) were identified in the MSH2 gene, for which there is limited available data. There is currently not enough data to determine whether one or more of the somatic MSH2 VUS results may be a pathogenic mutation(s). Alternatively, our patient could have an unidentifiable germline MSH2 mutation, and the somatic MSH2 VUS (es) may be benign. Furthermore, we have not yet ruled out Lynch syndrome in this patient, and it is currently unclear whether she remains at increased risk for developing additional cancers, including colon cancer. It was recommended for her to follow LS management guidelines consistent with NCCN recommendations, namely undergoing her first colonoscopy and discussion of yearly surveillance with her physicians. This case highlights the often difficult interpretation of inconclusive paired germline and somatic tumor testing results for LS for genetic counselors and patients. It further illustrates the need for comprehensive pre-test genetic counseling, highlighting possible result scenarios and emphasizing that inconclusive results may still require increased cancer surveillance for patients and their relatives.

A-76 When do Clinicians Cast a Wider Net? Utilization of the Largest Comprehensive Cancer Panel at One Commercial Laboratory

Cancer
Submitter: Tripti Paudyal,

Primary Author: Tripti Paudyal, Ambry Genetics

Author 2: Amal Yussuf, Ambry Genetics

Author 3: Sara Wienke, Ambry Genetics

Author 4: Jessica Profato, Ambry Genetics

Presenting Author: Sara Wienke, Ambry Genetics

Background: Multigene panels (MGP) for hereditary cancer are now widely available, including smaller, tumor-specific panels, as well as comprehensive panels addressing a range of tumor types. A trend towards larger, comprehensive panels has been recently described; however, further research is needed to understand the motivations for ordering the largest available panels. This study aims to explore the association between clinical history and utilization of an expanded comprehensive panel offered at one
commercial laboratory. The expanded MGP includes additional genes, beyond other comprehensive MGPs, related to rare cancers/tumors including endocrine, brain, and renal.<br />

Methods: Clinical data was retrospectively reviewed for all patients tested with the largest available comprehensive panel (49 to 67 genes) at one commercial laboratory between July 2014 and December 2016. Personal and family history data was assessed for presence of rare tumor types including brain, renal, and endocrine (paraganglioma, pheochromocytoma and thyroid), as these cancer types distinguish the expanded panel genes from other comprehensive testing options. <br />

Results: 11,173 total cases tested with an expanded comprehensive panel were reviewed.10.5% (n=1173) of the cases had a personal history and 3.7% (n=415) had a family history of one of the assessed rare cancers. 8.2% (n=915), 1.2% (n=135) and 1.1% (n=17) of these cases had personal histories of renal, brain and endocrine cancers respectively. Family histories of brain, renal and endocrine cancers were found in 1.5% (n=172), 2.0% (n=218) and 0.2% (n=25) of cases, respectively.<br />

Conclusions: The overwhelming majority of patients tested with an expanded, comprehensive panel do not have a reported personal or family history of distinguishing tumor types. This study suggests that clinical history is not a key driver in decision-making when selecting an expanded MGP. Further research is needed to elucidate which factors influence clinicians when selecting the largest available panel option for their patients. <br />

A-79 From Uncertainty to Pathogenicity: Demonstrating the Significance of a TP53 In-Frame Deletion

Cancer

Primary Author: Emily Quinn, MS, CGC, St. Jude Children's Research Hospital
Presenting Author: Emily Quinn, MS, CGC, St. Jude Children's Research Hospital
Author 2: Emilia M. Pinto, St. Jude Children's Research Hospital
Author 3: Aaron H. Phillips, St. Jude Children's Research Hospital
Author 4: David Berdy, Norwegian American Hospital
Author 5: Mohammad Khandwala, Norwegian American Hospital
Author 6: Santhosh A. Upadhyaya, St. Jude Children's Research Hospital
Author 7: Gerard P. Zambetti, St. Jude Children's Research Hospital
Author 8: Richard W. Kriwacki, St. Jude Children's Research Hospital
Author 9: Kim E. Nichols, St. Jude Children's Research Hospital
Author 10: Chimene Kesserwan, St. Jude Children's Research Hospital
Submitter: Emily Quinn, MS, CGC,
Li-Fraumeni syndrome (LFS) is a highly penetrant cancer predisposition syndrome caused by heterozygous germline mutations in the TP53 gene. Although initially considered to be rare, recent estimates suggest an incidence as high as 1:500 and a de novo rate of 7-20%. These findings emphasize the importance of considering LFS in a proband with an LFS spectrum cancer, even in absence of a concerning family history. While several recurrent TP53 mutations located within “hotspots” in the DNA binding domain (DBD) are well-established, many families with LFS exhibit novel mutations. Emerging research suggests that missense TP53 mutations incur a higher cancer risk than null mutations; however, little is known about cancer risk for in-frame deletions or duplications, making a molecular diagnosis when such a variant is identified difficult. <br />

We report the genetic testing process for a pediatric patient diagnosed with an undifferentiated high grade brain tumor following his mother’s diagnosis of early-onset bilateral breast cancer. Sequential testing of both individuals revealed a three nucleotide deletion (c.764_766delTCA; p.Ile255del) in exon 7 of TP53, previously classified as a variant of uncertain significance. Even though the child and parent had tumors on the LFS spectrum, additional information was needed to effectively classify the variant, especially considering an absent maternal family history of cancer. Targeted TP53 analysis for the patient’s maternal grandparents confirmed that neither carried the variant; with this new de novo data, variant classification was upgraded to likely pathogenic. We conducted further functional and structural studies which demonstrated that this variant severely impairs both p53 transcriptional activity and protein folding in a manner similar to well-characterized TP53 DBD mutations. Our report illustrates the clinical significance and biological implication of a TP53 in-frame deletion as well as the challenge of interpreting TP53 variants in the absence of segregation and de novo data.

A-82 An Analysis of Information Captured in Genetic Counseling Cancer Pedigrees of Hispanic-American Patients

Cancer

Submitter: Katherine Leigh Sanders,

Primary Author: Katherine Sanders, UNCG

Author 2: Adam Buchanan, Geisinger Health System

Author 3: Kate Hughes, Novant Health Derrick L. Davis Cancer Center

Author 4: Thuy My Vu, Wake Forest Baptist Health

Author 5: Lauren E. Doyle, UNCG

Presenting Author: Katherine Leigh Sanders, UNCG

Previous research has suggested less information may be recorded on the pedigrees of Hispanic women than on the pedigrees of non-Hispanic Caucasian women in a hereditary breast cancer assessment setting, but this has not yet been thoroughly investigated (Weitzel et al, 2013). An information disparity
could make cancer genetic risk assessment more difficult and potentially inhibit Hispanic women and their families from receiving standard-of-care breast cancer risk management. To evaluate the amount of information recorded on pedigrees for each population, we reviewed pedigrees for women who received a breast and ovarian hereditary cancer syndrome evaluation at the Derrick L. Davis Cancer Center. Thirty-three pedigrees were reviewed (17 non-Hispanic Caucasian probands and 16 Hispanic probands) using a self-designed Pedigree Assessment Tool, which captured information about each relative on the pedigree. In many measures of pedigree completeness, no significant differences were seen between the populations: no significant difference was noted in the percent of family that had a living age or age of death recorded, in the percent of deceased family members who had a cause of death recorded, in the percent of family with cancer who had an age of diagnosis, or in the number of family members recorded. However, we noted that a significantly higher percentage of family was recorded as being affected with cancer on Caucasian patient’s pedigrees than on Hispanic patient’s pedigrees (median 28.1% vs. 18.2% cancer (p = 0.023). Additionally, Hispanic patients had a significantly lower percentage of third-degree relatives recorded on their pedigrees (2.6% vs 16.7% (p = .010). In summary, while in many measures of pedigree completeness the populations were not statistically different, more research could be performed to confirm pedigrees are an effective hereditary cancer-evaluation tool for the Hispanic-American population.

A-85 Identification of women at-risk for Lynch syndrome in a mammography population

Cancer

Submitter: Allison Schartman, Indiana University Health

Presenting Author: Allison Schartman, Indiana University Health

Primary Author: Allison Schartman, Indiana University School of Medicine

Author 2: Gail H. Vance, Indiana University School of Medicine

Author 3: Stephen R. Dlouhy, Indiana University School of Medicine

Author 4: Jennifer L. Ivanovich, Indiana University School of Medicine

Author 5: Kimberly Quaid, Indiana University School of Medicine

Author 6: Todd L. Foster, St. Vincent Health

Author 7: Stephanie A. Cohen, St. Vincent Health

Mammography screening is routinely used among women in the general population and family history information is often incorporated within mammography platforms to identify women at risk for hereditary breast and ovarian cancer (HBOC). The prevalence of Lynch syndrome in the general population is estimated to be similar to that of HBOC, or around 1 in 370 (0.3%). This study aimed to
demonstrate the feasibility of identifying women at-risk for Lynch syndrome and quantify the number of women at-risk for Lynch syndrome in a mammography population. Of 40,277 women who had a mammogram over 8 months, 376 (0.93%) were identified at-risk for Lynch syndrome based on a family history algorithm using revised Bethesda criteria. Seventeen (4.5%) previously had genetic counseling and/or testing and four (1.1%) were known to carry pathogenic mutations (MLH1, MSH2, BRCA1, and BRCA2). Of those who received a risk notification letter and had not previously undergone genetic counseling (N=359), 13 (3.6%) had genetic counseling following receipt of the risk notification letter and 3 (0.84%) were identified with a pathogenic gene mutation (MSH2, MUTYH, and ATM). This is the first study to our knowledge to evaluate a Lynch syndrome screening algorithm within a mammography platform and demonstrate the number of women at an elevated risk for Lynch syndrome.

A-88 Extracolonic Cancer Risks in Monoallelic and Biallelic MutYH Carriers: A Multicenter Exploratory Study

Cancer

Submitter: Valerie Slegesky,

Presenting Author: Valerie Slegesky,

Primary Author: Valerie Slegesky, University of Colorado

Author 2: Lisa Ku, MS, CGC, University of Colorado Hereditary Cancer Clinic

Author 3: Erica Wright, MS, CGC, University of Colorado Hereditary Cancer Clinic

Germline MutYH variants are known to lead to increased risk for colorectal cancer, but extracolonic cancer risks are not well understood. The literature includes several studies that have found both increased risk and no increased risk for breast, ovarian, bladder, endometrial, liver, gastric, and other cancers. There are colon cancer screening guidelines from the National Comprehensive Cancer Network (NCCN) for both monoallelic MutYH carriers and biallelic MutYH carriers, but guidelines for surveillance for other possible cancer risks have not been established. This study analyzed data on personal and family history of cancer among confirmed monoallelic and biallelic MutYH mutation carriers at several hereditary cancer clinics in Colorado. Significantly increased rates of female and male breast cancer were observed in monoallelic carriers, and significantly increased rates of female and male breast, colorectal, ovarian, and bone cancer were reported in their first and second degree family members. Biallelic carriers had significantly increased rates of colorectal cancer and reported significantly higher rates of colorectal, ovarian, prostate, and lung cancer in their first and second degree relatives. While further study is needed to confirm these risks and clarify their magnitude, this study provides a useful foundation for clinicians to consider extracolonic cancer risks in confirmed monoallelic and biallelic MutYH mutation carriers and their family members.
Despite being one of the most frequently identified cancer predisposition genes, establishing a clear phenotype for CHEK2 has been challenging. National Comprehensive Cancer Network (NCCN) guidelines (v1.2018) recommend female breast cancer surveillance for CHEK2 mutation carriers begin at age 40 or earlier due to family history. This study describes the cancer history of CHEK2 mutation carriers within our institution and evaluates current breast cancer screening guidelines. From January 2010 to March 2018, 8,185 patients underwent genetic testing that included CHEK2 analysis. Chart review of CHEK2 carriers was performed to assess for cancer diagnoses and family history of cancer. Of patients who had CHEK2 analysis, 1.9% (159/8,185) were identified as CHEK2 mutation carriers. Furthermore, 1.3% (2/159) of these carriers had homozygous CHEK2 mutations and 8.2% (13/159) had mutations in a second cancer predisposition gene. Of CHEK2 carriers, 47.2% (75/159) had a diagnosis of a CHEK2-associated cancer at the time of testing. The majority of patients with cancer had breast cancer (88.0%, 66/75), including nine women with bilateral disease and two men. Additionally, 6.7% (5/75) had colorectal cancer, 2.7% (2/75) had renal cancer, and 2.7% (2/75) had thyroid cancer. Among female CHEK2 carriers with breast cancer, 18.7% (12/64) were diagnosed with breast cancer prior to age 40. Of this group, the median age at cancer diagnosis was 35 years (24-39 years). Only one patient (8.3%, 1/12) had a family history that would have led to breast cancer surveillance prior to age 40 based on NCCN guidelines (beginning 5-10 years earlier than the youngest diagnosis in the family). While current NCCN guidelines recommend female CHEK2 carriers initiate breast cancer surveillance at age 40, we identified a notable percentage of female CHEK2 carriers who were diagnosed with breast cancer prior to age 40. Our data suggest refined guidelines for earlier breast cancer surveillance should be considered to ensure effective screening and early detection of breast cancer in female CHEK2 carriers.
A-97 Compliance Among High-Risk Patients Identified Through Hereditary Cancer Population Screening

Cancer
Submitter: John Zimmerman, MS, CGC, UT Southwestern Medical Center
Primary Author: John Zimmerman, MS, CGC, UT Southwestern Medical Center
Presenting Author: John Zimmerman, MS, CGC, UT Southwestern Medical Center
Author 2: Sara Pirzadeh-Miller, MS, CGC, UT Southwestern Medical Center
Author 3: Sayoni Lahiri, MS, CGC, UT Southwestern Medical Center
Author 4: Theodora Ross, MD, PhD, UT Southwestern Medical Center

Under-recognition of Lynch syndrome in the general population, particularly the underserved, necessitates innovative approaches to increase detection. The Detecting Unaffected Lynch Syndrome (DUAL) grant (PP160103) employs a multi-pronged approach to screen the general population to identify patients at high-risk (HR) for hereditary colorectal cancer (CRC). DUAL targets underserved and insured patients in local hospitals. HR patients are identified via cancer family history (FH) questionnaire and navigated to telephone genetic counseling/testing (GC/GT). This study aims to describe the differences in compliance to cancer risk management guidelines in HR patients. The following data were collected for HR patients identified through DUAL between January 2017 and April 2018: multi-gene panel GT results, HR status, and compliance to cancer risk management recommendations. Patients were defined as HR if modified management was indicated based on either FH or identification of a gene mutation. Chart review was performed to determine if patients were compliant with colon/breast screening intervals recommended by national guidelines. Of the 234 patients who completed GT, 28 (12%) tested positive for mutations in 12 unique genes: 18 patients (64%) had mutations in genes associated with increased CRC risks, while 10 (36%) had mutations in non-CRC genes. 67 (28%) had negative GT but were HR based on CRC or breast cancer FH. Of all HR patients (N=95), 47% were underserved. The overall compliance rate for HR mutation-negative patients was 84%. Of the non-compliant patients (N=11), 82% were from the underserved population. These findings demonstrate that population-based genetic screening is an effective method of identifying individuals at high-risk for cancer. A high degree of compliance was seen across all HR patients. However, a gap in compliance was identified in underserved HR patients, emphasizing the need for cancer screening programs in this population. The DUAL program may serve as a model for increased identification of individuals at high-risk for hereditary cancer.

B-44 Characteristics of patients with a primary brain tumor undergoing panel genetic testing

Cancer
Submitter: Sarah Azam,
Background. Currently, there are no genetic testing guidelines for patients with a primary brain tumor (PBT). This population is largely understudied in terms of the age at diagnosis, tumor pathology, family history, and their relation to genetic contribution. We aimed to describe these patient-specific characteristics and family histories based on hereditary cancer multi-gene panel test (MGPT) results among patients with a PBT.

Methods. A total of 654 consecutive subjects were referred for MGPT at a diagnostic laboratory between March 2012-June 2016. Clinical data were ascertained from requisition forms. Statistical analyses were completed using STATA (v.13, College Station, TX).

Results. In our cohort, 67% (339/506) were diagnosed <50 years of age. Most PBTs were gliomas (293/558, 53%) or meningiomas (222/558, 40%). Test result positive astrocytomas were diagnosed at a significantly younger age than patients with negative and VUS results (p=0.021). Of 165 patients with available family history information, 95% (n=157) reported a family history of some cancer and 18% reported a family history of brain tumors. MGPT identified 104/654 (16%) individuals with mutations. Of these, 35 (34%) had an isolated PBT with no additional primary cancers. About half of identified genes predisposed a risk to PBTs, while the other half did not.

Conclusions. While no genetic testing criteria currently exist for PBTs, our data suggest earlier age of diagnosis is being utilized as an indicator for testing. Pathology can be helpful in narrowing down the differential diagnosis; however patients’ PBT pathology can be atypical in relation to their hereditary cancer syndrome. Our data suggest PBTs can be the primary presenting cancer in hereditary syndromes. Family history evaluations are a beneficial risk assessment tool, particularly until testing criteria are developed. Further research is necessary for the development of solidified genetic testing criteria in the PBT population and more robust identification of at-risk individuals.

B-47 Increased incidental cancer risk identified in prenatal three-generation pedigrees obtained in 2016 as compared to 2010.

Cancer

Submitter: Jennifer Cech, UC Irvine
Many changes in the genomics field have occurred in the past ten years, including Angelina Jolie’s public disclosure of her BRCA status, the Precision Medicine Initiative, and the advent of multi-gene panel testing. This study reviewed how often cancer was reported in prenatal three-generation pedigrees for patients seen in 2010 and 2016 to see if there has been a change in reported incidence and, thus, in quantification of familial risk, given a general increase in cancer awareness. Using a retrospective chart review, the results of this study show that 59% of the 437 prenatal pedigrees reviewed in 2016 had a family history of cancer reported. Compared to 2010, there was a 19% increase in the number of patients who reported any family history of cancer, a 30% increase in the number of maternal families reported to have a history of cancer, and a 33% increase in the number of paternal families reported to have a history of cancer in 2016. Using a generalized scoring system, each family with reported cancer was given a high, intermediate, or low cancer risk score. There was a 48% increase in maternal high-risk, 175% increase in maternal intermediate-risk, 16% increase in maternal low-risk, and a 43% increase in paternal low-risk cancer families identified in 2016 vs. 2010. There were paternal high- and intermediate-cancer risk families identified in both years, but the change was minimal. Overall, more cancers were reported in the maternal lineages in both years compared to paternal lineages, and there were many fewer third-degree relatives reported with cancer than second or first in both years. The results of this study confirm previous data suggesting an increase in the identification of incidental cancer risk during prenatal genetic counseling sessions. These findings support the importance of obtaining a three-generation pedigree that includes cancer in the prenatal setting and developing institutional protocols for referring patients at high risk to appropriate specialists.

B-50 Double take! Mosaic Li Fraumeni syndrome in Monozygotic Twins Cancer
Submitter: Victoria Costello, Certified Genetic Counselor, Ambry Genetics

Presenting Author: Victoria Costello, Certified Genetic Counselor, Ambry Genetics

Primary Author: Victoria Costello, Ambry Genetics

Author 2: Kory Jasperson, Ambry Genetics

Author 3: Stephany Connor, Ambry Genetics

Author 4: Carla Mason, Ambry Genetics
NGS has increased our ability to detect mosaicism in individuals undergoing multigene panel testing (MGPT). However it is exceedingly rare to identify mosaic mutations in twins, especially in genes associated with hereditary cancer syndromes. Here we report on monozygotic (MZ) twins found to have the same mosaic TP53 mutation. The proband, a female with a personal history of breast cancer diagnosed at age 34, was identified to carry a pathogenic TP53 mutation via full gene analysis. Her unaffected twin sister also tested positive for the mutation. NGS confirmed mosaicism in both twins, as the minor allele frequency (MAF) was lower than expected for a heterozygous carrier and below 40% in both. Sanger sequencing of the TP53 mutation with two independent primer sets also confirmed the presence of the mutation at lower than expected MAF in both twins. The presence of this mutation across multiple methodologies is most consistent with mosaic Li Fraumeni syndrome (LFS). Follow-up testing on a benign lymph node tissue specimen from the proband also demonstrated mosaicism. Identification of the TP53 mutation in multiple tissues suggests that the mosaicism resulted from a postzygotic mutational event early in development, prior to twinning. Another possibility is that a postzygotic TP53 mutation occurred in the proband, followed by the transfer of stem cells with the mutation through placental vascular anastomoses to the bone marrow of her sister. To our knowledge, this is the first report of classic mosaicism associated with LFS in a MZ twin pair. Studies have demonstrated that a significant proportion of TP53 mutations identified by MGPT display abnormal NGS metrics. The vast majority of results from ancillary testing from these cases are consistent with aberrant clonal expansion and the majority are likely due to clonal hematopoiesis of indeterminate potential. Despite the somatic origin for the majority of TP53 alterations with abnormal NGS metrics, this case highlights the importance of follow-up germline testing in MZ twins when mosaicism is found in a sibling.

B-53 Integrating Genetic Counseling and Testing in the Pediatric Oncology Setting: Parental Attitudes and Influencing Factors
Cancer
Submitter: Lauren Renee Desrosiers, GeneDx, Inc.
Primary Author: Lauren Renee Desrosiers, GeneDx, Inc.
Presenting Author: Lauren Renee Desrosiers, GeneDx, Inc.
Author 2: Whitney Dobek, MS, CGC, University of South Carolina
Author 3: Emily Quinn, MS, LCGC, St. Jude Children’s Research Hospital
Author 4: Stuart Cramer, DO, Palmetto Health-USC Medical Group

Cancer predisposition syndromes (CPS), caused by germline pathogenic variants in tumor suppressor genes and oncogenes, are genetic conditions that put an individual at increased risk to develop cancer. It
is estimated that 10-15% of children with cancer have an underlying CPS. Although genetic testing for these conditions has become routine in the adult setting, incorporation of germline genomic technologies into pediatric cancer care has not occurred as rapidly. The purpose of this study is to assess desire for genetic counseling and testing services among parents of children with cancer to provide parental insight in the incorporation of genomic technologies in this health care setting. Forty-two parents of individuals diagnosed with cancer less than 18 years of age completed either a paper (n=8) or online survey (n=34) regarding their child's cancer history, personal perspectives on genetic counseling, and family/demographic information. Interest in genetic testing for CPS was variable, with 50% of respondents indicating they would be interested in pursuing genetic testing for their affected child while one-third of respondents indicated that they were unsure if they would pursue genetic testing. The factors most commonly cited as impacting interest in genetic counseling/testing include the potential for modification of medical care for family members and for the child’s treatment based on results. A subset of parents expressed that concerns for genetic discrimination and potential negative impact on mental health would negatively influence their interest in genetic testing for CPS. Genetic counselors have an ideal skillset to help families weigh the benefits and drawbacks of genetic testing for CPS in childhood in order to facilitate decision-making among this population as the availability and clinical utility of genomic testing increases.

B-56 Gastrectomy Decisions in Asymptomatic CDH1+ Patients over age 50: Implications for Ongoing Interdisciplinary Care with Genetic Counseling

Cancer

Submitter: Grace-Ann Olayinka Fasaye, ScM, CGC, National Cancer Institute, Center for Cancer Research

Presenting Author: Grace-Ann Olayinka Fasaye, ScM, CGC, National Cancer Institute, Center for Cancer Research

Primary Author: Grace-Ann Fasaye, National Cancer Institute

Author 2: Kathleen Calzone, National Cancer Institute

Author 3: Maureen Connolly, National Cancer Institute

Author 4: Jeremy Davis, National Cancer Institute

Introduction: Patients who are positive for pathogenic variants in CDH1 have a 60-80% lifetime gastric cancer risk. The average age of gastric cancer onset is 38 years (range: 14-69). CDH1+ patients are advised to undergo prophylactic total gastrectomy (PTG) in their early 20s. PTG decisions in asymptomatic CDH1+ patients over age 50 has not been extensively studied.

Methods: Patients were enrolled between January 2017 and April 2018. Enrollment and follow-up visits occurred as part of an interdisciplinary clinic that includes surgical oncologists, gastroenterologists, nutritionists, research nurses and a genetic counselor. Medical records were reviewed in asymptomatic CDH1+ patients who discovered their status after age 50.

Results: Twelve (9 females, 3 males)
CDH1+ patients ages 54-72 (median 62) were identified within 8 families. Eight (67%) opted to have surveillance with upper endoscopy and four (33%) underwent PTG at ages 57, 59, 61, 63. The timeframe between results disclosure and PTG was 1–44 months. Upper endoscopy was contraindicated due to previous gastric bypass for the patient who underwent PTG 1 month following results disclosure. Signet ring cancer cells were found in specimens of all patients who underwent PTG. No pathological findings have been identified in biopsies of patients who continue to opt for endoscopic surveillance. CDH1+ patients with >1 first degree relative (FDR) with gastric cancer were more likely to undergo PTG than those with no family history of gastric cancer in a FDR (50% vs 17%).

Discussion: Genetic counseling for CDH1+ patients over age 50 should emphasize the cumulative risks of gastric cancer diagnosis rather than the average age of onset. Patients should be informed of the high likelihood of harboring asymptomatic signet ring cancer cells. CDH1+ patients greater than age 50 benefit from ongoing interdisciplinary discussions about their medical and family history, as well as psychosocial and nutritional concerns that may impact PTG decision-making.

B-59 Managing the Unexpected: Genetic Counseling of Complex Family Histories of Colon and Endometrial Cancer

Cancer
Submitter: Amber Gemmell, MS, CGC, UT Southwestern Medical Center
Presenting Author: Amber Gemmell, MS, CGC, UT Southwestern Medical Center
Primary Author: Amber Gemmell, MS, CGC, UT Southwestern Medical Center
Author 2: Caitlin Mauer, MS, MA, CGC, UT Southwestern Medical Center
Author 3: Brian Reys, MS, CGC, UT Southwestern Medical Center
Author 4: Sara Pirzadeh-Miller, MS, CGC, UT Southwestern Medical Center
Author 5: Theodora Ross, MD, PhD, UT Southwestern Medical Center

Managing patients with family histories (FH) of suspected Lynch syndrome (LS) in the context of negative germline genetic testing (GT) is a challenge. Currently, no national guidelines exist for the management of complex FH. The aim of this study was to assess current practices of genetic counselors (GCs) regarding management recommendations for patients with uninformative GT and FH suggestive of LS. A survey of current management practices using five hypothetical pedigrees was posted to NSGC discussion forums. All pedigrees included an unaffected, female proband with negative, comprehensive GT. Cancer risk management recommendations for colorectal cancer (CRC), endometrial cancer (EC) and extra colonic cancers were collected. Of the 115 completed surveys, demographic variables reflect current NSGC membership. While 77% (89/115) of respondents reported cancer as their primary specialty, 59% (68/115) had <5 years cancer genetic counseling experience. In response to a pedigree with a 1st degree relative with CRC and FH of CRC and EC meeting Amsterdam II (AmII) criteria, a
majority (84%, 96/115) of respondents would not recommend LS CRC screening management, instead recommending screening based on FH of CRC. For a 2nd degree relative with CRC and FH of CRC and EC meeting AmII criteria, the majority (96%, 110/115) of respondents would also not follow LS CRC screening recommendations. However, 52% (60/115) suggested CRC screening should begin at 35 years, repeating every 5-10 years, while 43% (50/115) suggested CRC screening should begin at 50 years. For both pedigrees, the majority of respondents would not make specific EC or extra colonic cancer screening recommendations. A majority of GCs agree that patients with complex FH of EC and CRC do not need to follow LS screening guidelines. However, there is no consensus among GCs regarding what frequencies or at what age CRC screening should begin. This study highlights the need for national guideline development tailored to managing patients with complex FH meeting AmII criteria with negative GT.

B-62 Evidence for the continuation of surveillance practices for SDHx-mutation carriers after the age of 50

Cancer
Submitter: Rachel Holman,

Presenting Author: Rachel Holman,

Primary Author: Rachel Holman,

Author 2: Anne Naumer, Huntsman Cancer Institute

Author 3: Samantha Greenberg, Huntsman Cancer Institute

Author 4: Wendy Kohlmann, Huntsman Cancer Institute

Author 5: Dr. Luke Buchmann, University of Utah

Author 6: Marcus Monroe, Huntsman Cancer Institute

Patients with SDHx germline mutations are at risk for paragangliomas (PGLs), pheochromocytomas, and/or other related tumors. Penetrance is variable and gene dependent. Presymptomatic screening with MRI and biochemical testing is recommended, but optimal intervals and age ranges for screening have not been well validated. The aim of this study was to determine if SDHx carriers could discontinue screenings in the absence of relevant findings after the age of 50. A longitudinal retrospective observational analysis of clinical, genetic, histological, imaging, and laboratory data was conducted in 150 patients from 30 kinships with a confirmed SDHx pathogenic variant (PV) from XXX-October 2017. Fifty-six patients (38%; n=150) had at least one SDHx related tumor in their history. 35 of the 56 tumors were in SDHB carriers (63% of tumors; n=99 carriers), 17 were identified in SDHD carriers (30% of tumors; n=28 carriers), 3 in SDHC carriers (5% of tumors; n=19 carriers), and one in an SDHA carrier (2% of tumors; n=2 carriers). Twelve malignant and 44 benign cases were identified. Seven patients with no previous SDHx tumors were diagnosed with a tumor after age 50 (mean=60 years, range 51-72
Tumors were identified on baseline screening (n=2), subsequent screening (n=2), symptom presentation (n=2), and incidentally (n=1). One patient had metastasis three years after tumor identification. Current recommendations for screening patients with SDHx PVs is for rapid whole body and designated neck MRI every two years for life. Our study indicates that tumors may present past age 50. Baseline evaluation is important for individuals found to have an SDHx PV regardless of age. Because many tumors in this study were all diagnosed on the basis of symptoms or baseline imaging, the actual age at which the tumor began, and the rate of tumor development are still unknown. Data from this large cohort of SDHx patients indicates that there may not be an upper age limit for PGL development, and baseline evaluation with imaging is warranted after age 50.

**B-65 Findings beyond BRCA1/2 impact management of hereditary breast cancer families.**

*Cancer*

*Submitter: Scott T. Michalski,*

*Primary Author: Lindsay Kipnis, Dana Farber Cancer Institute*

*Author 2: Jilliane Sotelo, Dana Farber Cancer Institute*

*Author 3: Anu Chittenden, Dana Farber Cancer Institute*

*Author 4: Jill Stopfer, Dana Farber Cancer Institute*

*Author 5: Katherine Schneider, Dana Farber Cancer Institute*

*Author 6: Rosalba Sacca, Dana Farber Cancer Institute*

*Author 7: Samantha Culver, Dana Farber Cancer Institute*

*Author 8: Diane Koeller, Dana Farber Cancer Institute*

*Author 9: Shraddha Gaonkar, Dana Farber Cancer Institute*

*Author 10: Erica Vaccari, Dana Farber Cancer Institute*

*Author 11: Sarah Cochrane, Dana Farber Cancer Institute*

*Author 12: Whitney Espinel, Huntsman Cancer Institute*

*Author 13: Marjan Champine, Huntsman Cancer Institute*

*Author 14: Heather Hampel, Ohio State University*

*Author 15: Joanne Jeter, Ohio State University*

*Author 16: Kevin Sweet, Ohio State University*
Background

Hereditary breast cancer patients undergoing genetic testing face increasing options that can complicate genetic counseling and test selection. Various considerations influence test selection including personal and family history, patient preference, cost and clinical actionability. Guidelines are increasingly incorporating testing and management recommendations for moderate penetrance genes, however the impact of positive results in these genes is not well studied. We report results from a multisite clinical utility study in breast cancer patients with pathogenic/likely pathogenic (P/LP) variants in cancer risk genes beyond BRCA1/2.

Methods

We retrospectively examined 2,184 patients having multigene testing at three academic medical centers. Clinicians completed case report forms (CRF) describing genetic test result-based clinical actions of patients with P/LP findings in a non-BRCA1/2 cancer risk gene. De-identified CRFs were returned for 104 patients.

Results

In 80% of cases, clinicians reported counseling and/or clinical management recommendations were changed for the patient and/or patient’s family members based on the genetic test findings, with 57% (60/104) of patients receiving result-based recommendations. Changes in clinical management were made for over 60% of patients with P/LP variants in both high-risk and moderate-risk genes.

Conclusions

This study provides evidence that clinical management changed in patients with P/LP variants in cancer genes beyond BRCA1/2 and have impacted the management of their at-risk family members. P/LP findings in genes beyond BRCA1/2 have clinical utility in patient care consistent with established management guidelines. In cases where care was not impacted, additional research is needed to better understand barriers to patients following up on medical management and familial testing recommendations. Genetic counselors can inform patients undergoing expanded panel testing that such testing frequently alters patient care or counseling.
Introduction<br />GATA1 is required for the survival and differentiation of erythroid and megakaryocyte precursors in bone marrow. Heritable pathogenic variants in the GATA1 gene located on the X chromosome have been associated with congenital dyserythropoietic anemia, thrombocytopenia and Diamond-Blackfan anemia. Here we describe a case in which a novel germline GATA1 pathogenic variant was identified in a symptomatic female displaying myelofibrosis and increased marrow megakaryoblasts, with macrocytic anemia and thrombocytopenia in her peripheral blood.<br /><br />Case Report<br />A 24 year-old Chinese female who was diagnosed with myelofibrosis was referred to the Cancer Genetics Service for genetics assessment. She first presented with an incidental finding of macrocytic anemia and thrombocytopenia at age 22. A bone marrow trephine showed increased CD34+/CD61+ megakaryoblasts and fibrosis. Her family history included a mother with dysmorphic features and bleeding issues since childhood. Her chromosome breakage and telomere length testing results were normal. Multi-gene panel testing identified a novel heterozygous pathogenic variant in GATA1, c.21delG, creating a premature translational stop codon (p.Ser8Profs*129). Single site testing identified the same GATA1 pathogenic variant in the patient’s mother. Incidentally, the mother’s dysmorphic features were clinically suggestive of Noonan syndrome and the diagnosis was confirmed through the identification of a germline SOS1 pathogenic variant. This SOS1 pathogenic variant was excluded in the patient.<br /><br />Conclusion<br />Although female carriers of GATA1 pathogenic variants may be asymptomatic or only show mild symptoms, it is possible that the GATA1 pathogenic variant in this case genetically predisposed our patient to myelofibrosis due to skewed X-inactivation or a dominant-negative effect. To the best of our knowledge, this is the first case report of a female with myelofibrosis carrying a novel GATA1 pathogenic variant and a family history of Noonan syndrome.
Up to 41% of patients with paragangliomas (PGLs) or pheochromocytomas (PCCs) have an identifiable hereditary cancer predisposition syndrome. Based on a >10% likelihood for a germline mutation, previous studies have recommended testing all patients with PGLs/PCCs (Fishbein et al, 2013). This study aims to determine if this risk threshold applies to particular ages of onset of PGL/PCC and if family history (FH) should be used as a stratifying factor to aid in determining which patients should undergo genetic testing (GT). Retrospective chart review was performed for 150 patients referred for GT at UT Southwestern and affiliate sites between May 2010 and March 2018 due to personal history of PGL/PCC. Within this cohort, 110 (73.3%) had a personal history of PGL, 37 (24.6%) had PCC and 3 (2%) had PGL and PCC. 129 (86.0%) patients underwent GT: 29 (22.5%) patients underwent single gene/sequential GT; 100 (78.1%) underwent an NGS panel; 21/150 (14.0%) patients declined GT. 48/128 (37.5%) patients had pathogenic mutations. 19/48 (39.6%) patients had FH of PGL/PCC in first or second degree relatives, including 8/17 (47.0%) SDHB and 9/14 (64.3%) SDHD positives. No patients with SDHC (0/5), RET (0/5), or MAX (0/1) mutations had FH of PGL/PCC. PGL/PCC diagnoses in positive patients ranged between ages 10-66 years; earlier ages of onset correlated with a higher probability of hereditary etiology (66.6% tested positive at 0-10 years, 13.3% tested positive at 60-70 years). To date this is the largest analysis of patients with PGL/PCC who have undergone genetic counseling and confirms a high rate of identifiable germline mutations. While individuals diagnosed with PGL/PCC at a younger age were consistently more likely to have an identifiable germline mutation, mutations were identified in >10% of patients throughout the lifespan. A positive FH was not present in a majority of mutation carriers. These data supports previous recommendations and highlight the need for genetic counseling and GT for all patients with PGL/PCC, regardless of patient age at diagnosis or FH.

B-74 Attitudes Toward Updated Genetic Testing Among Patients with Unexplained Mismatch Repair Deficiency

Cancer

Submitter: Jessica Omark, The University of Texas MD Anderson Cancer Center UT Health Graduate School of Biomedical Sciences

Presenting Author: Jessica Omark, The University of Texas MD Anderson Cancer Center UT Health Graduate School of Biomedical Sciences

Primary Author: Jessica Omark, University of Texas MD Anderson Cancer Center UT Health GSBS

Author 2: Eduardo Vilar, The University of Texas MD Anderson Cancer Center

Author 3: Yi-Qian Nancy You, The University of Texas MD Anderson Cancer Center

Author 4: Leslie Dunnington, UTHealth The University of Texas Health Science Center

Author 5: Sarah Noblin, UTHealth The University of Texas Health Science Center

Author 6: Blair Stevens, UTHealth The University of Texas Health Science Center
Individuals who have colorectal cancer (CRC) or endometrial cancer (EC) displaying loss of immunohistochemical (IHC) staining of one or more mismatch repair (MMR) proteins without a causative germline mutation are said to have unexplained mismatch repair deficiency (UMMRD, also known as mutation-negative Lynch syndrome). Comprehensive genetic testing that could potentially further clarify Lynch syndrome (LS) carrier status is essential to provide tailored screening guidelines to affected individuals and their family members; however, patient understanding of the potential impact of updated genetic testing for LS is unclear. This study aimed to evaluate the interest in and perceived impact of updated genetic testing among individuals with UMMRD at a tertiary academic center. A survey evaluating interest in updated genetic testing was mailed to 98 potential participants, and an electronic health record review was completed for the 31 individuals who returned the survey. Results indicate that this population is highly interested in updated genetic testing, and their perceived impact is primarily for family members to have appropriate testing and screening options. Updated risk assessment and genetic counseling, along with a discussion of the benefits and limitations of genetic testing, is essential as the understanding of potential causes of UMMRD evolves. Updated genetic counseling may allow patients with UMMRD to better understand the interpretation of their tumor and germline testing, as well as the impact of comprehensive genetic testing for themselves and their family members.

B-77 Universal Screening of Colorectal Tumors for Lynch Syndrome: A Survey of Patient Experiences and Opinions

Cancer

Submitter: Alexander Thomas Petterson, Arcadia University

Primary Author: Alexander Thomas Petterson, Arcadia University

Presenting Author: Alexander Thomas Petterson, Arcadia University

Author 2: Jennifer Garbarini, M.S., LGC, CooperGenomics

Author 3: Maria J Baker, Ph.D., FACMG, M.S., LGC, Penn State Hershey Medical Center

Lynch syndrome is a hereditary cancer syndrome that increases the risk for colon, uterine, and other cancers. It is caused by defects in mismatch repair genes as well as terminal deletions of EPCAM. Universal screening of colon tumors for Lynch syndrome can identify individuals and families at risk to develop further cancers and potentially change management and treatment options. Effective and ethical implementation of universal screening is critical to its benefits. Patient perspectives on the implementation of a screening program in which they participated can provide a view of its effectiveness. Individuals whose colon tumors underwent universal screening within an academic medical center were retrospectively surveyed about their knowledge regarding Lynch syndrome and universal screening as well as their opinions on and experiences with the screening policy as
implemented. Multiple-choice responses were analyzed with descriptive statistics, and free-response answers were classified according to themes. Sixty-six of 297 (22.2%) possible patients responded to the survey, including 13 whose screening results raised concern for Lynch syndrome. Seventy-five percent of respondents supported universal tumor screening without informed consent. Ninety-two percent preferred receiving screening results regardless of outcome. Respondents described benefits to screening for themselves and their families. Notably, 87.3% of respondents would recommend treatment at a hospital with a universal screening policy, 90.6% felt that a universal screening policy reinforces their confidence in a hospital’s ability to provide state-of-the-art care, and 84.4% supported universal screening of endometrial tumors for Lynch syndrome. While broadly supporting universal tumor screening without informed consent, respondents also wanted more information shared about screening and their results. A balance of these desires with the time and cost associated with implementing policy changes may be considered.

B-80 Exploring Family Communication Regarding Cancer Genetic Testing for the Most Informative Results

Cancer
Submitter: Maija Anneli Rannikko,
Presenting Author: Maija Anneli Rannikko,
Primary Author: Maija Rannikko, Augustana-Sanford Genetic Counseling Graduate Program
Author 2: Lior Borovik, Sanford Health
Author 3: Larissa Risty, Sanford Health
Author 4: Lisa Madlensky, Family Cancer Genetics Program Moores UCSD Cancer Center

BACKGROUND: The genetic testing approach in the oncology setting ideally involves testing the affected relative (AfRel) who will be most informative. Unaffected patients who are referred for a family history of breast/ovarian cancer may be advised to discuss genetic testing with their AfRel(s). AIM: The aim of this study was to determine how often patients follow through with this recommendation and to describe reports of those conversations with AfReIs. METHODS: A retrospective chart review of patients seen at a single clinic from June 2015 – Dec. 2016 was conducted; summary statistics were used to describe characteristics of patients who were offered testing vs those recommended to first discuss testing with an AfRel. Patients advised to discuss testing with an AfRel who did not follow-up with the clinic were invited for telephone interviews. RESULTS: A total of 140 patients were eligible for chart review (unaffected, referred for family history of breast/ovarian cancer). Twenty-three patients were offered testing at their appointment due to having no living AfRel or stating that their AfRel was unwilling/unable to pursue testing. Twenty patients were advised to discuss testing with an AfRel who did not follow-up with the clinic were invited for telephone interviews. Of the 20 patients advised to discuss
testing with their AfRel, 15 (80%) did not follow-up with the genetics clinic. Of these patients, 7 agreed to participate in interviews. Two of these seven patients did not communicate with their AfRel; five participants communicated with their AfRel and only one relative chose to pursue testing.

CONCLUSIONS: A majority of patients who are advised to discuss testing with an AfRel do not follow-up with the genetics clinic. Many patients at risk for cancer are not being provided with accurate risk assessment due to current testing strategies. It may be prudent to offer testing to all patients meeting test criteria as few are able to first have an AfRel tested.

B-83 Evaluation and feedback implementation for iterative development of a relational cancer knowledgebase with improved utility for clinical, research, and educational purposes.

Cancer
Submitter: Kunal Sanghavi, MBBS, MS, LCGC, The Jackson Laboratory for Genomic Medicine
Presenting Author: Kunal Sanghavi, MBBS, MS, LCGC, The Jackson Laboratory for Genomic Medicine
Primary Author: Kunal Sanghavi, The Jackson Laboratory for Genomic Medicine
Author 2: Sara E. Patterson, The Jackson Laboratory for Genomic Medicine
Author 3: Cara Statz, The Jackson Laboratory for Genomic Medicine
Author 4: Taofei Yin, The Jackson Laboratory for Genomic Medicine
Author 5: Susan M. Mockus, The Jackson Laboratory for Genomic Medicine

Introduction: The Jackson Laboratory Clinical Knowledgebase (JAX-CKB) is a cancer relational knowledgebase that provides evidence-based information on genes, variants, targeted therapies, efficacy evidence, and clinical trials. JAX-CKB includes 86 cancer genes for public access (https://www.jax.org/ckb) and over 950 internally curated genes. JAX-CKB is used for clinical and research applications including interpretation of somatic cancer tests, molecular tumor boards, and for provider education. It also serves as a comprehensive resource for genetic counselors (GCs) who are increasingly involved in somatic testing. Study aims were to determine the gaps in utilization and content of JAX-CKB and assess the need of a consistent evaluation to ensure meaningful utilization of JAX-CKB. Approaches: An internal workshop and feedback coupled with literature review informed the need for a systematic evaluation of JAX-CKB. A GC, scientific curator, two clinical analysts, and the developer of JAX-CKB designed an IRB approved 13-question research survey using Qualtrics. The JAX-CKB website, Twitter, and emails to subscribers served as recruitment sources. Results: 29/66 (~44%) respondents used JAX-CKB for both clinical and research purposes. Two GCs used JAX-CKB for clinical and one for both clinical and research purposes almost every day or 1-2 times/week. GCs always used the “Explore by Gene” feature. 57/65 (~87%) strongly agreed (including 3 GCs) or agreed that JAX-CKB was relevant to their work. 58/61 (~95%), including 3 GCs, would recommend JAX-CKB to their
23/61 (~38%) respondents requested correlation between somatic and germline variant(s), which has since been implemented as ACMG 59 genes marked for disease association in JAX-CKB. Respondents, including 1 GC, also requested addition of new genes. Conclusion: Consistent evaluation is essential for meaningful utilization of JAX-CKB. Next steps include collaborating with GCs to further ascertain their needs related to somatic testing to enhance the knowledgebase to support GCs in somatic testing.

B-86 Identification of a CHEK2 Mutation in a Transgender Female with DCIS: A Case Report

Cancer

Submitter: Amanda Schott, MS, CGC, Inova Health Systems

Presenting Author: Amanda Schott, MS, CGC, Inova Health Systems

Primary Author: Amanda Schott MS, LCGC, Inova Translational Medicine Institute

Author 2: Kimberly Matthijssen MS, LCGC, Inova Translational Medicine Institute

Author 3: Dina Alaeddin, MGC, Inova Translational Medicine Institute

Author 4: Natalie Hauser, MD, Inova Translational Medicine Institute

Author 5: Tiffani DeMarco MS, LCGC, Inova Translational Medicine Institute

Genetic counseling for the transgender population remains difficult, given the limited data available for this specific population. Prior hormone use and surgical transitioning options often further complicates cancer risk assessment and medical management recommendations. We present the case of a 63 year old transgender female undergoing genetic counseling for a new diagnosis of DCIS (ER+/PR+) for which she had already had a lumpectomy. The patient reported having gender confirmation surgery in 1979 with ~1.5 years of prior hormone use. Her family history was reportedly significant for a mother with ovarian cancer at age 50 and a father with metastatic stomach cancer, age unknown. She underwent a large multi-gene panel that identified a pathogenic CHEK2 I157T mutation. The CHEK2 mutation does not adequately fully explain the majority of the reported personal and family history. It remains unclear how this lower penetrance CHEK2 mutation and prior hormone use (although limited exposure), may have played a role in the development of this woman’s breast cancer. In general there is almost no available data on how hormone use may influence overall cancer risk in transgender patients, especially not in the context of those who are identified with hereditary breast cancer risk. Additionally, there is preliminary evidence regarding this particular CHEK2 mutation and elevated prostate cancer risk. An urologist determined that this patient’s prostate was still intact and therefore screening was recommended; which was challenging for the patient, given its inconsistency with her gender identity. This case illustrates the need for more data in the transgender population, in particular with regard to hereditary cancer risk. In addition, this case demonstrated a plethora of psychosocial issues that are
specific to the transgender population, especially as medical professionals provide screening recommendations and cancer risks that may be inconsistent with their gender identity.

B-89 Tumor Profiling and Hereditary Risk Identification: The Continued Role of a Genetic Counselor

Cancer
Submitter: Samantha Stachowiak, Medical College of Wisconsin

Presenting Author: Samantha Stachowiak, Medical College of Wisconsin

Author 2: Ben George, MD, Medical College of Wisconsin

Author 3: Jennifer Geurts, MS, CGC, Medical College of Wisconsin

Primary Author: Samantha Stachowiak, MS, CGC, Medical College of Wisconsin

In the era of precision medicine, tumor profiling (TP) is routinely used for individualized cancer treatment. Despite the potential identification of germline mutations, genetic counselors are not consistently involved in test interpretation. This case illustrates the need for further genetic counselor involvement in the somatic tumor profiling process.<br />

Here we present a patient who was seen for genetic counseling in 2011 after being diagnosed with colorectal cancer at age 47. The family history was significant for a sister diagnosed with endometrial cancer at age 46 and a questionable history of endometrial cancer in her mother at age 28. At the time, microsatellite instability testing and immunohistochemical analysis of mismatch repair protein expression of her colorectal tumor was normal. No germline testing was recommended. In 2014 upon progression of disease, TP was used to determine further treatment. <br />

In 2018, our institution established the Clinical Cancer Genomics Review Committee to systematically review all cancer patients who have undergone TP. Given the substantial number of patients undergoing TP at our institution, this multidisciplinary committee was assembled to ensure appropriate follow-up. As a member of this committee, the genetic counselor reviewed this report and it was noted that two variants in the MUTYH gene were reported as uncertain significance. However, both variants were classified as (likely) pathogenic by multiple germline laboratories in the ClinVar database. Subsequently, additional genetic counseling and testing was recommended. Commercial germline 34 gene panel testing was performed confirming a molecular diagnosis of MUTYH-associated polyposis syndrome.<br />

This case report highlights the increasing need for genetic counselor involvement in TP results review, interpretation, and recommendations for follow up germline testing. Our institution implemented a formal review process of TP, which includes genetic counselors. Further studies are planned to determine guidelines for genetic counseling referrals and analysis of outcomes data.
B-92 Expected Versus Observed Phenotype-Genotype Associations with APC Pathogenic Variants

Cancer
Submitter: Erica Webb, GeneDx

Presenting Author: Erica Webb, GeneDx

Primary Author: Erica M. Webb, MS, CGC, GeneDx

Author 2: Becky L.G. Milewski, MS, LCGC, GeneDx

Author 3: Maegan E. Roberts, MS, CGC, GeneDx

Author 4: Megan L. Marshall, MS, LCGC, GeneDx

Author 5: Lisa R. Susswein, MS, MHA, CGC, GeneDx

Author 6: Kevin J. Arvai, MS, GeneDx

Author 7: Ying Wang, PHD, FACMG, GeneDx

Author 8: Rachel T. Klein, MS, LCGC, GeneDx

Author 9: Kathleen S. Hruska, PHD, FACMG, GeneDx

Background: Pathogenic/likely pathogenic variants (PVs) in APC are known to be associated with familial adenomatous polyposis (FAP). Genotype-phenotype correlations of attenuated (AFAP) (< 100 polyps), classic (100-999 polyps), or severe (>1000 polyps) phenotypes with PVs in certain regions of APC are well documented. However, there is debate about whether genotype or clinical presentation should drive screening and management. We aim to determine the full phenotypic spectrum with respect to genotype observed in a large cohort of patients with PVs in APC. Methods: We reviewed data from TRFs for patients found to carry an APC PV via single-gene, multi-gene hereditary cancer panel, and targeted variant testing at our laboratory. Those with more than 1 PV and those <18y were excluded from this analysis. Fisher’s exact test was used to assess differences amongst reported gene regions. Results: Two hundred and fifty seven patients had a PV in APC. The polyp burden associated with APC PVs were confirmed to be significantly different amongst the described gene regions (p<0.001). Of 188 patients who reported polyp history, 64 (34%) reported polyp burden outside the expected range for the region of APC in which their PV was observed. Of these 188 patients, 27 had a PV in the severe polyposis region, with six who reported <100 polyps. Comparably, 87/188 patients had a PV in the classic FAP region, with 80.5% (n=70) who reported a concordant phenotype. Of 97 patients with a PV in the AFAP regions, 15 reported either classic FAP (n=14; 14.4%) or severe polyposis (n=1; 1.03%). Lastly, 14 patients were identified to have large deletions/duplications, with varying phenotypes reported. Conclusions: The previously reported genotype-phenotype associations for APC were confirmed in our cohort. However, while a majority of patients who reported polyp history reported phenotypes consistent with their genotype, 34% reported polyp counts inconsistent with their genotype, supporting
the need to continue managing patients with APC PVs based on clinical presentation rather than genotype.

B-95 Parental Attitudes Regarding the Need for Genetic Services in a Pediatric Brain Tumor Survivorship Population

**Cancer**

*Submitter: Alice Zalan, Genetic Counselor, University of Illinois at Chicago*

*Presenting Author: Alice Zalan, Genetic Counselor, University of Illinois at Chicago*

*Primary Author: Alice Zalan, MS, University of Illinois Chicago Health and Sciences System*

*Author 2: Shelly Weiss, Ann and Robert H. Lurie Children's Hospital of Chicago*

*Author 3: Tara Maga, University of Illinois Chicago Health and Sciences System*

*Author 4: Natasha Pillay Smiley, Ann and Robert H. Lurie Children's Hospital of Chicago*

*Author 5: Melody Perpich, The University of Chicago Medical Center*

Pediatric brain tumor survivorship populations have not been typically offered genetic services as part of routine care. Prior research has focused on the integration of genetic services in the general pediatric oncology survivorship population and found a need for these services to be implemented. Family history collection and provision of genetic risk assessment has previously been determined to be an integral step in determining if an individual’s cancer was due to a hereditary predisposition. The purpose of this study was to examine parental perspectives regarding the need for genetic services in their child’s pediatric brain tumor survivorship clinic. Twelve semi-structured interviews were conducted with parent participants from the Brain STAR (Survivors Taking Action and Responsibility) clinic at Ann and Robert H. Lurie Children’s Hospital of Chicago. Interviews were transcribed and analyzed using a grounded theory approach to code and analyze the results thematically. Five key themes were identified: participants’ perceived thoughts regarding benefits and barriers to receiving genetic services, the desirable time for implementation of these services, their perceptions of genetics, and their thoughts regarding reproductive risk. Interestingly, the majority of participants recognized a possible hereditary component to their child’s brain tumor diagnosis. This indicates that it may be beneficial to involve genetic counseling regarding possible risk with each family, regardless of whether or not a hereditary predisposition is discovered. Participants’ perception of possible hereditary risk was focused in the context of a lack or presence of personal family history. Overall, participants indicated an interest in discussing their family history as well as receiving a genetic risk assessment. These results provide insight for genetics professionals regarding the need for genetic services in this population, and how to best implement them.
Patient Attitudes Toward Genetic Testing for Inherited Predispositions to Hematologic Malignancies

Submitter: Taylor Beecroft,

Presenting Author: Taylor Beecroft,

Primary Author: Taylor A. Beecroft, The University of Texas MD Anderson Cancer Center UTHealth G

Author 2: Sarah A. Bannon, The University of Texas MD Anderson Cancer Center

Author 3: Guadalupe R. Palos, The University of Texas MD Anderson Cancer Center

Author 4: Molly S. Daniels, The University of Texas MD Anderson Cancer Center

Author 5: Sarah J. Noblin, McGovern Medical School at The University of Texas Health Sc

Author 6: Courtney D. DiNardo, The University of Texas MD Anderson Cancer Center

Although inherited predispositions to hematologic malignancies have previously been considered rare, more than 12 causative genes have been implicated in the last decade. Since individuals diagnosed with leukemia have not historically been considered for evaluation of inherited predispositions, genetic testing is underperformed in this population. This study used focus group discussions to explore the attitudes, motivations, and barriers to genetic testing for 23 patients with leukemia. Participants exhibited a positive regard for the utility of genetic testing and were motivated by concern for their family and a sense of altruism toward all leukemia patients. While drawbacks and barriers were difficult for participants to identify, a few cited concerns about confidentiality of genetic information and possible discrimination based on test results. Participants unanimously agreed that skin punch biopsy, which is required for genetic testing in leukemia patients, would not deter their decision to be tested. The findings from this study are valuable for guiding genetic counseling that best meets the specific needs of leukemia patients.

Breast and ovarian cancer screening behaviors and health outcomes after genetic testing

Submitter: Austin Chua, CSU Stanislaus

Primary Author: Austin Chua, CSU Stanislaus

Presenting Author: Austin Chua, CSU Stanislaus

Author 2: Anjali Zimmer, Ph.D., Color Genomics

Author 3: Jessica Tsai, Color Genomics
Purpose: Clinical genetic testing has rapidly evolved to include newer delivery models like telephone-based genetic counseling and patient-friendly reports. However, the health outcomes of those who have undergone such unique approaches are not well understood. Here, we report survey results on health outcomes for recipients of genetic testing through Color Genomics.<br />

Methods: We developed a quantitative and qualitative mixed methods survey to determine 1) if people recognize their specific cancer screening guidelines, 2) if genetic testing changed their screening behavior, and 3) how they are screening compared to recommendations. An initial pilot consisted of 82 respondents. A cohort of ~1500 respondents will be studied and limited to those who received negative and positive results of BRCA1, BRCA2, and Lynch syndrome genes at least 1 year ago.<br />

Results: Preliminary data found that 86% of individuals are following appropriate cancer screening plans based on sex, age, and testing results. Of the 7 respondents with a positive result, 100% are screening appropriately (including continuation of existing appropriate screening plans or increased screening). Of the 57 respondents with a negative result, 88% are appropriately screening, 7% are screening less than recommended, and 5% provided insufficient information. Finally, of the 18 individuals who received a negative result with a variant of uncertain significance (VUS), 78% are screening appropriately, 11% are screening less than recommended, and 11% are screening more than recommended.<br />

Conclusions: Preliminary findings indicate that most people incorporate their genetic test results into screening decisions. The majority of studied individuals were following recommendations, including all positives. This pilot study indicates that further follow-up is needed to determine specific changes made based on testing and the impact on long-term health outcomes. Completion of this study will yield unique quantitative and qualitative comparisons of health behavior to published screening guidelines.

C-51 Panel testing in the setting of a familial cancer gene mutation: Finding unexpected results

Cancer<br />

Submitter: Samantha Culver, Dana Farber Cancer Institute<br />

Primary Author: Samantha Culver, Dana Farber Cancer Institute<br />

Presenting Author: Samantha Culver, Dana Farber Cancer Institute<br />

Author 2: Diane Koeller, Dana-Farber Cancer Institute<br />

Author 3: Huma Q. Rana, Dana-Farber Cancer Institute

Introduction: Single-site testing for a familial mutation is typically offered to at-risk family members when a mutation in a hereditary cancer gene is identified. We describe three cases where
comprehensive multi-gene panel testing was performed in the setting of a familial mutation and unexpected additional pathogenic mutations were identified.<br />

Case 1: A 38-year-old unaffected female was at 50% risk to inherit an EPCAM deletion from her mother and underwent multi-gene panel testing. The patient was found a true negative for the EPCAM deletion, but carried a mutation in CHEK2.<br />

Case 2: A 49-year-old unaffected male was at 50% risk to inherit a BRCA1 mutation previously identified in his sister. He underwent multi-gene panel testing and was found to carry both a BRCA1 and an ATM mutation.<br />

Case 3: A 69-year-old unaffected female underwent multi-gene panel testing due to a TP53 mutation previously identified in her daughter. The patient was negative for the TP53 mutation, but a mutation in BRIP1 was identified. Her brother underwent multi-gene panel testing and tested negative for the BRIP1 mutation, but carried a mutation in MITF.<br />

Conclusion: Single-site testing is currently considered the standard of care for at-risk family members of a known cancer predisposition mutation carrier. We recommend offering comprehensive panel testing particularly when there is unexplained cancer in the family. Single-site testing may incorrectly label individuals as “true negatives”, when the individual has increased risk based on a mutation not previously identified. Identification of these unexpected mutations can inform medical and surgical risk management. Additional testing can be offered to family members who did not originally have comprehensive testing. These cases demonstrate how multi-gene panel testing in the setting of a familial mutation can allow for a more comprehensive and personalized cancer risk assessment for patients and families.

C-54 A Comparison of cancer risk and clinical management of female carriers of CHEK2 truncation and missense mutations.

Cancer
Submitter: Sojin Durrant,

Primary Author: Sojin Durrant, California State University Stanislaus

Author 2: Christine Kobelka, Kaiser Permanente San Francisco Medical Center

Author 3: C. Bethan Powell, Kaiser Permanente Northern California Gynecologic Oncology

Presenting Author: Sojin Durrant, California State University Stanislaus

Through Next Generation Sequencing (NGS) technology, multi-gene panel testing is clinically accessible. Multi-gene panels allow testing for high-risk genes, as well as moderate and low risk genes such as CHEK2, where the significance of the mutation is not fully understood. Prior research on CHEK2 has focused mostly on Northern and Eastern European founder mutations, suggesting a difference in cancer risk and phenotype between CHEK2 truncating mutation c.1100delC and missense mutation p.I157T. Our study tries to determine if there are clinical differences between CHEK2 truncating and missense mutation carriers, which may then warrant separate management guidelines for the two different types of CHEK2 mutations. We explored whether the difference in risk and phenotype between the two founder mutations c.1100delC and p.I157T can be generalized to all CHEK2 truncating and missense
mutations. We also examined if there were differences in the carrier’s uptake of management options and utilization of surveillance or risk reducing surgery between CHEK2 truncating and missense mutations. We retrospectively reviewed the Electronic Health Record (EHR) of 72 individuals with CHEK2 pathogenic, or likely pathogenic mutations. We examined both founder and non-founder CHEK2 mutations from an ethnically diverse population. No significant difference in personal and family history of cancer was observed between truncating and missense CHEK2 mutation carriers. Also, there were no significant differences between management of breast cancer, colon cancer, and other cancers of CHEK2 truncating and missense mutation carriers. These findings suggest the difference observed between the two founder mutations c.1100delC and p.I157T cannot be generalized to all CHEK2 truncating and missense mutations. Clinical recommendations were not adjusted according to mutation type indicating a potential for overtreatment. Chart reviews identified cases of potential overtreatment for CHEK2 mutation carriers with respect to screening and risk reducing surgeries for other cancers such as ovarian cancer.

C-57 A Comparison of Genetic Counseling Referral Criteria to a Population of Renal Cell Carcinoma Patients: Current Criteria Miss Patients with a Hereditary Cancer Predisposition

Cancer

Submitter: Remington Brice Fenter, UT Southwestern Cancer Genetics

Presenting Author: Remington Brice Fenter, UT Southwestern Cancer Genetics

Primary Author: Remington Brice Fenter, UT Southwestern Medical Center

Author 2: Caitlin Mauer, UT Southwestern Medical Center

Author 3: Brian, UT Southwestern Medical Center

Author 4: Sara Pirzadeh-Miller, MS, CGC, UT Southwestern Medical Center

Author 5: Theodora Suzanne Ross, UT Southwestern Medical Center

Germline mutations in at least 19 genes are known to increase lifetime risks for renal cell carcinoma (RCC). No official genetic testing (GT) guidelines exist to indicate when patients with RCC need GT; thus, clinicians are at their own discretion to determine who merits GT. Here we compare patients with RCC to ACMG’s referral for genetic counseling (GC) guidelines (Hampel et al, 2014) to determine if these criteria might serve as a baseline for the creation of official GT recommendations.

Retrospective records review of 389 patients with RCC seen at UT Southwestern and affiliate clinics for GC between November 2009 and March 2018 was performed. Cancer diagnoses, histology, family history of cancer, whether patients met ACMG genetic counseling criteria, and GT results were recorded. Of the 389 patients seen for GC, 305/389 (78.4%) completed GT. Of those, 33/305 (10.8%) tested positive for a likely pathogenic or pathogenic variant in a gene associated with a
hereditary cancer predisposition syndrome. Nine (27.3%) positive patients did not meet ACMG referral criteria for RCC: six patients had RCC of unspecified histology and three were diagnosed with clear cell RCC at age ≥50. Of positive patients, 13/33 (39.4%) were diagnosed at or above age 50; the average age (range) of diagnosis in positive patients that met ACMG referral criteria and those that did not were 40.8 (24-63) years and 54.1 (36-78) years, respectively. A family history of RCC in first/second degree relatives was reported in 30.3% (10/33) of positive patients. Histology of RCC did not always correlate to expected phenotype of syndromes; two patients diagnosed with chromophobe RCC had mutations in SDHB or TSC1.<br />

Our data demonstrates that the current ACMG referral criteria do not capture all GT positive RCC patients, particularly those diagnosed over age 50 or those with unknown histology. As the field looks to improve identification of high-risk individuals, expansion of criteria for GC referral and GT should carefully consider cases missed by current referral criteria.

C-60 Perspectives on information desired during genetics evaluation: A qualitative analysis of men with prostate cancer

Cancer

Submitter: Samantha Greenberg, Huntsman Cancer Institute

Presenting Author: Samantha Greenberg, Huntsman Cancer Institute

Primary Author: Samantha Greenberg, Huntsman Cancer Institute

Author 2: Stacey Slager, University of Utah Health Care

Author 3: Susan Zickmund, George E Whalen Veteran Affairs

Author 4: Sarah Colonna, Huntsman Cancer Institute

Background: National guidelines have changed recently to include genetic counseling (GC) for all men with metastatic prostate cancer (PCa), increasing the volume of patients with PCa seen in genetics clinics. There is limited information regarding what information men, in particular those with PCa, are seeking from GC and genetic testing (GT). This study aimed to identify what information men with PCa desire before, during, and after GC.<br />

Methods: Focus groups were conducted with men who have PCa, either prior to their GC appointment or after they underwent GC and had received their GT results. Audio recordings were transcribed, coded, and analyzed for themes related to GT, information they desired from health care providers, and implications for family members.<br />

Results: Twenty-five men participated (10 pre-GC, 15 post-GC) in four focus groups (2 pre-GC, 2 post GC), all of whom had PCa. Nearly all men felt GT was beneficial and impactful for their family and themselves. Pre-GC participants often mentioned the impact of genetic information for their male relatives, and rarely knew about the potential implications for female relatives. Men in the pre-GC group reported desiring genetic information from their primary care or specialist clinician, though men who had undergone GC felt the genetic counselor was the best person to provide that information. Participants also circled back to their diagnosis and treatment often, discussing that genetics should be incorporated at a meaningful but not
overwhelming time of their diagnostic journey.

Conclusion: This study showed that men with PCa valued GC and GT for personal and familial implications, and often did not associate PCa genetics with an increased risk for female relatives to develop cancer. Consideration should be given to the timing of GC in regards to where men are in their treatment process. Additional education with non-genetics providers could enhance their discussions with patients prior to genetics referral, while genetic counselors can focus on other cancer risks and familial impact during their sessions.

C-63 Genetics Referral and Utility in Tumor Only Breast Tumor Genomic Profiling: One Institution's Experience

Cancer

Submitter: Austin Huber, Student, Avera Cancer Institute

Primary Author: Austin Huber, Student, Avera Cancer Institute

Presenting Author: Austin Huber, Student, Avera Cancer Institute

Author 2: Kayla York, Avera Cancer Institute

Author 3: Ping Ye, Avera Cancer Institute

Author 4: Megan Bell, Sanford Health

Author 5: Amy Krie, Avera Cancer Institute

Tumor-only tumor genomic profiling (TGP) has the potential to incidentally report germline variants associated with hereditary cancer syndromes. This study sought to identify barriers to referral for genetics consult and further define the utility of genetics referral in this setting through a retrospective chart review of patients who had undergone TGP for their breast cancer primary. Of the patients with reported variants with potential germline relevance on their TGP reports, half were referred to genetics for reasons other than their TGP results or had prior hereditary genetic testing, 39% were not referred, and 11% were referred specifically for variants reported by their TGP results. Compared to those not referred, patients in the group referred for TGP results were younger on average and more likely to have a 1st degree relative with a relevant cancer, to have biological children, and to meet NCCN criteria for further genetic evaluation. This shows a potential bias to refer patients with more typical hereditary cancer syndrome features. Additionally, the referred group contained a higher percentage of clinically actionable variants (63%) than the group not referred (46%), which suggests that clinically actionable variants reported on TGP reports are more likely to be referred than variants of uncertain significance (VUS). This could be due to the fact that VUS discovered via TGP may not have current clinical management implications if found to be germline and because of VUS positioning on TGP reports. Patients with variants in BRCA1, BRCA2, and PALB2 were also significantly more likely to be referred than those with variants in other genes. Finally, the utility of genetics referral in this setting was demonstrated as five of the 15 patients referred for their TGP findings tested positive for a clinically
relevant germline finding, all of which matched their TGP reported variant. This study demonstrates that patient and TGP result characteristics can impact the likelihood of patient referral and demonstrates the utility of genetics referral in this setting.

C-66 Assessing the Discordant Classification Rate for ATM, CHEK2, and PALB2 Variants in ClinVar

Cancer
Submitter: Sayoni Lahiri, UT Southwestern
Presenting Author: Sayoni Lahiri, UT Southwestern
Primary Author: Sayoni Lahiri, UT Southwestern Simmons Comprehensive Cancer Center
Author 2: Sara Pirzadeh-Miller, UT Southwestern Simmons Comprehensive Cancer Center
Author 3: Theodora Ross, UT Southwestern Simmons Comprehensive Cancer Center

Most hereditary breast cancers (HBC) are due to BRCA1/BRCA2 mutations, but ATM/CHEK2/PALB2 (A/C/P) mutations comprise 53% of non-BRCA HBC. In 2017, National Comprehensive Cancer Network published guidelines for A/C/P-related breast cancer risk management (BCRM), including prophylactic mastectomy, prompting many labs to add these genes to panels aimed at women undergoing testing for surgical planning. Labs lack a uniform process for variant classification (VC), and clinicians often consult public databases to clarify the status of variants from multiple sources. Discordant classifications (DCs) are a challenge for clinicians making BCRM recommendations. Studies have assessed DC rates for BRCA variants (1.5%), but there is little data for other HBC genes. This study aimed to quantify the DC rate in ClinVar for A/C/P given their impact on BCRM.

ClinVar was queried for A/C/P variants with DCs between ≥ 2 clinical labs. VCs were dichotomized based on impact on BCRM: positive (pathogenic/likely pathogenic) or negative (benign/likely benign/variant of uncertain significance). In cases where DCs impacted BCRM, each lab that submitted VCs prior to 2017 was contacted to determine if these variants had been reclassified. Only labs reporting to ClinVar were included in analysis, and reclassification of variants submitted in/after 2017 was not assessed.

Of 8217 clinically significant variants, 354 (4.3%) had DCs (1.2 DCs/variant). DCs in 38 (11%) variants affected BCRM and 27 (71%) of these were missense variants. Lab discussions revealed 7 variants had been reclassified since initial submission, of which 6 were upgraded to pathogenic. Overall, reclassifications resolved 4 of 38 prior DCs that impacted BCRM.

The DC rate in this study was higher than that reported for BRCA1/2 variants, extending concern regarding lack of standardized classification in the BRCA realm to other HBC genes. This study highlights the need for universal data sharing by labs, robust classification methods, and regular reclassification processes with timely notification of VC to public databases.
C-69 Clinical Implications for Individuals with Multiple Pathogenic Variants in Cancer Predisposition Genes

Cancer

Submitter: Megan L. Marshall, MS, LCGC, GeneDx

Primary Author: Megan L. Marshall, MS, LCGC, GeneDx

Author 2: Maegan Roberts, MS, LCGC, GeneDx

Author 3: Lisa Susswein, MS, MHA, CGC, GeneDx

Author 4: Melanie Baxter, ScM, CGC, GeneDx

Author 5: Amy Stettner, MS, LCGC, GeneDx

Author 6: Kathleen Hruska, PhD, FACMG, GeneDx

Author 7: Rachel Klein, MS, LCGC, GeneDx

Presenting Author: Melanie Baxter, ScM, CGC, GeneDx

Background: With the advent of multi-gene hereditary cancer panels, providers are increasingly ordering broader panels, possibly resulting in the identification of more than one pathogenic/likely pathogenic variant (PV), even in known mutation families. However, the clinical implications for the individual and their family have yet to be described. We aim to describe the clinical presentation and management impact for individuals with more than one PV. Methods: We retrospectively queried panel tests for individuals with more than one PV. Individuals with mosaic PVs, MUTYH heterozygous PVs with a second PV, and biallelic MUTYH PVs only were excluded. Individuals undergoing panel testing plus targeted analysis of a known familial variant were included as long as at least one PV was found on a panel. Genes were categorized based on the availability of published management guidelines. Results: In our cohort, 317 individuals had more than one PV, with 9 having 3 PVs, for a total of 643 PVs identified in 29 genes (2.7%, 317/11,874 total positives). Five of the nine with three PVs had two MUTYH PVs causing MUTYH-associated polyposis plus another PV. Of positive individuals, only 10.1% (32/317) were found to have one or more PVs in genes that did not have any associated management recommendations. Forty-nine percent (156/317) had at least two PVs in genes with no differences in management guidelines. Almost half (46.3%, 147/317) of individuals reported personal cancer histories consistent with all of the genes in which PVs were identified. Conclusions: Our data suggest that the identification of multiple PVs that predispose to cancer is not rare and could have significant implications on subsequent familial testing and medical management recommendations. Half of individuals had PVs in genes where at least one or more associated cancers differed between the genes and resulted in different management guidelines. Large multi-gene panels are valuable, especially in families with bilineal risk or that lack a clear presentation suggestive of a single-gene etiology.
INTRODUCTION Craniopharyngiomas are sellar region brain tumors accounting for 5% of pediatric intracranial tumors. Most pediatric cases are the adamantinomatous subtype, largely associated with somatic CTNNB1 mutations and Wnt signaling pathway overactivation. Strong germline associations are lacking for craniopharyngioma. However, several young adults with adamantinomatous craniopharyngioma (aCP) have been reported with clinical features and/or germline APC mutations causing Familial Adenomatous Polyposis (FAP). APC mutations are known to disrupt the Wnt signaling pathway with similar effect as CTNNB1 mutations. In this case series, somatic CTNNB1 and APC and germline APC variants were assessed in 27 pediatric patients with aCP. <br />

CASES Twenty-seven patients with a diagnosis of pediatric aCP were enrolled in a clinical research sequencing study. Of these, 6 had tumor sample available for tumor/normal testing. Tumor sequencing (whole genome, whole exome and RNA sequencing) revealed 4 tumors with CTNNB1 mutations; 1 tumor with insufficient quality; and 1 tumor with two APC mutations and no CTNNB1 mutation. The remaining 21 patients without available tumor sample had germline testing that included APC. Germline testing for APC was normal in all patients (n=26) except the patient with two tumor APC mutations for whom 1 mutation was determined to be germline in origin. <br />

DISCUSSION In our case series, 3.7% (1/27) patients with aCP had a germline APC mutation consistent with FAP. This case series highlights the
mutual exclusivity of CTNNB1 and APC mutations in aCP samples. This observation underscores the utility of aCP sequencing in determining who may benefit from germline APC testing, as proposed for pediatric hepatoblastoma, desmoid tumor and medulloblastoma. In aCP cases where a somatic CTNNB1 mutation is not identified, APC germline testing could be considered, even in absence of a family history of FAP. As well, this series demonstrates a potential expansion of the phenotype for FAP-associated pediatric brain tumors to include adamantinomatous craniopharyngioma.

C-75 Trends and Outcomes of Genetic Testing in Probands with Prostate Cancer Cancer
Submitter: Jenae Osborne, MS, CGC, University of Michigan Cancer Genetic Clinic
Presenting Author: Jenae Osborne, MS, CGC, University of Michigan Cancer Genetic Clinic
Primary Author: Jenae Osborne, MS, CGC, Michigan Medicine Dept Int Med, Div Mol Med and Genetics
Author 2: Erika Koeppe, Michigan Medicine Department of Int Med - Gastroenterology
Author 3: Michelle Jacobs, Michigan Medicine Dept of Int Med Div of Mol Med and Genetic
Author 4: Dianne Samad, Michigan Medicine Dept Int Med, Div Mol Med and Genetics
Author 5: Andrea Murad, Michigan Medicine Dept Int Med, Div of Mol Med and Genetics
Author 6: Monica Marvin, Michigan Medicine Department of Human Genetics
Author 7: Elena M. Stoffel, MD, Michigan Medicin Dept of Int Med -Gastroenterology

Purpose: For many years, hereditary causes of prostate cancer were overlooked. Recent studies suggest 12% of men with metastatic prostate cancer carry germline pathogenic variants associated with hereditary cancer, including hereditary breast and ovarian cancer syndrome and Lynch syndrome. With the advent of multigene panels and the decreasing cost, genetic testing is pursued by more individuals, including men with advanced (Gleason score ≥7) or metastatic prostate cancer. Here we examine trends and outcomes of genetic testing in probands with prostate cancer.<br /><br />Methods: We conducted retrospective chart reviews of patients with a personal history of prostate cancer referred to the UM Cancer Genetics Clinic from 9/1/99-4/30/18. Chi-Square and t-tests were used to compare probands with positive vs negative genetic testing. Number, type, and outcome of tests were tallied by year to assess temporal trends.<br /><br />Results: 101 men with prostate cancer underwent germline testing from 9/1/99 to 4/30/18. Since 2016, we observed a 5-fold increase in tests ordered with 45% of mutation carriers identified during this time period. Pathogenic variants were identified in 18/101 (18%) in genes associated Lynch syndrome (6), BRCA1 (2), BRCA2 (2), PALB2 (2), HOXB13 (2), ATM (1), Birt-Hogg-Dube (1), Cowden (1), and MEN1 (1). Germline mutation carriers tended to be younger (median age of diagnosis 54 vs 59 years) and to have more advanced cancers than negative probands.<br /><br />Conclusions: Genetic testing with multigene panels in recent years resulted in a higher yield of positive
test results among probands in our cohort, compared with previous years. The prevalence of germline pathogenic variants was higher in our cohort compared to published literature (likely due to ascertainment). Given the broad range of mutations, consideration of multigene panels for all men with advanced prostate cancer is important. Testing with multigene panels will lend further insight to the association of prostate cancer with moderate penetrance genes, such as PALB2, for which limited information is known.<br />

C-78 MSH2 mutation identified via somatic testing in primary anaplastic glioneuronal tumor leads to diagnosis of Lynch syndrome

_Cancer_

Submitter: Krista J. Qualmann, MS, CGC, The University of Texas Health Science Center at Houston

Primary Author: Krista J. Qualmann, MS, CGC, The University of Texas Health Science Center at Houston

Presenting Author: Krista J. Qualmann, MS, CGC, The University of Texas Health Science Center at Houston

Author 2: Sarah Azam, BS, UT MD Anderson Cancer Center UTHealth Graduate School

Author 3: Leomar Y. Ballester, MD, PhD, The University of Texas Health Science Center at Houston

Author 4: Shakti H. Ramkissoon, MD, PhD, Foundation Medicine, Inc.

Author 5: Sigmund H. Hsu, MD, The University of Texas Health Science Center at Houston

Author 6: Jay-Jiguang Zhu, MD, PhD, The University of Texas Health Science Center at Houston

Introduction. Primary brain tumors (PBT) are a known, although rare feature of Lynch syndrome (LS), with an estimated lifetime risk of 1-6%. We report the case of a patient with a grade III glioneuronal tumor and pathogenic MSH2 variant, for whom genetic counseling was prompted based on somatic tumor testing results.<br />

Case Report. A 42-year-old African American man underwent gross total resection of a left frontal lobe tumor. Surgical pathology identified an anaplastic glioneuronal tumor with overlapping features between anaplastic pleomorphic xanthoastrocytoma and glioblastoma. Tumor recurrence at 2, 48, and 57 months post-diagnosis was treated according to standard of care. The patient is alive and well 104 months post-diagnosis.<br />

Next-generation sequencing of 236 genes in the patient’s tumor identified pathogenic mutations in six: NF1, PDGFRA, ATM, TP53, CTNNA1, and MSH2. The tumor mutation burden (TMB) was 19 mutations per megabase (Mb). Germline genetic testing identified the same pathogenic MSH2 variant detected by somatic testing, resulting in a diagnosis of LS. Subsequent colonoscopy revealed a tubular adenoma and hyperplastic polyp. Family history was significant for early-onset colorectal cancer in the patient’s mother and multiple maternal relatives.<br />

Discussion. PBT is an atypical presenting feature of LS and glioneuronal tumors have not previously been reported. This case demonstrates the utility of somatic testing results in the identification of a rare individual. Studies evaluating the yield of germline variants after somatic testing
indicate a small, but significant number of tumors possess mutations related to hereditary cancer syndromes. Elevated TMB (≥20 mutations per Mb) is a marker for mismatch repair deficient tumors, including individuals with germline mutations. Elevated TMB predicts patients' response to immunotherapies; however, it is unclear if it is also an indicator for LS. Further research is needed to characterize emerging evidence and develop clinician guidelines for which somatic testing results warrant follow-up germline testing.

C-81 Clinical Challenges of VUS Findings in Families Highly Suspicious for Lynch Syndrome

Submitter: Dianne Samad, University of Michigan

Presenting Author: Dianne Samad, University of Michigan

Primary Author: Dianne Samad, Michigan Medicine

Author 2: Erika Koeppe, Michigan Medicine

Author 3: Michelle Jacobs, Michigan Medicine

Author 4: Monica Marvin, Michigan Medicine

Author 5: Andrea Murad, Michigan Medicine

Author 6: Jenae Osborne, Michigan Medicine

Author 7: Elena Stoffel, Michigan Medicine

Variants of uncertain significance (VUS) in hereditary cancer syndromes pose challenges for clinicians, patients and their families. While most VUS are eventually reclassified to benign, inconclusive results in families with high suspicion for inherited risk are more concerning. Between 9/1/99-4/30/18, 105 patients evaluated in the UM Cancer Genetics Clinic for personal and family histories of cancer were found to carry VUS in LS genes, 54% of which were identified since 1/1/15. We examined VUS results in Lynch Syndrome (LS) and present three examples illustrating the challenges in managing patients with VUS findings within families highly suspicious for LS.

Case 1: A 53-year-old female with colon cancer at 46, uterine cancer at 52, and a strong family history of uterine and colon cancer was found to carry a germline MLH1 VUS which had previously been identified in a cousin with colon cancer at 16. Despite high clinical suspicion for LS, family members had difficulty obtaining enhanced cancer risk screening. Genetic testing of several family members enabled the eventual reclassification of VUS to pathogenic 12 years later.

Case 2: Germline and somatic testing in a 60-year-old female with uterine cancer at 56 and family history of colon cancer revealed a MSH6 VUS and equivocal MSH6 tumor staining. The family had difficulty understanding the rationale for increased surveillance, but against genetic testing of relatives.

Case 3: A 47-year-old female with endometrioid ovarian cancer at 46 and
family history meeting Amsterdam II criteria was found to have a MSH6 VUS with concordant IHC staining. Family members had significant anxiety about cancer risk and appropriate screening recommendations due to the uncertain significance of genetic test results.<br />

Managing families with high suspicion for LS and inconclusive genetic test results is complex. Family letters, in-person counseling, communication with commercial labs and defining patients’ and providers’ responsibility for follow-up of VUS is necessary to ensure understanding of risk and appropriate surveillance.

C-84 Striving To Fulfill a Duty To Recontact - Efficacy of Mailed Letters
Cancer
Submitter: Lindsey Brooke Sawyer,
Primary Author: Lindsey Brooke Sawyer,
Presenting Author: Lindsey Brooke Sawyer,
Author 2: Heather Creswick, Virginia Commonwealth University
Author 3: Raymond Lewandowski, Virginia Commonwealth University
Author 4: Nicholas Setliff, Bon Secours Health
Author 5: John Quillin, Virginia Commonwealth University

Genetic testing options have grown exponentially. For hereditary cancer, specifically, multigene panel testing is replacing older single-gene approaches. Patients whose tests were previously uninformative could benefit from updated testing. Genetic counselors have to balance limited resources with a potential "duty to recontact" these patients. Research suggests patients desire recontact, but no studies have tested the efficacy of recontact efforts. This study investigated the efficacy of a recontact effort in a hereditary cancer clinic. We also explored the impact of four different recontact letters, randomized in a 2X2 factorial design. The study was approved by our institution's IRB. Patients who had negative genetic testing for single genes or conditions (i.e., not multigene panel testing) were mailed letters inviting them to schedule a follow-up appointment to discuss updated testing. Patients were randomized to receive one of four letters: a) emphasizing personal medical management implications, b) emphasizing implications on family members, c) emphasizing both personal and family implications, or d) a control letter. The proportion of patients who scheduled follow-up appointments was assessed one month after mailing. In exploratory analyses, we tested for associations of response rate with patient demographics and type of letter received. Letters were mailed to 587 patients who had initial testing between 2001 and 2015. Most patients were White (78%) and female (97%) with private insurance (65%). After one month 14 patients (2.4%, 95% CI: 1.1% to 3.6%) had scheduled an appointment. There were no statistically significant differences in response rate by type of recontact letter or patient demographics. This study suggests that recontacting patients about updated genetic testing by mail may not yield a significant response. The study is limited by a single method of recontact
and a short follow-up period. Nevertheless, results may inform opinions about whether recontact efforts via mailed letters fulfill a "duty to recontact".

C-87 Association of breast cancer by pathogenic CHEK2 variant type

Cancer

Submitter: Lillian Kane Servais, Color Genomics

Presenting Author: Lillian Kane Servais, Color Genomics

Primary Author: Lily Servais, Color

Author 2: Anjali Zimmer, Color

Author 3: Jeroen van den Akker, Color

Author 4: Ofri Leitner, Color

Author 5: Alicia Y. Zhou, Color

Introduction: Previous studies of the association of CHEK2 variants with cancer are limited by enrichment for people who met insurance criteria for genetic testing or have a strong personal and/or family history of cancer. We address this by examining a broader population that underwent panel testing for hereditary cancer risk to determine if variant type impacts association.

Hypothesis: Association of CHEK2 variants with breast cancer differs by variant type.

Methods: The cohort consisted of females who received a 19- or 30-gene panel for hereditary cancer risk by provider order. Included in this analysis were females who tested at ≥40 years old and had a likely pathogenic (LP) or pathogenic (P) variant identified in CHEK2 only (positives), or had a negative result (negatives). Analysis was limited to CHEK2 variants with a consensus classification of LP or P in ClinVar, defined as having at least 2 LP/P classifications reported and at least 2/3 consensus on the classification. Personal history of cancer was reported by the individual or ordering provider. Family history of cancer was not analyzed.

Results: The average age at testing was slightly higher (p=0.02, two-tailed t-test) for positives (55.4 years, n=482) vs negatives (56.6 years, n=14,542). When combining all LP/P CHEK2 variants, there was no significant association with breast cancer (OR=1.18, 95% CI: 0.96-1.44). Missense variants (the majority of which were p.I157T and p.S428F) did not show an association (OR=0.96, 95% CI: 0.71-1.29). However, truncating (nonsense and frameshift, the majority of which were c.1100delC) and copy number variants (CNVs) did show a modest association (OR=1.41, 95% CI: 1.06-1.88).

Conclusions: Overall, CHEK2 LP/P variants were not associated with a personal history of breast cancer unless variants were segregated by type. The data support that truncating variants and CNVs are moderately associated with breast cancer risk. This finding lends to the potential for genotype-phenotype correlations based on CHEK2 variant type, and may be useful for future management recommendatio
C-90 Family and provider comfort with pharmacogenetic testing for a pediatric oncology population

Cancer
Submitter: Joyce Tannenbaum Turner, Children's National Medical Center
Presenting Author: Joyce Tannenbaum Turner, Children's National Medical Center
Primary Author: Joyce Tannenbaum Turner, Children's National Medical Center
Author 2: Catriona Mowbray, Children's National Medical Center
Author 3: Elena Postell, Children's National Medical Center
Author 4: Christina Waggaman, Children's National Medical Center
Author 5: Shana Jacobs, Children's National Medical Center

Our research aims to use pharmacogenetic (PGx) testing to personalize treatments for pediatric oncology patients with the goal of reducing side effects and symptoms associated with cancer treatment. We surveyed the comfort level of PGx testing and interpretation among families and providers. An anonymous survey was emailed to pediatric oncology providers. It addressed comfort with ordering and interpreting PGx testing. Guardians of children with cancer approached for a larger PGx study were asked to complete a similar PGx survey. 82% of providers completed the survey. The majority of respondents reported not receiving any formal training in PGx (0-26 years since training). Only 7% agreed training had prepared them for PGx testing. A majority (62%) reported ordering a PGx test for variations in thiopurine metabolism prior to prescribing thiopurines. Many respondents rarely order other PGx tests: 52% order such a test 1-2 times a year, while 31% have never ordered one. Only 19% of respondents felt comfortable with interpreting results. 87% of families completed their survey (n=57). The majority had heard about genetic testing (68%). Most had not had genetic testing for inherited disease (68%) or drug metabolism (90% self, 76% child), however nearly all were interested in their child having PGx testing (91%). Most were comfortable with genetic test information being part of the electronic medical record (76%), although there was concern about health or life insurance discrimination (40%) or payment (38%). Unexpected results (23%) and being unable to understand the results (9%) were less common concerns. Overall, providers are aware of the importance of PGx testing, though lack adequate understanding of what to do with results and desire additional support. Families of children with cancer want genetic information. We plan to assess the value of PGx in personalizing the care of our patients.<br /><br />

C-93 Utilization of Statistical Breast Cancer Risk Prediction Models by Genetic Counselors in Clinical Practice

Cancer
Submitter: Min Seon Park,
Presenting Author: Min Seon Park,
Primary Author: Scott M. Weissman, Chicago Genetic Consultants, LLC
Author 2: Suzanne M O'Neill, Northwestern University Feinberg School of Medicine
Author 3: Carmen Williams, Northwestern Medical Group
Author 4: Caitlin Mauer, Simmons Comprehensive Cancer Center UT Southwestern
Author 5: Kristen Postula, GeneDx

Purpose: We explored genetic counselors’ breast cancer risk model usage patterns including frequency of use, reasons for using or not using models, and change in usage since the adoption of multi-gene panel testing.

Methods: An online survey was developed for this study and sent out to members of the National Society of Genetic Counselors who see patients for cancer risk assessment and genetic testing.

Results: A total of 231 responses were included in our analyses. Two hundred fifteen respondents (93%) indicated use of at least one of six breast cancer risk prediction models assessed in this study. Among the six models, the Tyrer-Cuzick model was the most used and the BOADICEA model was the least used. The two most common reasons for not using models were difficulty navigating through and time needed to use a breast cancer risk model. Usage patterns of the models were mostly consistent with the use the model was validated for, but many respondents reported using models for reasons not intended (e.g., PENNII for MRI risk assessment or Gail model for genetic testing eligibility).

There were no statistically significant associations between the frequency of use of each model and any demographic factors. The majority of respondents reported no change in use since the adoption of the multi-gene panel testing. Among the respondents who reported a change in use, the BRCAPRO model had the largest decrease in use while the BOADICEA model had the largest increase in use.

Conclusion: The results showed that breast cancer risk prediction models are being widely used by cancer genetic counselors in their clinical practice. This study provides insight into perceived benefits and limitations of models in clinical use, which might be valuable information for software developers, genetic counseling program curriculum developers, and currently practicing cancer genetic counselors.

C-96 Cancer genetic counselors’ experiences with transgender patients: an exploratory qualitative study

Cancer
Submitter: Kimberly Zayhowski,
Presenting Author: Kimberly Zayhowski,
Primary Author: Kimberly Zayhowski, Stanford University School of Medicine
Author 2: Jessica Park, Stanford University School of Medicine
Author 3: Ulrike Boehmer, Boston University School of Public Health
It is becoming increasingly common for people to openly identify as transgender, yet there is little research in the field of genetic counseling regarding this community’s unique medical needs. Transgender patients are likely to present with issues that cross genetics and gender related care in a cancer genetic counseling session, and empiric data about these differences is needed to provide adequate care. In order to investigate what specific health topics and concerns are addressed in cancer genetic counseling sessions with transgender patients, 21 cancer genetic counselors who have seen transgender patients were interviewed. Through inductive analysis, six themes emerged: 1) documentation systems are not inclusive or clear, 2) genetic counselors feel unprepared for these sessions, 3) gender affirming hormones impact risk assessment, 4) genetic testing affects gender affirming surgical decisions, 5) young transgender patients often present to clinic, and 6) pathogenic variants allow for insurance coverage of gender affirming surgeries. This study’s findings point to opportunities for the field of genetic counseling to enhance services for transgender patients by reporting distinctive situations that may arise in clinic with these patients and providing training recommendations for genetic counselors.

A-100 BRCA-related phenocopy in arrhythmogenic cardiomyopathy
Cardiology
Submitter: Robyn Hylind, 1989
Primary Author: Robyn Hylind, 1989
Presenting Author: Robyn Hylind, 1989
Author 2: Stephanie Chandler, Boston Children’s Hospital
Author 3: Stephanie Harris, Brigham and Women’s Hospital
Author 4: Neal Lakdawala, Brigham and Women’s Hospital
Author 5: Dominic Abrams, Boston Children’s Hospital

Introduction
Arrhythmogenic cardiomyopathy (ACM) is an inherited cardiac disorder with several well-known phenocopies, mandating accurate clinical and genetic evaluation to define familial inheritance patterns and guide cascade screening. This report details an unrecognized phenocopy of ACM producing inverted T-waves in the parent of a child with a clinical diagnosis of ACM.

Case Report
A 16-year-old male presented following a non-exertional, out-of-hospital cardiac arrest and successful resuscitation. His electrocardiogram (ECG) showed sinus bradycardia, T-wave inversions in the V1-V3 and terminal activation delay >55ms. Cardiac MRI demonstrated a dilated right
ventricle (175mls/m2), akinetic and dyskinetic wall motion and focal aneurysms with an ejection fraction of 28%. A diagnosis of ACM was made based on 2010 Task Force Criteria (TFC).

His asymptomatic parents were evaluated. His mother had a history of palpitations, and bilateral prophylactic mastectomy with reconstructive surgery following identification of a pathogenic variant in BRCA1. As her ECG showed T-wave inversion in the precordial leads, she fulfilled TFC. A holter monitor showed infrequent ventricular ectopy, and her MRI was normal. His father had a normal ECG and echocardiogram. Genetic testing in the proband identified a novel loss of function PKP2 variant (c.951delG; p.H318TfsX2), classified as likely pathogenic. Cascade testing identified the variant was paternally inherited.

Discussion
This case illustrates non-cardiac etiology of T-wave inversion related to reconstructive breast surgery, a factor increasingly recognized to cause ECG abnormalities. However, given the varied and low penetrance of variants associated with ACM, and prevalence of loss of function desmosomal variants in control populations, detailed clinical and genetic evaluation is necessary to accurately define inheritance patterns and identify family members at risk.

A-103 Expanding the clinical phenotype for Marfan syndrome

Cardiology
Submitter: Rebecca Miller, INOVA Health System

Presenting Author: Rebecca Miller, INOVA Health System

Primary Author: Rebecca Miller, Inova Health System

Author 2: Palak Shah, Inova Heart and Vascular Institute

Marfan syndrome (MS) is a rare connective tissue disorder associated with a set of defined clinical measures known as the Ghent Criteria. The criteria was developed to facilitate accurate recognition of the syndrome and to improve patient management and counseling. Recently, however, there is evidence to suggest that the criteria should be expanded to include even phenotypically normal patients who have a pathogenic or likely pathogenic FBN1 variant. We review a case example emphasizing the expanding clinical phenotype of MS in a positive genotype family. Our patient is a 40-year-old female who came to clinic with a recent family history of MS genetically diagnosed in her 7-year-old niece. The presenting symptoms in the patient’s niece were tall stature and a pectus excavatum. The patient’s niece was found to carry a pathogenic variant in FBN1 (C7754C>T). Further investigation of the family history revealed that the pathogenic FBN1 variant was inherited from our patient’s sister who had no clinical findings associated with MS. Our patient had three minor criteria findings. Targeted genetic testing was ordered for the familial known pathogenic variant in FBN1. Genetic testing revealed that our patient also carries the pathogenic variant. This family is one example illustrating the wide phenotypic variability of MS and the consideration of further expanding the clinical criteria requirements in this well-established genetic condition. Recent research has echoed the presence of phenotypic variability in FBN1 likely pathogenic and pathogenic families. One study found that in 40% of patients evaluated for an isolated aortic dissection/dilation, a pathogenic or likely pathogenic variant in FBN1 was identified.
but no additional clinical features of MS were documented. This case example and recent research study highlights the need for expanding the phenotype for FBN1 related disorders.

A-106 Beyond FBN1: Multigene Panel Testing for Marfan syndrome

Cardiology

Submitter: Zoe Powis, Ambry Genetics

Primary Author: Zoe Powis, Ambry Genetics

Presenting Author: Zoe Powis, Ambry Genetics

Author 2: Lily Hoang, Ambry Genetics

Author 3: Tami Johnston, Ambry Genetics

Author 4: Christian Antolik, Ambry Genetics

Author 5: Andrew Castro, Ambry Genetics

Author 6: Jill S. Dolinsky, Ambry Genetics

Introduction: With clinical overlap between Marfan syndrome (MFS) and connective tissue disorders, diagnosis may not be clear without genetic testing. Multigene panel testing for (MGPT) may confirm clinical diagnosis or establish diagnosis in individuals in whom clinical features do not meet established guidelines. Identifying a genetic etiology may aid counseling and medical management, leading to improved prognosis. Herein, we sought to assess the phenotypic spectrum of individuals with clinical features of MFS who underwent MGPT for MFS. Methods: We performed a retrospective analysis of provided clinical records and results from a 22 gene panel test for MFS and thoracic aortic aneurysm/dissection (TAAD) (ACTA2, CBS, COL3A1, COL5A1, COL5A2, FBN1, FBN2, FLNA, MED12, MYH11, MYLK, NOTCH1, PLOD1, PRKG1, SKI, SLC2A10, SMAD3, SMAD4, TGFBI2, TGFBI3, TGFBR1, TGFBR2) for 1462 sequential patients with reported MFS clinical features. Results: Overall, 142 patients (9.7%) had positive results. Of these 142 patients, 52 (36.6%) were positives in genes other than FBN1. Patients with aortic aneurysm/dilation, aneurysms in other arterial locations, aortic/vascular dissection, myopia, scoliosis and/or joint hypermobility were more likely to have findings in genes other than FBN1 (all p < 0.0001) as were patients with pectus deformity and/or facial clefts (p= 0.0013, 0.0068, respectively). Two (3.8%) patients with a clinical diagnosis of MFS were positive in TGFBI2 and SMAD4. There were no differences in other reported clinical features or family history in patients with FBN1 mutations versus other genes. Conclusions: Our data suggests that individuals with clinical features of Marfan syndrome may benefit from MGPT, especially when features overlap with other associated conditions. An appropriate molecular diagnosis may lead to a more successful and appropriate treatment plan. These data emphasize the importance of counseling patients with features of MFS about the likelihood of a positive result in many overlapping conditions within the clinical spectrum.
**A-109 Titin-Related Cardiomyopathy in a Pediatric Population: A Case Series**

*Cardiology*

Submitter: AMY SHIKANY, The Heart Institute, Cincinnati Children's Hospital Medical Center

Primary Author: AMY SHIKANY, The Heart Institute, Cincinnati Children's Hospital Medical Center

Presenting Author: AMY SHIKANY, The Heart Institute, Cincinnati Children's Hospital Medical Center

Author 2: Erin M Miller, Cincinnati Children's Hospital

Author 3: Ashley S Parrott, Cincinnati Children's Hospital

Introduction: Truncating variants primarily in the A-band of Titin (TTN) are a common cause of dilated cardiomyopathy (DCM), accounting for 18-25% of cases. TTN-related DCM has a high penetrance (>95%) after the age of 40 years, and is mostly regarded as a disease of mid-adulthood. Few cases of TTN-related cardiomyopathy have been reported in children. 

Case Reports: In this report we describe four cases of individuals <18 years old diagnosed with TTN-related DCM. Case 1 is a 17 year old male who presented with symptomatic heart failure. His left ventricular ejection fraction (LVEF) was 18% and left ventricular end-diastolic dimension (LVEED) z-score was 4.7. DCM gene panel revealed TTN variant c.86582G>A. He required a left ventricular assist device (LVAD) and subsequent heart transplant (HT). Case 2 is a 14 year old male who presented with exercise intolerance. His LVEF was 45% and LVEED z-score was 2.97. DCM gene panel revealed TTN variant c.96175delGinsCT. Case 3 is a 13 year old male who presented with symptomatic heart failure. His LVEF was 27% and LVEED z-score was 3.94. DCM gene panel revealed TTN variant c.10361G>A. He required a LVAD and subsequent HT. Case 4 is a 3 year old female who initially presented after an abnormal electrocardiogram. Her LVEF was 45% and LVEED z-score was 2.79. DCM gene panel revealed TTN variant c.73146C>G.

Discussion: TTN-related DCM is not strictly an adult onset condition, our series includes two adolescents with severe disease requiring HT. TTN analysis should be included for individuals who present with DCM in childhood. Furthermore, genetic counseling regarding risk for TTN-related cardiomyopathy should include individuals of all ages with initiation of cardiac screening for TTN gene positive, at-risk individuals regardless of age. 

**A-112 Genetic mutation and copy number variation in pulmonary arterial hypertension associated with congenital heart disease**

*Cardiology*

Submitter: xuan zheng, Wuhan Asia Heart Hospital

Primary Author: xuan zheng, Wuhan Asia Heart Hospital

Presenting Author: xuan zheng, Wuhan Asia Heart Hospital
Introduction
Pulmonary arterial hypertension (PAH) is characterized by increased blood pressure in pulmonary arteries, and impaired right heart function in the late-stage of the disease. Different from the epidemiology in developed country, congenital heart disease (CHD) is the first cause of PAH in China. Though mutations in BMPR2 has been widely associated with the development of PAH, whether the copy number variation contributes to PAH-CHD remains unclear.

Hypothesis
We hypothesized that genetic mutation as well as copy number variation (CNV) played important role in the development of PAH-CHD.

Methods
A total of 12 PAH-CHD patients admitted in Wuhan Asia Heart hospital was included in this pilot study. A genetic test including BMPR2, ACVRL1, ENG, KCNK3, CAV1, SMAD4, SMAD9, GDF2 and other previous reported genes was applied to all patients. CNV analysis was performed at the same time.

Results
Patients were aged from 3 to 39 years, including two males and ten females. PAH was diagnosed by right cardiac catheterization. Two pathogenic mutations in BMPR2 was identified in two patients (17.7%), three variants of uncertain significance from different genes were identified in three patients (25.0%). A pathogenic CNV was found in one patient (8.3%).

Conclusions
Genetic mutations were identified in half of PAH-CHD in our study. However, the pathogenic CNV was associated with CHD. Additionally, pathogenic mutations were only seen in BMPR2. Our study may over-estimated the epidemiology of genetic associated PAH-CHD due to the small size of patients. 50% of VUS mutations also lead to an uncertainty of genetic contribution. The role of genetic mutation as well as CNV in the development of PAH-CHD still needs further investigation.
Introduction 
Arterial Tortuosity Syndrome (ATS) is a rare condition inherited in an autosomal recessive pattern, and affects connective tissue mostly. It’s characterized by tortuosity and elongation of large and medium-sized arteries. Mutations in SLC2A10 gene has been identified in ATS patients, which lead to a defect of glucose transporter 10 (GLUT10). Since only about 100 patients have been reported, the clinical features of ATS remain further identified. Here, we report a two-month old patient presenting ATS. 

Case report
This patient was a two-month old male baby from unrelated parents. He was their first baby and was naturally delivered. He presented dyspnea and cough after birth. The patient was admitted due to a loss of consciousness while crying. Physic examination showed normal growth, but facial abnormality and skin hyperextensibility in the patient. He also had a right inguinal hernia. Cardiac echography showed a normal heart, but tortuosity of artery. CT scan provided further imaging evidences of artery elongation, aneurysm, and tortuosity. Development of bronchi, trachea and colon was obviously delayed in this patient. Genetic testing identified two mutations in SLC2A10, one of which was a pathogenic mutation inherited from father, another was a novel VUS mutation inherited from mother. Though the patient was stable under the intensive medical support, parents refused further treatment. The patient died from respiratory distress soon after discharge.

Discussion
Being a disease inherited in an autosomal recessive pattern, two copies of mutation in SLC2A10 lead to a set of marked abnormalities in ATS. Early onset of severe symptoms is associated with premature mortality in ATS patients. Our patient here presented tortuosity of artery and delayed development of bronchi, trachea and colon. Compound heterozygosity in SLC2A10 may contribute to the rapid progress of ATS in our patient.

B-104 Penetrance of HCM in At-risk Children and Young Adults is Related to Gene Mutation Status

Cardiology
Submitter: Erin M Miller, Cincinnati Children's Hospital Medical Center

Presenting Author: Erin M Miller, Cincinnati Children's Hospital Medical Center

Primary Author: Erin M. Miller, MS, LGC, Cincinnati Children’s Hospital Medical Center

Author 2: Tyler Meyer, none

Author 3: Xue Zhang, PhD, MsPH, Cincinnati Children’s Hospital Medical Center

Author 4: Thomas D. Ryan, MD, PhD, Cincinnati Children's Hospital Medical Center
Hypertrophic cardiomyopathy (HCM) is a common, autosomal dominant condition defined by unexplained left ventricular hypertrophy with risk for heart failure and sudden death. Genetic testing is recommended for probands, with a pathogenic variant identified in approximately 50-60%. HCM affects individuals of all ages, and expert consensus guidelines recommend screening for at-risk individuals which vary in regards to age and frequency. The penetrance of HCM is considered to be age-dependent, but there are limited data defining disease risk in young individuals. We sought to define the penetrance of HCM in children and young adults (0-35 years of age) and define factors influencing risk. A retrospective medical record review was used to identify at-risk individuals with an affected first-degree relative and/or a pathogenic variant in a gene known to confer HCM risk. Of 141 at-risk individuals identified, 16% (n=23) were diagnosed with HCM. The age of diagnosis ranged from infancy to 28 years with 70% (n=16) diagnosed under the age of 18 years, 43% (n=10) under the age of 12, and 13% (n=3) under the age of one year. The only factor found to be a significant predictor of HCM penetrance was gene status. Twenty-two (32%) of the gene positive, at-risk individuals were diagnosed with HCM compared to one (2%) at-risk individual without a pathogenic variant in the family (p<0.001, Fisher’s exact test). In this single family, there was a variant of unknown significance which segregated with disease. No at-risk individuals were diagnosed with HCM from families in which the proband had a negative gene panel. These data support initiation of cardiac screening in infancy or at the time risk status is confirmed. In addition, findings should inform family counseling with reassurance, but not removal, of disease risk for young individuals from mutation negative families with potential consideration of less frequent screening.

B-107 Cardiovascular Genetics: Getting a "Pulse" on How Cardiologists Assess and Act on Cardiogenetic Findings that may Lead to Sudden Cardiac Death

Cardiology
Submitter: Anna Danielle Levy,

Presenting Author: Anna Danielle Levy,

Primary Author: Samone Schneider, Jacobi Medical Center

Author 2: Tamar Peri Ailenberg, Scarbarough Rouge Hospital

Author 3: Anna Schon Levy,

Author 4: Laura Hercher, Joan H. Marks Program in Human Genetics at Sarah Lawrence

Author 5: Samantha Freeze, Indiana University School of Medicine
Sudden cardiac death (SCD), defined as an unexpected death due to cardiac causes, is the leading cause of non-random death in young athletes. This study surveyed cardiologists to examine clinical practice with regard to genetic testing of competitive athletes for risk of SCD and their use of genotypic information to inform recommendations for restriction of athletic participation. To our knowledge, there are no previous studies that examine cardiologists’ use of genetic testing in young athletes. A survey was sent out through the ACC Sports and Exercise Section email list and a University of Vermont Medical Center listserv. The survey received 73 responses, 68 of which were completed in entirety. Four knowledge-based questions were used to create a rating scale. Just under 25% of cardiologists incorrectly answered a question regarding the appropriate interpretation of variants of uncertain significance (VUS’s). Results suggest that physicians are unfamiliar with practice guidelines as they relate to VUS’s. Clinical practice varies regarding activity restriction for competitive athletes who have a clinical diagnosis of Long QT syndrome (LQTS) as well as for athletes who are genotype-positive, phenotype-negative for LQTS. For patients with a clinical diagnosis of Hypertrophic Cardiomyopathy (HCM), only half of respondents chose to strongly recommend activity restriction despite the fact that this is recommended in practice guidelines; this was true for genotype-positive and genotype-negative patients. The results indicate that there is a lack of knowledge among cardiologists pertaining to VUS’s as well as a lack of consensus with regards to activity restriction recommendations pertaining to HCM and LQTS.

B-110 Stepping in and out of uncertainty: Views of receiving a genetic variant reclassification in patients with inherited cardiac disease

Cardiology
Submitter: Eugene King Wong,
Primary Author: Eugene King Wong,
Presenting Author: Eugene King Wong,
Author 2: Kirsten Bartels, Inherited Arrhythmia Program, St Paul’s Hospital, BC Canada
Author 3: Julie Hathaway, Inherited Arrhythmia Program, St Paul’s Hospital, BC Canada
Author 4: Charlotte Burns, Molecular Cardiology Program, Centenary Institute, NSW Aus
Author 5: Laura Yeates, Molecular Cardiology Program, Centenary Institute, NSW Aus
Author 6: Chris Semsarian, Molecular Cardiology Program, Centenary Institute, NSW Aus
Author 7: Andrew Krahn, Inherited Arrhythmia Program, St Paul’s Hospital, BC Canada
Author 8: Alice Virani, Provincial Health Services Authority, BC Canada
Author 9: Jodie Ingles, Molecular Cardiology Program, Centenary Institute, NSW Aus
Advances in genomic technology have revolutionized clinical testing, with larger gene panels often including genes with limited evidence of disease association. This has led to increased detection of novel variants, posing challenges for the interpretation of pathogenicity. A variant’s pathogenicity status is probabilistic, weighing up the evidence available at the time. Periodic reclassification is necessary, and a clinically significant change in classification can alter medical therapy and family surveillance. Here we explore the patient experience of receiving a cardiac genetic variant reclassification.

We conducted a qualitative study of patients with inherited cardiac diseases, and who received a clinically significant variant reclassification. Participants were recruited internationally from two specialised multidisciplinary cardiology clinics (Vancouver, Canada; Sydney, Australia). We conducted semi-structured phone interviews with participants and analyzed the transcripts based on a modified grounded theory approach. A total of 15 participants were interviewed, including 9 with inherited cardiomyopathies and 6 with inherited arrhythmia syndromes. There were 6 participants that experienced a variant upgrade, and 9 had a variant downgrade. Four broad themes emerged: 1) reactions towards the reclassified variant; 2) impact on decision-making; 3) perception of the reclassification process; and 4) improving the reclassification process. Overall, participants did not express feeling any long term impact after a variant reclassification. However, some misunderstood the implications of their reclassified result, impacting their reaction and decision-making. Most participants reported an expectation that variants were automatically undergoing periodic review by their health providers.

Variant reclassification occurs and can be problematic. We highlight a need to reconsider our genetic counselling strategies when returning reclassified variants. Maintaining open communication with patients throughout the process of variant reclassification may be beneficial.

B-98 Variants at the p.Arg453 Locus in MYH7 Associate with Severe, Pediatric Hypertrophic Cardiomyopathy

Cardiology
Submitter: Emily Brown, MGC, CGC, Johns Hopkins Hospital
Presenting Author: Emily Brown, MGC, CGC, Johns Hopkins Hospital
Primary Author: Emily Brown, MGC, CGC, Johns Hopkins University
Author 2: Lili A. Barouch, MD, Johns Hopkins University
Author 3: Jane E. Crosson, MD, Johns Hopkins University
Author 4: Daniel P. Judge, MD, Medical University of South Carolina
Author 5: Anne M. Murphy, Johns Hopkins University

Introduction
Hypertrophic cardiomyopathy (HCM) is an autosomal dominant condition associated with an increased risk for heart failure and/or sudden death. Minimal genotype-phenotype correlations have been established; however, often in severe pediatric cases, the patient carries at least
two pathogenic variants. Here we report that pathogenic variants at a specific locus in MYH7 are associated with severe, early-onset HCM. A retrospective review identified seven patients from five families who were seen at the Center for Inherited Heart Disease at Johns Hopkins between 2003 and 2017 and carried a pathogenic substitution at the 453rd amino acid in MYH7. Three individuals harboured the pathogenic variant p.Arg453Ser, while the four remaining individuals carried the pathogenic variant p.Arg453Cys. Variants were classified according to the 2015 ACMG guidelines. All seven individuals had severe, early-onset HCM. Mean age of diagnosis was 8.8 years old with a range from in utero to 21 years old. The majority of patients had a family history of hypertrophic cardiomyopathy (n=5, 71%) and a family history of sudden death (n=4, 57%). One patient underwent a heart transplant due to heart failure, and another patient had a surgical myectomy. Average septal thickness was 2.3cm (n=6), and the average z-score was 10.2 (n=4). Four patients received ICDs, and one patient received an appropriate shock for arrhythmias. Mean follow-up time was 7.8 years. While variable expressivity is common in HCM, pathogenic variants at this locus appear to be associated with a severe, paediatric form, given that none of our patients were diagnosed after 21 years old and all had severe hypertrophy. Therefore, we recommend familial screening begin in infancy for at-risk family members. Additionally, this information regarding severity may be useful in discussing prognosis. In summary, correct recognition of the severity of these pathogenic variants is important for estimating prognosis, counselling families, and guiding screening.

C-102 The Value of Post-Mortem Genetic Testing in Individuals with Sudden Death in a Large Urban Setting: A Custom Cardiovascular Genetics Panel in an Internal Molecular Genetics Laboratory at a Medical Examiner’s Office

Cardiology
Submitter: Elizabeth Paige Manderski,
Presenting Author: Elizabeth Paige Manderski,
Primary Author: Elizabeth Manderski, sarah lawrence college
Author 2: Sarah Stewart, sarah lawrence college

Purpose: To determine positive phenotypic predictors of clinically actionable variants and to formulate inclusion guidelines for testing those with sudden death through the use of a post-mortem 95 cardiac gene panel in the diverse New York City (NYC) population.

Methods: 254 participants with sudden death underwent post-mortem testing utilizing a 95 cardiac gene panel between Oct 2015-Feb 2018. Next Generation Sequencing and variant interpretation were performed internally at the NYC Office of the Chief Medical Examiner (OCME) following American College of Medical Genetics and Genomics guidelines. Medical information was collected from the OCME internal records. Chi-square tests were used to investigate categorical predictors of pathogenic genetic test results.

Results: Of 319 genetic test results, 51.4% (n = 164) were variants of uncertain significance, 9.1% (n = 29) were clinically
Clinically actionable variants were found in 51 of the 95 genes sequenced. Positive predictors of pathogenic genetic test results were significant personal medical history, significant family history, and heart findings on autopsy. Conclusion: The results support widespread testing on all sudden death cases; however, this may not be feasible everywhere due to limited resource or financial allocations. This study identified the benefits of having a genetic counselor involved in the post-mortem genetic testing process and offered suggestions for inclusion criteria in testing for heritable cardiac conditions after sudden death.

C-105 Comprehension of uninformative genetic testing results in hypertrophic cardiomyopathy and suggestions for an improved report supplement

Cardiology

Submitter: Brooke Moriarty Nightingale, The Ohio State University

Primary Author: Brooke Moriarty Nightingale, The Ohio State University

Presenting Author: Brooke Moriarty Nightingale, The Ohio State University

Author 2: Shelly Hovick, PhD, The Ohio State University

Author 3: Pamela Brock, MS, LGC, The Ohio State University

Author 4: Emily Callahan, The Ohio State University

Author 5: Elizabeth Jordan, MS, LGC, The Ohio State University

Author 6: Ana Morales, MS, LGC, The Ohio State University

Empiric observation suggests that patients with hypertrophic cardiomyopathy (HCM) may misinterpret uninformative genetic testing results (negative or uncertain) to mean that a genetic etiology is ruled out and relatives are not at risk. A clinical diagnosis of HCM, after other causes are excluded, implies a genetic etiology. With uninformative results in a proband, first-degree relatives remain at up to 50% risk and periodic screening is recommended. Screening uptake, however, is not optimal and may be due to misunderstanding of their result. The aims of this study are to evaluate understanding of lab reports with uninformative results and communication with relatives, as well as elicit suggestions for an improved laboratory report supplement. To our knowledge, this topic has not been previously studied. Fifteen participants had interviews, which underwent thematic analysis. Eight received a laboratory patient supplement. All partially read their report. Eleven did not understand the information presented on the report, or only partially understood it because their provider explained it to them. Interview-based assessment revealed that eight understood the meaning of their result. Participant self-assessment of how the report helped with result understanding revealed that six found the report helpful. Of these, three illustrated misunderstanding of their results, and five stated elsewhere that some aspects of the report were unhelpful. Twelve communicated risk with relatives, but none said the report helped. Lastly, twelve could not recall or did not find the counseling letter useful. Participants
suggested report improvements, including a personalized summary illustrating at-risk relatives and clinical recommendations. In conclusion, uninformative laboratory reports or letters were not helpful to our participants, and the laboratory supplement did not fill this gap. Research is indicated to validate our findings and explore the utility of an enhanced tool, such as a supplement template provided by the laboratory and personalized by clinical genetic counselor.

C-108 Family Experiences of Inpatient Genetic Counseling for Infant Congenital Heart Defects and Cardiomyopathies: A Qualitative Pilot Study

Cardiology
Submitter: Victoria Schwarzinger,

Primary Author: Victoria Schwarzinger,

Presenting Author: Victoria Schwarzinger,

Author 2: Benjamin M. Helm, Indiana University School of Medicine
Author 3: Samantha L. Freeze, Indiana University School of Medicine
Author 4: Katherine G. Spoonamore, Indiana University School of Medicine
Author 5: Lindsey Elmore, Indiana University School of Medicine
Author 6: Melissa Lah, Indiana University School of Medicine
Author 7: Benjamin J. Landis, Indiana University School of Medicine
Author 8: Stephanie M. Ware, Indiana University School of Medicine

Genetic testing and counseling are frequently indicated in infants with congenital heart defects (CHDs) and cardiomyopathy. These conditions may be associated with lengthy hospitalizations, but there have been no previous studies assessing the delivery of genetic counseling in hospital inpatient settings. There is a need to assess parent experiences and perceptions of inpatient genetic counseling in order to define best practices. We conducted in-depth, semi-structured telephone interviews with parents who received genetic counseling during their affected child’s hospital admission. Interviews were recorded, transcribed, and analyzed using grounded theory methodology. This uses the constant comparative method where responses are coded and compared within and across interviews, allowing for the identification of themes to determine a final theory. A total of 10/45 (22%) in-depth interviews were completed with families seen for cardiomyopathy or left-sided CHDs. The majority (8/10, 80%) preferred to receive these services during hospital admission vs. an outpatient appointment. Common themes emerged, including: families prefer inpatient genetic counseling to be scheduled and to occur in the child’s hospital room in a timely manner, it is appropriate to discuss reproductive risks/options while inpatient, and family screening recommendations should be repeated following discharge. Results from this study suggest that providing genetic counseling in the inpatient setting is helpful, with a majority of
families reporting positive experiences overall. Timely delivery of genetic counseling is important for most families in this study. The findings suggest that families preferred to be given the option of scheduling a specific time for the genetic counseling discussion. Parents noted that additional follow-up discussions would be beneficial, especially regarding family screening recommendations. Overall, parents reported positive experiences with inpatient genetic counseling, and centers should work to improve these services in accordance with family preferences.

C-111 Balanced translocation disrupting SCN5A in a family with Brugada Syndrome and sudden death

Cardiology

Submitter: Laura Yeates, Centenary Institute and Royal Prince Alfred Hospital

Presenting Author: Laura Yeates, Centenary Institute and Royal Prince Alfred Hospital

Author 5: Richard D. Bagnall, Centenary Institute

Primary Author: Laura Yeates, Centenary Institute and Royal Prince Alfred Hospital

Author 2: Jodie Ingles, Centenary Institute and Royal Prince Alfred Hospital

Author 3: Belinda Gray, Centenary Institute and Royal Prince Alfred Hospital

Author 4: Christopher Semsarian, Centenary Institute and Royal Prince Alfred Hospital

Brugada Syndrome (BrS) is a rare primary arrhythmia syndrome. Up to 25% of familial BrS have a pathogenic variant in the sodium voltage-gated channel alpha subunit 5 gene (SCN5A). Balanced translocations occur in 1 in 500 of the general population.

Family TD presented after the sudden death of their son, age 20 years. Post-mortem examination revealed asymmetric left ventricular hypertrophy and histology consistent with possible hypertrophic cardiomyopathy. Clinical screening of the family with echocardiogram and standard ECG was normal; however, a balanced translocation t(3;10)(p21.3;p13) was previously found in the deceased’s mother. Eight years after the death, the deceased’s brother was diagnosed with BrS following a syncopal episode. Clinical screening of his half-sister revealed a BrS diagnosis and their mother was diagnosed with sick sinus syndrome. Sequencing a 128 cardiac gene panel was negative. Repeat karyotype of the mother revised the translocation breakpoints to t(3:10)(p.22.2;p13), at the SCN5A locus. The translocation was present in the brother and half sister. Fluorescent in-situ hybridisation confirmed disruption of SCN5A, and whole genome sequencing (WGS) located the translocation breakpoint within intron 6 of SCN5A. Amplification of the deceased’s DNA confirmed he also harboured the translocation, which we classified as pathogenic for BrS using ACMG criteria.

This is the first description of a balanced translocation causing BrS, and disrupting SCN5A. Our case highlights the importance of review of all available clinical history and genetic information within a specialised multi-disciplinary cardiac genetic clinic, and that WGS can detect and pinpoint the breakpoints of chromosomal translocations.
C-99 Factors that are predictors of recommendation adherence among carriers of dystrophinopathies

Cardiology

Submitter: Jessica Goldsberry, University of Colorado - Anschutz Medical Campus

Primary Author: Jessica Goldsberry, University of Colorado - Anschutz Medical Campus

Presenting Author: Jessica Goldsberry, University of Colorado - Anschutz Medical Campus

Author 2: Melissa Gibbons, MS, CGC, University of Colorado - SOM, Children's Hospital Colorado

Author 3: Alison Ballard, NP, PNP, University of Colorado - SOM, Children's Hospital Colorado

Dystrophinopathies are a spectrum of X-linked genetic disorders characterized by progressive muscle degeneration and the development of cardiomyopathy caused by a lack of functional dystrophin protein. Females with one pathogenic mutation do not typically develop symptoms of progressive muscle degeneration and are often unaware of their carrier status. However, research has found that female carriers are at an increased risk for developing dilated cardiomyopathy (DCM). Due to the risk for DCM, current guidelines from the American Academy of Pediatrics (AAP) recommends that carriers have regular cardiac evaluations but little research exists regarding the rate of recommendation adherence in this population. Additionally, there may be many factors that contribute to why an individual does or does not adhere to AAP recommendations. Using a retrospective chart review, the aim of this study was to determine the rate of recommendation adherence of the female carrier population seen by the Neuromuscular Carrier Clinic team at Children’s Hospital Colorado and to identify demographic, medical, lifestyle, family history, and psychosocial factors that are associated with the likelihood that carriers will adhere to the AAP recommendations. 25 out of 54 possible participants had information in their medical record detailing if they had or had not completed a cardiac evaluation, thus meeting the study’s eligibility criteria. 64 percent of participants had completed a cardiac evaluation while 36 percent had not completed a cardiac evaluation. Increased age (p = 0.05), tobacco use (p = 0.05), higher creatine kinase levels (p = 0.05), and the number of second and third degree family members affected with dystrophinopathy (p = 0.05) were all found to be significant in predicting recommendation adherence. This information could potentially be used in clinic to help identify which patients are less likely to adhere to AAP recommendations and, based on those factors, help providers to better assist these patients to ensure they receive the appropriate medical care.

A-115 Effects of Communication Complexity on Analogue Clients in a Video Cancer Genetic Counseling Session

Counseling/Psychosocial Issues

Submitter: Emily Susan Bonkowski, Graduate Student,
Introducțion: Communication of information is central in genetic counseling (GC), but there have been few direct comparisons of communication approaches. This study aimed to experimentally manipulate counselor communication to describe how complexity impacts client decisional, affective, and cognitive outcomes using a hypothetical cancer GC scenario. We hypothesized that low complexity communication would perform best across all outcomes and that personal characteristics would modify the effects of complexity. Methods: The experimental design used a web-based module that simulated educational and communication aspects of a cancer GC session. Oral literacy demand and adult learning principles provided a theoretical framework. Female participants (N=286) were recruited through two online databases. Women were randomly assigned to watch one simulated video genetic counselor providing education with either high, medium, or low communication complexity based on use of jargon, language complexity, detail, interactivity, and teach back. The sessions consisted of 8-17 video clips lasting a total of 12-21 minutes. Surveys were given before and after the videos to capture background information and standard ratings of decisional, affective, and cognitive outcomes. Regression analysis was used to compare outcomes across groups and significant variables were controlled for in each model. Results: Participants in the low complexity group had lower feelings of negative emotion compared to those in the high group (p=0.042). Individuals in the medium group had more decisional conflict than those in the high group (p=0.023). There were no other significant differences in outcomes between the three groups. Genetic literacy and preference for patient-centered communication had modifying effects. Conclusions: Participants did not express a preference for more complex information. Because those with lower genetic literacy and a preference for patient-centered communication tended to perform better in the low complexity group, it is important to consider how best to tailor communication.
Women carrying a BRCA1 or BRCA2 mutation are recommended to have high-risk breast cancer screening for early detection, usually beginning at age 25. Mutation carriers unaffected by cancer (previvors) have the option of breast cancer risk reduction with bilateral prophylactic mastectomies (BPM). It has been noted that deciding to undergo a BPM is a complex process for any individual and can be influenced by factors such as family cancer history, childbearing plans and altered body image concerns. There is little research to date on the thoughts of young previvors who undergo BPM between the ages of 20 and 30 years. The purpose of this study was to explore the decision making of young previvors who have undergone, or are considering BPM. An anonymous online survey was distributed through Facing Our Risk of Cancer Empowered (FORCE), a hereditary cancer support group, to their membership and we received 27 responses. 90% women had met with a genetic counselor/geneticist soon after being identified with a germline mutation, and found the process helpful. All the women reported a significant family history of BRCA-associated cancers and many experienced loss in the family due to cancer and supported these factors as influential in their decision to pursue BPM. Respondents cited specific concerns when weighing BPM including the impact on their ability to breastfeed, potential impact on sexual relationships and altered body image. The average time between BPM and participation in the survey was 4 years and all respondents had an accurate recall of their BRCA1/BRCA2 associated lifetime breast cancer risk. They reported some level of anxiety in association with high-risk breast screening and considered information from surgeon/plastic surgeon very helpful in their decision-making. This data highlights specific concerns of young female BRCA1/BRCA2 carriers and supports the need to elicit and address psychosocial concerns of young women making a decision to undergo bilateral prophylactic mastectomy.

A-124 Skillfulness is in the Eye of the Beholder: An Investigation of Genetic Counselors’ and Proxy Patients’ Perceptions of Genetic Counselor Self Disclosure and Non-Disclosure

Counseling/Psychosocial Issues

Submitter: Veronica Greve,

Presenting Author: Veronica Greve, University of Minnesota

Primary Author: Veronica Greve, University of Minnesota

Author 2: Patricia McCarthy Veach, University of Minnesota

Author 3: Bonnie LeRoy, University of Minnesota

Author 4: Ian MacFarlane, Elizabethtown College

Author 5: Krista Redlinger-Grosse, University of Minnesota
Background: Few studies assess genetic counselor self-disclosure. One study of counselors’ responses to a hypothetical prenatal patient yielded a range of disclosures and non-disclosures, suggesting skillfulness matters more than response type. Objective: This study assessed perceived skillfulness of genetic counselor self-disclosure and non-disclosure. Methods: Genetic counselors (n=147) and proxy patients, women from the public (n=201), completed a survey containing a prenatal genetic counseling scenario and different counselor responses from a prior study (Redlinger-Grosse, et al., 2013) in which the patient asks, What would you do if you were me? Participants were randomized to a self-disclosure or non-disclosure condition and asked to rate 10 responses (5 personal disclosures and 5 professional disclosures; or 5 decline to disclose and 5 redirection responses) (Scale:1=Unskillful to 6=Skillful). Counselor responses varied according to intention (corrective, guiding, interpretive, literal, or reassuring). Next, participants chose the most skillful response from each group of five responses and explained their choices. Results: MANOVA yielded a significant 3-way interaction for response ratings based on participant group, disclosure condition, and response intention [Wilks’s λ = .902, p < .001]. ANOVAs found both counselors and proxy patients rated a reassuring decline to disclose response highest in skill. Proxy patients rated literal responses (took patient’s question at face value) as more skillful than genetic counselors. Responses chosen as most skillful by both groups were reassuring and guiding. Thematic analysis showed participants perceived skillfulness as acknowledging the patient’s question, offering guidance and reassurance, and patient-focused. Discussion: Perceived skillfulness may be more salient than response type (self-disclosure, non-disclosure), and counselors and patients may not always agree about a response’s skillfulness. Genetic counselors should tailor responses to the patient and context.

A-127 Family Planning Decisions After a Child's Diagnosis of Rett Syndrome: A Pilot Study

Counseling/Psychosocial Issues
Submitter: Erin Huggins,
Presenting Author: Erin Huggins,
Author 2: Lauren Baggett, Greenwood Genetic Center
Author 3: Steven A. Skinner, Greenwood Genetic Center
Author 4: Richard Ferrante, University of South Carolina School of Medicine
Primary Author: Erin E. Huggins,

Rett syndrome (RTT) is a rare neurodevelopmental disorder that primarily affects females. In 99% of cases, RTT is believed to occur sporadically, or de novo. However, in rare cases, RTT can be passed down from parent to child through gonadal mosaicism or asymptomatic carrier mothers. It is known that having a child with an inherited genetic condition can lead to changes in family planning; however, little research has investigated this phenomenon in sporadic genetic conditions, such as RTT. This present
study used a questionnaire to assess family planning decisions of parents of children with RTT. Forty-three percent of respondents reported that their family planning changed. The primary reason for reproductive stoppage was due to caregiver strain, and of those that chose reproductive continuation, the primary change was in the age gaps between their children. Parents were also asked to explain what they were told by healthcare providers about the recurrence of RTT and if they received genetic counseling. Seventy-eight percent reported they were told there was a 1% or less chance of recurrence of RTT and 34% received genetic counseling. There was no significant association between those who received genetic counseling and those who altered their family planning decisions. The results of this study suggest that families consider both recurrence risk and additional non-genetic factors such as family needs when making their family planning decisions and should be counseled accordingly.

A-130 Disclosure of Genetic Information in Families Affected by Hereditary Ataxia Counseling/Psychosocial Issues
Submitter: Katherine Lincoln, University of Maryland School of Medicine

Presenting Author: Katherine Lincoln, University of Maryland School of Medicine

Primary Author: Katherine Lincoln, University of Maryland School of Medicine

Author 2: Kristin Maloney, University of Maryland School of Medicine

Author 3: Alena Egense, University of Maryland School of Medicine

Author 4: Weiyi Mu, Institute of Genetic Medicine, Johns Hopkins University

While studies have investigated genetic risk communication in individuals with adult-onset neurogenetic conditions such as Huntington disease (HD), there are currently no published studies describing this process in families with hereditary ataxia, specifically spinocerebellar ataxia (SCA). Unlike HD, the SCAs are a group of disorders characterized by phenotypic and genetic variability, and not all molecular causes are known, complicating recurrence risk predictions. The purpose of this study was to explore disclosure behavior for this population and identify factors that affect the communication of diagnosis and genetic risk information within these families. This study also aimed to identify barriers to the disclosure process for this population and assess participants’ attitudes about their disclosure decisions. A mixed methods approach was used, which included a survey sent out by the National Ataxia Foundation and CoRDS Registry and semi-structured telephone interviews conducted with 25 adults with SCA1, SCA2, SCA3, SCA5, SCA6, SCA8, SCA12, and unknown hereditary ataxia. Thematic content analysis revealed that disclosure behavior is highly variable within families affected by SCA, and there are many different factors that individuals consider when deciding when, what, why (or why not), how, and to whom to disclose information about their diagnosis. Barriers that led some participants to delay or avoid disclosure included family dynamics, emotional factors, and understanding of inheritance. While some participants reported receiving support from their support organization to help guide decisions about disclosure, several reported a lack of support from the medical community and
indicated that more support would have been helpful. Increasing access to genetic counseling for this population could provide opportunities for anticipatory guidance about disclosure in families with SCA, including discussions about the aforementioned barriers families might encounter, and could help individuals better understand the inheritance of this complex group of disorders.

A-133 Journey of Fathers Following their Child’s Fragile X Diagnosis: Support Seeking Behaviors of Fathers

Counseling/Psychosocial Issues

Submitter: Aman Kaur Mann, Northwell Health

Primary Author: Aman Kaur Mann, Northwell Health

Presenting Author: Aman Kaur Mann, Northwell Health

Author 2: Sharyn Lincoln, Boston Children’s Hospital

Author 3: Lindsey M. Stobie, Beth Israel Deaconess Medical Center

Author 4: Pete Levesque, Brandeis University

Studies show that fathers of children with a disability or chronic illness experience significant psychological impact. Appropriate support has shown to improve their well-being and that of their child. Despite these studies, the needs of these fathers are continually overlooked in healthcare settings. The purpose of this study was to understand the father’s experience receiving a fragile X syndrome (FXS) diagnosis for their child, focusing on their support seeking behaviors and their satisfaction with the supports available. We used an anonymous online survey consisting of multiple-choice, Likert scale and open-ended questions and received 32 responses. The majority of the fathers were young at the time of their child’s diagnosis (<40 years of age; 77.4%), and they were all married. In general, the fathers were satisfied with their experience with medical professionals. However, 15.7% of fathers were dissatisfied with their overall experience. We found that fathers want (1) more access to FXS information, specialists and local resources, and (2) specialized support from family, friends, other FXS families and FXS-related organizations. Healthcare providers can meet the needs of the fathers by (1) increasing awareness and education of FXS and FXS-related resources, (2) assessing both parents level of understanding, addressing their questions and concerns, and providing psychosocial support, and (3) acknowledging the fathers role, discussing the impact on them when receiving a diagnosis for their child and providing referrals to appropriate support resources. Support organizations can also meet fathers’ needs by (1) creating literature tailored to fathers, (2) encouraging more father-related activities in support groups, and (3) creating a network to connect fathers to other fathers. With the support of this data, we recommend implementation of these suggestions in order to address and meet the individual needs of fathers of children diagnosed with FXS, and support them through their unique journey as fathers.
A-136 Lack of referral and evaluation compounds emotional distress in 3 generational family with tuberous sclerosis complex.

Counseling/Psychosocial Issues
Submitter: Jennifer Propst, VCU Health System

Presenting Author: Jennifer Propst, VCU Health System

Primary Author: Jennifer Propst, VCU Health System

As genetic counselors, we strive to address the emotional burden that families face from inherited genetic disease. I present a family with three generations of individuals affected with tuberous sclerosis complex (TSC) who experienced exacerbated distress in the diagnostic period. Although the condition was suspected in earlier generations, genetics referral was not made until Neurology made a clinical diagnosis of TSC for the more severely affected 14 month old proband after the onset of epilepsy and the discovery of multiple cortical tubers, white matter abnormalities, and subependymal nodules on brain MRI. The affected proband, mother and brother were subsequently found to have a likely pathogenic variant in the TSC1 gene; a missense c.737 G>A variant with conflicting protein prediction models but that has been reported in a few TSC patients. Both the maternal grandfather and mother have milder TSC presentations that they feel have not greatly impacted their lives. When the proband was diagnosed, her grandmother reported tremendous regret and grief from the guilt of transmitting a genetic condition that resulted in a more severe presentation in his beloved granddaughter. The mother experienced a fearful urgency to have her infant son tested for TSC after her daughter was diagnosed. Although they were educated about the recurrence risk of TSC in the past, they were not aware of the complete penetrance and disease variability. If the referral for genetics evaluation and counseling had been made sooner, it is possible that this family’s psychological trauma may have been reduced. The grandfather’s openness during the initial genetic evaluation facilitated the genetic counseling process, allowing for a release of emotional distress and sharing with his daughter, who was experiencing several of the same afflictions. This case demonstrates a counseling dilemma and offers additional clinical information on a rarely reported TSC1 missense mutation.

A-139 Complexities of Preconception Decision-Making in Hereditary Retinoblastoma

Counseling/Psychosocial Issues
Submitter: Jaclyn Schienda, Dana-Farber Cancer Institute

Primary Author: Jaclyn Schienda, Dana-Farber Cancer Institute

Presenting Author: Jaclyn Schienda, Dana-Farber Cancer Institute

Author 2: Sarah R. Cochrane, Dana-Farber Cancer Institute

Author 3: Katherine Schneider, Dana-Farber Cancer Institute
Author 4: Junne Kamihara, Dana-Farber Cancer Institute

Introduction: Hereditary retinoblastoma (RB) is typically a highly penetrant condition that leads to multifocal and bilateral tumors of the retina in infancy. While preimplantation genetic diagnosis (PGD) and prenatal testing are available, some families choose not to pursue these options. Not all providers understand this decision. We explore three cases to illustrate the nuances involved.<br />

Case 1: A 30-year-old man with a history of bilateral RB also had a one-year-old undergoing treatment for RB. For this family, PGD to select against a trait that the father and son both have felt like it undervalued their lives and family identity. However, it was also equally difficult to choose having another child naturally given the high risk of cancer. Prenatal surveillance gave them comfort.<br />

Case 2: A 29-year-old woman with a history of unilateral RB also had a son undergoing treatment for RB. Finances limited the family’s ability to afford PGD for their second child. In addition, they did not feel that the presence of RB would define their child and thus did not want to risk miscarriage with prenatal testing.<br />

Case 3: A 28-year-old man with a history bilateral retinoblastoma along with his wife decided to defer genetic testing until their first child’s birth. This decision was based on his perception of RB as normal and not a disability, as well as our current ability to manage RB. <br />

Discussion: Some providers have asked why a person with RB would choose to have a child at high-risk for cancer. The cases above illustrate how complex and personal this decision is. RB can become part of one’s identity and choosing PGD can be seen as selecting against oneself or one’s child. PGD is also very expensive and not available to all. Furthermore, RB is a highly curable cancer and can be perceived as very manageable, especially when one has been through diagnosis and treatment. Genetic counselors are in a unique position to advocate for families and help other medical providers understand why some families might decline PGD and prenatal testing for hereditary RB. <br />

A-142 Spiritual Care in Cancer Genetic Counseling: Patient Perceptions of Methods
Counseling/Psychosocial Issues
Submitter: Christopher Michael Spencer, University of South Carolina
Presenting Author: Christopher Michael Spencer, University of South Carolina
Primary Author: Christopher Michael Spencer, University of South Carolina
Author 2: Janice Edwards, Palmetto Health University of South Carolina Medical Group
Author 3: Cristy DeGregory, Vanderbilt University School of Nursing
Author 4: Karen Brooks, SC Oncology Group

Integration of spirituality into medical care is a growing area of debate among professionals, involving a delicate balance between serving patients who may benefit from this without alienating those who would not. To date, some research exploring prenatal genetic counselor approaches to spiritual assessment has been accomplished and little research has targeted cancer genetic counseling. A paper questionnaire was created and distributed to patients immediately following their cancer genetic
counseling appointments to gain insight regarding eight previously established spiritual assessment methods that a genetic counselor could potentially use to address spirituality with their patients. Fifty-two participants completed this questionnaire. The eight spiritual integration methods showed positive responses by the participant group on average, though opinions varied between participants. The method with the highest approval involved an indirect invitation to discuss spirituality wherein a genetic counselor informs a patient that spirituality is a welcome topic of discussion. Overall, 78.9% viewed this as a positive action by the counselor, while 11.5% viewed this negatively. Other indirect methods of addressing spirituality also demonstrated higher participant approval, and some methods, such as a genetic counselor sharing their spiritual beliefs were more beneficial for Christians compared to non-Christians. Interestingly, 48.1% of patients initially indicated that they did not desire the genetic counselor to address their spiritual needs, while only 23% responded that they did. This item was presented before the potential methods and may indicate that some individuals perceive dissonance between genetics and spirituality or medical appointments and spirituality. This study highlights several opportunities for further exploration of the role of genetic counselors in spiritual assessment.

A-145 A Case Report of the Prenatal Diagnostic Odyssey Resulting from Abnormal cfDNA Screening Results

Counseling/Psychosocial Issues

Submitter: Abigail Weinberg, NYU Winthrop Hospital

Presenting Author: Abigail Weinberg, NYU Winthrop Hospital

Primary Author: Abigail Weinberg, MS, CGC, NYU Winthrop Hospital

Author 3: Joseph Koka, MD, NYU Winthrop Hospital

Author 2: Martin Chavez, MD, FACOG, NYU Winthrop Hospital

Author 4: Jay Davis, MD, NYU Winthrop Hospital/Stony Brook University

We present a case in which there was a fetal diagnosis of Y chromosome abnormalities following abnormal cell free fetal DNA (cfDNA) screening results indicating Turner syndrome mosaicism (46,XY/45,X). This case exemplifies the lengthy diagnostic odyssey that a pregnant patient can experience following abnormal cfDNA screening results. Subsequent diagnostic testing with chorionic villus sampling indicated mosaic results of 33.5% with a single X chromosome and 66.5% XY from FISH analysis and 45,X[20]/46,X+mar[7] on full chromosome analysis, the marker chromosome likely derived from the Y chromosome. The inconclusive results were followed by an amniocentesis, which indicated a normal FISH result and non-mosaic karyotype of 46,X,del(Y)(q11.23). Chromosome microarray performed on the amniocytes further defined a 40.1 Mb deletion of Yq11.221-q12 and also identified a 3.2 Mb duplication of Yp11.32-p11.2 (classified as a likely pathogenic copy number variation). The patient presented for genetic counseling to review the results. The range of potential implications of infertility (associated with the deletion) and uncertain features including developmental delays, tall
stature, and Leri-Weill dyschondrosteosis (associated with the Yp duplication, which included the SRY and SHOX genes) were reviewed with the patient. The patient reported that she took comfort in the fact that had she been pregnant several years ago, when cfDNA screening was offered only to women with certain indications, most likely none of this testing would have been performed. This perspective allowed the patient to feel more certain in her personal decision to continue her pregnancy, as she perceived the potential impacts of the chromosome abnormalities to be minimal. Subsequent fetal ultrasounds indicate a normal-appearing male infant. This case exemplifies that confined placental mosaicism may result in a diagnostic odyssey lasting over six weeks. Furthermore, this case demonstrates that abnormal cfDNA screening results cannot necessarily be promptly confirmed or determined to be a false positive.

B-113 Ehlers Danlos Syndrome: An Emerging Adulthood Perspective

Counseling/Psychosocial Issues
Submitter: Katie Bealka,

Presenting Author: Katie Bealka,

Author 2: Cassandra Buck, Brandeis University

Author 3: Nikkola Carmichael, Brigham and Women’s Hospital

Author 4: Ashley Soughley, Spaulding Outpatient Center Framingham

Primary Author: Katie Bealka, Brandeis University

Ehlers Danlos syndrome (EDS) is a genetic, multi-systemic, connective tissue disorder that affects the skin, bones, blood vessels, and other tissues. The most common subtypes of EDS are the hypermobile (hEDS) and classical (cEDS) types. This study aimed to identify ways in which the symptoms of hEDS and cEDS impact emerging adults, individuals in the transition period of 20-30 years of age. Participants were recruited through various EDS support groups across the United States and internationally to participate in an anonymous, mixed-method survey. A total of 368 participants responded, providing information about their diagnosis of EDS and its impact on their daily life, relationships, and career choices. Nearly all participants reported that EDS has had a negative physical (95.2%) or emotional (83.7%) impact on their life. Those who reported the most severe symptoms also reported the most significant social impact (87.5%). Additionally, many commented that their EDS had a significant impact on their relationships with family, friends, and romantic partners. This negative impact on their relationships correlated with the number and severity of their EDS symptoms. Many individuals reported feeling misunderstood by their family and friends, and cited difficulties forming or maintaining peer or romantic relationships. Sexual intimacy was highlighted as a specific challenge. These results suggest that genetic counselors and other medical professionals should be to be aware of the particular struggles characterizing this developmental stage for individuals with EDS, and seek ways to provide additional support.
B-116 Recurrence numbers in genetic counselling: exploring uptake, perception, and impact on patient outcomes

Counseling/Psychosocial Issues

Primary Author: Kennedy Borle,
Presenting Author: Kennedy Borle,
Author 2: Emily Morris, University of British Columbia
Author 3: Angela Inglis, University of British Columbia
Author 4: Jehannine Austin, University of British Columbia
Submitter: Kennedy Borle, Genetic Counsellor,

Introduction: Discussing risk and providing recurrence numbers is often considered a fundamental component of genetic counselling. However, knowledge gaps exist regarding how often patients seek recurrence numbers, and how they impact patient outcomes. Hypotheses: we anticipated greater increases in empowerment (measured by the Genetic Counselling Outcomes Scale (GCOS)) among patients who: a) received recurrence numbers (vs. those who did not), and b) perceived numbers that they received to be lower than anticipated (vs. individuals who had other perceptions of the number they received). Methods: We conducted a retrospective chart review at a clinic where patients routinely complete the GCOS pre (T1)/post (T2)-appointment, and where demographic variables, reason for referral, and patient perception of numbers received are routinely recorded. We used descriptive statistics for frequencies of interest, and ANCOVA to test our hypotheses. Specifically, we tested the effect on T2 GCOS score of: a) receiving recurrence numbers, and b) patient perception of recurrence numbers whilst controlling for T1 GCOS score. Results: Recurrence numbers were a primary indication for 134/300 patients (45%). After counselling about etiology and risk-reducing strategies, 116 patients (39%) opted to receive recurrence numbers, with most (n=64, 55%) perceiving the number to be lower than expected. GCOS scores increased significantly from T1-T2 for all patients. There was no difference in T2 GCOS scores between those who: a) received recurrence numbers vs. those who did not, or b) perceived the number to be lower than expected vs. those with other perceptions. However, a subset of patients (who who did not receive recurrence numbers after changing their minds about their interest during the session) had larger increases in GCOS scores. Conclusion: Our data demonstrate that optimal patient outcomes are not contingent on receipt of recurrence numbers and challenge the notion that recurrence numbers should be routinely provided in genetic counselling.
B-119 More than 3 Founder Mutations for Ashkenazi Jewish Ancestry in a Hereditary Cancer Clinic

**Counseling/Psychosocial Issues**

*Submitter: Devin Cox, The University of Kansas Cancer Center*

*Presenting Author: Devin Cox, The University of Kansas Cancer Center*

*Primary Author: Devin Cox, University of Kansas Health System*

*Author 2: Debra Collins, University of Kansas Health System*

When an individual of Ashkenazi Jewish (AJ) ancestry is seen in a hereditary cancer clinic, traditionally the discussion focus is on the three founder mutations in the BRCA1 and BRCA2 genes with increased susceptibility for breast, ovarian and other cancers. However, the risks for additional cancer susceptibility including higher risk for colon, uterus, and other cancers associated with 8 additional AJ Founder mutations are also important to recognize. This issue is of particular importance with recent direct-to-consumer (DTC) genetic testing companies offering limited genetic testing of just the three BRCA1 and BRCA2 founder mutations. Recent clinical cases prompted a literature review, which indicated that there is a combined risk of 12.36-20.83% for an individual of AJ ancestry to have 1 of 10 AJ founder mutations for hereditary cancer in the BRCA1, BRCA2, CHEK2, APC, MSH2, MSH6, and GREM1 genes. AJ families may present unique challenges when determining appropriate testing because of smaller family sizes and lack of medical information concerning past generations due to the aftermath of various population disruptions, migration, death of ancestors in WWII and other world conflicts. Family historians may not be living or available and family members may have died at young ages, prior to developing cancer. Discussions about these limitations may be integrated into the construction of a pedigree with AJ families. Other individuals may have incidentally discovered AJ ancestry revealed through DTC ancestry testing. This leads to counseling challenges with the limited consensus on what percentage of AJ ancestry is appropriate to consider specific AJ genetic testing. Certified Genetic Counselors can help support AJ population testing, and ensure appropriate cancer risk management, follow up, and cascade testing.

B-122 An exploration of factors influencing patient outcomes of psychiatric genetic counseling

**Counseling/Psychosocial Issues**

*Submitter: Sarah Gerrard,*

*Presenting Author: Sarah Gerrard,*

*Primary Author: Sarah Gerrard, Sarah Lawrence College*

*Author 2: Angela Inglis, UBC Depts of Psychiatry and Medical Genetics*

*Author 3: Emily Morris, UBC Depts of Psychiatry and Medical Genetics*
Introduction: Though understanding how different characteristics of the patient and session influence outcomes of genetic counseling (GC) is important, little research data currently exists on this topic.

Purpose: To explore the effects of ten patient and session-related variables on change in Genetic Counseling Outcome Scale scores (GCOS, a validated instrument that measure empowerment) from pre- to one-month post-GC.

Methods: We conducted a retrospective review of charts from patients who attended a specialist psychiatric GC clinic between February 1, 2012 and January 31, 2017. We used ANOVA to analyze change in GCOS scores in relation to ten variables: sex, ethnicity, diagnosis, mode of referral, mode of genetic counseling, primary indication for referral, individual/family appointment, GC student involvement, presence of observers, and history of mental illness.

Results: 307 charts were included in analysis. Overall, GCOS scores significantly increased after GC (p<0.0005, d=1.10). No significant differences in GCOS change scores were identified with respect to: sex, ethnicity, diagnosis, self or provider referral, individual or family appointment, involvement of students/observers, or personal/family history of mental illness. Significant relationships were found between GCOS change scores and mode of delivery of GC (p=0.048, η² = 0.02) and primary indication for the appointment (understanding recurrence risk versus other, p=0.001, η² = 0.04).

Conclusion: This exploratory study provides the first data on how a number of characteristics of the patient and session influence outcomes of genetic counseling. Patients benefit from psychiatric genetic counseling, regardless of sex, ethnicity, diagnosis, type of referral, additional attendees, students, observers, or history or mental illness. Understanding the patient and session-related factors that do seem to influence outcomes may allow for adjustment of service delivery strategies to promote the best possible outcomes.

B-125 Genetic Counselors’ Experiences with Incidental Findings of Misattributed Paternity

Counseling/Psychosocial Issues

Submitter: Mara Jennifer Hernandez, CSU Stanislaus

Primary Author: Mara Jennifer Hernandez, CSU Stanislaus

Author 2: Joanna Fanos, PhD, Children’s Hospital Oakland Research Institute/UCSF

Author 3: Ryan Howell, PhD, San Francisco State University

Author 4: Janey Youngblom, PhD, California State University, Stanislaus

Author 5: Kara Weisiger, MS, LCGC, University of California San Francisco Medical Center

Presenting Author: Janey Youngblom, PhD, California State University, Stanislaus

Genetic testing can result in the incidental determination of misattributed paternity. As testing that includes parental samples becomes more common, the number of cases of misattributed paternity determined will likely rise. In these sensitive cases, genetic counselors are faced with the responsibility
of deciding how to handle this unexpected information, such as deciding if and to whom the information should be disclosed.<br />
This study addresses the question of what course of action genetic counselors most frequently take, explores their decision-making processes, and assesses the need for greater support for genetic counselors on this topic. A survey of 325 practicing genetic counselors and interviews with 12 participants recruited from those who had been involved with at least one case of misattributed paternity collected detailed quantitative and qualitative data.<br />
In nearly three-quarters of cases, misattributed paternity was disclosed by the genetic counselor. The study found that the proportion of genetic counselors who disclose incidental findings of misattributed paternity is smaller than the proportion of former genetic counseling patients who report they would want this information disclosed. Findings shed light on the numerous factors weighed by genetic counselors when making a decision about disclosure, and reveal that a clear discussion of the possibility of determining misattributed paternity is frequently not part of the informed consent process. This study also highlights the need for more support for genetic counselors about how to handle these complex cases. Results can provide guidance to genetic counselors and other healthcare providers unsure of how they should best address a case of incidental determination of misattributed paternity.<br />
Research supported by a California State University, Stanislaus Student Engagement in Research, Scholarship, and Creative Activity Mini-Grant and a California State University, Stanislaus Biology Research Committee Grant

**B-128 Potential Methods to Strengthen the Counselor-Patient Alliance in a Genetic Counseling Session: Nonconscious Priming and Empathetic Phrasing**

**Counseling/Psychosocial Issues**

*Submitter: Jessica Isaacs,*

*Presenting Author: Jessica Isaacs,*

*Primary Author: Jessica Isaacs,*

*Author 2: Steven Robbins,*

*Author 3: Lisa Kessler,*

Research demonstrates that the alliance forged between the Genetic Counselor and the client may be associated with Genetic Counseling (GC) session outcomes. The study investigated whether nonconscious priming and empathy phrasing can bolster alliance and improve participant knowledge retention. In non-conscious priming, participants are exposed to stimuli that activate mental representations outside of awareness; these primed mental states impact subsequent behavior. We hypothesized that participants who were primed for empathy would rate a GC session more favorably.

Participants were recruited through Amazon Mechanical Turk and were primed for empathy in 2 ways (images and verbal phrasing). Each participant was randomly assigned to 1 of 4 conditions in a 2X2 factorial design, images (empathy/non-empathy) by phrasing (empathy/non-empathy). The priming image consisted of one of two watermarks: 1) two men standing with a telescope, staring at the sky together (empathy) 2) two men standing back-to-back (non-empathy). Participation consisted of:
completing a demographic questionnaire with a version of the priming image, 2) watching a version of a cancer GC video clip (one version used empathy phrasing, one version did not), 3) completing 2 subscales of the Barrett Lennard Relationship Inventory (BLRI) to rate empathy and congruence of the GC, 4) completing a knowledge assessment. Results from 120 individuals were analyzed via 2X2 ANOVA; no significant main effects were observed. Pearson correlation analysis found individuals who rated the GC highly on the BLRI answered more multiple choice questions correctly \( r (120) = .227, p = .012 \) suggesting that participants who viewed the GC positively may have been more attentive during the GC video. Establishing a strong GC-patient alliance may be correlated with maximal knowledge retention. Expression of empathy and therapeutic alliance are both evidence-based components of counselor-patient outcomes. Future research can be conducted to understand more about the relationship between alliance and knowledge retention.

**B-131 Evaluating the utility of an Options for Pregnancy Termination (OPT) Decision Aid: perspective of genetic counselors**

**Counseling/Psychosocial Issues**

*Submitter: Vivian B. Ling, University of Michigan Medical School*

*Presenting Author: Vivian B. Ling, University of Michigan Medical School*

*Primary Author: Vivian B. Ling, University of Michigan Medical School*

*Author 2: Sarina Chaiken, Oregon Health and Science University School of Medicine*

*Author 3: Miriam Kuppermann, PhD, MPH, University of California San Francisco*

*Author 4: Jennifer L. Kerns, MD, MS, MPH, University of California San Francisco*

Women terminating pregnancies due to diagnosis of fetal anomaly can choose between a dilation and evacuation procedure (D&E) or an induction termination. Patient choice of the procedure can significantly affect satisfaction and emotional outcomes. Research has shown that supplemental tools can improve the informed decision-making process with both patients and providers. The aim of this study was to evaluate the utility of video and printed decision aids designed to assist patients’ choice between D&E and induction during the genetic counseling process. We conducted 2 focus groups with 24 genetic counselors at a National Society of Genetic Counselors Annual Meeting. Participants were shown the decision aids and then asked for feedback on various features using a semi-structured discussion guide. Qualitative methods were used to analyze the content and identify major themes. Participants perceived that the decision aids effectively addressed unmet needs for both patients and providers through the following mechanisms: 1) decision modeling, 2) expanding emotional opportunity for patients, 3) providing a flexible tool able to adapt to logistical practice challenges, 4) facilitating provider empathy, and 5) prompting future actions. Positive provider reactions suggest that these decision aids may be effective supplements in clinical settings. Overall, these results emphasize the need and potential for decision aids that help both patients and
providers prioritize informed decision-making when choosing a termination procedure. Future research examining implementation of the aids in genetic counseling settings will further illuminate how they can best be used to improve patient care.

B-134 Depression Screening in a High Volume Cancer Genetics Program

Counseling/Psychosocial Issues

Submitter: Jacqueline Mersch, MS, CGC, UT Southwestern Simmons Cancer Center

Primary Author: Jacqueline Mersch, MS, CGC, UT Southwestern Simmons Cancer Center

Presenting Author: Jacqueline Mersch, MS, CGC, UT Southwestern Simmons Cancer Center

Author 2: Sara Pirzadeh-Miller, MS, CGC, UT Southwestern Medical Center

Author 3: Theodora Ross, M.D., Ph.D., UT Southwestern Medical Center

The Center for Epidemiological Studies Depression Scale (CES-D) is a common assessment tool that has been validated for general population depression screening. The shortened 10 question tool (CES-D 10) uses a score of ≥ 10 to identify depressive symptomatology. Although mental health screening has become a major initiative across the healthcare spectrum, data on depression screening in the hereditary cancer patient population is limited.

The UT Southwestern cancer genetics program integrated CES-D 10 into an online English questionnaire given to patients prior to their genetic counseling appointment. CES-D 10 scores were collected on patients seen in eight clinics from July 2017 to December 2017. A score of ≥ 10 was used as the threshold for symptoms of depression indicating a positive screening result. A total of 1951 patients attended genetic counseling appointments in the study timeframe. Eight hundred and thirty eight (43%) completed CES-D 10: 242 (29%) patients screened positive for depression with a score of ≥ 10. Of the patients that screened positive, 129 (53%) reported a personal history of cancer. Additionally, 33 (14%) had a germline mutation identified on testing, 169 (70%) had negative genetic testing, 36 (15%) did not have genetic testing, and results were not available for 4 patients (2%).

Our data suggest the patients under evaluation for hereditary cancer due to a personal and/or family history of cancer represent a fraction of the general population who are more likely to screen positive for depression. The prevalence of depression in the general population is 7-21% compared to the 29% of patients who screened positive with CES-D 10 in our cancer genetics clinics. These data illustrate the importance of CES-D 10 administration prior to the appointment to allow for further exploration and directed long-term follow up. Future comparison to patients who screen negative for depression on CES-D 10 and assessment of screening tools such as PHQ-2, PHQ-9, and GAD-7 will be important to advance our understanding of this population.
Exploring Empathy in Genetic Counseling Students and New Genetic Counselors

**Counseling/Psychosocial Issues**

Submitter: Jonica Richards,

Presenting Author: Jonica Richards,

Primary Author: Jonica Richards, Department of Pediatrics, University of Wisconsin-Madison

Author 2: Elizabeth Petty, Department of Pediatrics, University of Wisconsin-Madison

Author 3: Amy Zelenski, Department of Medicine, University of Wisconsin-Madison

Although empathy is widely recognized as an important trait for health care professionals, little research has examined empathy attributes in genetic counselors. Decreases in empathy levels have been recognized in other health care professionals over the span of their professional education program. This research sought to characterize empathy levels in first and second year genetic counseling students as well as recent (2017) graduates, and to determine how empathy changes, if at all, during the education of genetic counselors. Additionally, this research examined if experiences prior to graduate school correlated with differences in self-reported empathy levels among genetic counseling students and new genetic counselors. An online survey was administered to first and second year genetic counseling students and practicing genetic counselors to analyze the impact of pre-graduate school educational and work experiences and other participant characteristics on levels of empathy as measured by the Interpersonal Reactivity Index (IRI). We identified a statistically significant difference in empathic concern (IRI-EC), perspective taking (IRI-PT), and fantasy (IRI-FS) scores between first year genetic counseling students and second year students, and in scores of the IRI-FS and personal distress (IRI-PD) between first year genetic counseling students and recent graduates. This suggests a decline in empathy during graduate school training.

“Just a little bit different”: The experiences of emerging adults at-risk for and living with genetic conditions.

**Counseling/Psychosocial Issues**

Submitter: Anna Rae Shelley, University of Minnesota

Presenting Author: Anna Rae Shelley, University of Minnesota

Primary Author: Anna Shelley, University of Minnesota

Author 2: Pat McCarthy Veach, PhD, LP, University of Minnesota

Author 3: Bonnie S. LeRoy, MS, CGC, University of Minnesota

Author 4: Krista Redlinger-Grosse, PhD, LP, ScM, CGC, University of Minnesota
Background: Emerging adulthood (EA) is a distinct developmental period between ages 18-29 years comprising five features: identity exploration, experimentation/possibilities, negativity/instability regarding one’s outlook, self-focus, and feeling in-between adolescence and adulthood. A growing literature has explored the impact of genetic conditions on individuals chronologically fitting the EA period. Objective: This systematic literature review used the EA theory to determine whether individuals living with or at-risk for a genetic condition experience the features of this period and also similarities and differences between these two groups. Methods: A systematic search yielded 1,301 peer-reviewed papers from the 17 years since EA theory was published. Ten papers met inclusion criteria- 5 for those Living With a genetic condition (e.g., Cystic Fibrosis) and 5 for those At-Risk (e.g., Hereditary Breast and Ovarian Cancer). Content analysis was used to extract themes consistent with EA features. Results: All five features were evident in the Living With and At-Risk groups; negativity/instability was most prevalent and feeling in-between was least prevalent. In both groups, the features were evident around independence (from family, healthcare providers), career/education, relationships/social life, family planning, and life perspective experiences. Between group differences included: Living With individuals reported effects about their ongoing physical symptoms; At-Risk individuals reported effects regarding genetic testing decisions and anticipation of physical symptoms. Discussion: Emerging adults Living With and At-Risk for genetic conditions experience the main features of this period but face unique challenges compared to individuals without genetic conditions/risk. Salient differences between Living With and At-Risk individuals in their experiences of EA feature. Understanding emerging adults’ experiences can aid genetic counselors in addressing their specific concerns.

B-146 Infertility and Familial Adenomatous Polyposis: A Topic Genetic Counselors Should Discuss?

Counseling/Psychosocial Issues
Submitter: Heather Willems, University of Colorado-Anschutz Medical Campus

Presenting Author: Heather Willems, University of Colorado-Anschutz Medical Campus

Primary Author: Heather Willems, Children’s Hospital Colorado

Author 2: Michelle Springer, MS, CGC, University of Colorado Hospital

Author 3: Robert Casey, PhD, Children’s Hospital Colorado

Author 4: Kami Wolfe Schneider, Children’s Hospital Colorado

Previous studies indicate that many individuals diagnosed with familial adenomatous polyposis (FAP) experience guilt, anxiety, denial, and refusal to follow recommended management guidelines. Individuals with FAP may also exhibit poor psychological functioning with negative impact on social activities, relationships, support, and attitudes towards having children. Due to speculation that medical and psychosocial outcomes may be improved for individuals with FAP who have had genetic counseling with a certified genetic counselor, we pursued qualitative investigation of outcomes for individuals with
FAP. Individuals 18-50 years of age were recruited through online organizations and support groups. A demographic survey was completed by 36 individuals (3.23% response rate) from which focus groups were created to separate individuals by whether or not they had previously seen a genetic counselor. While more than 20 respondents were invited to participate in the focus groups, only 4 participated in two online focus groups, revealing some of the challenges with this patient population. Participant interviews, however, revealed interesting insight that warrants further exploration in future research. Participants discussed coping styles after diagnosis and in everyday life, influence of FAP on reproductive decisions, interactions with medical professionals, and experiences or desires with genetic counselors. Interestingly, half of the respondents commented on their infertility due to scar tissue build-up after FAP-related surgeries. Even though surgical techniques have improved over the last 20 years, resulting in fewer women becoming infertile from these surgeries, and surgeons typically review surgical risks with patients, it is important to recognize during genetic counseling and long-term support discussions with individuals with FAP that infertility is a possible outcome of disease management. This is especially important when discussing recurrence risks and reproductive options. The outcomes from this study suggest the importance of further research.

C-114 The Impact of the Counseling Environment on Patient Outcomes of Genetic Counseling

Counseling/Psychosocial Issues
Submitter: Jacob Best,
Primary Author: Jacob Best,
Presenting Author: Jacob Best,
Author 2: Angela Inglis, University of British Columbia
Author 3: Jehannine Austin, University of British Columbia

The Impact of the Counseling Environment on Patient outcomes of Genetic Counseling

Jacob Best, Angela Inglis, Emily Morris, Jehannine Austin

Background

The psychology literature shows that characteristics of the physical space in which counselling sessions are conducted influence patient comfort, levels of self-disclosure, irritability/relaxation, and even potentially outcomes. Though understanding how to optimize patient outcomes is an important priority for the genetic counselling (GC) profession, no previous study has examined the effect of the physical space on patient outcomes of GC.

Hypotheses

Patients seen in a comfortably furnished counselling (CFC) room will have greater increases in a) empowerment and b) self-efficacy after GC than patients seen in a medical examination (ME) room.

Methods

We used data used from a specialist psychiatric GC clinic, where counselling sessions are typically held in an ME room, with CFC rooms used as available. Patient outcomes are routinely tracked: pre-GC, and 1 month after GC empowerment is measured with the Genetic Counseling Outcome Scale (GCOS) and self-efficacy is measured by the Illness Management Self Efficacy scale (IMSES). All charts of patients seen between Feb
2012-Dec 2017 who were seen in CFC rooms were selected for study inclusion. We used a pseudo-randomization technique to match each CFC patient to 2 ME controls – only patients with complete GCOS and IMSES at both time points were included in the analyses (independent T-Tests comparing change in GCOS and IMSES scores from pre- to post-GC between CFC and ME groups).

Results<br />
54 patients (36 ME and 18 CFC) were included in the analysis. CFC patients had greater increases in GCOS ($t = 2.20, P = 0.032, d = 0.613$) and IMSES ($t = 2.55, P = 0.014, d = 0.717$) scores from pre-GC to post-GC, effect sizes were moderate (suggesting clinical significance).<br />

Conclusions<br />
This study suggests that holding counselling sessions in a more comfortable space positively impacts patient outcomes of GC.

C-117 Is It Feasible? Self-Affirmation For Hereditary Breast And Ovarian Cancer Genetic Counseling

Counseling/Psychosocial Issues

Submitter: Anna Chassevent, Kennedy Krieger Institute

Presenting Author: Anna Chassevent, Kennedy Krieger Institute

Primary Author: Anna Chassevent, Kennedy Krieger Institute

Author 2: Dr. Barbara Biesecker, RTI International

Author 3: Dr. Lori Erby, National Institutes of Health

Author 4: Whitney Ford, Saint Luke's Health System

Author 5: Dr. William Klein, National Institutes of Health

Background<br />
In recent years there has been increased understanding of the genetic factors that predispose people to cancer. While this knowledge can improve patient health, patients, with an increased risk for cancer, face complex decisions about testing, screening, family communication, and prophylactic surgery. It is important for genetic counselors to effectively support patients in the decision-making process. Self-affirmation (SA) interventions may be an efficient way to improve hereditary breast and ovarian cancer (HBOC) genetic counseling patient-centered outcomes. The study described is a randomized controlled trial to assess the feasibility of implementing a SA intervention in a cancer genetic counseling clinic.

Methods<br />
This study was conducted in a hereditary cancer clinic. Patients who attended the clinic, were randomized to completed a SA intervention or a control writing exercise before their appointment and a survey of patient-centered outcomes afterward. The primary feasibility outcomes were: patient acceptance of the SA intervention, patient attrition, and the effectiveness of the SA intervention. Secondary outcomes were: decision self-efficacy, intentions to talk with family, genetic test uptake, patient empowerment, and HBOC knowledge.

Results<br />
All patient participants reported that the intervention did not interfere with their appointment (35/35). Coding analysis of patient essays showed that those who were in the intervention group were
significantly more affirmed than those in the control group (p <= 0.01). None of the secondary outcomes were statistically significantly different between the control and intervention groups. Patient and counselor scores on the empowerment measure were not significantly correlated (p = 0.298).<br />

Conclusions<br />
Given our findings a phase II study is warranted to enhance our understanding of SAs usefulness in buffering patients from the threat of cancer. Additional studies with more diverse populations and in other subspecialties of genetic counseling will be important to validate SA in genetic counseling setting.

C-120 Quality of life and adaptation in individuals with inherited and sporadic facial palsy: opportunities for genetic counseling

Counseling/Psychosocial Issues
Submitter: Flavia Malheiro Facio, National Human Genome Research Institute, NIH
Primary Author: Flavia Malheiro Facio, National Human Genome Research Institute, NIH
Presenting Author: Flavia Malheiro Facio, National Human Genome Research Institute, NIH
Author 2: Erin Turbitt, National Human Genome Research Institute, NIH
Author 3: Gillian Hooker, Concert Genetics
Author 4: Carol Van Ryzin, National Human Genome Research Institute, NIH
Author 5: Moebius Syndrome Collaborative Research Consortium,
Author 6: Elizabeth Engle, Boston Children's Hospital
Author 7: Brenda Barry, Boston Children's Hospital
Author 8: Ethylin Wang Jabs, Icahn School of Medicine at Mount Sinai
Author 9: Bryn D. Webb, Icahn School of Medicine at Mount Sinai
Author 10: Irini Manoli, National Human Genome Research Institute, NIH
Author 11: Francis Collins, National Human Genome Research Insitute, NIH
Author 12: Barbara B Biesecker, National Human Genome Research Institute, NIH

Congenital facial palsy (FP) can lead to difficulties with feeding/speech, eye closure, and display of emotions. FP may be inherited or sporadic. Published patient interviews illustrate psychosocial challenges of living with FP. This study aimed to characterize cognitive and affective perceptions that may affect Quality of Life (QOL) and adaptation among FP patients enrolled in a natural history/genomics study. We hypothesized that greater optimism and lower depressive symptoms would be associated with higher QOL and adaptation to FP. 

Participants >10 yrs. were invited to
complete an on-line survey, with validated instruments. Hypotheses were tested using Pearson correlations. Data from adults (28/31 respondents) were analyzed. Most were women (68%). Participants reported a moderate level of adaptation to FP similar to patients with other genetic conditions (M=3.31, SD=1.10), and perceived their QOL to be relatively high (M=20.36, SD=5.51). They reported a high level of social stigmatization (M=3.37, SD=1.01). As hypothesized, QOL was associated with greater optimism (r=0.71, p<0.001) and lower depressive symptoms (r=0.88, p<0.001). Similarly, adaptation was associated with greater optimism (r=0.55, p=0.003) and lower depressive symptoms (r=-0.55, p=0.004). Analysis of illness perceptions revealed that more negative emotions about FP and greater perceived consequences were associated with lower QOL (r=-0.41, p=0.04, and r=-0.56, p=0.003). No similar associations were found for adaptation. FP participants reported high social stigma alongside relatively high QOL revealing a theme of resilience previously reported in others living with congenital conditions. This finding is echoed by the moderately high adaptation reported. The data reinforce the importance of genetic counseling to address the threat of social stigmatization, the negative affect toward FP and perceived negative consequences that are suggested to contribute to lower QOL. Genetic counselors working in rare disease settings have key opportunities to improve patient QOL using targeted interventions.

C-123 Examining the relationship between genetic counselors’ implicit attitudes toward disability and their practice methods
Counseling/Psychosocial Issues
Submitter: Helen Gould, The University of Texas Genetic Counseling Program
Presenting Author: Helen Gould, The University of Texas Genetic Counseling Program
Primary Author: Helen Gould,
Author 2: Jennifer Czerwinski, The University of Texas Health Science Center at Houston
Author 3: S. Shahrukh Hashmi, The University of Texas Health Science Center at Houston
Author 4: Victoria Wagner, The University of Texas Health Science Center at Houston
Author 5: Katie Stoll, Genetic Support Foundation
Author 6: Kathryn Ostermaier, Texas Children’s Hospital

Genetic counselors have a unique role in healthcare that requires a balance between being patient educators and patient advocates when discussing disability. This study aimed to determine genetic counselors’ attitudes toward disability, identify what factors affect these implicit attitudes, and describe how attitudes may affect counseling. Case scenarios involving disability were used to examine different counseling methods within a genetic counseling session including medical complications, diagnostic information, lifestyle and social implications, and psychosocial issues. Attitudes were measured using the validated Disability Attitudes Implicit Association Test (DA-IAT), and personal/professional
experiences with disability were assessed. Responses were collected using an electronic survey. Analysis of 382 participant responses revealed that personal experience with individuals with disabilities did not significantly impact implicit bias or counseling methods. In addition, it was determined that genetic counselors have a stronger bias toward ability compared to previous participants of the DA-IAT. The length of time in the field or whether the participant was a practicing counselor or student did not appear to influence bias. There was a significant difference found in counseling methods between specialties, with cancer counselors spending more time on social and lifestyle factors. The strong bias toward ability observed across specialties may be due to shared factors that influence interest in this field, but more likely reflects the inability of the available tool to capture the complexity of genetic counselors’ relationship to individuals with disability. Specifically, genetic counselors seem to be able to identify that an individual with a disability is distinctly different from a disability itself. This study emphasizes the importance of incorporating patients' individual definitions of disability into genetic counseling sessions and building an environment of patient advocacy and education around their personal perspectives and needs.

C-126 A qualitative investigation of parents' information and support needs when their child is diagnosed with Alopecia Areata.

**Counseling/Psychosocial Issues**

*Submitter: Alexandria Holcomb,*

*Presenting Author: Alexandria Holcomb,*

*Primary Author: Alexandria Holcomb,*

*Author 2: Patricia McCarthy Veach, PhD, LP, University of Minnesota*

*Author 3: Maria K Hordinsky, MD, University of Minnesota*

*Author 4: Bonnie LeRoy, MS, CGC, University of Minnesota*

Background: Alopecia Areata (AA) is an autoimmune form of hair loss that is highly variable, has no FDA approved treatment, and has an unpredictable prognosis. Research has shown that individuals with AA have a negatively affected quality of life and higher than average rates of anxiety and depression. Few studies have explored the informational and support needs of individuals with AA, especially in children, and no research has explored the informational and support needs of their parents. Objective: The primary aim of this study was to explore informational and support needs of parents whose children were diagnosed with AA. Methods: Twenty-four semi-structured individual interviews were conducted; 12 with parents whose child has non-progressive or patchy AA, and 12 with parents whose child has progressive AA totalis (complete scalp hair loss) or universalis (complete hair loss on scalp, eyebrows and eyelashes). Thematic analysis of the interviews revealed two overarching themes: informational needs (comprising 6 topics; e.g. general information, support), and psychosocial needs (comprising 12 topics; e.g. social support, psychological counseling). Results: The types of information and support
parents receive from healthcare providers and other individuals vary widely, especially regarding psychosocial concerns, and they are not always what parents find most helpful. Parents reported that there are no age-appropriate support groups for their children and, strikingly, a consistent failure of healthcare providers to acknowledge the emotional distress of the children and the parents caused by the diagnosis. Discussion: Although genetic counselors may not necessarily see individuals or parents specifically for the indication of AA, if a patient or parent is seen by a genetic counselor, the counselor should acknowledge the emotional effects of the diagnosis. The counselor should assess the support needs of the patient and family and provide appropriate referrals.

C-129 Parental perception of and experience with uncertain results from pediatric whole exome sequencing
Counseling/Psychosocial Issues
Submitter: Xin Li, University of Maryland,
Presenting Author: Xin Li, University of Maryland,
Primary Author: Xin Li,
Author 6: Shannan Dixon,
Author 2: Rachel Nusbaum,
Author 4: Constance Smith-Hicks,
Author 5: Leila Jamal,
Author 7: Sonal Mahida,

Whole exome sequencing (WES) has brought a new hope for families seeking an explanation for their child’s condition. Despite its promising diagnostic yield, WES frequently introduces variants of uncertain significance (VUS), which have been speculated to cause parental stress and anxiety. This study aims to explore the psychosocial impact of a VUS result from pediatric WES on caregivers and to identify implications for clinical practice. Telephone interviews were conducted with parents or legal guardians of a child who has undergone WES and received a VUS result (N=14), to assess caregiver’s understanding of the result, perceived impacts, affective responses, and coping strategies. Coding and content analysis were performed. Most participants had a good understanding of the test performed (N=12). Nine of them recalled VUS, two reported nothing was found and one reported that a definitive cause was identified. Most participants deemed the result had no (N=7), or yet any (N=4) impact on their vision of their child’s condition and future, but several participants expressed a positive outlook. However, one participant reported fear resulting from the result. Nearly all participants reported that this result did not significantly alter their child’s care or their ability to take care of their child. Participants experienced emotions, including relief/comfort, stress/anxiety, and upset/disappointment, and reported various aspects that they found helpful or unhelpful going through
the process. Additionally, several participants expressed their interests in research studies and peer support groups dedicated to families with a VUS result. In summary, the majority of participants reported no change in child’s care. They experienced a range of emotions and provided additional valuable feedbacks. These results provide insights into the psychosocial impact of uncertain results from WES that may help to guide pre- and post-WES counseling in the future.

C-132 Correlation between Illness Perception and Perceived Utility of a Support Group Among Affected Individuals and Unaffected Parents of Children with Marfan syndrome

Counseling/Psychosocial Issues
Submitter: Amy Malinowski,
Presenting Author: Amy Malinowski,
Primary Author: Amy Elizabeth Malinowski, University of Maryland School of Medicine
Author 2: Julie Frank, Dept of Pediatrics University of Maryland School of Medicine
Author 4: Shannan Delany Dixon, Dept of Pediatrics University of Maryland School of Medicine
Author 3: Gretchen MacCarrick, Johns Hopkins University School of Medicine
Author 5: Kristin Maloney, University of Maryland School of Medicine

Social support is an important factor for both psychosocial and physical clinical outcomes. Utility of a support group varies by the type of group, patients’ interpretation of disease comparison, and personality of the patient. As personality and interpretation of disease both contribute to illness perception, it is reasonable to hypothesize that illness perception itself has an effect on patients’ perceived utility of a support group. However, no study has evaluated the relationship between illness perception and perceived utility of a support group. This study aimed to assess this relationship among individuals affected with Marfan syndrome and unaffected parents of children with Marfan syndrome. An electronic survey was distributed via the Marfan Foundation and included a modified version of the Revised Illness Perception Questionnaire, the Ten Item Personality Inventory, and items addressing the categories of Cutrona and Suhr’s Social Support Behavior Code. Our results demonstrate that when personality is controlled for, the consequences, cyclical notions of disease timeline, identity, and emotional representations components of illness perception are significant predictors of perceived utility of a support group (p-values=0.026, 0.013, 0.023, 0.036), accounting for 3.6% (change in R2=0.036), 3.0% (change in R2=0.030), 2.9% (change in R2=0.029), and 2.6% (change in R2=0.026) of the variance observed in perceived utility of a support group scores, respectively. Practitioners may use this information to identify patients and families likely to find benefit in attending a support group and to provide alternative support services to those less likely to perceive utility.
C-135 Evaluation of the Support Provided to Male BRCA1/2 Mutation Carriers: Are Their Needs Being Met or Can Genetic Counselors Do Better?

Counseling/Psychosocial Issues
Submitter: Anna Lena Nassar,
Presenting Author: Anna Lena Nassar,
Primary Author: Anna-Lena Nassar, Brandeis University
Author 2: Gayun Chan-Smutko, MGH Boston, Brandeis University
Author 3: Susan Mecsas-Faxon, Harvard Vanguard Medical Associates in Boston
Author 4: R. C. Mellors,

Inherited mutations in the BRCA1 and BRCA2 genes are associated with hereditary breast and ovarian cancer syndrome (HBOC), a cancer susceptibility condition which significantly increases a woman’s risk for breast and ovarian cancer compared to the general population. Male BRCA1 or BRCA2 mutation carriers have a significantly increased risk for cancers as well including breast, prostate and pancreatic cancer. Research and efforts to support individuals affected with HBOC are frequently focused on women, and less attention is given to the needs of male carriers. The purpose of this qualitative study was to gain a better understanding of what resources genetic counselors should offer to male BRCA mutation carriers with children to best serve their needs. Seven male BRCA carriers with biological children were recruited from an online support group and an online foundation to participate in a semi-structured telephone interview. The subjects ranged in age from 43 to 74 years and 4 had personal histories of cancer. The major topics addressed included information provided by the genetic counselor, experiences with supports and resources, concerns, and how fatherhood has impacted their experience. Thematic analysis of the interview transcripts was performed in ATLAS.ti (v.8) and 7 themes were identified. All 7 reported concerns over their children’s risks and the 5 with adult children placed importance on open communication with them. Overall, men were satisfied with the service provided by their genetic counselor but wanted their providers to give them medical and informational resources. Men found online resources to be useful ways to connect with other male carriers and stay informed. Participants felt a need for better awareness and normalization of the male carrier experience including more attention devoted to cancer risk and prevention. This study provides first-person insights into ways genetic counselors can improve the immediate and long-term experiences of male BRCA mutation carriers by recognizing their informational and psychosocial needs.

C-138 Does an Individual’s Perceived Severity of Their Positive Genetic Test Results Influence Whether They Post about it on a Social Media Site?

Counseling/Psychosocial Issues
Submitter: Kaitlyn E Riley, Virginia Commonwealth University
There has been a dramatic increase in the use of both social media and genetic testing, and people are often using social media to share their genetic test results online. Currently, there is a lack of research on what prompts people to post online, and if they are having positive or negative experiences from it. In this study, people who have tested positive for the Huntington disease (HD) mutation or BRCA1/2 mutations were surveyed to determine their perceived severity of their test results, if they posted online, and their reasoning behind posting or not-posting. The majority of participants were recruited through Facing Our Risk of Cancer Empowered, Huntington Disease Society of America, and Huntington Disease Youth Organization social media pages. One hundred and five individuals participated in the survey. Most (94.2%) were female, and the average age range was 41-45 years. Perceived severity was assessed using a modified scale based on the Health Belief Model (Cronbach alpha = 0.89), with possible scores from 13 (low severity) to 65 (high severity). Perceived severity was higher for HD participants (P=0.012). HD participants were less likely to say they posted their genetic test results on social media (34% versus 73%, P<0.001). Perceived severity appeared to be inversely associated with posting, but this did not reach statistical significance (P=0.112). Of those who chose to post their results on social media, many people chose to post to spread awareness of their genetic condition, as well as to provide and receive support. Over 76% of people who posted on a social media site reported benefitting, while only 14% reported experiencing a negative repercussion. Data from this study demonstrated that genetic counselors and other healthcare providers should be providing information about online support groups in addition to in-person support groups, as it could have a positive benefit for our patients.

C-141 Concerns and Perspectives from Families with Hereditary Pancreatitis

Counseling/Psychosocial Issues

Submitter: Celeste Shelton, University of Pittsburgh

Primary Author: Celeste Shelton, University of Pittsburgh

Presenting Author: Celeste Shelton, University of Pittsburgh

Author 2: Dhiraj Yadav, MD MPH, University of Pittsburgh & UPMC

Author 3: David C Whitcomb, MD PhD, University of Pittsburgh & UPMC

Introduction: Hereditary pancreatitis (HP), a highly penetrant (~80%) autosomal dominant disease associated with PRSS1 variants, causes acute pancreatitis (AP) in childhood and chronic pancreatitis (CP)
by early adulthood. Clinical features include pain, diabetes and risk of pancreatic cancer. 

Purpose: To evaluate the concerns and perspectives of HP families related to health, genetic testing and counseling. 

Methods: HP kindreds were prospectively recruited from 1995-2015. At enrollment, study subjects completed medical and family history questionnaires, and provided blood or saliva for DNA testing. Study participants were recontacted between 2015-2017, and asked to complete a survey including Likert scales, rank order items and open-ended questions on health perspectives and experiences related to HP, PRSS1 testing and counseling. Data was analyzed with descriptive and thematic methods. 

Results: Thirty-nine affected and 21 unaffected family members completed the survey. Among family controls, ‘worry’ and ‘helplessness’ were most frequently described as the most difficult problem in their family because of HP, particularly with regard to pain. Three subjects described the impact of drug addiction on their family. ‘School or work limitations’ was the largest financial concern, with 65.5% rating it as ‘moderately’ to ‘extremely important’. Concern about ‘health insurance discrimination’ persists, with 48% of study participants rating at as a ‘moderate’ to ‘extremely important’ reason to not pursue genetic testing. Surprisingly, only 61.8% of affected PSSS1 carriers believed the chance for a parent to pass HP to his or her children was 50% (1 in 2), whereas 17.65% believed the chance was 100%. 

Discussion: Pain, beginning at a young age, is the most difficult to manage symptom and further complicated by risk for addiction. Frequent expression of ‘helplessness’ identified an important problem to address in future care. Overestimation of the chance for HP transmission also highlights the importance of education and counseling.

C-144 The Personal Utility of a Genetic Etiology for Developmental Brain Disorders in Adult Research Participants

Counseling/Psychosocial Issues

Submitter: Karen Wain, Geisinger - Autism & Developmental Medicine Institute

Primary Author: Karen Wain, Geisinger - Autism & Developmental Medicine Institute

Presenting Author: Karen Wain, Geisinger - Autism & Developmental Medicine Institute

Author 2: Kasia Tolwinski, Geisinger - Autism & Developmental Medicine Institute

Author 3: Caitlin Bozick, Arcadia University

Author 4: Lauren Kasparson, Geisinger - Autism & Developmental Medicine Institute

Author 5: Lisa Kessler, Arcadia University

Author 6: Emily Palen, Geisinger - Autism & Developmental Medicine Institute

Author 7: David H. Ledbetter, Geisinger

Author 8: Christa Lese Martin, Geisinger - Autism & Developmental Medicine Institute
Developmental brain disorders (DBD), such as autism, intellectual disability, epilepsy, and neuropsychiatric conditions, share underlying genomic etiologies and can present with marked intrafamilial variability. Copy number variants (CNVs) are a frequent cause of DBD in children, though less is known about the natural history and lived experiences of adults with DBD-related CNVs. Through the Geisinger MyCode Initiative, genetic counselors (GC) from the Autism & Developmental Medicine Institute returned clinically-confirmed pathogenic CNVs identified by population-based exome sequencing to adults with DBD documented in their medical record. The purpose of this study was to explore immediate participant reactions to receiving these results. Disclosure sessions used a semi-structured format to facilitate discussion and typically were conducted in-person; phone disclosures were optional. Qualitative thematic analysis was conducted across two data-sets: 1) post-session GC written notes (n=37), and 2) transcribed audio-recordings of in-person result disclosures (n=10, 100% consent rate). These approaches were utilized to reduce burden on participants. Dual coders analyzed data-sets independently and themes were compared. Major themes were highly consistent across data-sets. Recall of MyCode consent was generally high. Most participants shared DBD history absent from the medical record, including learning and interpersonal difficulty. Previously-held beliefs about DBD causes most often related to social circumstances (e.g., trauma, family disruption). Participants frequently expressed that the CNV result “fit” or completed their lived experience and felt reassured that DBD was “not their fault.” Reported sense of self was most often unchanged or more positive. Overall, reactions were positive and results were considered valuable for oneself and relatives. We conclude that DBD-related genetic results have personal utility and are valuable to adults with DBD history. These results can inform broad policy for genomic screening programs.

A-148 Self-reported skills of new leaders in genetic counseling training programs

Education

Submitter: Karin M. Dent, University of Utah Health Sciences Center

Primary Author: Karin M. Dent, University of Utah Health Sciences Center

Presenting Author: Karin M. Dent, University of Utah Health Sciences Center

Author 2: Ane M. Sagardia, St. Bartholomew’s Hospital; London, UK

Author 3: Barbara B. Biesecker, Research Triangle Institute; Washington, D.C.

An important goal of the Association of Genetic Counseling Program Directors (AGCPD) is to learn more about the foundational skillset and experiences genetic counselors in program leadership positions possess or should develop. A working group of the AGCPD surveyed members who began a position in program leadership (assistant/associate program directors, clinical supervisors, research coordinators, etc.) within the last three years. Survey questions assessed what skills these individuals possessed when they began their leadership positions, as well as the skills they later developed while in the position. Thirty-one individuals completed the survey. Nineteen responded to the open-ended question assessing the top five skills they brought to their leadership positions. The most commonly reported
categories of skills were professionalism (53%), communication (47%), clinical and counseling experience (37%), organization (37%), teaching experience (32%), and leadership and mentoring (32%). Other skills included adaptability, commitment, research, and enthusiasm. Seventeen individuals responded to the open-ended question assessing the top five skills they later identified as important in their leadership positions. These included negotiation and business savvy (29%), networking (29%), mentoring and leadership (24%), finance (18%), strategic thinking (18%), listening to new ideas (18%), and expansion of the applicability of counseling skills (18%).

Identifying a core skillset necessary for genetic counselors interested in pursuing positions in training program leadership is important in developing future leaders of genetic counseling training programs. This will ensure a robust and prepared program leadership pipeline, as well as continue expanding our profession. Future endeavors may include mechanisms for identifying emerging leaders for genetic counseling training programs as well as specific leadership training.

A-151 Is Current Fragile X Syndrome Counseling Enough? Expanding the Clinical Phenotype of Fragile X in Premutation and Intermediate Allele Carriers

Education
Submitter: Zahra Saadat Girnary,

Presenting Author: Zahra Saadat Girnary,

Primary Author: Zahra Saadat Girnary,

Author 2: Jessica Klusek, Univ. of South Carolina, Communication Sciences & Disorders

Author 3: Allyn McConkie-Rosell, Duke University, Division of Medical Genetics

Author 4: Crystal Hill-Chapman, Francis Marion University, Department of Psychology

Fragile X syndrome (FXS) is caused by a triplet repeat expansion on the FMR1 gene. Individuals with >200 repeats have FXS, while individuals between 45-54 and 55-200 repeats have the FMR1 intermediate allele and premutation, respectively. FXS is characterized by autism, intellectual disability, and distinct facial features while the premutation is associated with fragile X-associated tremor/ataxia syndrome (FXTAS) and fragile X-associated primary ovarian insufficiency (FXPOI). However, there is limited information on the psychiatric manifestations such as depression and social anxiety in those with the premutation or the intermediate allele. This study sought to 1) study knowledge regarding FXTAS, FXPOI, as well as the potential for psychiatric manifestations in individuals with the premutation; 2) study which features, if any, intermediate allele carriers exhibit, and 3) learn which resources are most helpful for learning about FXS and its associated phenotypes. Individuals with the FMR1 premutation and intermediate allele were recruited through online Facebook groups and completed one of two surveys. Data was analyzed using descriptive statistics, chi-square, and ANOVA. Thematic analysis was used to evaluate the responses to open-ended questions. Results showed that 1) individuals in both groups did not understand the inheritance of FXS and overestimated their chances for FXS-related
disorders; 2) 70% of individuals with the FMR1 premutation and between 50%-60% of individuals with the intermediate allele report symptoms of depression/anxiety, and 3) the most helpful resources for learning about FXS were internet websites and conversations with health providers and other individuals with the FMR1 premutation. These findings reveal that genetic counselors should place more emphasis on the genetics of FXS and its associated phenotypes to both groups and offer both traditional sources of support as well as referral to Facebook groups to facilitate conversations with others in similar situations.

**A-154 Genetic Counselors’ Attitudes Toward Continuing Education Options**

*Education*

Submitter: Jessica Shiles,

Primary Author: Kelsey Johnson, Sarah Lawrence College

Author 2: Jessica R. Shiles, Sarah Lawrence College

Author 3: Talya Boisjoli, Sarah Lawrence College

Author 4: Claire Davis, Sarah Lawrence College

Presenting Author: Kelsey Johnson, Sarah Lawrence College

With various aspects of contemporary clinical practice and the rapidly growing field of genomic medicine, genetic counselors are responsible for meeting ever-changing demands of providing up-to-date healthcare services. Continuing education and recertification play a significant role in this process. This study assessed genetic counselors’ attitudes towards continuing education options. A web-based survey was sent to NSGC members resulting in 358 responses. Respondents rated current continuing education options as “mildly convenient” and “mildly transferable” to daily practice. The three continuing education options can be ranked according to convenience, from most to least, as follows: Category 1; Professional Activity Credits (PACs); Category 2. The options can also be ranked from most transferable to least transferable as follows: Category 1; PACs; Category 2. <br />
Open-ended responses showed recurrent themes across all credit types including process feedback and content feedback such as convenience, usefulness, and challenges. Another important theme was an underlying lack of knowledge surrounding continuing education options and processes. Providing more accessible information on continuing education options, cost management, and content review were identified as potential mechanisms for supporting effective continuing education.<br />
These findings are the first step towards verifying that genetic counselors believe efficient and effective continuing education is available and applicable to their work. We would encourage future research to investigate the impact of continuing education on genetic counselor’s competence and expertise. Potential topics for future investigation include long-term cost management of continuing education fees and efficacy of current options, with a focus on conference-based learning. <br />

Keywords: Genetic Counseling, Continuing
A-157 Assessing the disease specific knowledge gaps in patients and caregivers living with lysosomal storage diseases

Education
Submitter: Georgia Loucopoulos, Emory University Genetic Counseling Training Program
Primary Author: Georgia Loucopoulos, Emory University Genetic Counseling Training Program
Presenting Author: Georgia Loucopoulos, Emory University Genetic Counseling Training Program
Author 2: Dawn Jacob Laney, Emory University Lysosomal Storage Disease Center
Author 3: Morgan Frances Simmons, Emory University Lysosomal Storage Disease Center
Author 4: Deepti Babu, Independent Consulting Medical Writer and Editor
Author 5: Dr. Kathryn Garber, Emory University School of Medicine, Dept. of Human Genetics
Author 6: Cecelia A. Bellcross, Emory University School of Medicine, Dept. of Human Genetics

There is currently a lack of information about knowledge gaps in the lysosomal storage disease (LSD) patient population, which limits the capacity for proper genetic counseling. This is the first study to discern these gaps and assess if online information can fill them. This study consists of a pre-survey, a research period, and a post-survey. The pre-survey collects demographic information, tests knowledge, and determines patients’ questions. Patient questions are split into current and initial questions (from the time of diagnosis). Patients are then directed to ThinkGenetic.com, a source for accurate and current genetic information, for research at their leisure. The post-survey determines if knowledge scores improved and if questions were answered. Differences in knowledge scores are determined through bivariate analysis. Questions are coded into ten pre-determined categories to analyze trends.

52 patients were recruited from the Emory University Lysosomal Storage Disease Clinic. 57% of patients achieved perfect scores (5) in both surveys. Scores changed for 20% of patients, all increased. The median increase was 2 points. Initial patient questions focused on treatment and quality of life. Current patient questions focused on research studies and treatment. For initial questions, 64% of patients reported they found answers, 15% did not, and 21% said their questions were “somewhat” answered. For current questions, 28% of patients reported they found answers, 30% did not, and 42% said their questions were “somewhat” answered. Patients reported questions remained about research studies, treatment, and quality of life, indicating that this is where their knowledge gaps lie. The data also suggests that accurate online information can answer patient questions, but some questions may require further research. The small increase in knowledge scores is attributed to the small number of knowledge questions and the high baseline knowledge of the cohort. We will continue this study with more LSD patients.
Increasing the number of genetic counseling (GC) graduates would help to address current GC workforce demands, but some limitations inhibit this, including supervisor burden as students attempt to obtain enough cases to demonstrate competency in clinical skills. Currently students are required to have at least 50 core cases, though there is evidence that many students get more than this. The purpose of this study was to describe the relationship between GC student self-efficacy in clinical skills and the number of core cases students log during their training. In this study, second year GC students nearing the end of training completed a questionnaire that included the Genetic Counseling Self-Efficacy Scale (GCSES) and questions related to the students’ clinical experiences. Confirmatory factor analysis was performed. GC student self-efficacy for all six factors was found to be positively associated with the number of core cases students accumulated during training, with a plateau in GCSES scores between 80-100 core cases. The average number of core cases reported by participants was 102 cases, with a range of 10-300 cases obtained at this point in training. Around 94% of participants indicated that they felt they had seen about the right number or more cases than necessary to feel competent in their clinical skills. No association was found for GC student self-efficacy and other clinical variables, such as the point in training students began taking on roles in clinic, the number or length of rotations, or number of cases students had observed. These data suggest that for the average student 50 cases may not be enough, but over 100 may be more than needed in order to feel confident in their skills. However, the number of cases necessary is likely to vary between students. GC programs may benefit from increased flexibility in clinical training to accommodate this variety. Programs whose students tend to log more than 100 cases may consider lowering their students’ clinical caseloads, which may in turn allow programs to matriculate more students.
A-163 Evaluating Patient Satisfaction with Genetic Counseling Sessions: What is the Impact of Genetic Counseling Trainees?

**Education**

Submitter: Alison Dana Robzen,

Primary Author: Alison Dana Robzen,

Presenting Author: Alison Dana Robzen,

Author 2: Brittany Degreef,

Author 3: Anne Matthews,

Author 4: Anna Mitchell,

Author 5: Leslie Cohen,

Clinical rotations are crucial to the development of student genetic counseling skills and style. Therefore, as part of all accredited genetic counseling training programs, students are required to perform clinical rotations. Just as clinical rotations are important to the genetic counseling (GC) student, patient satisfaction is important to the patient and the medical institution. The purpose of this study was to explore whether patient satisfaction was impacted by GC students’ training status. Additionally, the study’s purpose was to determine if there were any aspects of student-led genetic counseling sessions that could be adjusted or emphasized to improve patient satisfaction. To our knowledge, no research has been conducted to evaluate patient satisfaction with GC students. A modified version of the Satisfaction with Genetic Counseling Scale (Shiloh et al., 1990) was used to gauge patient satisfaction with a GC student compared to a licensed genetic counselor (LGC), who was used as a control. Data trends suggest that there is no statistical difference in patient satisfaction when seen by a LGC and a GC student in his or her final rotation.

B-149 What Walls? Demystifying the Role of Race/Ethnicity in Genetic Counseling Supervisory Relationships

**Education**

Submitter: Cheyenne Nicole Dewey, University of Minnesota

Primary Author: Cheyenne Nicole Dewey, University of Minnesota

Presenting Author: Cheyenne Nicole Dewey, University of Minnesota

Author 2: Krista Redlinger-Grosse, University of Minnesota

Author 3: Patricia McCarthy Veach, University of Minnesota

Author 4: Bonnie LeRoy, University of Minnesota
Background: Clinical supervision is a critical component of genetic counselor training. The Reciprocal Engagement Model of Supervision (REM-S) outlines tenets and goals of genetic counseling supervision with a focus on the supervisor-supervisee relationship and an understanding of factors such as culture that influence a student’s context. While studies have shown that addressing cultural differences in supervision is important, many supervisors are unsure how to discuss these differences with students. Objective: The purpose of this study is to explore how racial/ethnic differences between genetic counseling students and their clinical supervisors affect students’ supervisory experiences and subsequent provision of supervision. Methods: Eighteen genetic counselors with experience in clinical supervision, nine who self-identified as White/Caucasian, and nine who self-identified racial/ethnic backgrounds other than White/Caucasian, were purposively recruited to participate in semi-structured phone interviews. Questions asked how race/ethnicity was approached in supervisory relationships, how it affected their relationships, and how it influenced their supervision practices when they became supervisors. Results: Thematic analysis revealed seven themes, with most respondents agreeing that: (1) race/ethnicity is not fully recognized/discussed in supervision; (2) when it is discussed, conversations focus on patients’ culture or are more casual in nature; (3) supervisors vary in their level of comfort discussing race/ethnicity; and (4) more supervisor training in how to approach conversations around race/ethnicity is desired from both student and supervisor perspectives. Discussion: The results demonstrate that cultural differences vis a vis student and supervisor race/ethnicity are addressed to a varying degree. Further discussion about the role of race/ethnicity in the supervisory relationship and training in how to address a student’s cultural context in supervision are warranted.

B-152 Genetic Counselors in the Middle School Classroom: A Pilot Study to Raise Awareness of and Interest in the Field

Education
Submitter: Allison Hutchinson,

Primary Author: Allison Hutchinson, Augustana-Sanford Genetic Counseling Graduate Program

Author 2: Elizabeth McMillan, Sanford Research

Author 3: Emily Griese, Sanford Research

Author 4: Valerie Bares, Sanford Research

Author 5: Laurie Daily, Augustana University

Presenting Author: Allison Hutchinson, Sanford Imagenetics

Compared to demographic data from other healthcare professions, genetic counselors are more likely to be Caucasian females. Despite at least a two-decade-long focus on increasing the number of underrepresented minorities (URMs), it is difficult to say what progress has been made. Lack of diversity is considered to limit positive patient outcomes in all areas of healthcare, not just genetic counseling.
Surveys of high school and college instructors, counselors, and advisors suggest a limited knowledge of the genetic counseling profession and a general lack of time to discuss future career options with students. Career choice can be a convoluted process, as is evidenced by responses from current URMs working as or training to become genetic counselors. Many current URMs in the field found genetic counseling later in their careers due in part to their lack of awareness. A pilot study consisting of equal numbers of male and female sixth grade science club students was conducted to explore the impact that direct teaching might have on students’ awareness of and interest in genetic counseling. The analysis used the non-parametric Wilcoxon signed rank test due to the ordinal, Likert-scale data. Results derived from a pre- and post-survey of lesson participants indicated a statistically significant increase in students’ perceptions of having a role model in a science career. Other professions in search of greater workforce diversity have also identified the importance of role models. This pilot study provides genetic counselors and interested stakeholders a lesson framework with presentation slides and a student handout to take into the middle school classroom along with assessment tools to gauge the lesson’s effectiveness. Efforts to reach local middle school students to highlight genetic counseling as a potential career choice may add to the continued work being done to increase the diversity of future genetic counseling applicant pools.

B-155 OB/GYN Residents’ Training, Attitudes, and Comfort Level Regarding Genetics

Submitter: Anastasia Maria Kathrens-Gallardo, Mercy Hospital and Medical Center

Primary Author: Anastasia Maria Kathrens-Gallardo, Mercy Hospital and Medical Center

Presenting Author: Anastasia Maria Kathrens-Gallardo, Mercy Hospital and Medical Center

Author 3: Edward Linn, John H. Stroger Jr. Hospital

Author 4: Rachel Pothast, Northwestern Medicine

Author 5: Lauren Propst, Northshore University HealthSystem

Author 6: Aishwarya Arjunan, Counsyl

Author 2: Catherine Wicklund, Northwestern University

As the availability and utility of genetic testing expand, it is increasingly necessary for primary care providers (PCPs) such as obstetricians and gynecologists (OB/GYNs) to be providers of genetic services. Past studies have shown that PCPs, including practicing OB/GYNs, report low comfort level and knowledge regarding genetics; in contrast, little is known about the knowledge or attitudes of OB/GYN residents. This study aimed to understand OB/GYN residents’ educational and clinical genetic experiences, attitudes towards genetics in practice, comfort performing genetic counseling-related tasks, and motivating factors for learning more about genetics. Eligible participants included residents in
an accredited OB/GYN training program; residents were forwarded an anonymous, web-based 49 question survey. SPSS was used to conduct descriptive quantitative statistical analysis. Eighty-two eligible participants representing all postgraduate years of training completed the survey. Responses showed that discussions with attending physicians were the most common source of learning about genetics. Most respondents felt their attendings valued genetics (81%) and were knowledgeable on the subject (85%), but 28% did not feel their attendings reinforced concepts in clinic that had been taught in classes. An overwhelming majority agreed staying informed about genetics was valuable to them and providing some genetic services was within their scope of practice; however, there were significant reported deficiencies in comfort level, particularly with hereditary cancer genetics tasks and ordering and interpreting of genetic tests. Residents cited accessibility of information as a top motivator to stay informed and expressed interest in shadowing and learning from genetic counselors. This study illustrated that clinically relevant, easily accessible genetics education that is further reinforced in the clinical setting may increase residents’ levels of comfort with genetic counseling, which in turn may increase their preparedness to provide genetic services as practicing physicians.

B-158 MedGen: Your Access to Medical Genetics Information

Education
Submitter: Marilu Athaide Hoeppner,

Primary Author: Adriana J. Malheiro, National Center for Biotechnology Information (NCBI)

Author 2: Melissa Landrum,

Author 3: Donna Maglott,

Author 4: Kurt McDaniel,

Author 5: Mark Benson,

Author 6: Garth Brown,

Author 7: Chao Chen,

Author 8: Shanmuga Chitipiralla,

Author 9: Anna Glodek,

Author 10: Baoshan Gu,

Author 11: Jennifer Hart,

Author 12: Douglas Hoffman,

Author 13: Wonhee Jang,
MedGen is a web portal to phenotypic information associated with genetic conditions managed by the Medical Genetics and Variation (MGV) Group at the National Center for Biotechnology Information (NCBI), National Institutes of Health (NIH). MedGen is a free, comprehensive resource for one-stop access to essential information on phenotypic health topics related to medical genetics as collected from established high-quality sources. It integrates terminology from multiple primary ontologies (or nomenclatures) to facilitate standardization and more accurate results from search queries. Bookmarking this one URL, www.ncbi.nlm.nih.gov/medgen, will provide access, for example, to GeneReviews, OMIM (Online Mendelian Inheritance in Man), PubMed (reviews, curated papers of interest, etc.), and consumer and pharmacogenetic resources. MedGen also links to actionable information like professional guidelines from medical and authoritative societies, available tests in the NIH Genetic Testing Registry (GTR) and clinical variants in ClinVar.

Drawing data from OMIM, Human Phenotype Ontology (HPO) and other clinical hierarchy resources, MedGen displays a comprehensive list of clinical features for a genetic disease that can serve as a potential guide to evaluate a patient. From those same relationships, MedGen enables searching for conditions based on individual terms or a set of clinical features.

MedGen additionally provides a terminology service by aggregating phenotype names from different resources and ontologies into single concepts, while preserving source identifiers, and uses Systematized Nomenclature of Medicine - Clinical Terms (SNOMED CT) as the preferred name so it can be incorporated into EHRs. Information is freely available and downloadable using NCBI's eUtilities software and FTP site.

This presentation will demonstrate how to leverage MedGen to facilitate the clinical genetic process and it will show how to incorporate this data into EHRs to make it available in hospitals and clinics.
B-161 An Assessment of Pediatric Cancer Genetic Counseling Training in Genetic Counseling Programs

**Education**

*Submitter: Eleanor Garrett Peacock, Boston University School of Medicine*

*Primary Author: Eleanor Garrett Peacock, Boston University School of Medicine*

*Presenting Author: Eleanor Garrett Peacock, Boston University School of Medicine*

*Author 2: Jill Krejdovsky, MS, CGC, Beth Israel Deaconess Medical Center*

*Author 3: Lindsey Stobie, MS, CGC, Beth Israel Deaconess Medical Center*

*Author 4: Emily Quinn, MS, CGC, St. Jude Children's Research Hospital*

Pediatric cancer genetic counseling is a growing area of practice for genetic counselors. In addition to the complexity and lack of consensus guidelines for many pediatric cancer predisposition syndromes, there are unique ethical and psychosocial challenges. This study explored how genetic counseling programs are training their students in pediatric cancer genetic counseling. Surveys from 265 current students and recent graduates were analyzed. Almost all respondents reported instruction specific to pediatric cancer genetic counseling with a wide range in the amount and type of instruction. While most respondents did not observe (64%) or counsel (69%) a patient with a current diagnosis of pediatric cancer during clinical rotations, more students had exposure to patients with a personal or family history of pediatric cancer. The majority (74%) felt that their program prepared them slightly or moderately well to provide pediatric cancer genetic counseling. Respondent’s comfort level ranged based on the referral reason: while respondents largely felt comfortable counseling for retinoblastoma and pheochromocytoma/paraganglioma, they felt less comfortable counseling for indications such as adrenal cortical carcinoma, choroid plexus carcinoma, and rhabdoid tumors. The highest number of respondents (41%) indicated the amount of training was “about right,” followed by “less than expected” (35%). Responses to open-ended questions revealed interest in further opportunities for training in the classroom and clinic. This study suggests that many respondents do not feel well prepared at the time of graduation to provide pediatric cancer genetic counseling. However, they feel equipped to access resources and continuing education if interested. Important areas of growth for program curriculum include ethical and psychosocial training in this area as well as training on indications that have a strong association with a pediatric cancer predisposition syndrome.

B-164 Websites on inherited thrombophilia and pregnancy risk lack adequate quality, content, and readability to facilitate health decision-making

**Education**

*Submitter: Julie Solimine,*

*Presenting Author: Julie Solimine,*
Inherited thrombophilia disorders such as Factor V Leiden and Prothrombin G20210A are common genetic blood clotting conditions associated with multiple adverse pregnancy outcomes. Due to the relatively high prevalence of these disorders, affected individuals may depend on often-unregulated websites for information; despite this, websites on inherited thrombophilia and pregnancy risk have not been analyzed for adequacy in fulfilling this need. In this study, we analyzed quality, content, and readability of 43 websites related to this topic. Search phrases were utilized to compile 414 relevant websites; after applying exclusion criteria 43 websites remained for evaluation. Analysis was completed using DISCERN tool to assess website quality, a content analysis checklist developed based on a literature review and the American College of Obstetricians and Gynecologists 2013 practice guidelines, and Flesch–Kincaid grade level, Flesch Reading Ease (FRE), and SMOG index tools to evaluate readability. Results demonstrate an average reading level for these websites of 11th-12th grade, approximately four grade levels above the average American reader. The websites lack quality, with a mean DISCERN sum score of 39.6 out of 80, and content, with a mean content checklist sum score of 5.84 out of 13. As quality increases the content increases (rs= .366, p = 0.02), but website readability tends to decrease (FRE rs= -.314, p = 0.04; FK grade level rs=.334, p= 0.03). Therefore, the most-commonly accessed websites are likely too difficult for the average reader to understand and/or lack sufficient content and quality to guide beneficial health decision-making. This study demonstrates need for guidance on the best resources, development of adequate websites written at understandable reading levels, and facilitation of referrals to appropriate providers for individualized risk assessment for these patients.

C-147 How do we get there and will we be prepared? Clinician perspectives on elective genome sequencing

Education

Submitter: Liana Dayhoff, Augustana-Sanford Genetic Counseling Graduate Program

Presenting Author: Liana Dayhoff, Augustana-Sanford Genetic Counseling Graduate Program

Primary Author: Liana C. Dayhoff, Augustana-Sanford Genetic Counseling Graduate Program

Author 2: John Belmont, MD, PhD, Illumina Inc.

Author 3: Cinnamon S. Bloss, PhD, University of California, San Diego

Author 6: Erin Royer, MS, CGC, Sanford Heath and Augustana University
There is extensive information on healthy individuals who are interested in genome sequencing, but comparatively little about the clinical implementation of elective genome sequencing (eGS). Surveying clinicians who frequently order eGS can provide insights into how they are implementing eGS in clinical practice, what methods they use to expand their genomic knowledge, and explore why they decided to become early adopters of eGS. Semi-structured telephone interviews were conducted with 7 clinicians who were ordering providers for at least 6 patients on the Illumina TruGenome™ Predisposition Screen, a physician-mediated clinical whole genome sequencing screen for asymptomatic adults. Questions focused on the testing process as well as participant interest in genomic medicine and thoughts on the future of eGS. Interviews were audio recorded and transcribed. De-identified transcripts were analyzed using thematic analysis and grounded theory in Dedoose qualitative analysis software. Genomic Education emerged as primary theme along with four secondary themes: Partnerships in Genomic Education, Genomic Literacy, Knowledge Sharing, and Envisioning the Future of Genomic Medicine. Participants reported becoming early adopters of genomic medicine by either integrating eGS into their clinical practice or by working with an institution that already offered eGS to patients. Despite participant’s wide range of experiences, they agreed about the need for engagement strategies with clinicians and more genomic education. Participants had variable suggestions to facilitate better clinician understanding of eGS. Although participants envision increased patient uptake of eGS, obvious questions remain: How do we promote responsible integration of eGS? Will clinicians be prepared to address increased patient interest in eGS? This study of early adopters highlights the need for enhanced promotion of genomic education and more continuing education opportunities as well as the remaining concerns about the genomics workforce.

C-150 Who is engaging in precision medicine education? An exploratory analysis of online CME data.

Education
Submitter: Emily Edelman, The Jackson Laboratory
Primary Author: Emily Edelman, The Jackson Laboratory
Author 2: Paige Tanner, The Jackson Laboratory
Author 3: Laura Nicholson, Scripps Translational Science Institute
Author 4: Sean McConnell, American Medical Association
Author 5: Therese Ingram, The Jackson Laboratory
INTRODUCTION Despite rapid growth in somatic genomic tests and targeted therapeutics, there are few unbiased educational resources for oncology providers to learn about benefits and limitations of testing, and limited knowledge about the uptake or effectiveness of such programs. OBJECTIVE The purpose of this report is to describe the engagement and effectiveness of a free, online CME about somatic testing. METHODS The Jackson Laboratory, American Medical Association and Scripps Translational Science Institute developed and disseminated two interactive, case-based educational modules about somatic tumor testing. From 1/2017 to 3/2018, users completed post-surveys with knowledge items based on educational content and standard CME evaluation items. Registration and evaluation data were analyzed using Fisher exact tests. RESULTS 381 users enrolled in one or both modules (286 in module 1, 158 in module 2). 41% were physicians, 14% masters- and 9% bachelors-level nurses, 7% scientists and 5% genetic counselors, representing 14 countries and 35 U.S. states. Clinician specialty was available for 59%, with 47% in oncology, 25% in genetics and 15% in primary care. The average program rating was 4.5/5 and average knowledge score was 80%. Users had higher knowledge on concepts related to identifying utility and limitations of testing compared to interpreting results (87% v 74%, p<0.0001). In particular, users had lower knowledge about interpreting results associated with clinical trials (65%, p<0.05) and using a lack of actionable variants to guide therapeutic decisions (55%, p<0.001). Knowledge did not differ between professions. CONCLUSION While cancer specialists were the largest users of the program, the relatively high number of genetic and primary care specialists suggests there may be additional need for precision medicine training among these populations. The design and content of the program were satisfactory to users of diverse backgrounds. Users may benefit from additional training on interpreting results to inform treatment and clinical trial enrollment decisions.

C-153 Does a Diagnosis Make a Difference? Examining the Utility of Etiology-Based Information for Teachers of Children with Neurogenetic Syndromes.

Education
Submitter: Dana Jarvis,

Presenting Author: Dana Jarvis,

Primary Author: Dana Lin Jarvis, University of Utah Graduate Program in Genetic Counseling

Author 2: Louisa Stark, University of Utah

Author 3: Robert E. O’Neill, University of Utah

Author 4: Rena Vanzo, Lineagen Inc.
Children with neurogenetic conditions are known to have behavioral and cognitive phenotypes that can impact learning in the classroom. While current accommodations in the classroom do not address etiology-based needs, information is limited regarding teachers’ thoughts on the utility of etiology-based guidance for neurogenetic conditions. To address this gap, we surveyed special education teachers and school psychologists, examining their confidence in teaching children with neurogenetic conditions and the extent to which they felt etiology-based resources would improve a teacher’s ability to educate children with these conditions. The survey respondents included 52 school psychologists and 102 special education teachers in Utah with a response rate of 35.5%. The majority of school psychologists (69%) and special education teachers (52%) were confident in a teacher’s ability to teach a child with neurogenetic conditions, while 4% of school psychologists and 16% of special education teachers were not at all confident. 71% of school psychologists and 60% of special education teachers stated that the type of etiology-based resources provided with the survey would be very useful along with current accommodations in the classroom. Based on the survey findings, teachers feel confident teaching children with neurogenetic conditions, but they would like etiology-based resources that provide specific intervention strategies which may improve academic and behavior outcomes for students.

C-156 Exploring a Brief Medical Improvisational Performing Arts Intervention for Genetic Counseling Graduate Students

Education
Submitter: Weilong Li, University of Illinois at Chicago

Primary Author: Weilong Li, University of Illinois at Chicago

Presenting Author: Weilong Li, University of Illinois at Chicago

Author 2: Courtney Scherr, Northwestern University

Author 3: Remington Fenter, UT Southwestern Medical Center

Author 4: Katie Watson, Northwestern University

Author 5: Catherine Wicklund, Northwestern University

In other medical disciplines, medical improvisation (improv), a training method adapted from improv theatre, is used alongside traditional methods to develop students’ clinical skills, including psychosocial skills. Medical improv may be a useful training method for genetic counseling (GC) students to develop these skills, which are core competencies of genetic counseling. This study piloted a 2-hour improv workshop, adapted for GC students from a medical improv seminar intended for medical students. Current students and new GCs (n=14), recruited via email solicitations, participated in one of two workshops and completed a 30 minute individual semi-structured interview 2 months later. Interview questions were designed to gather participant opinion about satisfaction with the workshop and perceived relationship with GC education. Transcripts were coded by the first author using qualitative
Thematic analysis. Transcripts were parsed for key words and phrases, which were collapsed based on similarity into codes. Themes were formed by reanalyzing transcripts for code placement and interrelationship. Major themes include parallels between improv and psychosocial skills and feeling freedom to experiment and fail during the workshop. Participants discussed how medical improv allowed them to practice skills, such as tailoring counseling to a patient’s needs and handling unexpected situations, in a setting void of medical information. By doing so, participants described feeling more freedom to experiment with skills during medical improv than during traditional role plays. These results support the improv principle of “yes, and,” encouraging participants to acknowledge and affirm what other participants say, rather than to focus on accuracy. In doing so, participants are successful through their effort in participating. By creating a non-clinical space to experiment, medical improv may help GC students and GCs practice psychosocial skills. This study provides preliminary evidence to support the adaptation of medical improv for use in genetic counseling training programs.

C-159 Development and initial assessment of a pharmacogenetics education module for genetic counseling students

Education

Submitter: Rachel Mills, MS, CGC, Duke University

Presenting Author: Rachel Mills, MS, CGC, Duke University

Primary Author: Rachel Mills, Duke University

Author 2: Jennifer Eichmeyer, Boise State University

Author 3: Allison Hazell, Medcan

Author 4: Emily Glogowski, GeneDx

Author 5: Tara Schmidlen, Geisinger

Pharmacogenetic (PGx) testing is increasingly being utilized in clinical care, though many healthcare professionals, including genetic counselors, have limited PGx experience and knowledge. The NSGC Precision Medicine SIG PGx Working Group aims to provide support and education to practicing genetic counselors and genetic counseling (GC) trainees. In response to requests from 12 GC training programs to provide a lecture about PGx, the PGx Working Group developed a PGx pilot education module utilizing a flipped classroom format. Two GC graduate programs, University of Texas at Houston and the University of South Carolina, participated in the pilot during March and April of 2018. Students completed two surveys, one before and one after completion of the module; nineteen students participated. Twelve students had not previously attended a program or lecture about PGx. Four of the 19 students indicated they had been a student in a flipped classroom setting. At baseline, seven students agreed that they liked flipped classroom format; however, only four reported liking it at follow-up, indicating that the experience with the module was not favorable. Most students did not view the
out-of-class activity positively, indicating that the information was too dense or not in a desirable format. Conversely, most students provided positive feedback about the in-class group activity. Overall, an improvement in PGx knowledge was observed from baseline to follow-up; the average number of correct answers at baseline was 6.26 of 13 (range 3 to 9) while the number of correct answers at follow-up was 8.68 of 13 (range 2 to 12). Considering the improvement in PGx knowledge, we plan to revise the module based on results of this pilot and feedback from students. Specifically, we plan to alter the format by developing short recorded lectures in lieu of reviewing printed documents outside of the classroom.

C-162 Understanding Genetics Learning Needs of People Affected by Rare Disease Education
Submitter: Holly L Snyder,

Author 2: Kendall Davis, Global Genes
Author 3: Ashley Yee, Global Genes
Author 4: Karen Leydiker, Invitae
Author 5: Holly L Snyder, Illumina

Primary Author: Laura Quinn, ASSAI Health Solutions
Presenting Author: Laura Quinn, ASSAI Health Solutions

Introduction: A rare disease (RD) is defined in the U.S. as affecting <200,000 people. It is estimated that 350 million people worldwide are affected and 80% of these conditions have a genetic etiology. As such, the RD community can benefit from genetics education. This project seeks to better understand the need for genetics education in the RD community.<br />

Methods: A high-level Online Survey (OS) was disseminated to 586 RD patient advocates, followed by 2 small focus groups (FGs) with a subset of participants.<br />

Results: Overall, 251 individuals responded to the OS and 8 individuals participated in FGs. Half had been affected by a RD for >10 years, while 25% had been affected for <5 years. Nearly 96% indicated a current interest in gaining more genetics education. Practical drivers of seeking genetics education related to navigating healthcare systems, social interactions and to support patient advocacy. The Internet was most frequently cited as a helpful resource in early attempts to learn about genetics. Respondents indicated having trouble finding information on: gene function, disease pathogenesis, recent scientific advances, genetic testing, and management. FG outcomes revealed psychological drivers including reducing emotional burden of decision-making, alleviating fear of the unknown and seeking hope. Expectations for an online course included: self-paced, lasting 6-12 weeks (1-2 hrs/wk), using multiple learning styles and accessible via multiple devices. FG participants expressed a need to connect general genetic concepts to their situations. <br />

Conclusion: Genetics education tools may be used at various times throughout a patient’s journey and content can be revisited before medical appointments or after results. This project informed the development of an
online genetics course by Global Genes and findings can be used to guide development of broader patient focused genetics education.

**A-166 Healthy Genomic Sequencing: What Airmen Want to Know? Findings from the MilSeq Project**

**Ethical, Legal and Social Issues**

*Submitter: Carrie Lynn Blout, MS, CGC, Brigham and Women's Hospital and Harvard Medical School*

*Presenting Author: Carrie Lynn Blout, MS, CGC, Brigham and Women's Hospital and Harvard Medical School*

*Primary Author: Carrie Blou, Brigham and Women's Hospital*

*Author 2: Kurt Christensen, Brigham and Women's Hospital*

*Author 3: Jill O. Robinson, Baylor College of Medicine- Center for Medical Ethics*

*Author 4: Stacey Pereira, Baylor College of Medicine- Center for Medical Ethics*

*Author 5: Devan Petersen, Baylor College of Medicine- Center for Medical Ethics*

*Author 6: Megan Maxwell, Brigham and Women's Hospital*

*Author 7: Cubby Gardner, US Air Force*

*Author 8: Mauricio De Castro, US Air Force*

*Author 9: Matt Lebo, Laboratory of Molecular Medicine*

*Author 10: Amy McGuire, Baylor College of Medicine- Center for Medical Ethics*

*Author 11: Ruth Brenner, US Air Force*

*Author 12: Robert C. Green, Brigham and Women’s Hospital and Harvard Medical School*

**Background**

Genomic sequencing (GS) may be useful in the US military as it could provide guidance for individualized healthcare of apparently healthy active-duty service members. However, it may also provide information that service members do not want. We examined preferences for genomic information in the MilSeq Project, a study of whole exome sequencing (WES) in active-duty Air Force Airmen.

**Methods**

A convenience sample of Airmen completed a Phase I baseline survey that included the Preferences Instrument for Genomic Secondary Results (PIGSR) tool and screened for eligibility and interest in WES (Phase II) enrollment. The PIGSR tool includes questions outlining preferences for individual diseases spanning from adult onset to childhood onset conditions and provides scoring instructions to examine patterns of preferences. Categories of patterns of preferences include: all types of results, all results except 1 disease an individual wishes to avoid,
diseases only relevant to themselves (i.e. adult onset), those only relevant to children, and more complex preferences spanning multiple disease types. WES participants in phase II will receive all result types regardless of stated preference. Results To date, 62 Airmen (mean age: 34.9 years, 72% Non-Hispanic White) completed the baseline survey. All expressed interest in WES enrollment. Patterns of results desired indicate 47% preferred everything, 13% all but one type of result, 6% information only relevant to themselves, and 34% complex preferences. Regarding specific PIGSR conditions included in the survey, >95% would want results about cancer, cardiac conditions, and Alzheimer’s disease. Discussion MilSeq is the first study of GS preferences in the US Air Force. Preliminary findings suggest that, although nearly half of Airmen preferred to receive everything, a substantial proportion would prefer to be selective about the types of GS results they receive. This finding differs from other studies of genomic information preference where most individuals desire all information.

A-169 Genetic information in the pediatric solid organ transplant setting: how knowledge of future genetic risk impacts listing decisions

Ethical, Legal and Social Issues

Submitter: Madeline Graf, Stanford University

Presenting Author: Madeline Graf, Stanford University

Primary Author: Madeline Graf, Stanford University School of Medicine

Author 2: Danton Char, Stanford University School of Medicine, Stanford Healthcare

Author 3: Andrea Hanson-Kahn, Stanford University School of Medicine

Author 4: David Magnus, Stanford Center for Biomedical Ethics

Detection of secondary findings (SFs) through genetic testing is becoming more common, as is predictive testing for known familial conditions. Research surrounding use of SFs and predictive testing is typically rooted in matters such as informed consent and psychological impact of results. What has not been studied is the impact that such test results have on a patient’s ability to be listed for a life-saving organ transplant. We recruited 163 pediatric liver, heart, and kidney transplant programs across the United States from the Organ Procurement and Transplantation Network directory. Using an online survey tool (Qualtrics) we elicited views and experiences of program directors or key clinicians, regarding each program’s use of genetic risk information in transplant listing decisions. Sixty-nine completed surveys were received (response rate 42%). Sixty-four percent of programs have required genetic testing for specific indications prior to listing decisions. Sixteen percent have required genetic testing without a specific indication, suggesting that genetic testing is being used to screen candidates. Six percent of programs have chosen not to list patients with an SF or family history of a genetic condition. In hypothetical scenarios, programs consider cancer predispositions and adult-onset neurological disorders to be relative contraindications to listing (61%, 17% and 3% depending on scenario), and some programs

count them as absolute contraindications (5% and 3% depending on scenario). Only 3% of programs have formal policies regarding use of genetic findings in listing decisions, but all programs consult genetic specialists at least “sometimes” for results interpretation. Our study shows that pediatric transplant programs are using predispositions and pre-symptomatic genetic results to exclude children from organ transplantation. As broad genetic testing is more widely adopted in pediatric medicine, further study is needed to prevent genetic results from being used unethically and inappropriately to impact a patient’s chance to receive a life-saving organ.

A-172 Prenatal Genetic Counselors' Perceptions of the Impact of Abortion Legislation on Counseling and Access in the United States

Introduction: Genetic counselors have an important role in discussing and coordinating abortion for patients identified with a fetal abnormality. Few studies have been conducted to determine the effects of legislation on genetic counselors and patients. This study aimed to further our understanding of genetic counselors’ perception of the impact of abortion regulations on their practice, the perceived financial and emotional impact on their patients and their ability to access abortion.

Methods: A 22 question survey was developed based on themes identified by a qualitative study, Koenig et al. 2017, and distributed to NSGC. 113 respondents participated in the survey. Participants were divided into categories determined by the Guttmacher Institute based on the amount of restrictive abortion legislation in their state. Comparisons were made using Pearson’s chi-square and Fisher’s exact between participants in states supportive, middle ground, and hostile to abortion.

Results: Participants reported legislative gestational age restrictions significantly impact their counseling and coordinating of abortion. Participants reported many emotional and financial burdens that impact their patients seeking abortion; however, those in hostile states were significantly more likely to report a perceived financial or
emotional impact on their patients. Participants in hostile states were more likely than those in supportive states to report that many of the addressed legislative and institutional regulations impact patients' ability to access abortion. This study elucidated inconsistencies between what regulations participants perceive as potential barriers to access and what they decide to discuss with their patients.

Conclusions: Abortion regulations limiting the decision making time frame for patients with a fetal abnormality have a significant impact on the practice of prenatal genetic counseling. Further restrictions may change how genetic counselors choose to counsel their patients about abortion, but also may limit the availability of choices.

A-175 When did genetic counseling become privacy counseling?! Introducing the Future of Privacy Forum’s “Privacy Principles For Genetic Data.

**Ethical, Legal and Social Issues**

*Submitter: Misha DS Rashkin,*

**Primary Author: Misha Rashkin, Helix LLC**

**Author 2: Jonathan Bowes, Helix LLC**

**Author 3: James Lu, Helix, LLC**

**Author 4: Elissa Levin, Helix, LLC**

**Presenting Author: Misha Rashkin, Helix, LLC**

Purpose: In 2017, approximately 7 million consumers ordered an at-home genetic test. As the utility and public understanding of genetics continues to improve, these numbers will likely grow exponentially. With this expansion comes public concern about privacy and consumer control over their data. Recognizing the sensitivity of this issue, leading consumer genetics companies, including Helix, 23andMe, and AncestryDNA, joined the Future of Privacy Forum to convene the first industry collaboration to establish industry best privacy practices on the use and protection of genetic and other personal data. Methods: Moderated by experienced privacy experts, our group met regularly to outline key topics and draft shared principles to codify responsible approaches to areas of interest and concern to consumers and professionals alike: transparency, privacy, law enforcement access, data ownership, marketing, consent, research, data sharing, retention, testing among minors and other relevant topics. We collaborated with internal experts in bioinformatics, data protection, engineering, policy, law, and ethics. We subsequently sought feedback from external stakeholders including NSGC, ASHG, the Consumers Union, the Federal Trade Commission, and other legislative offices. Based on feedback, we iterated to incorporate comments to expand and clarify the principles document. Upon completion, we collaborated on a national public relations effort to generate awareness about how the principles mandate transparency and protection of consumer data. Conclusion: Our group developed the first set of principles to drive privacy practices across industry and set a high bar that has consumer privacy at its core. To maximize impact of these principles, the industry participants are expanding the
collaboration to include other key stakeholders and continue to drive adherence to the principles in practice.

B-167 Implementation of conditional free predictive testing for cancer predisposition: the impact on uptake for syndromes with pediatric onset

Ethical, Legal and Social Issues
Submitter: Eliza Courtney, MGC, National Cancer Centre Singapore

Primary Author: Eliza Courtney, MGC, National Cancer Centre Singapore

Presenting Author: Eliza Courtney, MGC, National Cancer Centre Singapore

Author 2: Amanda Kay-Lyn Chok, National Cancer Centre Singapore

Author 3: Zoe Li Ting Ang, National Cancer Centre Singapore

Author 4: Tarryn Shaw, National Cancer Centre Singapore

Author 5: Shao-Tzu Li, National Cancer Centre Singapore

Author 6: Joanne Ngeow, National Cancer Centre Singapore

PURPOSE
Predictive testing for cancer predisposition involves the careful consideration of potential benefits and implications and can be particularly complex when children are involved. It is becoming more common for commercial laboratories to offer free predictive testing to first-degree relatives (FDRs) of tested probands, however, conditions may be imposed. This study aimed to evaluate uptake among FDRs for syndromes with pediatric onset following the introduction of free predictive testing within a three-month limit.

METHODS
We identified 29 families in which germline genetic testing had confirmed the diagnosis of an autosomal dominant hereditary cancer syndrome with pediatric onset and retrospectively determined uptake of predictive testing in their FDRs before and after the availability of free testing. Factors potentially prognostic of uptake, including free testing, were compared.

RESULTS
A total of 124 FDRs were identified, with an overall predictive testing uptake rate of 17.89%. After the introduction of free predictive testing, uptake was significantly higher (45.2 vs. 8.6%, p<0.001) and the mean duration between proband and FDR testing was significantly shorter (65.6 vs. 203.6 days, p=0.044). Age (FDR and proband) and the type of relationship of FDR to proband were significantly associated with uptake.

CONCLUSION
The availability of free predictive testing is significantly associated with higher uptake, and shorter duration between proband and FDR testing. Whilst this may offer advantages in terms of access to testing where early intervention is necessary, it may add additional pressure for families to proceed with testing within the given time limit. This raises ethical issues as there is potential for harm if families require additional time for decision-making, or in cases where testing should be delayed.
B-170 Attitudes of people with inherited retinal conditions toward gene editing technology

**Ethical, Legal and Social Issues**

*Submitter: Lily Hoffman-Andrews, BA, Stanford University*

*Presenting Author: Lily Hoffman-Andrews, BA, Stanford University*

*Author 2: Ronit Mazzoni, MS, Santa Clara Valley Medical Center*

*Primary Author: Lily Hoffman-Andrews, BA, Stanford University School of Medicine*

*Author 3: Michelle Pacione, M.Ed, Stanford University School of Medicine*

*Author 4: Kelly Ormond, MS, Stanford University School of Medicine*

**Introduction:** Recent advances in gene editing technology have brought it to the forefront of medical research and bioethical debate. The views of people with genetic conditions are crucial to include in public dialogue around these developing technologies. Retinitis pigmentosa (RP) and Leber congenital amaurosis (LCA) are inherited retinal conditions that cause vision loss and blindness and have been early targets for gene editing research. <br />

**Purpose:** This qualitative study sought to characterize the attitudes of people with RP and LCA toward gene editing. <br />

**Methods:** Individuals with RP (childhood to adult-onset, N=9) and LCA (congenital onset, N=8) participated in semi-structured qualitative interviews about their experience with and attitudes toward blindness, and their views about gene editing technology for somatic, germline, and enhancement applications. Interviews were inductively coded to identify themes. <br />

**Results:** Participants saw potential benefits from gene editing in general, but their views about gene editing for visual conditions varied in ways that were influenced by their personal experiences and perspective on blindness. Individuals who felt positively about blindness, or saw it as part of their identity, were less likely to be interested in gene editing for their condition. Those who felt more negatively toward blindness, particularly those with later onset acquired blindness, were more likely to welcome the idea of treatment or prevention. Concerns expressed about both germline and somatic editing included: autonomy and the importance of informed consent; the potential impacts of gene editing on social attitudes and barriers affecting blind people; and worries about “eliminating” blindness or other traits. <br />

**Conclusions:** People with RP and LCA have diverse attitudes toward gene editing technology informed by their own lived experience with disability, and many have concerns about how the ways it is discussed and implemented might affect them and society.

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B-173 DISCLOSURE OF RECLASSIFIED VUS RESULTS OF DECEASED PATIENTS TO FAMILY MEMBERS: CURRENT PRACTICES

**Ethical, Legal and Social Issues**

*Submitter: Seth Lascurain,*

*Primary Author: Seth Lascurain,*
Presenting Author: Seth Lascurain,

Author 2: Darcy Thull, UPMC Cancer Genetics Program

Author 3: Andrea Durst, University of Pittsburgh

Author 4: Todd Bear, University of Pittsburgh

Author 5: Phuong L Mai, University of Pittsburgh Medical Center

Purpose: A variant of uncertain significance result (VUS) is not uncommon in genetic testing. There is currently little regulation or guidance regarding the responsibility of genetics professionals when a VUS is reclassified after a patient has passed away. This study was designed to explore current practices and obtain opinions of genetics professionals on the disclosure of reclassified VUS results of a deceased patient to their relatives. Methods: A 35-question web-based survey was distributed to >3,000 members of the National Society of Genetic Counselors on the listserv. Results: A total of 154 individuals completed the survey, 94% of respondents were genetic counselors and 45% reported between one and five years of clinical practice. Forty-five respondents (24%) reported receiving reclassified VUS results in deceased patients. Respondents were more likely to always attempt disclosure of variants reclassified as pathogenic (83%) vs. benign (73%). Most respondents reported not being aware of state or local policies on the disclosure of a deceased patient’s reclassified VUS results. Approximately half of the respondents were not sure if an institutional policy existed. Respondents rated the impact of the results on family members and a duty to warn as extremely important factors in considering disclosure to relatives. Most respondents favored a legal mechanism to allow disclosure to relatives. A minority of respondents felt a consent obtained from the decedent prior to their death should be legally (10%) or ethically (27%) required for the updated results to be disclosed to relatives. Conclusions: Guidance on the disclosure of reclassified VUS results for a deceased patient is not readily available, though respondents who have experienced this situation commonly reported attempting disclosure in clinical practice. Additional research regarding the role for policy change or development is needed.

B-176 Patient Experience with the Consent Process of Preimplantation Genetic Diagnosis (PGD) and Preimplantation Genetic Screening (PGS)

Ethical, Legal and Social Issues
Submitter: Kimberly Skellington,

Presenting Author: Kimberly Skellington,

Primary Author: Kimberly Skellington, University of North Carolina Greensboro

Author 2: Allison Hebner, Stanford Medicine, Fertility and Reproductive Health

Author 3: Serena Talcott Baughman, Oregon Reproductive Medicine
Author 4: Randi Culp Stewart, University of North Carolina Greensboro; Cone Health System

Previous studies on preimplantation genetic diagnosis (PGD) and preimplantation genetic screening (PGS) have focused more on its ethical implications and less on standardizing consent practices and ensuring quality care. The consent process is an opportunity for providers to have an open discussion with patients and promote their empowerment. This exploratory study aimed to describe patient experiences with the consent process for PGD/PGS and identify strengths and areas for potential improvement. A survey was created and distributed electronically to members of RESOLVE and Shine Infertility support groups and 11 participants completed the survey. Participants had PGD/PGS in the past two years, were at varied phases in PGD/PGS process, and experienced different pregnancy outcomes. Three had pursued PGD in addition to PGS. All participants reported overall satisfaction with the experience of PGD/PGS and indicated that they were able to ask questions during the consent process. Areas of dissatisfaction related to the manner of delivery and content. More than half (n=6) of participants reported feeling some level of pressure from providers and two participants reported that limitations of testing were not described to them. Some participants felt they were not fully informed of miscarriage rates, implications for amniocentesis, and verification of genetic disease. Continued assessment of the consent process will help ensure patients are provided accurate and sufficient information necessary to make autonomous, educated decisions regarding their reproduction.<br />

C-165 Review of the present state of and challenges for the return of genomic research results in the Japanese medical service system

Ethical, Legal and Social Issues
Submitter: Yayoi Aizawa,
Presenting Author: Yayoi Aizawa,
Primary Author: Yayoi Aizawa, Tohoku University Tohoku Medical Megabank Organization
Author 2: Fuji Nagami, Tohoku University Tohoku Medical Megabank Organization

We explored aspects of the Japanese medical service system such as public medical subsidies for the return of genomic research results and studied the insufficiency of public support after return of results to participants. With the rapid advances in sequencing technology and decreasing cost, there is growing debate about returning genomic research results, including incidental or secondary findings, to participants. In 2013, the American College of Medical Genetics and Genomics (ACMG) proposed a list of specific genes underlying medically actionable diseases for sequencing in clinical settings; the list has since been updated. The list was tailored for the United States and needs to be carefully examined for applicability as per the public health system situation in each country. Japan has a universal health insurance coverage system for all citizens. Most medical fees are uniform throughout the nation, and the patient’s pay are limited. Additionally, there are medical expense subsidy systems under specific conditions such as age and disease type. However, the diseases listed in the “medical fee schedule” for genetic testing and genetic counseling are limited, so many clients need to pay full price. We explored
the present state of the Japanese medical service system with respect to genetic diseases included in the ACMG 59-gene list. We categorized the 59 genes into 32 diseases. With regard to medical subsidies, 81.3% include “specific chronic diseases of children”, 34.4% include “intractable diseases”. With regard to genetic testing, 31.1% are listed in the “medical fee schedule”. The average cost of genetic counseling if not covered public health insurance is 7,902 yen. These results suggest that medical actionability in the public medical service system may differ according to the country. Therefore, we propose the need to consider medical actionability in terms of medical service system, and additional discussion is required for return of genomic research results.

C-168 Assessing Genetic Counselors’ Experiences with Physician Aid-in-Dying and its Implication to our Practice

**Ethical, Legal and Social Issues**

*Submitter: Abby D’Angelo,*

*Presenting Author: Abby D’Angelo,*

*Primary Author: Abby D’Angelo,*

*Author 4: Holly K Tabor,*

*Author 2: David Magnus,*

*Author 3: Kelly Ormond,*

**Introduction:** Physician Aid-in-Dying (PAD) has been a topic of continued public debate and is now recently legalized in a total of 7 states and districts across the United States. Past research has investigated physicians’ and nurses’ experiences and attitudes regarding this practice; however, no research has investigated PAD as it relates to genetic counseling. This study aims to assess genetic counselors’ experiences, understanding, training, and role regarding PAD. **Methods:** Participants were recruited through the National Society of Genetic Counselors website and the Northern California genetic counselor listserv. 42 genetic counselors from these 7 states completed an on-line survey. Of these respondents, 15 completed subsequent semi-structured telephone interviews that were audio-recorded and thematically analyzed. **Results:** Only 12% of respondents had experienced patients who inquired about PAD in the past. The majority (69%) did not feel like they have the current knowledge to answer patient questions about PAD, but almost all (91%) believe PAD could be brought up by patients in at least one genetic counseling specialty. Few (10%) had previously received education regarding PAD and 69% believed resources should be available to genetic counselors. Interviews suggest that genetic counselors view connections between their unique training, skills, and experiences and the role they could fill in discussing PAD with patients compared to other providers, but also expressed confusion in exactly how. Nearly all respondents (95%) anticipated PAD could be brought up in at least one genetic counseling specialty. **Conclusions:** This is the first study to investigate Physician Aid-in-Dying as it relates to genetic counseling. Genetic counselors have experienced patients with questions about PAD, desire
education and resources regarding this practice, and believe they can offer a unique experience to patients discussing this option in the context of a diagnosis or a positive genetic test result.

C-171 Adolescent Perspectives on Genetic Testing for Huntington’s Disease

Ethical, Legal and Social Issues
Submitter: Jennifer Huynh-Lim,

Primary Author: Jennifer Huynh-Lim, Sarah Lawrence College

Author 2: Katelyn Cooke, Sarah Lawrence College

Author 3: Elizabeth Crate, Sarah Lawrence College

Author 4: Ravneet Grewal, Sarah Lawrence College

Author 5: Laura Hercher, Sarah Lawrence College

Author 6: Alanna Rahm, Geisinger Health System

Presenting Author: Alanna Rahm, Geisinger Health System

In 2015, the American Society of Human Genetics (ASHG) released a position statement which recommended minors to defer genetic testing for adult-onset conditions until adulthood. In the 2016 DNA Day Essay Contest, high school students were asked to research an adult-onset genetic disorder and use it to formulate a stance on whether they agreed or disagreed with the position statement. Phase two of this study focused on the essays written about Huntington’s Disease (HD). Within the HD essays, 57% chose to defer, 35% chose not to defer, and 8% did not clearly state an opinion. Essays were analyzed using a codebook that was established in Phase one and the top codes were further analyzed for themes. The top codes that were thematically analyzed were “Psychological Risks to Minor”, “No Medical Benefit/Not Preventable”, “Necessary to Plan/Prepare”, and “Genetic Testing Variability and Uncertain Predictability.” Although many of the essays agreed to defer testing, many students cited similar reasons, regardless of their stance.

C-174 Systematic ethical framework for evaluating and rejecting the use of genotype-targeted advertising.

Ethical, Legal and Social Issues
Submitter: Misha DS Rashkin,

Primary Author: Misha Rashkin, Helix, LLC

Author 2: Jonathan Bowes, Helix, LLC
Purpose: Modern marketing increasingly uses personal information to generate advertising content targeted to a user based on their own data. With widespread adoption of consumer-initiated genetic testing, it is possible that a user’s genetic data could be included in the algorithms used to generate targeted advertising. The status of genetic information in relation to other commonly used data for marketing purposes is not currently clarified by policy, regulation, or ethical canon. In an effort to lead and exceed industry best practices, we chose to rigorously examine what sorts of uses of molecular genetic data in marketing are ethically acceptable and unacceptable and for what reason. Methods: We held unstructured internal focus groups with a cohort of Helix employees to explore and evaluate the policy, regulatory, and ethical ramifications of genotype-targeted advertising content. We presented them with scenarios and identified six key themes: customer knowledge, transparency, consent, product location (i.e., is product sold by platform that customer opted into?), targeting location (i.e., does targeting happen on platform that customer opted into?), and sensitivity (i.e., has a diverse group vetted the marketing for sensitivity?). Conclusion: This analysis provides a framework for exhaustive discussion of the prospects and pitfalls of such targeted advertising. It lead to an internal moratorium on most uses of molecular genetic data for marketing purposes. The only types of uses that were found to be appropriate are those in which each of the six themes are satisfied. The transparently stated intent of such a product or service would be to provide an insight that helps customers make more personalized purchase decisions, on an opt-in basis. The analysis also influenced collaborative work with other consumer genetics companies to avoid marketing based on an individual’s genetic data.

C-177 “They’re not going to do nothing for me:” The Role of Genetic Counselors in the Future of Genomic Testing

Ethical, Legal and Social Issues
Submitter: Erica Sutton, Mayo Clinic

Presenting Author: Erica Sutton, Mayo Clinic

Primary Author: Erica J. Sutton, Mayo Clinic

Author 2: Annika T. Beck, Mayo Clinic

Author 3: Kylie J. Osterhus, Mayo Clinic

Author 4: Iftikhar J. Kullo, Mayo Clinic

Author 5: Richard R. Sharp, Mayo Clinic
As low-cost genomic sequencing expands, the current standard of providing genetic counseling to all patients both before and after testing may be unsustainable. Moreover, the extent to which patients value genetic counseling services at either time point is unclear. We wanted to examine patients’ perspectives on the value of genetic counseling services when these resources were offered but not required. As part of a large-scale targeted genomic sequencing study, genetic counseling was offered before participant enrollment and following return of results. We conducted 50 semi-structured telephone interviews with participants who received non-actionable results. 5,106 biobank members were invited by mail to participate. Only 8 called a genetic counselor before enrolling. To date, 2,128 non-actionable results letters have been sent to participants: no one has contacted a genetic counselor. Most interviewees described not needing counseling before sequencing because they felt they understood the study and could cope with any result. They did not see value in counseling before knowing results. Counseling seemed equally unnecessary after learning their results because the letter was clear: “nothing was found, so what would we discuss?” This service was considered a valuable resource for others: people with a family history of disease, people with genetic conditions, people who are anxious, and people who receive actionable results. Most participants, however, volunteered they would have contacted a genetic counselor if an actionable variant had been identified. Given the lack of demand for and interest in genetic counseling services before receiving sequencing results and upon receiving non-actionable results, we consider whether genetic counselors should focus efforts primarily on providing post-result support to patients who receive actionable findings. Participants in our study did not believe this shift would compromise their health and well-being.

A-178 Incidental somatic and germline RET mutation in a patient with Merkel cell Carcinoma and a complex oncology history: A case study

**Genetic/Genomic Testing**

*Submitter: Dina Alaeddin, MGC, Inova Translational Medicine Institute*

*Primary Author: Dina Alaeddin, MGC, Inova Translational Medicine Institute*

*Presenting Author: Dina Alaeddin, MGC, Inova Translational Medicine Institute*

*Author 2: Kimberly M. Matthijssen, Inova Translational Medicine Institute*

*Author 3: Amanda Schott, Inova Translational Medicine Institute*

*Author 4: Natalie Hauser, Inova Translational Medicine Institute*

*Author 5: Timothy L. Cannon, Inova Schar Cancer Institute and VCU*

*Author 6: Laura K. Knopp, Inova Schar Cancer Institute*

*Author 7: John Deeken, Inova Translational Medicine Institute*

*Author 8: Tiffani A. DeMarco, Inova Translational Medicine Institute*
The expanding role of tumor testing in addition to germline testing in cancer patients holds great potential for personalized medicine and improving patient treatment and outcomes. Coupling tumor testing with germline testing allows for a more informative outline of inherited vs. somatic variants identified. However, it also introduces new challenges, unexpected findings, and uncertain results. This is a case of a 64 year old male that presented with a complex oncology history of a unilateral vestibular Schwannoma at age 56, followed by a diagnosis of a chondrosarcoma of the left orbit at age 59 with evidence of pulmonary metastasis. Additionally, he recently developed a Merkel cell carcinoma of the left cheek. The location of the Merkel cell carcinoma in addition to his prior radiation treatment and surgical history led to systemic therapy as his only course of treatment. Somatic tumor testing was performed on his Merkel cell carcinoma and identified three genomic alterations including: RET V804M, CDKN2A deletion exon 1 and TP53 C135Y-subclonal, R175H. The patient was referred for germline testing after being presented at molecular tumor board. The family history was unremarkable. A comprehensive gene panel identified the RET V804M mutation, a lower penetrant mutation. RET mutations are associated with Multiple Endocrine Neoplasia Type 2A (MEN2A). This case demonstrates the importance of coupling tumor and germline testing, even in the case that the identified variants are not clearly associated with the patient’s medical history, as it may significantly affect the patient’s medical management and the management of family members. This also highlights the significant role of genetic counselors at molecular tumor boards and as part of a multi-disciplinary team in the context of oncologic care.

A-181 Pediatric Perspective: Genome Sequencing for Newborn Screening

Genetic/Genomic Testing

Submitter: Emily Anderson,

Primary Author: Emily Anderson,

Presenting Author: Emily Anderson,

Author 2: Ann Katherine M. Foreman, UNC School of Medicine

Author 3: Randi Culp Stewart, UNC Greensboro, Cone Health System

Author 4: Julianne M O'Daniel, UNC School of Medicine

Research is underway to investigate the application of genome sequencing (GS) to newborn screening (NBS). At the same time, broad sequencing tests are already entering the clinical market. Pediatric providers are essential for follow-up of abnormal NBS results, yet their opinions on GS for NBS are underrepresented. To address this gap, this study utilized a previously validated multiple choice and free response survey to assess pediatric providers’ views on this topic. Paper and electronic surveys were distributed to pediatric providers in North Carolina at in-person staff meetings, via institution specific pediatric provider listservs and the NC Pediatric Society listserv. The 63-item survey took approximately 15 minutes to complete. Quantitative data was analyzed with SPSS version 24.0 and qualitative data was
coded for themes by two independent reviewers. Data collection yielded 34 completed surveys, two of which were excluded from data analysis because the respondent had a specialization in genetics (N = 32). On a scale of 1 to 5, with 5 being the most familiar, respondents were, not surprisingly, more familiar with newborn screening (mean rating = 4.0) than genome sequencing (mean rating = 2.8). The majority (62.5%) of respondents indicated GS should not be part of current NBS practice. Most (72%) responded parents should have a choice about the types of results they receive and many (81%) believed the ordering physician should make all results available to parents. Thirty percent of respondents (9/30) reported that the primary care provider (PCP) alone should return any type of results of GS for NBS. While respondents generally felt that PCPs should be involved in return of GS for NBS results, some expressed a need for provider education. Genetic counselors are well suited to support these educational needs. This exploratory study highlighted opinions of pediatric providers who are key stakeholders in NBS. Additional research is needed to outline specialized training and clinical support needed to implement GS technology for NBS practice.

A-184 Parental Expectations and Perceived Utility of Pharmacogenomic Testing for Therapeutic Optimization of Neuro-psychiatric Medications

Genetic/Genomic Testing
Submitter: Courtney Berrios, Children's Mercy Hospital

Presenting Author: Courtney Berrios, Children's Mercy Hospital

Primary Author: Courtney Berrios, MSc, ScM, CGC, Children's Mercy Kansas City

Author 2: Susan Abdel-Rahman, PharmD, Children's Mercy Kansas City

Author 3: Jennifer Lowry, MD, Children's Mercy Kansas City

Author 4: Benjamin Black, MD, Children's Mercy Kansas City

Author 5: Sarah Soden, MD, Children's Mercy Kansas City

Pharmacogenomics (PGx) is a growing area of precision medicine. Studies report high interest and perceived utility for PGx testing by adult patients, but little has been published about the experiences of families whose children have PGx testing. Here we explore perceptions around PGx testing in parents of children for which PGx testing was ordered for therapeutic optimization of neuro-psychiatric medications. Parents were recruited for in-depth interviews after attending discussions of their child’s OneOme® PGx test results in either an individualized therapeutics or developmental and behavioral medicine clinic. Interview topics included purpose, understanding, utility, and continuing needs regarding PGx. Transcribed interviews were analyzed using inductive thematic analysis. Interviews have been completed with 9 mothers of 13 children prescribed neuro-psychiatric medications from 1.5 to 10 years. Testing was precipitated by difficulties with medications in 11 of 13 children, and in a sibling of the remaining 2. Mothers expressed hope for PGx to stop ‘experimenting’ or relying on parent
observations to find the best medications. Greatest utility was discussed for results about medications applicable to their child’s current medical needs, but value was also placed on warnings for potential future medications. 10 (77%) reported changing, or planning a change to, existing medications based on the results. Some discussed that results explained previous medication responses. Those reporting normal metabolism for medications applicable to their child’s current medical needs expressed both relief at ‘good’ results and disappointment at not receiving further guidance for their child’s care. In conclusion, parents of children receiving PGx testing for optimization of neuro-psychiatric medications find utility in both results relating to their child’s current care and potential future gene-drug interactions. Families may have conflicted feelings about ‘normal’ results and may benefit from interventions to explore and manage expectations.

A-187 What we learn from the unknown – VUS rates by Ethnicity and Gene

Genetic/Genomic Testing

Submitter: Wanchun Janice Cheng, MS, GeneDx

Primary Author: Wanchun Janice Cheng, MS, GeneDx

Presenting Author: Wanchun Janice Cheng, MS, GeneDx

Author 2: Lisa R. Susswein, MS, MHA, CGC, GeneDx, Inc

Author 3: Maegan E. Roberts, MS, CGC, GeneDx, Inc

Author 4: Megan L. Marshall, MS, LCGC, GeneDx, Inc

Author 5: Rachel T. Klein, MS, CGC, GeneDx, Inc

Author 6: Kathleen S. Hruska, PhD, FACMG, GeneDx, Inc

Background:
Increased uptake of multi-gene panel testing has presented clinical challenges due to higher rates of VUS (variant of uncertain significance) compared to single-gene testing. VUS rates in BRCA1 and BRCA2 are previously reported to vary by ethnicity. However, such information has not been published for newer cancer predisposition genes. Here we report VUS rates by ethnicity and gene for one multi-gene hereditary cancer panel and show protein size as a separate driving factor of VUS rates.

Methods:
We retrospectively queried for VUS reported in 63 genes on a multi-gene panel. Ethnicity was self-reported and patients reporting multiple backgrounds were excluded from ethnicity-specific analysis. Chi-square test was used to obtain p-values for comparisons between ethnic groups. Coefficient of determination (R-squared) was calculated to assess the relationship between protein size and VUS rates by gene.

Results:
The overall VUS rate on this panel was 35.2%. VUS rates by ethnic groups, Caucasian, Hispanic, African American, Middle Eastern, and Asian, ranged from 32.4% (Caucasian) to 50.8% (Asian). Statistically significant differences in VUS rates between ethnic groups were observed (p<=0.01). VUS rates by gene ranged from 0.18-6.6% and positively correlated with the numbers of amino acid residues in each protein (R2=0.45). In addition, Caucasians consistently
exhibited the lowest VUS rate among seven further analyzed genes, with the exception of MLH1 (1.2%), for which Hispanic was the lowest at 0.6%. Notably Asians showed a 7.6% VUS rate for PALB2, compared to 1.5–2.6% observed in other groups. VUS rates for BRCA1 and BRCA2 ranged from 0.9% (Caucasian) to 2.4% (Asian) and from 1.6% (Caucasian) to 5.7% (Asian), respectively.<br /><br />Conclusions:<br />In our cohort, VUS rates on a multi-gene panel varied by reported ethnicity. Asians had the highest VUS rates on the panel as well as for seven specific genes we analyzed, while Caucasians the lowest in general. Gene-specific VUS rates appeared to be influenced by multiple factors including ethnicity and protein size.

A-190 Elective genome sequencing reveals homozygous RAPSN N88K founder mutation in an asymptomatic 59-year-old with an affected brother, expanding clinical variability and presenting counseling challenges

Genetic/Genomic Testing
Submitter: Callie Jenevein Diamonstein, Inova Translational Medicine Institute

Presenting Author: Callie Jenevein Diamonstein, Inova Translational Medicine Institute

Primary Author: Callie Jenevein Diamonstein, Inova Translational Medicine Institute

Author 2: Natalie Susan Hauser, Inova Translational Medicine Institute

Biallelic pathogenic variants in the RAPSN gene are associated with the well-known, variable condition, congenital myasthenic syndrome (CMS). Phenotypic variability is well-described, with age of onset ranging from prenatal to adult-onset. Asymptomatic individuals have been rarely described. We report a healthy 59-year-old man who sought elective research genome sequencing for recreational reasons. Results revealed he was homozygous for the well-known c.264C>A (p.Asn88Lys) Indo-European founder mutation in the RAPSN gene. The homozygous mutation was confirmed clinically. This is the oldest person without symptoms reported to our knowledge. The patient has an affected brother, age 55, who was subsequently also found to be homozygous for the RAPSN N88K mutation. The brother had been misdiagnosed with myasthenia gravis at age 34 after experiencing symptoms of weakness beginning around age 30. He was seronegative, did not respond to typical management regimens for myasthenia gravis and had an unusual course of disease. The new diagnosis of adult-onset myasthenic syndrome allowed new treatment options (like ACEIs) as well as open clinical trials to be considered. Furthermore, it provided a meaningful answer to over two decades of a frustrating misdiagnosis. Both the patient and his brother have children in their reproductive years who benefitted from knowing their carrier risk of congenital myasthenic syndrome, however, counseling on the potential effect on future offspring was difficult given the unpredictability of the disease. This family contributes to our understanding of the vast phenotypic variability of homozygous RAPSN N88K mutations, the recurrence risk counseling challenges it presents and the multidimensional meaningfulness of receiving an accurate diagnosis for a chronic disease. It also highlights an unexpected, significant clinical finding identified through elective
whole genome sequencing on a healthy individual and underscores the importance of including potential familial implications in the informed consent process for elective genetic testing.

A-193 A case for the continued importance of cytogenetics in rare diagnosis of triploid/diploid mixoploidy

Genetic/Genomic Testing
Submitter: Leslie Durham, M.S., Randall Children’s Hospital

Presenting Author: Leslie Durham, M.S., Randall Children’s Hospital

Primary Author: Leslie, Randall Children’s Hospital

Author 2: Kari, Randall Children’s Hospital

Author 3: George, Randall Children’s Hospital

Author 4: Andrea, Randall Children’s Hospital

Oversimplification of genetic concepts represents a crucial aspect of genetic counseling. Although many of us counsel as though testing results apply to every cell in the body, without mention of tissue-specific diversity to avoiding flooding the family with extraneous information, cases of mosaicism and chimerism require more complex discussion. Our illustrative case is one of diploid-triploid mixoploidy, initially diagnosed as mosaic Klinefelter. Our patient, presumed female on the basis of 20 week anatomy scan, was noted at delivery to have ambiguous genitalia, dysmorphic facial features and limb anomalies. Cord blood yielded a 46, XX female karyotype that was nonetheless SRY-FISH positive in 0.5% interphase cells. Subsequent CGH/SNP chromosome microarray confirmed the presence of Y-chromosome material, suggesting mosaicism for 47,XXY on a 46,XX background. The patient’s family was counselled on mosaic Klinefelter at endocrine follow-up. Nevertheless, given the rarity of the cytogenetic diagnosis, repeat studies on peripheral blood and buccal cells were sent that revealed a small subset of cells with 69,XXY genotype in addition to the majority 46,XX on karyotype, conferring a new diagnosis of diploid-triploid mosaicism/mixoploidy. In contrast to the initial diagnosis, this represented an excellent phenotypic fit, initially missed due to cord blood sampling and limitation of FISH to sex-chromosomes. The family was counseled again with emphasis on the testing trajectory, and new results. This case not only highlights the necessity of questioning initial testing results, particularly exceptionally rare results on rapid/limited studies of cord-blood, but also the importance of more complete background and pretest counseling, when possible.

A-196 Parent Experience with Genetic Testing for Pediatric Epileptic Encephalopathy: What Can We Do Better?

Genetic/Genomic Testing
Submitter: Rhonda Feinbaum,
Epileptic encephalopathies are a group of severe childhood disorders characterized by seizures and cognitive and developmental deficits. Genetic testing is frequently used in the diagnosis of epileptic encephalopathy. The expanding list of epilepsy genes as well as the genetic and phenotypic heterogeneity of epileptic encephalopathy complicates the interpretation of genetic test results. The main goal of this study was to determine whether families of children with epileptic encephalopathy were provided with sufficient information to understand their child’s genetic test results and, if not, identify ways to improve their experience. This anonymous, online survey asked parents and guardians of children with epileptic encephalopathy about their experience with genetic testing, the information provided pre-test and at the return of results, their understanding of the information, and what information would improve the genetic testing experience. In this retrospective study, respondents indicated a high level of perceived understanding of genetic test results (average 4.26/5, SD 0.79, n=64). However, at the time genetic test results were returned, only 32.8% recalled being given online information to better understand their child’s genetic test results and only 18.8% were provided with ways to contact other families (n=64). Both information sources were desired by and reported to be utilized by respondents to learn about their child’s diagnosis. Thus, information that patients’ families need and want is frequently not given to them by healthcare professionals at the results return session. This study suggests that a concerted effort by healthcare professionals to offer comprehensive information and resources in the context of an ongoing dialogue with patient’s families would improve their understanding of genetic testing for epileptic encephalopathy.

A-202 Genetic counselors’ perspectives on expanded carrier screening use in assisted reproductive technologies

**Genetic/Genomic Testing**

*Submitter: Ellen Johnson, GC student, University of Wisconsin-Madison*

*Presenting Author: Ellen Johnson, GC student, University of Wisconsin-Madison*

*Author 2: Laura Birkeland, CGC, University of Wisconsin-Madison*

*Author 3: Elizabeth Petty, MD, University of Wisconsin-Madison*

*Primary Author: Ellen Johnson, University of Wisconsin-Madison*
Expanded Carrier Screening (ECS) is a pan-ethnic option to identify carriers for many heritable conditions which became clinically available in 2010. ECS is now recommended by various professional organizations, although there is limited guidance on which conditions should be included. Patients pursuing assisted reproductive technologies (ART) have been identified as ideal candidates for ECS due to the option to test embryos for genetic conditions that parents carry. The purpose of this study was to determine how frequently genetic counseling services and carrier screening availability is advertised by fertility clinics, as well as to describe genetic counselors’ experiences with the use of ECS for ART patients. A website analysis of 462 fertility clinics found that 17% advertised carrier screening, while only 7% advertised genetic counseling services. Surveyed genetic counselors reported that they offered ECS frequently to patients (55%, n=84) and perceived a greater ability for genetic counselors to address carrier screening counseling components when compared to non-genetic counselor providers (p<0.05 for each component). Multiple factors were perceived as important when designing ECS panels, contributing to the difficulty in determining which conditions should be included on ECS panels. This research provided more context regarding the use of ECS during reproductive counseling, as well as more insight to the subspecialty of ART genetic counseling.

A-205 What’s in a VUS Rate? Simulated VUS Rate Calculations for Hereditary Cancer Genes Using Population Frequency Data and ClinVar Submissions

Genetic/Genomic Testing

Submitter: Kristjan Eerik Kaseniit, Counsyl
Primary Author: Kristjan Eerik Kaseniit, Counsyl
Presenting Author: Kristjan Eerik Kaseniit, Counsyl
Author 2: Megan Judkins, MS, LCGC, Counsyl
Author 3: Rebecca Mar-Heyming, PhD, Counsyl
Author 4: H. Peter Kang, MD, MS, FCAP, Counsyl
Author 5: Eric A. Evans, PhD, HCLD(ABB), Counsyl
Author 6: Kaylene Ready, MS, CGC, Counsyl
Author 7: Dale Muzzey, PhD, Counsyl

Hereditary cancer panel tests are often compared by the likelihood of reporting a variant of uncertain significance ("VUS"), yet this "VUS rate" has questionable value as multiple factors influence it (e.g., the patient population). By permuting various parameters, we explore the extent to which the reported VUS rate can vary even if the underlying information about variants is the same. Methods. We simulated hypothetical laboratories by sourcing assertions from ClinVar and allele frequencies (AF) from gnomAD. We permuted six parameters: (1) the AF above which variants were automatically classified as
benign; (2) the number of exon-padding intronic bases sequenced; (3) the cohort's ethnic composition; (4) whether to include patients with both VUS and pathogenic variants in the rate; (5) how variants with multiple ClinVar assertions were interpreted, and (6) the genes on the test's panel. Unless in ClinVar, low-AF variants were classified using Variant Effect Predictor (HIGH/LOW impacts only). Variance-based sensitivity analysis was used to assess the relative importance of parameters.<br />Results. The main determinants of the VUS rate were panel composition (VUS rate increased with more genes), the ethnicity composition of the patient cohort (an African/African American cohort had the highest VUS rate at 88.1% on average for the largest panel, and a European cohort had the lowest, 70.5%), and the method used to reconcile variants with multiple ClinVar assertions (a simple majority rule had a smaller VUS rate than a full consensus rule). The other three parameters had smaller effects. Across all simulations, the VUS rate varied from 1.5% to 96.5%.<br />Conclusions. VUS rates can vary widely, in part due to variables not under laboratory control. As ethnicity was a key VUS-rate determinant, further research of the genetic variants of minority populations is warranted. Our results indicate that the VUS rate in isolation is not a reliable measurement of quality, suggesting that multiple criteria should be considered when evaluating which genetic tests to offer to patients.

A-211 The Use of Pheno Analysis to Reclassify Variants in Moderate Penetrance Genes (CHEK2, ATM, BARD1) with Analysis of the Effects of Reported Cancer History Errors

Genetic/Genomic Testing
Submitter: Erin Mundt,
Primary Author: Erin Mundt, Myriad Genetics, Inc.
Author 2: Karla Bowles, Myriad Genetics, Inc.
Author 3: Brian Morris, Myriad Genetics, Inc.
Author 4: Jamie Willmott, Myriad Genetics, Inc.
Author 5: Susan Manley, Myriad Genetics, Inc.
Presenting Author: Jamie Wilmott, MS, CGC, Myriad

Background: Pheno analysis is a computerized statistical tool used to provide evidence for classification of variants in genes associated with hereditary cancer. The Pheno calculation has been used in the reclassification of numerous variants in multiple genes. Pheno is continually reviewed and validated and was recently enhanced to include upgrades in CHEK2 and ATM as well as downgrades in BARD1. Data for Pheno is obtained from the personal and family cancer histories provided on test request forms (TRFs). TRFs are completed by providers based on self-reported cancer histories so errors may occur.<br />Methods: Pheno combines clinical and genetic data from probands
pursuing comprehensive genetic testing in routine clinical practice. Pheno classification thresholds were constructed targeting >99.5% PPVs and NPVs and pathogenic and benign composite variants were analyzed through two-fold cross-validations. PPVs, NPVs and the average number of probands required for Pheno to make a calculation were calculated. Errors on TRFs were evaluated to determine if these affect the overall variant Pheno score. 

Results: Validation with composite pathogenic and benign variants in CHEK2 and ATM revealed a positive predictive value of 99.9% and 99.8% respectively. Additionally, validation of BARD1 revealed a negative predictive value of 99.8%. The testing of random errors in personal and family history provided on TRFs revealed Pheno PPVs and NPVs of >99.5%. TRF errors did lead to an additional number of probands required for Pheno to make a call. 

Conclusions: Pheno provides accurate evidence for use in variant classification. The inclusion of BARD1, CHEK2 and ATM highlights the important ability of Pheno to provide information about the classification of variants in moderate risk genes that would otherwise remain uncertain. Results of analysis of errors reported on the TRF further confirms the accuracy and confidence in this classification tool.

A-214 Genetic Counselors’ Perceptions and Experiences of Counseling and Testing for Low Penetrance Alleles

**Genetic/Genomic Testing**

*Submitter: Kaylin O’Brien-Miner,*

*Presenting Author: Kaylin O’Brien-Miner,*

*Primary Author: Kaylin O’Brien, Boston University Division of Medical Sciences*

*Author 2: Meghan Towne, MS CGC, Ambry Genetics*

*Author 3: Elicia Estrella, MS CGC, Boston Children’s Hospital*

This study explored genetic counselors’ experiences, knowledge, and opinions surrounding genetic testing and available guidelines for testing of five genes with low penetrance: APOE (Alzheimer’s disease), F5 (thrombophilia), GBA (Parkinson’s disease), HFE (hemochromatosis), and MTHFR (indications unrelated to folate metabolism). The study assessed the current state of clinical genetic testing and examined genetic counselors’ perceptions of “Direct to Consumer” (DTC) testing for the five alleles. We found that genetic counselors are more willing to order clinical testing for alleles with low penetrance when they believe there is strong evidence to support the association with disease, and when there are actions that can be taken to mitigate the effects of the associated conditions (e.g. impact to clinical care or lifestyle). Additionally, genetic counselors reported they are more likely to order testing for the alleles if there is a known family history of the condition. Of the genes we covered, the most commonly ordered tests were for variants in HFE and F5, which were also the genes participants considered to be the most evidence-based and actionable. Our results show that there is often discordance between the number of patients requesting testing for these low penetrance alleles and the reported number of times clinical testing has been ordered. In the case of APOE, 29.9% of
genetic counselors reported having testing requested from them, while just 1.7% had ordered clinical testing. Finally, while this study shows that most genetic counselors would not recommend DTC testing for any of the alleles covered by this study (greater than 80% of genetic counselors surveyed said they would never recommend DTC testing for each allele) it is possible that patients will pursue testing independent of their clinical care. <br />

A-217 Genome-wide cfDNA testing: Clinical laboratory experience screening for select microdeletions

Genetic/Genomic Testing
Submitter: Jill Rafalko, MS, LCGC,

Primary Author: Jill Rafalko, MS, LCGC, Integrated Genetics

Author 2: Kimberly Fanelli, MS, LCGC, Integrated Genetics

Author 3: Theresa Boomer, MS, CGC, CG/MB(ASCP), Sequenom/Integrated Genetics

Presenting Author: Kimberly Fanelli, MS, LCGC, Integrated Genetics

Introduction<br />
Genome-wide cell-free DNA (cfDNA) testing was introduced for clinical use in August 2015. Since its release, over 40,000 samples were submitted for analysis. We describe the clinical laboratory experience of this screening test for the identification of select chromosomal microdeletions.<br />

Methods<br />
Maternal blood samples submitted to Sequenom Laboratories® for MaterniT® GENOME testing were subjected to DNA extraction, library preparation, and whole-genome massively parallel sequencing as previously described by Jensen et al. Sequencing data were analyzed using a novel algorithm to detect aneuploidies and other subchromosomal events as described by Lefkowitz et al. For all positive results, outcome data (e.g. cytogenetic/molecular results and/or birth outcomes) were requested by phone or email from the ordering provider.<br />

Results<br />
Analysis of approximately 40,000 samples yielded 65 results that were positive for select chromosome microdeletions, specifically: 1p, 4p, 5p, 8q, 11q, 15q, and 22q. The majority (~71%) of samples were submitted during the second trimester of pregnancy. Diagnostic follow-up testing was available for ~50% of cases, of which >90% of these results confirmed the cfDNA finding. The most commonly identified microdeletion was 22q, accounting for ~58% of the positive results. There were 14 cases in which the microdeletion was suspected to be maternal in origin (13 involving 22q, and 1 involving 8q), which precluded assessment of fetal status for that particular chromosomal region. At least half of the predicted maternal events were confirmed by FISH or microarray in the mother. Parental confirmatory testing was declined in the remaining cases or results were lost to follow-up.<br />

Conclusion<br />
Genome-wide cfDNA testing allows for the identification of select microdeletion syndromes. Though the uptake of diagnostic testing in these cases is limited, knowledge of a potential chromosome abnormality in these pregnancies may help families arrange for appropriate diagnostic testing at birth.
A-220 A retrospective analysis of clinical whole genome sequencing results after non-diagnostic microarray or whole exome sequencing

**Genetic/Genomic Testing**

*Submitter: Alicia M. Scocchia, Illumina Inc.*

*Presenting Author: Alicia M. Scocchia, Illumina Inc.*

*Primary Author: Alicia Scocchia, Illumina Inc.*

*Author 2: Maya Rajan,*

*Author 3: Maren Bennett,*

*Author 4: Erin Thorpe,*

*Author 5: Carolyn M Brown,*

*Author 6: Amanda Buchanan,*

*Author 7: Ryan J Taft,*

*Author 8: Denise L Perry,*

Patients with a rare and undiagnosed genetic disease (RUGD) often undergo years of serial testing, commonly referred to as the “diagnostic odyssey”. Often, clinicians must navigate the patient’s health insurance policy and choose whether to investigate copy number variation (CNVs) using microarrays (CMA) or target single nucleotide variants (SNVs)/indels using whole exome sequencing (WES). Clinical whole genome sequencing (cWGS) combines detection of SNVs, indels, CNVs, aneuploidy, and other chromosomal changes in a single clinical test. Here, we provide a case series of 262 probands who underwent cWGS testing for a RUGD indication at the Illumina Clinical Services Laboratory from 2015-2018. As part of routine analysis, details about prior genetic testing were collected from test requisition forms and medical notes submitted by the ordering clinicians. A reported 64% (n=167) of probands received at least one genetic test prior to cWGS, including CMA (n=104) and WES (n=17). Over half of these probands (57%; n=96) received two or more genetic tests, including nine probands who received both CMA and WES. After cWGS, new information was reported for 62.5% (n=65) of probands with prior CMA and 53% (n=9) with prior WES. Of these cases, most probands received pathogenic or likely pathogenic findings (66%, n=49). Most often, a SNV/indel was identified by cWGS after non-diagnostic CMA (n=36). In five cases, CNVs >100 bp but <87kb were identified by cWGS that were not reported on CMA. In two cases, CNVs were detected after non-diagnostic WES. In five cases, new gene-disease relationships had emerged since last testing. Importantly, a compound heterozygous SNV/CNV pair was detected by cWGS in one case, which may not have been detected until a multi-platform approach was pursued. These data highlight the added value of simultaneous detection
of multiple variant types by cWGS over serial molecular testing approaches and reinforce the need for reanalysis of sequencing data over time.

A-223 Primary care Physicians’ perspectives on positive newborn screens for cystic fibrosis: a statewide survey

**Genetic/Genomic Testing**

*Submitter: jessica tarnowski,*

*Presenting Author: jessica tarnowski,*

*Primary Author: Jessica Marie Tarnowski, Mayo Clinic*

*Author 2: Peggy Modaff, MS, CGC, University of Wisconsin - Madison*

*Author 3: Catherine Reiser, MS, CGC, University of Wisconsin - Madison*

*Author 4: Mei W. Baker, Wisconsin State Laboratory of Hygiene*

**Background**

NBS for cystic fibrosis (CF) incorporates DNA analysis in the screening methodology. Results for screen-positive infants can be challenging to interpret, especially in states that use advanced next generation sequencing technology. This survey aimed to provide the first systemic evaluation of primary care physicians’ information needs when receiving positive newborn screens for CF.

**Methods**

A web-survey was distributed to the Wisconsin pediatrician population. Major question domains addressed preferences for information and communication practices, familiarity with the methodology for screening newborns for CF, and knowledge of risk stratification in screening.

**Results**

Fifty-four physicians completed the survey (6% response rate). Major findings of this study indicate physicians with a higher familiarity with the methodology for screening for CF had a higher level of comfort communicating results to parents (p-value < 0.001). Respondents indicated the value of the immunoreactive trypsinogen (IRT) measured in the first-tier screen for CF was important for to include on the NBS report, as well as the normal range of IRT (N=52, 98%). In addition, respondents indicated statistical information on the likelihood a newborn is affected would be helpful (N=53, 98%). There were no major differences in preferences for information based on the respondent’s experience with NBS or years in practice.

**Conclusion**

The findings of this study indicate the following information included in newborn screen reports is useful: 1) the next steps in the diagnostic process 2) methodology for screening for CF, and 3) information on the genetic basis of the condition. It may be helpful if NBS laboratories also included specific values for IRT and DNA analysis as well as evidence-based estimates of residual risk on reports.
A-226 Genetic Testing Preferences and Intentions in Patients with Clinically Diagnosed Familial Hypercholesterolemia

Genetic/Genomic Testing
Submitter: Hannah Wand, Stanford Healthcare

Primary Author: Hannah Wand, Stanford Healthcare

Presenting Author: Hannah Wand, Stanford Healthcare

Author 2: William Klein, National Cancer Institute

Author 4: Lori Erby, NHGRI; Johns Hopkins

Author 5: Iris Kindt, Familial Hypercholesterolemia Foundation

Author 3: Amy Sturm, Geisinger

Description of Study: Familial Hypercholesterolemia (FH) is a common (1/250) Mendelian disorder that results in elevated LDL cholesterol levels from birth, and if left untreated can result in premature heart disease. Only up to 10% of affected individuals are clinically identified. This is problematic as early statin intervention reduces morbidity and mortality. Currently, there are no standard diagnostic criteria in the US. Few patients in the US have a genetic diagnosis, and little is known about patients’ reasons to pursue or not pursue FH genetic testing. The primary objective of this study is to identify predictors of FH genetic testing intentions in patients with a clinical FH diagnosis. We recruited patients with a clinical diagnosis of FH who have not had genetic testing through the FH Foundation, in lipid clinics throughout the US, and at the FH Summit. Participants completed the survey online or on paper in person. Exploratory factor analysis was used to collapse survey items related to benefits, risks and barriers of genetic testing into independent factors. We then used linear regression to test which factors predicted genetic testing intentions, after controlling for age and gender. We also tested for interactions between factors.

Results: Exploratory factor analysis identified three factors: (1) aversion of information (e.g. genetic testing for FH would cause me a lot of anxiety/stress), (2) curiosity regarding medical/family history (e.g. I am curious about my genetic make up), (3) and psychological reassurance (e.g. If I knew my high cholesterol was genetic, it would encourage me to be healthier). Psychological reassurance was the only significant predictor for genetic testing intention in our regression. There was a significant interaction between aversion and reassurance, such that aversion was inversely related to genetic testing intentions when there was low perceived psychological reassurance. These results are useful in enhancing informed decision-making for patients with Familial Hypercholesterolemia.

A-229 Patients’ Reactions and Follow-Up Testing Decisions Related to Tay-Sachs (HEXA) Variant of Uncertain Significance Results

Genetic/Genomic Testing
Submitter: Tiffany Yip, Emory University School of Medicine

Description of Study: Tay-Sachs (HEXA) is an autosomal recessive disorder that results in a deficiency of the enzyme Hexosaminidase A. While the condition may be severe, the clinical presentation can be highly variable. The HEXA variant of unknown significance (VUS) can cause the disease if both parents are carriers. The study aimed to analyze patients’ reactions and follow-up testing decisions related to the HEXA VUS.

Results: The study found that patients and families had varying reactions to receiving a HEXA VUS diagnosis. Some patients pursued additional genetic testing, while others preferred more conservative approaches. Follow-up testing decisions were influenced by multiple factors, including personal preferences, the severity of symptoms, and the availability of treatments. The study highlights the importance of providing personalized support and counseling to help families make informed decisions.
Introduction: The majority of laboratories do not report variant of uncertain significance (VUS) results from carrier screening panels. JScreen, a national public health initiative through Emory University that provides reproductive carrier screening, began reporting VUSs in the Tay-Sachs disease gene (HEXA) to patients in 2014. Patients received genetic counseling to discuss the VUS, and were offered blood HEXA enzyme screening to assist with VUS reclassification and to provide patients with more information regarding carrier status. Currently, there is a paucity of research regarding reactions to VUS results from carrier screening and little effort has been made to identify factors influencing follow-up testing decisions after receiving a VUS result.

Methods: We conducted a quantitative retrospective study through chart review and by administering online surveys to 62 patients with HEXA VUSs. Participants were eligible if they received a HEXA VUS through JScreen between 2014 and 2017. Using bivariate analyses, we compared demographic and survey responses between two groups: those who pursued enzyme testing and those who did not.

Results: Both groups experienced low levels of distress when receiving the VUS results (p=0.810). Most participants (79%) indicated that the VUSs had no impact on their decision to have children. Perceptions of HEXA carrier status after genetic counseling (p=0.033), decisional conflict levels, plans to have children in the near future, time available to pursue enzyme testing, and interest in and eligibility for research (p<0.001) are factors influencing decision-making related to follow-up testing.

Conclusions: When discussing follow-up testing with patients, it may be beneficial for genetic counselors to focus on these factors to help facilitate the patient decision-making process. Results suggest that patients may not experience intense anxiety after receiving a VUS from carrier screening panels in preconception settings. More research is needed to determine the clinical utility and impact of VUS disclosure in carrier screening.

B-179 The Role of Familial Cancer Risk on Predictors of Genetic Testing and Counseling for Hereditary Breast and Ovarian Cancer

Genetic/Genomic Testing
Submitter: Caitlin G Allen, Emory University

Presenting Author: Caitlin G Allen, Emory University

Primary Author: Caitlin G Allen, Emory University

Author 2: Megan Roberts, National Cancer Institute

Author 3: Colleen McBride, Emory University
Author 4: Ye Guan, Emory University

Background: Despite the increasing availability of clinical genetic testing and counseling for BRCA-related cancers, these services remain underutilized. While there is continued growth and exposure to genetic services, there have been limited efforts to understand the public’s level of awareness and use of genetic services, particularly for BRCA-related cancers. Methods: This quantitative analysis is based on data from the 2015 National Health Interview Survey (NHIS). Bivariate analyses were used to compute percentages and examine the associations of familial cancer risk for three genetic services outcomes. Multivariate logistic regression models were used to estimate the association of familial cancer risk and other demographic and health variables with each of the genetic services outcomes. Results: A total of 18,601 women were included in this sample and the average age was 50.3 years old. 87.9% were at low risk (no first degree female relatives with history of breast or ovarian cancer), 10.4% were at medium risk (at least one first-degree female relative with breast cancer) and 1.7% were at high risk (at least one first-degree relative diagnosed with breast cancer under 50 or any first-degree relatives with ovarian cancer) of developing BRCA-related cancers. A low number of women in the sample had ever had genetic counseling (2.8%), discussed genetic testing with their physician (4.6%), or had genetic testing (1.6%). Across all counseling and testing outcomes, individuals who were at higher risk and those with stronger risk perceptions were more likely to have received counseling or testing. Greater familial risk was significantly associated with the likelihood to receive cancer genetic services. Conclusion: Our findings highlight the low uptake of cancer genetic services among high risk populations in the US. Genetic counselors may address this challenge by supporting the positive role of familial risk information in undertaking appropriate cancer genetic counseling and testing.

B-182 Perspectives of Pediatric Providers Regarding Clinical Use of Pharmacogenetics

Genetic/Genomic Testing
Submitter: Kayleigh Avello,

Presenting Author: Kayleigh Avello,

Primary Author: Kayleigh Avello, Augustana-Sanford Genetic Counseling Program

Author 2: Megan Bell, LCGC, Sanford

Author 3: Megan Landsverk, Ph.D., FACMG, Ambry

Author 4: Eugene Hoyme, MD, Sanford

As healthcare progresses in the current personalized medicine era, one goal has been the utilization of pharmacogenetics (PGx) to influence how medications are prescribed. However, there are current healthcare disparities for prescribing medications between adults and children. Research has shown that
children are not just small adults and different challenges exist for pediatric providers (physicians, nurse practitioners and physician assistants) in regards to ordering and interpreting PGx tests. The goal of this study was to provide an initial understanding of current pharmacogenetic testing use by pediatric providers, as well as determine what perceived barriers currently exist. An online survey consisting of 22 multiple-choice questions was distributed to pediatric providers via email at six different institutions across the United States. Responses to the survey were downloaded from SurveyMonkey into an excel sheet and read into R for analysis. Of the 252 respondents who completed the survey, 24% reported having ordered PGx tests before, however, over 90% of respondents reported that they would feel more comfortable ordering and interpreting with the professional assistance of a pharmacist, geneticist, genetic counselor or expert in PGx. Additionally, pediatric providers identified barriers which prevent the utilization of routine clinical PGx testing as: cost (to patient), as well as lack of knowledge and/or experience with pharmacogenetics, clinical utility and PGx availability. Solutions to overcome these barriers could encompass increasing provider education regarding PGx testing, collaboration through a multidisciplinary team approach, as well as having established PGx programs. As the pharmacogenetic field continues to evolve and gain more utility for children, it will be important to continuously identify and address barriers and challenges that exist for pediatric providers in order to allow for a more successful implementation of PGx testing in the pediatric setting and enhance patient care.

B-185 Complex chromosomal rearrangements revealed through Genome-wide cfDNA: 40,000 samples

Genetic/Genomic Testing
Submitter: Theresa Hopkins Boomer,

Primary Author: Theresa Hopkins Boomer, Sequenom Laboratory / LabCorp

Author 2: Samantha Caldwell, Sequenom Laboratory / LabCorp

Author 3: Eyad Almasri, Sequenom Laboratory / LabCorp

Author 4: Jenna Wardrop, Sequenom Laboratory / LabCorp

Author 5: Sidra Boshes, Sequenom Laboratory / LabCorp

Author 6: Michelle Hackbardt, Sequenom Laboratory / LabCorp

Author 7: Philip Cacheris, Sequenom Laboratory / LabCorp

Author 8: Ron McCullough, Sequenom Laboratory / LabCorp

Presenting Author: Sidra Boshes, Sequenom Laboratory / LabCorp

Background: Genome-wide cell-free DNA prenatal screening continues to increase our insight into placental findings not previously recognized. Here we present data from the first two years of clinical testing for expanded cfDNA screening, including genome wide aneuploidy detection and
subchromosomal copy number variants (CNVs) larger ≥ 7Mb, with specific attention to complex chromosomal rearrangements. Methods: Maternal blood samples submitted for genome-wide cfDNA testing were subjected to DNA extraction, library preparation, and whole-genome massively parallel sequencing as described by Jensen et al. Sequencing data were analyzed using a novel algorithm as described by Lefkowitz et al. Results: 41,634 samples were submitted to the clinical laboratory. Positive results (n = 1957) were classified as follows: 53% Common trisomies 19% Sex chromosomal aneuploidies 3% Microdeletions 13% Esoteric chromosomal aneuploidies 8% Isolated CNVs 4% Complex CNVs (e.g. translocations) Complex CNV positive samples consistently report a higher proportion of ‘ultrasound findings’ (62% vs 22%) and ‘personal/family history’ (29% vs 8%) compared to the testing population as a whole. However, 24% of this cohort report being ‘average risk’ or ‘advanced maternal age’. Of the 83 complex CNVs reported, 63 were interpreted as possible translocations and 20 as possible interchromosomal recombinant events. Fetal confirmation was reported in 56%, with 24% pending, 15% lost to follow-up, and 5% discordant. Parental rearrangements (e.g. translocation, insertion, inversion) were previously known for 16% of these results, while 18% were consequently identified post positive screen, 6% proven de novo, and 58% pending full parental assessment. Conclusion: Genome-wide cfDNA prenatal screening with subchromosomal CNV detection has allowed noninvasive technology to reach the subset of patients at highest risk for chromosomal imbalance, many previously unaware. These high risk families can benefit from early identification or added reassurance, prior to diagnostic testing.

B-188 Primary findings from elective whole genome sequencing in an ostensibly healthy population

Genetic/Genomic Testing
Submitter: Meagan Cochran, MS, CGC, HudsonAlpha Institute for Biotechnology
Presenting Author: Meagan Cochran, MS, CGC, HudsonAlpha Institute for Biotechnology
Primary Author: Meagan Cochran, HudsonAlpha Institute for Biotechnology
Author 2: Kelly East, HudsonAlpha Institute for Biotechnology
Author 3: Whitley Kelley, HudsonAlpha Institute for Biotechnology
Author 4: Carol Aiken, The Smith Family Clinic for Genomic Medicine
Author 5: David Bick, HudsonAlpha Institute for Biotechnology

In July 2016, HudsonAlpha launched Insight Genome, an elective whole genome sequencing and pharmacogenetic test available through The Smith Family Clinic for Genomic Medicine. Since that time, 42 patients have completed testing including clinical WGS through the HudsonAlpha Clinical Services Lab and pharmacogenetic testing through Kailos Genetics. Patients undergo clinical evaluation prior to
testing which includes review of medical records, collection of medical and family histories, and physical examination. WGS results include primary findings related to a current or previous condition or family history as well as secondary findings based on patient preference. Of our 42 participants, 13 (30.1%) have had returnable primary findings identified. Of these 13, 3 have had two distinct primary findings potentially associated with different medical conditions. Identified primary variants range from those associated with hereditary cancer predisposition (MSR1 and MSH2) to neurologic/neuromuscular conditions (COL6A3, ANO5, SPTLC2) and even include a likely somatic variant representative of an underlying malignancy (TET2). The number of ICD10 codes for these patients ranges from 1-11 with an average of 5.4; the average number of ICD10 codes across our entire cohort is 4. The results from our case series suggest that elective genomic sequencing should no longer be considered the realm of the “worried well”. It is also important to note that of our 13 patients with primary findings, only three had personal or family histories that would likely have led to traditional genetics referrals and testing strategies. While the implementation of elective genomic testing for the general population is currently limited by economics and availability of providers, these results suggest that the rate of primary findings in an ostensibly healthy population may be higher than previously realized. Further research is warranted into whether patients seeking elective sequencing are representative of the general population or have additional motivations guided by underlying health issues.

B-191 Rapid exome identified dual diagnoses, congenital myasthenic syndrome and double-dominant MYBPC3-related neonatal cardiac disease, in critically ill neonate, allowing for heart transplant

Genetic/Genomic Testing
Submitter: Callie Jenevein Diamonstein, Inova Translational Medicine Institute

Presenting Author: Callie Jenevein Diamonstein, Inova Translational Medicine Institute

Primary Author: Callie Jenevein Diamonstein, Inova Translational Medicine Institute

Author 2: Natalie Susan Hauser, Inova Translational Medicine Institute

Author 3: Rebecca Tannenbaum Miller, Inova Translational Medicine Institute

Whole exome sequencing (WES) is increasingly appreciated as a diagnostic tool for critically ill neonates and championed for the ability to identify dual diagnoses that may be missed by panel testing. WES was ordered at a large community hospital for a neonate with respiratory failure, mild joint contractures, mild hypotonia and severe restrictive cardiomyopathy. The prenatal history was significant for maternal gestational diabetes, maternal chronic cardiomyopathy and suspected fetal cardiac disease. The parents were consanguineous and had a history of elective termination for a fetus with cystic hygroma and suspected cardiac disease. The current baby was born full term by repeat C-section. On day of life two, the baby developed tachypnea, increased work of breathing with retractions and desaturations, requiring ventilation. Restrictive cardiomyopathy was identified. The baby failed extubation three times in a three-week period. It become clear that heart transplant was likely the only option for cardiac
treatment, however, the clinical team was concerned about the possibility of a genetic syndrome based on the baby’s weakness, contractures and extreme respiratory failure. Withdrawal of care was considered. Semi-rapid (30-day) whole exome sequencing was ordered and revealed a known homozygous pathogenic variant (c.264C>A) in RAPSN as well as a homozygous, likely pathogenic, intronic variant (c.1927+1G>T) in MYBPC3. The results were consistent with dual diagnoses of congenital myasthenic syndrome (CMS) and rare, double-dominant MYBPC3-associated severe neonatal cardiac disease. Given the decent general prognosis of CMS, the family and team opted for cardiac transplant, and the infant was accepted to the cardiac transplant list. The baby’s parents were identified to be at risk for autosomal dominant MYBPC3-related cardiac disease. Rapid whole exome sequencing had a tremendous effect on the neonate’s care, identified many family members at risk for dominant disease and contributed phenotypic information to rarely described double-dominant MYBPC3 mutations.

B-194 Unexpected Findings from Clinical Whole Exome Sequencing for a Diagnostic Odyssey Patient: Results Suggestive of Leukemia

Genetic/Genomic Testing
Submitter: Marissa Ellingson, MS, LCGC, Mayo Clinic
Presenting Author: Marissa Ellingson, MS, LCGC, Mayo Clinic
Primary Author: Marissa S. Ellingson, Mayo Clinic
Author 2: Nicole J. Boczek, Mayo Clinic
Author 3: Douglas L. VanCuyk, Mayo Clinic
Author 4: Linda Hasadsri, Mayo Clinic
Author 5: Zhiyv (Neal) Niu, Mayo Clinic
Author 6: Jess F. Peterson, Mayo Clinic
Author 7: Linda B. Baughn, Mayo Clinic
Author 8: Deepti M. Warad, Mayo Clinic
Author 9: Brendan C. Lanpher, Mayo Clinic
Author 10: Matthew J. Ferber, Mayo Clinic

INTRODUCTION: A 10-year-old female was referred for genetics evaluation. Clinical features included global developmental delay, intellectual disability, ADHD, encephalopathy, delayed myelination, hypotonia, joint laxity, cardiac anomalies, feeding difficulty, splenomegaly, bleeding disorder, and suprarenal ganglioneuroblastoma. Because the features were suggestive of a genetic etiology but a particular syndrome was not recognized, whole exome sequencing (WES) was pursued.<br/>
METHODS: WES was performed on blood samples from the patient and both biological parents. Reported variants were confirmed by Sanger sequencing.

RESULTS: Analysis of WES data revealed homozygosity across a region of chromosome 11q. Within this region, a homozygous de novo pathogenic variant was identified in the CBL gene (c.1112A>C, p.Tyr371Ser; NM_005188.3), associated with autosomal dominant Noonan syndrome-like disorder with or without juvenile myelomonocytic leukemia (JMML). Based on 2016 World Health Organization criteria, a germline CBL mutation with loss of heterozygosity of CBL meets genetic criteria for a diagnosis of JMML; however, clinical correlation is necessary for a formal diagnosis. Results were communicated urgently to the ordering clinician. Subsequent bone marrow biopsy was normal. To better understand the natural history of her disease, previous blood and fibroblast samples were tested. The CBL variant was homozygous in a blood sample from age 2, but was heterozygous in fibroblasts (representative of germline). The hematologist suspects the patient had a leukemia-like episode prior to age 2 with spontaneous remission, which has been documented in several patients with germline CBL mutations.

CONCLUSIONS: In patients with germline CBL mutations, JMML develops following somatic LOH and acquired uniparental isodisomy of chromosome 11q, and may spontaneously regress. Because unexpected somatic findings may be discovered in patients evaluated for germline mutations by WES, variants must be carefully analyzed to determine their significance as germline versus somatic.

B-197 Information and Support Resources for Whole Exome Sequencing

Genetic/Genomic Testing

Submitter: Kathryn Gunther,

Presenting Author: Kathryn Gunther,

Primary Author: Kathryn Gunther, University of Alabama at Birmingham

Author 2: Christina Hurst,

Author 3: Aimee Brown Jennings, University of Alabama at Birmingham

Author 4: Dr. Anna Hurst, University of Alabama at Birmingham

Author 5: Dr. Sara Knight, University of Alabama at Birmingham

There have been several research studies based on whole exome sequencing (WES), as it is being increasingly used in clinic populations for previously undiagnosed disease. This study aimed to assess the resources used by patient families for support and information in the WES process. The participants were 26 parents (19% response rate) of pediatric patients from the University of Alabama at Birmingham whose children had undergone WES, and they were sent a retrospective survey about the resources they used. The survey responses were analyzed quantitatively, and free response answers looked for emerging themes. The most common information resource provided to the family was a handout from a laboratory and 58% of participants did not seek further information. Most participants did not receive support resources, but still felt supported in the process. Most participants utilized their
previously established support networks, like family or religion. Genetic counselors were a most utilized support, likely given their accessibility and knowledge. Patient perception of support and information were strongly correlated (p<0.05) and believed to be markers that synchronize to create an overall positive experience. Genetic counselors should strive to create a dynamic of support and information during the WES testing process to better serve the patient experience.

**B-200 Comprehensive analysis of the ACMG59 genes in parental samples submitted for exome evaluation yields a high positive rate**

*Genetic/Genomic Testing*

*Submitter: Eden Haverfield, DPhil, FACMG,*

*Primary Author: Eden Haverfield, DPhil, FACMG, Invitae Corporation*

*Author 2: Sienna Aguilar, MS, CGC, Invitae Corporation*

*Author 3: Edward D. Esplin, MD, PhD, FACMG, FACP, Invitae Corporation*

*Author 4: Rebecca Truty, Invitae Corporation*

*Author 5: Tina M Hambuch, PhD, FACMG, Invitae Corporation*

*Author 6: Kristin McDonald Gibson, PhD, FACMG, Invitae Corporation*

*Author 7: Jackie Tahiliani, MS, LCGC, Invitae Corporation*

*Author 8: Amira Khouzam, MS, CGC, Invitae Corporation*

*Author 9: Brandon Bunker, PhD, Invitae Corporation*

*Author 10: Keith Nykamp, PhD, Invitae Corporation*

*Author 11: Robert L Nussbaum, MD, Invitae Corporation*

*Author 12: Swaroop Aradhya, PhD, FACMG, Invitae Corporation*

*Presenting Author: Eden Haverfield, DPhil, FACMG, Invitae Corporation*

**Background**
The American College of Medical Genetics and Genomics recommends reporting secondary findings in 59 genes (ACMG59) associated with medically actionable monogenic disorders. This applies to all individuals undergoing whole exome (WES) or whole genome (WGS) sequencing, regardless of indication. Healthy parents who are tested alongside the proband for a trio analysis can also choose to receive secondary findings. Our study evaluates the frequency of medically actionable findings in the ACMG59 genes in probands and unaffected parents.

**Methods**
We analyzed de-identified data from 2,369 individuals who consented to receive secondary findings in the ACMG59 genes as part of exome sequencing. These analyses represent evaluations of probands and
parental samples. We analyzed every individual separately and provided personalized reports if positive variants were identified.

Results
Pathogenic/likely pathogenic (P/LP) variants were identified in 146 of 2,369 (6.1%) individuals, including probands and parents. If heterozygous P/LP variants for ATP7B (Wilson disease) and MUTYH (Familial Adenomatous Polyposis 2) were excluded, the detection rate was 84 of 2,369 (3.5%). Of 1,224 unique cases (representing 596 proband, 111 duo, or 517 trio cases), 46 had findings in a proband only (41%), 33 had findings in a proband and one parent (29%), and 33 had findings in a parent only (29%). Parent-only findings were present in genes including those related to HBOC, Lynch syndrome, familial hypercholesterolemia, and cardiomyopathy.

Conclusion
Medically significant secondary findings are identified in 3.5% of individuals undergoing exome sequencing, and 6.1% if heterozygous variants in ATP7B and MUTYH are included. Notably, investigating secondary findings in the ACMG59 genes identified previously unknown personal and familial risk for certain types of actionable disorders in a parent only in nearly one-third of positive findings. These findings may justify the use of a targeted gene panel including the ACMG59 genes to screen for hereditary disease risk in the general population.

B-203 Clinical validity of expanded carrier screening: high concordance of inter-lab variant classifications

Genetic/Genomic Testing
Submitter: Kristjan Eerik Kaseniit, Counsyl

Primary Author: Kristjan Eerik Kaseniit, Counsyl

Presenting Author: Kristjan Eerik Kaseniit, Counsyl

Author 2: Elizabeth Collins, PhD, Counsyl

Author 3: Christine Lo, PhD, Counsyl

Author 4: Krista Moyer, MGC, LCGC, Counsyl

Author 5: H. Peter Kang, MD, MS, FCAP, Counsyl

Author 6: Dale Muzzey, PhD, Counsyl

Introduction
Consensus in databases such as ClinVar is often used to establish the clinical validity of individual variants. The ACMG/AMP variant classification guidelines recommend using a higher bar of evidence for deleterious assertions when applied to an unaffected population, e.g., in expanded carrier screening (ECS), where the vast majority of patients are asymptomatic. We evaluated the clinical validity of ECS by analyzing variant-classification concordance between Counsyl's Foresight ECS and ClinVar submissions.

Methods
ClinVar entries were classified as either concordant with Counsyl interpretations, or falling into one of eight discordance categories: (1) legitimate interpretation difference ("LDiff"); (2) homozygotes observed in population studies; (3) unclear submitter classification; (4) no published cases; (5) adult onset; (6) dependent allele; (7) reduced penetrance; (8) variable
expressivity. Alleles were weighted by their population frequency to estimate the carrier rates of different categories.<br />

Results<br />
Out of 12,834 variants evaluated, 98.2% were concordant. Most discordances were due to deleterious assertions in ClinVar (76.8%) which we considered not to be reportable (VUS or benign). Of the discordances, 51.5% were LDiffs, 3.4% were variants with homozygotes observed in the population, 25.7% were due to unclear submitter classifications, 14.8% were variants with no cases, and 4.6% were due to categories 5-8, where reporting of variants in a carrier-screening setting might not be appropriate compared to a diagnostic setting. Overall, 31.7% of Foresight patients are carriers for concordant alleles, and only 0.9% carry LDiff alleles (0.7% carry variants which do not meet our ECS threshold for pathogenicity).<br />

Conclusions<br />
With a proper variant-interpretation workflow, ECS has high clinical validity. Residual discordances may be unavoidable because of different patient populations tested (e.g., affected vs. not). Routine evaluation of discordances with ClinVar is expected to boost clinical validity even further and ultimately better serve patients.

B-206 Pathogenic RET variant identified as secondary result in unaffected parent via trio whole genome sequencing for developmental delay: clinical, familial, and psychosocial implications

**Genetic/Genomic Testing**

*Submitter: Whitley V Kelley, HudsonAlpha Institute for Biotechnology*

*Presenting Author: Whitley V Kelley, HudsonAlpha Institute for Biotechnology*

*Primary Author: Whitley V Kelley, MS, CGC, HudsonAlpha Institute for Biotechnology*

*Author 2: Kyle B. Brothers, MD, PhD,*

*Author 3: Carla A. Rich, MA,*

*Author 4: Kelly M. East, MS, CGC,*

*Author 5: Michelle D. Amaral, PhD,*

*Author 6: Gregory S. Barsh, MD, PhD,*

*Author 7: Kevin M. Bowling, PhD,*

*Author 8: Meagan E. Cochran, MS, CGC,*

*Author 9: Candice R. Finnila, PhD,*

*Author 10: David E. Gray, MS,*

*Author 11: Susan M. Hiatt, PhD,*
As whole genome sequencing is increasingly used in the clinical setting, the identification of secondary findings commands a larger role in the downstream management of patients and their families. Here we describe a case from a research study utilizing trio whole genome sequencing in a pediatric patient and her parents for an indication of developmental delay. A pathogenic RET variant (c.1826G>A, p.C609Y) associated with multiple endocrine neoplasia, type 2A, was identified in the proband’s father. The proband did not inherit the variant, and no explanation for her developmental delay was identified. The father was 50 years of age at the time of testing and had no personal or family history indicative of medullary thyroid cancer or other features of MEN2A. The proband’s 13-year-old sibling, who was not part of the research study, had a diagnosis of Hirschsprung disease in infancy. She was later confirmed as part of her clinical care to have inherited her father’s pathogenic RET variant. Both the father and the sibling are currently being managed in a high-risk setting via regular biochemical screenings, but neither have received a prophylactic thyroidectomy. The initial disclosure and counseling of this result presented multiple psychosocial challenges, including dichotomous and volatile emotional reactions between the proband’s two parents. Furthermore, via a recorded and transcribed follow-up interview, we have learned that this information has continued to be a source of great emotional and financial concern for this family many months after the return of results appointment. This case not only highlights the incomplete penetrance of well-studied pathogenic variation in certain genes but also provides a counterexample to literature that suggests secondary findings do not increase distress levels in patients and family members. Examples such as these can serve as a reminder to counselors, other clinicians, and policymakers not to dismiss the possibility of distress in genomic results disclosure.
B-212 Detection of Copy-Number Variants in Expanded Carrier Screening Maximizes Identification of Cystic Fibrosis Carriers

**Genetic/Genomic Testing**

*Submitter: Dale Muzzey, Counsyl*

*Primary Author: Dale Muzzey, Counsyl*

*Presenting Author: Dale Muzzey, Counsyl*

*Author 2: Peter V. Grauman, Counsyl*

*Author 3: Lindsay Spurka, Counsyl*

*Author 4: Kyle A. Beauchamp, Counsyl*

**OBJECTIVE:** Medical-society guidelines recommend routine carrier screening for cystic fibrosis via targeted genotyping of 23 frequent single-nucleotide variants (SNVs) and short insertions or deletions (indels) in the CFTR gene. Screening for copy-number variants (CNVs) is recommended only when a reproductive partner is a known carrier. Here we assess the performance and clinical impact of routinely screening for SNVs, indels, and CNVs in a next-generation sequencing (NGS)-based expanded carrier screen (ECS).

**METHODS:** Pathogenic variants in CFTR from 103,718 patients were discovered via a validated NGS-based ECS. A custom algorithm identified CNVs via relative deviations in NGS read depth: downward depth deflections signified deletions and upward deflections indicated duplications. Approximate CNV breakpoints were inferred from the NGS-depth profile. Positive CNVs were orthogonally assessed via multiplex ligation-dependent probe amplification (MLPA). CFTR CNV sensitivity was explored across a range of length scales via in silico simulations.

**RESULTS:** Among carriers of cystic fibrosis, 98.7% had pathogenic SNVs or indels in the CFTR gene (79% had one of the 23 common variants), and the remaining 1.3% harbored a pathogenic CNV spanning at least one exon. We observed 25 unique CNVs in total, suggesting that algorithms must be configured to detect novel CNVs. Further, single-exon deletions were observed for seven different CFTR exons; analysis of confidence scores for these empirical deletions—coupled with extensive simulations—demonstrated that the bioinformatics pipeline was both accurate and robust, even for short CNVs. Additional analysis revealed that NGS-based CNV detection has expected accuracy comparable to MLPA.

**CONCLUSION:** CNV detection maximizes identification of cystic fibrosis carriers and can be applied to all patients undergoing NGS-based ECS validated to detect these complicated variants. Clinical guidelines recommending screening of only the 23 most frequent variants miss critical identification of carriers and should be revisited.

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B-215 Genetic Counselors’ Perception of Uncertainty in Pretest Counseling for Genomic Testing

**Genetic/Genomic Testing**

*Submitter: Jessica J Park, BS,*
Increased usage of genomic testing (including exome and genome sequencing) has made uncertainties associated with genomic testing more prevalent within medicine. Previous research has characterized aspects of this uncertainty and have proposed methods to assess uncertainty in practice. However, there is limited research exploring how professionals in genomics actually perceive uncertainties involved in their experiences of providing genomic testing, and if or how this impacts approaches to pretest counseling. In this study, we undertook semi-structured interviews with 20 genetic counselors in the US and Canada who provide pretest genetic counseling for genomic testing. Interviews explored genetic counselors’ views of uncertainty regarding genomic testing, how they classify it, how it manifests, and how they manage it during the counseling process. Many genetic counselors identified concepts that mapped to Han et al’s source, issue, and locus of uncertainty related to genomic testing (2017). Genetic counselors reported that patients perceive genomic tests as the “end all be all” test, which often led to overestimating diagnostic yield and expectations that the test will enable customization of all aspects of their health care. This contrasts with genetic counselors’ more skeptical views and expectations. They also described stressing uncertain aspects of genomic testing when patients overestimate its clinical and personal utility. All genetic counselors agreed that standardized guidelines for genomic testing pretest counseling would be helpful, particularly for novice genetic counselors and non-genetics providers. These findings highlight the perceived incongruencies between patients’ and providers’ perceptions of uncertainty regarding genomic testing and the need to further explore effective strategies for handling aspects of uncertainty during pretest genetic counseling.

B-218 Building a cohort from an “n of 1”: The story of GNB1

Genetic/Genomic Testing

Submitter: Anya Revah Politi, MS, CGC, Columbia University Medical Center

Presenting Author: Anya Revah Politi, MS, CGC, Columbia University Medical Center

Primary Author: Anya Revah Politi, Institute for Genomic Medicine, Columbia University

Author 2: Parisa Hemati, Institute for Genomic Medicine, Columbia University

Author 3: Louise Bier, Institute for Genomic Medicine, Columbia University

Author 4: David Goldstein, Institute for Genomic Medicine, Columbia University
Finding variants in genes that have not yet been associated with disease occurs frequently when doing whole exome sequencing (WES). Identifying additional patients is essential to interpret the significance of the variants, publish on new disease associations, and provide diagnoses to patients.

In 2015, research WES at the Institute for Genomic Medicine at Columbia University identified GNB1 variants in three patients with delays with or without seizures. These variants had strong bioinformatic signatures (Need et al., 2012; Zhu et al., 2015): they were de novo, and occurred in a region of GNB1 that was highly intolerant to variation based on population databases like ExAC (the Exome Aggregation Consortium). Through Genematcher we identified another patient with a GNB1 variant and then nine other cases by contacting previous collaborators and clinical laboratories, leading to the publication of a paper linking germline de novo GNB1 variants to neurodevelopmental disability, hypotonia and seizures (Petrovski, et al., 2016). After the publication, we were contacted directly by clinicians and laboratories, as well as parents of patients with GNB1 variants. Then two new patients were listed on DECIPHER (Database of Chromosomal Imbalance and Phenotype in Humans Using Ensembl Resources), and four other papers were published describing patients with GNB1 variants (Steinrucke et al., 2016; Lohmann et al., 2017; Szczaluba et al., 2017; Brett et al., 2017). After compiling clinical information for all new and published cases (46 total) we drafted a second paper describing the phenotype in more detail (currently under review). A “GNB1 gene disorder group” now exists on Facebook and has become a platform where over 40 families communicate.

Many useful websites exist today that connect researchers, clinicians and patients with rare genetic variants. These resources allow for the creation of cohorts, expediting new gene-disease associations. In addition, social media websites created by families allow for the building of a support network and the sharing of information.

B-224 Assessing a New Genetic Counseling Referral Source: Tumor Genomic Profiling

**Genetic/Genomic Testing**

*Submitter: Jennie Vagher, Huntsman Cancer Institute*

*Primary Author: Jennie Vagher, Huntsman Cancer Institute*

*Presenting Author: Whitney Espinel, Huntsman Cancer Institute*

*Author 2: Whitney Espinel, Huntsman Cancer Institute*

*Author 3: Jamie Warner, University of Utah*

*Author 4: Amanda Gammon, Huntsman Cancer Institute*
Background: The acquisition of new high-risk cancer populations is constantly evolving as new applications for genetic testing arise. One such application, tumor genomic profiling (TGP), has implications for targeting therapy to improve patient outcomes. However, implications of the results can extend beyond targeted therapies due to the potential identification of hereditary cancer syndromes.

Methods: This study analyzed both positive and unknown variants in 69 genes (chosen based on germline implications) from Foundation One tests (322 solid tumor gene panel) ordered at Huntsman Cancer Institute since 2014. Variants were organized into three categories: clear therapeutic implications, potential germline management changes, and potential germline research genes. The database was analyzed for patterns and potential genetic counseling consequences.

Results: 5,382 variants were identified in 1303 patients in the 69 selected genes. 837 variants were identified in 9 genes determined most likely to change therapeutic implications, most frequent being ATM (55 pathogenic and 146 unknown variants identified in 177 patients) and BRCA2 (41 pathogenic and 157 unknown variants in 180 patients). BRCA1 variants (23 pathogenic and 64 unknown) were the third most common variants, identified in 73 patients. 1,927 variants were identified in additional genes with potential germline implications and 2,655 variants were identified in other potential germline research genes. Testing was most commonly ordered for patients with a metastatic cancer of unknown origin followed by brain, colon, prostate, bladder, and lung cancer. Over half of the somatic alterations detected in this database were identified as a VUS by Foundation Medicine.

This database represents one institution’s experience with TGP over the last 4 years. Characterization of TGP at our institution is a first step to determining the burden that TGP may place on a genetic counseling clinic and help in creating a referral triage system for patients with TGP results.

B-227 Preimplantation Genetic Diagnosis following Whole Exome (WES) or Whole Genome Sequencing (WGS)

Genetic/Genomic Testing
Submitter: Nina Wemmer, MS, CGC, Natera
Primary Author: Nina Wemmer, MS, CGC, Natera
Presenting Author: Nina Wemmer, MS, CGC, Natera
Author 2: Katrina Merrion, Natera
Author 3: Melissa Maisenbacher, Natera

Introduction: WES and WGS are emerging tools in pediatric/adult genetics, increasing the diagnosis rate of rare mutations/conditions. This allows more patients reproductive testing options including in vitro fertilization (IVF) with preimplantation genetic testing for monogenic diseases (PGT-M).

Materials and Methods: PGT-M tests (N=1159) performed from April 2014 to February 2018 by a single lab were retrospectively reviewed for prior proband diagnosis by WES/WGS. Embryo samples were analyzed by Illumina CytoSNP-12 microarrays and informatics. Embryo and parent samples were compared across multiple SNP loci to determine disease chromosome homolog phase/mutation status,
Results: PGT-M testing was performed for 17 cases (20 cycles) with variations previously identified by WES/WGS. Average maternal age was 35.2 years (range 26-43). Four cases underwent PGT-M for two separate conditions resulting in evaluation of 19 conditions with varying inheritance patterns: autosomal recessive (13), autosomal dominant (4) and X-linked (2). At least one variant of uncertain significance (VUS) was tested for in 6/17 (35%) cases. The average number of embryos tested per IVF cycle was 5.7. A majority of cycles (14/20, 70%) had at least one embryo for transfer (unaffected for the monogenic condition[s] and euploid results).

Discussion: WES/WGS are expanding the diagnosis rate in clinical genetics and, thus, the number of conditions assessable by PGT-M. Identified variations introduce complicated counseling discussions around limited phenotypic data, population incidence, and disease progression information. VUS pose clinical and ethical challenges for providers and patients considering IVF and PGT-M. As new technologies transition from pediatrics into the preconception and prenatal arenas, educating patients and providers and ensuring informed consent will require the input, expertise, and collaboration of genetic counselors practicing within these subspecialties.

B-230 The role of cardiovascular, psychiatric and pain pharmacogenetics in predicting disease risk: A Systematic Review of Conditions Associated with Genes Commonly Tested for on Pharmacogenetic Panels

Genetic/Genomic Testing
Submitter: Rachel Brite Saunders,
Primary Author: Heather Zierhut,
Author 2: Thomas Felton,
Author 3: Rachel B. Saunders,
Author 4: Morgan Jackson,
Author 5: Megan Kocher,
Author 6: Kristen Cooper,
Author 7: Sabrina Southwick,
Author 8: Haley Tritch,
Author 9: Maddie Talamantes,
Author 10: Matt Bower,
Author 11: Katie Wiens,
Author 12: Jeffrey R. Bishop,

Presenting Author: Rachel Brite Saunders,

Background: Disease associations with genes found on pharmacogenetics (PGX) panels are not well elucidated, and models for inclusion of disease risk communication and genetic counseling during PGX testing differ or be ignored. Secondary findings of PGX testing exist, but significance of these unsubstantiated. The aim of this study was to systematically review previous publications to identify which diseases are significantly associated with genes on cardiovascular, psychiatric, and pain PGX testing panels and to what magnitude.

Methods: Thirty-two genes present on >1 PGX panel were identified through the Genetic Testing Registry (GTR) and the Concert Genetics websites. A systematic literature search identifying meta-analyses and systematic reviews was performed for each gene. The search produced 23,301 publications of which 481 met inclusion criteria.

Results: A total of 27 of the 32 genes were found to have at least one significant disease association: ABCB1, ADRA2A, BDNF, CACNA1C, COMT, CYP1A2, CYP3A4, CYP3A5, CYP2B6, CYP2C9, CYP2C19, CYP2D6, CYP2E1, CYP4F2, DRD1, DRD2/ANKK1, HLA-A, HLA-B, HTR2A, OPRM1, SLC6A4, SLCOB1, UGT1A1, UGT2B7, UGT2B15, and VKORC1. Statistically significant gene and disease pairs were most commonly found for psychiatric disorders (n=97) and cancer (n=75). Associations with other conditions (n=65) such as hypertension, type 2 diabetes, heart disease, were also found. We identified consistent associations with psychiatric conditions with odds ratios (OR) ranging from 0.33 (95% CI: 0.14-0.81) to 3.29 (CI: 1.43-7.53). For cancer associations, we noted less consistency but ORs ranged from 0.57 (CI:0.41-0.80) to 8.41 (CI: 4.92-14.37).

Conclusion: Clinically significant, and potentially actionable associations were identified for multiple genes on PGX panels. Additional research is needed to assess individual disease associations. Healthcare providers ordering PGX tests should be aware of secondary findings as they may be responsible for discussing disease associations with patients or may consider referring to genetics professional for counseling.

C-180 Genetic Counseling Following Consumer Driven Genetic Testing: Who, What and Why

Genetic/Genomic Testing

Submitter: Sharon Reid Altmeyer, MS, LCGC, GenCipher Consulting, LLC

Presenting Author: Sharon Reid Altmeyer, MS, LCGC, GenCipher Consulting, LLC

Primary Author: Sharon Reid Altmeyer, MS, LCGC, GenCipher Genetic Counseling

Author 2: Johanna Schmidt, MPH, MGC, LCGC, Westide Genetic Counseling

The demand for consumer driven genomic testing (CDGT) is increasing rapidly, but little is published about the demographics of those who seek this kind of testing, their motivations for testing, and outcomes of their genetic counseling sessions. Consumers obtain genomic information from companies that offer SNP-arrays, and, more recently, whole exome (WES) or whole genome sequencing (WGS).
Many times, the data that the consumer receives, either via laboratory devised reports/online user interfaces or from raw data files, comes with limited interpretation or counseling. Genomic test interpretation and counseling is within the scope of practice for genetic counselors (GCs); however, few offer it and there are no established practice guidelines. Presented here is initial data from 55 CDGT cases seen by two independent GCs to better elucidate: client demographics, reason for testing, test types, interpretation tools used, and GC session outcomes. Counseling sessions were by telephone or web-based platform. Clients ranged in age from 23-84 years, median age 53y. 64% were female and 36% male. Test types included WES (75%), SNP-array (20%), WGS (2%), WES&SNP (3%). 78% were referred by the testing company; 15% of clients self-referred from the NSGC website or from the GC’s website; and 7% were referred by a third-party interpretation company. 55% of clients sought testing and counseling for medical reasons and 45% for general interest and/or to optimize health. 24% of clients were referred on for clinical assessments and/or testing. GC after CDGT can help clients understand test results in the context of their personal and family medical history and can be used to formulate an appropriate clinical action plan. More work is needed to develop appropriate training and resources for GCs and other providers to help consumers understand, contextualize and utilize these genomic data from CDGT most effectively.

C-183 A Data-Driven Approach for Determining Conditions to Include in Expanded Carrier Screening Panels

Genetic/Genomic Testing

Submitter: Rotem Ben-Shachar, Counsyl

Presenting Author: Rotem Ben-Shachar, Counsyl

Primary Author: Rotem Ben-Shachar, Counsyl

Author 2: Ashley Svenson, Counsyl

Author 3: Dale Muzzey, Counsyl

Current guidelines issued by the American College of Obstetricians and Gynecologists (ACOG) provide criteria for determining if a disease should be included in an expanded carrier screening (ECS) panel. A data-driven approach is needed to evaluate the impact of these criteria on detection of couples at risk for conceptuses with serious disease. To that end, we analyzed de-identified data from 44,483 patients who underwent ECS on a 176-condition panel to evaluate how exclusion of diseases that do not meet certain criteria impacts the rates of detection of both individual carriers and at-risk couples. 170 (97%) of the 176 conditions met at least six of the seven ACOG criteria. Limiting an ECS panel to these 170 conditions would reduce identification of at-risk couples by 3%. The seventh criterion—that a disease must have a carrier frequency above 1-in-100—can be interpreted in different ways, as carrier frequencies vary widely by ethnicity. Depending on the definition used, the criterion is satisfied by between 12 (7%) and 75 (43%) conditions, and if met, would reduce identification of at-risk couples by between 5% and 51% and carriers by between 20% and 83%, respectively. We introduce a statistical
framework to determine an alternative and more clinically relevant carrier-frequency cutoff by modeling clinical sensitivity, an analysis based on the probability that sufficient reported cases exist in the literature to interpret the pathogenicity of observed variants. Our modeling suggests that a disease with a carrier frequency as low as 1 in 4,000 could still achieve a clinical sensitivity of 50%. In summary, we show that, while disease-inclusion criteria are needed for an ECS panel to be clinically meaningful, the 1-in-100 carrier-frequency threshold is unclear and arbitrary, limiting at-risk couple detection without yielding a substantial reduction in carrier detection. We suggest that this threshold should be revisited and propose an alternative model to determine a carrier-frequency threshold based on estimated clinical sensitivity.

C-186 Negative Whole Exome Sequencing...Now What?
Genetic/Genomic Testing
Submitter: Elly Brokamp,

Presenting Author: Elly Brokamp,

Primary Author: Elly Brokamp, Vanderbilt University Medical Center

Author 2: Laura Fairbrother, Vanderbilt University Medical Center

Author 3: John A Phillips, Vanderbilt University Medical Center

Author 4: Rizwan Hamid, Vanderbilt University Medical Center

Author 5: John Newman, Vanderbilt University Medical Center

Author 6: Joy Cogan, Vanderbilt University Medical Center

Author 7: Anna Bican, Vanderbilt University Medical Center

Author 8: Amy K Robertson, Vanderbilt University Medical Center

Author 9: Mary Koziura, Vanderbilt University Medical Center

Introduction: Individuals with undiagnosed diseases have significant symptoms leading to extensive evaluations and tests without discovery of the underlying etiology. Before patients are accepted into the Undiagnosed Diseases Network (UDN) their clinical diagnostic work up has typically included a chromosomal microarray (CMA), panel sequencing and copy number variant (CNV) testing, and possibly Whole Exome Sequencing (WES) without detection of obvious pathogenic mutations. 

Methods: We reviewed the first 30 diagnoses made by the Vanderbilt University Medical Center clinical site of the UDN to determine the methodologies that lead to their diagnosis.

Results: Of these diagnoses, 7/30 (23%) were made using WES and none of these 7 participants had WES previously done on a clinical basis. 10/30 (33%) were diagnosed using WGS and did not require any additional functional studies. Of the diagnoses made with WGS, 5/10 (50%) had previous non-diagnostic
WES. Of our total diagnoses, 5/30 (17%) required CNV analysis. Another 5/30 (17%) required cDNA analysis to prove the suspected functional effects of non-coding variants (NCV). The final 3/30 (10%) of diagnoses were made on a clinical basis without genetic testing. Discussion: Receiving a non-diagnostic WES result is often disheartening for families who are seeking a genetic diagnosis. Genetic counselors should be aware of additional testing techniques and resources for these families, in order to continue to give them hope for being diagnosed. Since 87% of our diagnoses were made with studies other than WES, we suggest that logical next steps be discussed with undiagnosed patients. Additional testing including WGS, repeat expansion sequencing, cDNA analysis, CNV analysis, methylation studies, high resolution CMA, and re-analysis of WES data should be considered in undiagnosed patients after WES has been performed. Research studies and support organizations, such as SWAN and GARD, are some of the resources for undiagnosed patients.

C-189 Personal genetic testing for future genetic counselors: Assessing interest in offering personal genetic testing as an educational experience in genetic counseling graduate programs

Genetic/Genomic Testing
Submitter: Brian Corner,
Primary Author: Brian Corner,
Presenting Author: Brian Corner,
Author 2: Kathleen Berentson Swenson,
Author 3: Allison Cirino,

Several medical training programs have offered personal genetic testing (PGT) to students as an educational experience. PGT is not being readily incorporated into genetic counseling training programs today and there is a clear gap in the literature pertaining to attitudes of genetic counseling students and faculty towards PGT in the graduate school classroom. A survey was administered to listserv members of the National Society of Genetic Counselors. Board certified or eligible genetic counselors were invited to participate. The survey assessed respondents’ opinion towards the practice of offering PGT in genetic counseling training programs and asked respondents to comment on their own experiences with PGT in the classroom. A self-identified “leadership cohort” of faculty members of genetic counseling training programs was compared to the other respondents. In total, 258 eligible participants completed the survey, the majority of whom serve as clinical genetic counselors. Twelve-percent of respondents met criteria for the leadership cohort. Almost half (42%) of respondents were offered PGT during their training, Karyotyping was rated as the most appropriate level of PGT to offer in training programs followed by carrier screening, while WGS and WES were rated as the least appropriate. Respondents strongly agreed that genetic counseling training programs are well equipped to address the ethical, legal, and social implications surrounding the use of PGT as an educational experience. The fear of abnormal results and infringement upon students’ autonomy were
reported as the two most significant concerns. The majority of respondents felt that with the appropriate protocols in place, the practice could be implemented responsibly. The majority of students who were offered PGT reported a positive experience that increased their understanding of the patient perspective. The most frequent recommendations for implementing PGT responsibly were: must be optional, carrier screening (as an appropriate level of testing) and anonymous data as an alternative.<br />

C-192 Unexpected findings via fragile X carrier screening, four case reports

Genetic/Genomic Testing

Submitter: Casey Duld,

Presenting Author: Casey Duld,

Primary Author: Casey Duld, MGC, LCGC, NxGen MDx

Author 2: Jonathan Karnes, NxGen MDx

Author 3: Robert Carlson, MD, FCAP, NxGen MDx

Author 4: Julie D. Stella, MS, LCGC, NxGen MDx

Author 5: Heather Fecteau, MS, LCGC, NxGen MDx

Author 6: Amelia Tahmassi, MS, LCGC, NxGen MDx

Fragile X syndrome is the most common inherited cause of intellectual disability, caused by a cytosine-guanine-cytosine (CGG)-trinucleotide repeat in the 5' region of the FMR1 gene, located on the X-chromosome. Affected individuals have greater than 200 CGG repeats, though premutation carriers (55-200 repeats) are at risk for adult onset conditions. Current guidelines from the American Congress of Obstetricians and Gynecologists (ACOG) and the American College of Medical Genetics (ACMG), along with the availability of the technology, have made carrier screening for fragile X syndrome more accessible to patients. Fragile X carrier screening allows patients to learn information regarding reproductive risks and provides information about their personal health. The guidelines surrounding carrier screening for fragile X highlight the need for appropriate pre- and post-test counseling due to the complex inheritance pattern and varying phenotypes associated with the FMR1 mutation in its premutation and full mutation forms. It is important for both providers and patients to understand the possible results they may receive via this test, and what implications they have. Here we highlight five cases of fragile X carrier screening performed by NxGen MDx where results were consistent with a diagnosis rather than a positive carrier status. Four of the cases indicated females with greater than 200 CGG repeats, suggestive of a molecular diagnosis of fragile X; and the fifth case was a male sample suggestive of a diagnosis of Klinefelter syndrome (47,XXY). The results of the male sample noted two different CGG repeat values, and a Y chromosome signal. Additionally, this sample was tested for chromosomal copy number variation using the Illumina VeriSeq-PGS platform, and results were
consistent with 47,XXY. These cases illustrate how fragile X carrier screening may provide unexpected, complex results that providers must be able to interpret and disclose to their patients.

C-195 Mate-pair sequencing: providing molecular resolution of structural rearrangements for improved diagnostic clarity.

**Genetic/Genomic Testing**

*Submitter: Anna A Essendrup, MS, LGC, Mayo Clinic*

*Primary Author: Anna A Essendrup, MS, LGC, Mayo Clinic*

*Presenting Author: Anna A Essendrup, MS, LGC, Mayo Clinic*

*Author 2: Richard T. Dineen, CGC, Rush University Medical Center*

*Author 3: George Hoganson, MD, University of Illinois College of Medicine at Peoria*

*Author 4: Daniel L. Jackson, M.D, M.S., F.A.C.O.G., University of Missouri Women’s and Children's Hospital*

*Author 5: Laura Baker, MGC, LCGC, Nemours/A.I. duPont Hospital for Children*

*Author 6: Karen W. Gripp, MD, FAAP; FACMG, Nemours/A.I. duPont Hospital for Children*

*Author 7: Beth Pitel, MS, CG(ASCP), Mayo Clinic*

*Author 8: Matthew Webley, Mayo Clinic*

*Author 9: Sarah Koon, Mayo Clinic*

*Author 10: Stephanie Smoley, Mayo Clinic*

*Author 11: Kyna Byerly, MS, CGC, Mayo Clinic*

*Author 12: Elyse Mitchell, MS, LCGC, Mayo Clinic*

*Author 13: Nicole Hoppman, PhD, Mayo Clinic*

*Author 14: Linda Baughn, PhD, Mayo Clinic*

*Author 15: Hutton Kearney, PhD, Mayo Clinic*

Approximately six percent of individuals with balanced rearrangements are observed to have an abnormal phenotype including congenital anomalies and developmental delays. As the field of genetic testing continues to evolve, our ability to further define apparently balanced genetic abnormalities has also improved. Utilizing NextGen Sequencing and a specialized bioinformatics approach, mate pair sequencing (MPseq) is able to further define the breakpoints of cytogenetically detected structural
C-198 NCAM2: A candidate for corpus callosum malformation

**Genetic/Genomic Testing**

*Submitter: Marcela Dias Hanna,*

*Presenting Author: Marcela Dias Hanna,*

*Primary Author: Marcela Dias Hanna, Instituto de Ciências Biológicas, Universidade de Brasília*

*Author 2: Claudiner Pereira de Oliveira, Secretaria de Estado de Saúde do Distrito Federal*

*Author 3: Patricia Natalia Moretti, Instituto de Ciências Biológicas, Universidade de Brasília*

*Author 4: Maria Teresa Alves da Silva Rosa, Secretaria de Estado de Saúde do Distrito Federal*

*Author 5: Silviene Fabiana de Oliveira, Instituto de Ciências Biológicas, Universidade de Brasília*

*Author 6: Aline Pic-Taylor, Instituto de Ciências Biológicas, Universidade de Brasília*

*Author 7: Juliana Forte Mazzeu de Araújo, Faculdade de Medicina, Universidade de Brasília*

The development of the central nervous system is a complex process involving several genes and environmental factors as well. In an attempt to contribute to the knowledge of the genetic etiology of brain malformations, we describe a 16-month-old boy with dysgenesis of the corpus callosum, colpocephaly and mild dysmorphic features. Chromosome microarray analysis was performed using Cytoscan 750K (Affymetrix) and revealed a 7.3Mb de novo deletion on the 21q11 region. The deleted segment comprises 19 genes. From these, we suggest the Neural cell adhesion molecule 2 gene.
to be the best candidate for the dysgenesis of the corpus callosum. NCAM2 is a paralog of NCAM1, a well characterized cell-cell adhesion molecule highly expressed in the nervous system and involved in important neurodevelopmental processes, such as outgrowth of neurites and synaptic plasticity. Likewise, recent studies on NCAM2 report its high levels of expression in the human brain and its nervous system-related functions. NCAM2 is important for neurite outgrowth, axon growth, fasciculation and compartmentalization and dendritic bundling in the olfactory system. The gene seems to be dosage-sensitive, suggesting a contribution to detrimental effects on neurodevelopment on Down syndrome patients. Besides, GWAS studies have found a strong association of NCAM2 with autism and Alzheimer’s disease. Hence, we propose this gene as a candidate for brain malformations and recommend further studies to test its contribution to neurodevelopmental disorders.

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C-201 Assessment of a Video on Genome Testing Expectations and Results: Parent and Adolescent Views and Understanding

Genetic/Genomic Testing
Submitter: Michaela Jazz Idleburg, MS, Cincinnati Children’s Hospital and Medical Center

Primary Author: Michaela Jazz Idleburg, MS, Cincinnati Children’s Hospital and Medical Center

Presenting Author: Michaela Jazz Idleburg, MS, Cincinnati Children’s Hospital and Medical Center

Author 2: Melanie Myers, Cincinnati Children’s Hospital Medical Center

Author 3: Cynthia Prows, Cincinnati Children’s Hospital Medical Center

Author 4: Alexandra Magnante, Cincinnati Children’s Hospital Medical Center

Author 5: John Lynch, University of Cincinnati

Return of results from genomic research raises issues about how best to help families understand the expectations and results of genomic tests, including testing limitations, the possibility of secondary findings, and the significance of positive and negative results. Parents (n=97) and their adolescents (n=97) viewed a video developed to address these issues and completed a 13-item post-video questionnaire to examine their understanding of its content. Differences in parent and adolescent scores were compared using two-sided independent t-tests and Fisher’s exact tests. Adolescents were less likely than parents to understand the limitations of testing, positive and negative results’ significance, and use of results. Significant differences were noted in average overall correct scores between parents and adolescents (p<0.001). To explore adolescents’ misunderstanding, ten additional adolescents watched the video, completed a modified post-video questionnaire, and were interviewed about their reactions to the video. All interviews were audio recorded, transcribed, coded, and analyzed for major themes. Most adolescents could not recall the limitations of testing, thought the video was long, and understood but struggled to explain basic genomic concepts in relation to positive and
negative results’ significance. In summary, adolescents did not comprehend video content equivalently to parents, and lacked confidence in describing key video concepts. It is possible that adolescent recall and responses are influenced by lack of experience with video concepts. Prior education and repeated viewings throughout the testing process may improve adolescent recall and understanding of this information.

C-204 Interpretation of microdeletion variants aided by population analysis of copy-number variation

Genetic/Genomic Testing
Submitter: Kristjan Eerik Kaseniit, Counsyl
Primary Author: Kristjan Eerik Kaseniit, Counsyl
Presenting Author: Kristjan Eerik Kaseniit, Counsyl
Author 2: Greg Hogan, PhD, Counsyl
Author 3: Kevin D’Auria, PhD, Counsyl
Author 4: Carrie Haverty, MS, LCGC, Counsyl
Author 5: Dale Muzzey, PhD, Counsyl

Introduction
While non-invasive prenatal screening (NIPS) has largely focused on detecting fetal trisomies of chromosomes 13, 18, and 21 due to their well-established clinical consequences, novel fetal microdeletions can also be identified by NIPS. However, these variants are challenging to interpret clinically and are often reported as findings without interpretations. We investigated whether copy-number variant (CNV) prevalence in an ostensibly healthy population could aid the interpretation of novel microdeletions.

Methods
We identified maternal copy-number variants (mCNVs) spanning at least 200kb in 87,255 NIPS samples and used these mCNVs to establish the prevalence of CNVs. We calculated the proportion of each autosomal, 10Mb sliding window that was covered by at least three observed deletions in our mCNV dataset, termed the "deletion span". The corresponding duplication span served as a proxy to control for CNV propensity. The ratio of the two spans ("dup:del ratio") and the gene density was evaluated for known pathogenic microdeletions. We calculated the proportion of each autosomal, 10Mb sliding window that was covered by at least three observed deletions in our mCNV dataset, termed the "deletion span". The corresponding duplication span served as a proxy to control for CNV propensity. The ratio of the two spans ("dup:del ratio") and the gene density was evaluated for known pathogenic microdeletions. We calculated the proportion of each autosomal, 10Mb sliding window that was covered by at least three observed deletions in our mCNV dataset, termed the "deletion span". The corresponding duplication span served as a proxy to control for CNV propensity. The ratio of the two spans ("dup:del ratio") and the gene density was evaluated for known pathogenic microdeletions.

Results
The deletion and duplication span measurements were significantly correlated (Pearson r = 0.73), consistent with there being an intrinsic positional-dependent propensity for CNVs. Three of five commonly tested pathogenic microdeletions (1p36, 4p16, 15q11) had high gene density and elevated dup:del ratio. The 22q11.21 region had a nearly 1:1 dup:del ratio (10th percentile), but high gene density. The 5p13 region had the opposite: an elevated dup:del ratio (≥99th percentile) but near-average gene density. Most additional expert-curated microdeletions of at least 1Mb were also outliers in one or both metrics, with two exceptions having low span values (≤10%), suggesting that general CNV-intolerance can be an additional metric to consider when interpreting novel
Conclusions<br />Novel microdeletions could be evaluated for their gene density and duplication:deletion ratio to determine possible pathogenicity. Either metric in isolation might miss some pathogenic variants.

C-207 Participants' Perceptions of Sequencing Accuracy and Its Correlations with Knowledge, Numeracy, and Optimism

Genetic/Genomic Testing
Submitter: Katie Lewis,

Presenting Author: Katie Lewis,

Primary Author: Katie Lewis, NHGRI

Author 2: Paul K. J. Han,

Author 3: Barbara B. Biesecker,

Author 4: William M. P. Klein,

Author 5: Kristen P. Fishler,

Author 6: Ilana M. Miller,

Author 7: Leslie G. Biesecker,

Patients expect sequencing to yield information relevant to their personal health, but many will receive negative results. How patients understand the accuracy of sequencing has not been studied but relates to whether they are falsely reassured by such results. We set out to describe participants' perceptions of sequencing accuracy and its correlates. We hypothesized that most participants would have realistic expectations of accuracy, which would be positively correlated with sequencing knowledge and subjective numeracy and negatively correlated with optimism. Participants in a sequencing study (N=349) were surveyed about those variables and demographics before receipt of results. Most had at least a college degree (70%) and were female (63%) and African-American (52%). Knowledge about benefits and limitations of sequencing were modest ($\bar{x}$=5.4 and 5.6, SD=2.4 and 2.9, respectively; ranges=0-10), and subjective numeracy was high ($\bar{x}$=4.8, SD=1.1, range=1-6), as was optimism ($\bar{x}$= 8.8, SD = 2.4, range = 0-12). Thirty-one percent had unrealistic perceptions of sequencing accuracy, including its sensitivity (19% - unlikely that they/their family had variations not detected by the test, 16% - test detects all possible variants) and negative predictive value (8% - negative result ruled out having an affected family member in the future). We conducted bivariate analyses comparing those with unrealistic (n=107) and realistic (n=242) perceptions on all potential correlates and demographics. Those who had realistic perceptions were more knowledgeable about sequencing limitations (t=4.2, p<0.01), and were more likely to be male ($X$=6.4, $p=0.01$) and not African American ($X$=7.3, $p<0.01$) than those with unrealistic perceptions. There were no other significant differences between those with realistic vs
unrealistic perceptions. Reassuringly, many participants had realistic expectations of sequencing accuracy. Genetic counselors have the opportunity to identify patients who misunderstand the accuracy of complex screening tests and help them build more realistic expectations.

C-210 Removing the barrier of cost for family variant testing in cancer predisposition genes significantly increases uptake among relatives

**Genetic/Genomic Testing**

*Submitter: Rachel F. Miller,*

*Primary Author: Rachel F. Miller, MS, CGC, Invitae*

*Author 2: Rebecca Trudy, PhD, Invitae*

*Author 3: Edward D. Esplin, MD, PhD, Invitae*

*Presenting Author: Rachel F. Miller, MS, CGC, Invitae*

Background: Family variant cascade testing (FVT) uptake is often limited by a variety of barriers, one of which is cost. In July of 2017, Invitae implemented a new policy, which includes FVT at no additional charge for first-degree relatives (FDR) of probands who test positive for a pathogenic or likely pathogenic (P/LP) variant within 90 days after the initial test report is released. We examined the number of relatives and the percentage of families that participated in FVT before and after this policy implementation.<br /><br />Methods: Probands with P/LP variants in hereditary cancer genes were studied. One cohort of 4,617 probands had their P/LP variants identified in Jan-July of 2017, at which time the charge for FVT was $200 for FDR. The subsequent cohort of 6,076 probands had their P/LP variants identified in July 2017-Jan 2018, during which time there was no additional charge for testing for FDR of probands.<br /><br />Results: Comparing the percentage of probands that had at least one relative tested, we observed a statistically significant increase in testing during the no-additional charge time frame (19.6% vs. 23.2%, p=7.8e-6). Among the families that underwent FVT, during the paid time frame an average of 1.9±0.1 (95% CI) relatives per proband had FVT, while during the no-additional charge time frame an average of 2.2±0.1 relatives per proband had FVT.<br /><br />Conclusion: These data indicate that there was a significantly increased uptake of FVT after the removal of the cost barrier. These data were taken right after the implementation of this policy, and therefore we suspect that this represents an upward trend. While other barriers to FVT exist and also warrant further study, removing the cost barrier as an obstacle appeared to enable more at-risk family members to obtain valuable information potentially relevant to their own healthcare management.
Fabry disease (FD) is an X-linked metabolic disorder resulting from a defect in the α-galactosidase A (α-Gal A) enzyme. This defect is due to mutations in the α-galactosidase A (GLA) gene and causes progressive accumulation of specific glycolipids. There are two major disease subtypes: early-onset type 1 classic phenotype and later-onset type 2 phenotype. Onset of the disease manifestations are seen in childhood or adolescence, typically characterized by acroparesthesias, angiokeratomas, hypohidrosis, and corneal and/or lenticular opacities. With advancing age, the progressive glycolipid deposition, leads to cardiac, renal, and cerebrovascular disease, resulting in premature demise if untreated. Due to the vast degree of heterogeneity, affected individuals typically have a significant delay in diagnosis of about 13 to 15 years. This delay prevents patients from receiving enzyme replacement therapy, a lifesaving treatment, in time to prevent disease manifestations. Newborn screening (NBS) pilot studies for FD have shown that the disease incidence is higher then initially suspected and babies who received treatment had a better prognosis. This study proposed that genetic counselors would be in favor of adding FD to the NBS panel. A survey that examined the perceived benefits and drawbacks of the addition of early and later-onset FD to NBS panels was sent out to the National Society of Genetic Counselors and the American Board of Genetic Counselors. A total of a 122 genetic counselors completed the survey. Results did confirm that the majority of genetic counselors agreed that adding FD to the NBS panel would be beneficial and potentially life saving for those who are diagnosed at birth. Furthermore, it was found that the study cohort was in favor of adding targeted sequencing of severely debilitating early-onset disease genes that had effective therapies but the majority disagreed with adding these disorder if no effective treatment was available.
C-216 Adherence to NCCN Guidelines Within One Hospital System: Comparison Between Sites and Genetic Counselor Utilization

**Genetic/Genomic Testing**

*Submitter: Karen Powell,*

*Primary Author: Karen Powell, MS, Cone Cancer Center*

*Author 2: Anna Villa, MS, CGC, Cone Cancer Center*

*Author 3: Leslie Hoyt, BS,*

*Presenting Author: Karen Powell, MS, CGC, Cone Cancer Center*

Genetic testing is an instrumental tool used to determine if an individual has a predisposition to certain cancers. Testing positive for a predisposition may allow a patient and their family to consider high risk screening or risk reducing options. Genetic counselors work with physicians to ensure that patients at increased risk are referred for genetic testing according to the National Comprehensive Cancer Network (NCCN) guidelines. Cases within one hospital system’s cancer registry were used to identify individuals who qualify for genetic testing. This includes patients with a history of breast (dx ≤45 and triple negative (TN) ≤60), ovarian, colon (dx ≤50) or uterine cancer (dx ≤50). Within this registry, there are four cancer centers. Two sites utilize genetic counselors (GC), and two do not (noGC). To determine if there is a difference in genetic testing rates between GC and noGC sites, cases were evaluated from the joint cancer registry. An analysis of 541 cases demonstrated a significantly higher proportion of eligible patients undergoing genetic testing at the GC site compared to the noGC site (85% vs 55%, p<0.0001). Further analysis of specific cancers showed a significantly higher proportion in genetic testing for eligible colon cancer (82% vs 16%, p<0.0001), breast cancer (97% vs 77%, p<0.0001), ovarian cancer (83% vs 55%, p<0.001), and uterine cancer (36% vs 0%, p<0.05) patients at the GC sites compared to the noGC sites. There was no significant difference in testing of TN ≤60 between sites. This data suggests that having a GC working within an institution increases the ability to identify and offer testing to patients who meet NCCN genetic testing guidelines based on their cancer type.

C-219 Patient-Derived Genomic Data from ClinGen’s GenomeConnect: Advancing Genomic Knowledge and Keeping Patients Informed of Variant Classifications

**Genetic/Genomic Testing**

*Submitter: Juliann Savatt, MS, LGC, Geisinger*

*Primary Author: Juliann Savatt, MS, LGC, Geisinger*

*Presenting Author: Juliann Savatt, MS, LGC, Geisinger*

*Author 2: Danielle R. Azzariti, Laboratory for Molecular Medicine, Partners*

*Author 3: Emily Palen, Geisinger*
Expanding testing technologies have allowed for simpler detection of genomic variants; however, understanding the effect of such variants remains challenging. Broad sharing of genomic and health data is needed to inform variant interpretation and patient care. GenomeConnect (GC), the Clinical Genome Resource (ClinGen) patient registry, is open to anyone who has had genetic testing and wishes to share their de-identified genomic and health information with public databases, including ClinVar. To date, 1615 participants have enrolled and 26% of participants (n=420) have shared genetic report(s) for curation. Most commonly, participants underwent panel testing (36.4%, n=153/420) or exome sequencing (37.8%, n=159). The majority of participants had genetic testing for diagnostic purposes (69.3%, n=291/420). Participants’ reports included 69 distinct copy number variants and 812 unique sequence variants in 568 genes. Testing was completed from 2007 to 2018, and 56.9% (n=502/881) variants were reported as uncertain. Of the curated sequence variants, 47.4% (n=385/812) are novel to ClinVar, demonstrating that patients can serve as a key genomic data source. For the 52.6% (n=427) of variants previously shared, GC submissions provide additional phenotypic data to inform variant interpretation. Data sharing through GC also provides participants with a means to receive updates about their reporting laboratory’s variant classification. To date, 97.3% (n= 727/747) of responding participants opted to receive such information if available and 13 updates have been identified. GC also supports connections with other participants, clinicians, and researchers to enable the exchange of information and support. Almost 13% (n=205/1615) of participants can match with another participant based on gene, and several participants have been informed of a research opportunity based on genetic results. Through data sharing, patients can contribute to the genomic knowledge base while forming connections and remaining informed about their test results.
C-222 Delay of Diagnosis: The Impact of a Lack of Physician Contact Information and Clinical History in Biochemical Genetic Test Result Interpretation

**Genetic/Genomic Testing**

*Submitter: April L. Studinski, Mayo Clinic*

*Primary Author: April L. Studinski, Mayo Clinic*

*Presenting Author: April L. Studinski, Mayo Clinic*

*Author 2: Amy White, Mayo Clinic*

*Author 3: Gisele Pino, Mayo Clinic*

*Author 4: Dawn Peck, Mayo Clinic*

**Introduction:** Laboratory genetic counselor (GC) notification of abnormal biochemical genetic test results is performed as a service to clinicians and for phenotypic correlation as a lab quality measure. The refusal of send out laboratories to provide contact information or provider lack of willingness to engage with lab GCs has been noted to interfere with the diagnosis and treatment of patients. **Purpose:** The aim of this study was to evaluate the impact of the lack of provider dialogue and clinical history for a subset of orders in a diagnostic biochemical genetics laboratory. **Methods:** All results were reported via our laboratory information system. In addition, a laboratory GC attempted to notify clinicians via telephone of abnormal results and review clinical presentation, family history, and recommendations for follow up. **Results:** Reasons result discussions did not occur were due to communication barriers with international clients and domestic send out labs refusal to provide caregiver contact information. In addition, themes cited among providers who declined to engage included concerns regarding potential Health Insurance Portability and Accountability Act (HIPAA) violations, care transfer to another provider/institution, test order errors, and presumed unauthorized research. New specimens received months to years later identified diagnostic and treatment delay as well as incorrect therapy implementation. Discussions with the provider often revealed a patient new to the practice engaged in a diagnostic odyssey. **Conclusions:** This study provides evidence that partnership and open discourse between providers and labs provides the best patient care. Follow up of abnormal test results by a lab GC helps to target referrals and additional testing. Increased understanding by the provider is needed regarding the value of clinical history in laboratory interpretation and how that information is further utilized. This study serves as a foundation for future research on methods to improve communication between clinical and biochemical genetic laboratory care providers.

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C-225 Exploring the Impact of Pharmacogenomic Results on Medical Management and Disclosure Behaviours

**Genetic/Genomic Testing**

*Submitter: Larissa Waldman,*
Introduction: Pharmacogenomic (PGx) tests represent significant advances in precision medicine, allowing for the identification of genetic markers that better predict an individual’s response to a medication. Current literature includes studies that evaluate public opinions regarding PGx testing, as well as clinical and personal utility of general genetic tests. However, no study thus far has investigated the experiences and behavioural responses of individuals who underwent PGx testing, including pre-and post-test genetic counseling (GC).

Purpose: Explore participants’ perceptions following the return of PGx results, as well as their medication management and disclosure behaviours.

Methods: In November 2016, Medcan, a health and wellness clinic in Toronto, Canada, began offering a PGx panel facilitated by a genetic counselor. We surveyed clients who had PGx testing, including pre- and post-test GC. The survey included both quantitative and open ended response questions.

Results: The survey was emailed to 166 eligible participants, with a response rate of 22%. 84% of participants found pre-test GC helpful to both understanding the possible results and the purpose of testing; 94% found the post-test GC helpful in understanding their PGx results. 50% of participants disclosed their results to a physician, 6% disclosed to a pharmacist, and 68% shared their results with family members. Qualitative analysis of participants’ open ended responses regarding their overall experience with PGx testing identified three recurring themes: 1) psychological reassurance, 2) perceived utility: informative and useful versus confusing and not impactful, 3) experiences with disclosure to other healthcare providers.

Conclusion: Our study findings support the provision of pre- and post-test GC services for a non-disease related genetic test, and the importance of managing expectations surrounding PGx testing in pre-test GC. As well, GC should include discussion regarding disclosure and communication of results with other members of the healthcare team, and at risk family members.

C-228 Custom reporting structure for accurate risk assessment of NPHS2-related nephrotic syndrome in Counsyl’s Foresight carrier screen

Genetic/Genomic Testing
Submitter: Domenic Previte, Counsyl
The c.686G>A(p.R229Q) allele is a high-frequency mutation in the NPHS2 gene that can cause nephrotic syndrome. R229Q is not pathogenic in homozygous individuals, but when found in trans with certain missense mutations, protein mislocalization causes a deleterious phenotype. Therefore, custom reporting of NPHS2 is needed to accurately describe reproductive risk for nephrotic syndrome. We separated NPHS2 pathogenic mutations into three categories, each associated with different risk, including: 1. R229Q, 2. a set of missense variants with sufficient evidence for pathogenicity in trans with either R229Q or other pathogenic mutations (R229Q-interacting pathogenic, RP), and 3. all other pathogenic mutations that act in a strictly Mendelian manner and do not interact with R229Q (Other Pathogenic, OP). Risk assessments were calculated using estimated incidence reported in literature (~1:312,500), and carrier rates of the R229Q (1:13.5) and RP (1:27,717) alleles. The carrier rate of OP mutations (1:367) was derived from the quadratic equation where the probability of all possible pathogenic genotypes are summed to equal incidence. Individuals heterozygous for R229Q are reported as carriers. Counsyl’s merged reporting for partners enables precise risk assessments that can be as low as 1:1,000,000 when paired with another R229Q carrier, or as high as 1:4 when paired with an RP carrier. When partner pairs are strictly carriers of RP and/or OP mutations, reproductive risk is reported in a standard Mendelian manner of 1:4. When only one partner is tested, risk is based on his/her carrier status and the estimated carrier frequency of a hypothetical partner. In this framework, an RP carrier would have a reproductive risk equal to 1:54, far greater than would be reported in the absence of locus-specific risk assessment. This approach to NPHS2 risk calculation allows for a precise numerical risk to be reported for all combinations of genotypes to guide counseling and clinical management.
A-232 Development of a Patient-Reported Outcome Measure in Mitochondrial Myopathy: Patient Perspective

Other
Submitter: Natalie Elizabeth Burrill, Arcadia University

Presenting Author: Natalie Elizabeth Burrill, Arcadia University

Primary Author: Natalie Burrill, MS, GC, Arcadia University

Author 2: Zarazuela Zolkipli-Cunningham, MBChB, MRCP, Children’s Hospital of Philadelphia

Author 3: Colleen Clarke Muraresku, MS, LCGC, Children’s Hospital of Philadelphia

Author 4: Kathleen Valverde, MS, CGC, Arcadia University

Mitochondrial diseases (MD) are heterogeneous and multi-systemic disorders that affect 1 in 5000 individuals. While commonality in these disorders is difficult to find, patients often experience fatigue, muscle weakness, and exercise intolerance affecting many body systems, including the central nervous system, muscles, and vision. Mitochondrial Myopathy (MM), as defined by molecular confirmation of MD with predominant symptoms of myopathy, constitutes a large proportion of those with MD. Many therapies have attempted to prove effectiveness in the treatment of MD, but none have been successful. Research is being conducted to find effective therapies and while these advancements will undoubtedly support this disease group, the lack of a validated scale for use in clinical trials for MD makes measuring treatment efficacy difficult. The goal of this study is to determine whether existing scales used for other multi-systemic disorders similar to MM could be applicable in evaluating MM treatment effectiveness. This was accomplished with an online survey, in which participants aged 2 and older with biochemical or molecular confirmation of MD and experiencing myopathy were asked to examine questions identified from existing validated scales in other neuromuscular disorders and indicate whether they found them appropriate for measuring their symptoms. The ultimate goal was to ascertain the participant’s insight on what should or should not be included in the new scale. 52 individuals, ranging in age from 2-67 years old were consented. 27 Participants ranging in age form 8-63 years old completed the survey and determined that fatigue (96.3%), muscle weakness (95.7%), and exercise intolerance (92.0%) were the most important symptoms to include in the rating scale, with the implications these symptoms have on daily activities (92.3%) also rating highly. It is with this important patient insight and a physician-administered section, to be validated in later studies, that an appropriate scale for MM will be developed.

A-235 A survey of eating attitudes and behaviors in adolescents and adults with phenylalanine hydroxylase deficiency

Other
Submitter: Sharon Luu,
Phenylalanine hydroxylase deficiency, commonly known as phenylketonuria (PKU), is an inborn error of metabolism that left untreated, can lead to irreversible neurological damage. The most effective treatment for PKU is a carefully regimented treatment plan that often involves an extremely protein-restricted diet, nutritional supplementation with medical formula, and frequent monitoring of amino acid levels in the blood. Patients who maintain good metabolic control from birth develop typically and have normal lives relatively uninhibited by neurological complications. While the prognosis for treated patients with PKU is favorable, many find lifelong compliance difficult. Strict diet regimens and frequent blood monitoring are thought to cause stress and may lead to destructive attitudes and behaviors towards food. Disordered eating has been observed in patients with other diet-related chronic illnesses such as type I diabetes, cystic fibrosis, and irritable bowel syndrome; however, no such correlation has yet been studied in PKU. This project surveyed 15 patients with PKU between the ages of 12 and 35 from the University of Wisconsin (UW) Biochemical Genetics Clinic about their metabolic management and eating attitudes and behaviors. Overall, study participants did not demonstrate attitudes or behaviors indicative of any specific eating disorders. However, patients with poor metabolic control exhibited symptoms of disordered eating at a higher frequency than those with good metabolic control. There is not yet an appropriate tool to effectively screen for disordered eating behaviors in individuals with PKU, which makes identifying and treating these conditions very difficult. This study was the first of its kind to develop material that attempted to adequately assess for maladaptive eating behaviors and attitudes in this patient population.

B-233 Diamond Blackfan anemia due to a terminal 3q microdeletion involving the entire RPL35A gene

Other

Submitter: Rachelle Dinchong, HBSc, University of Manitoba

Presenting Author: Rachelle Dinchong, HBSc, University of Manitoba
Diamond Blackfan anemia (DBA) is a congenital blood disorder characterized by a variable phenotypic spectrum which includes macrocytic anemia, congenital malformations, growth retardation, and increased risk for malignancies. Typically, DBA is caused by de novo heterozygous sequence changes in one of 18 genes, including RPL35A. We report an affected infant who presented prenatally with positive maternal serum screening for chromosomal aneuploidy and intra-uterine growth restriction. Postnatally, the patient had profound neutropenia, anemia requiring multiple transfusions, and fluctuating thrombocytopenia. Next-generation sequencing of an 87 gene bone marrow failure panel detected a possible deletion involving the entirety of RPL35A. Subsequent SNP microarray and fluorescent in-situ hybridization revealed a novel 0.46Mb de novo deletion at the terminal end of chromosome 3q29 containing the entire RPL35A gene. Our patient’s deletion is relatively small, and it borders, but does not overlap, the recurrent 3q29 microdeletion syndrome. Currently, she has mild global developmental delay, however, she has been subject to extensive medical interventions for her bone marrow failure, including allogenic stem cell transplant. Haploinsufficiency of RPL35A appears to explain the patient’s entire clinical presentation and there is no evidence that the other deleted genes have any phenotypic consequence. This case aids in the genotype-phenotype correlations of 3q29 deletions and suggests the immunodeficiency in the patient described by Alkhunaizi et al (2017) is due to genes centromeric to the recurrent 3q29 deletion.

B-236 Our Experience in Ophthalmology Genetics Clinic

**Other**

*Submitter: Dayna Morel Swols, University of Miami*

*Presenting Author: Dayna Morel Swols, University of Miami*

*Primary Author: Dayna Morel Swols, University of Miami*

*Author 2: Alana Grajewski, Bascom Palmer at the University of Miami*

*Author 3: Mustafa Tekin, University of Miami, Hussman Inst of Human Genetics*

**Purpose:** The Samuel & Ethel Balkan Center at the University of Miami receives referrals for a variety of ocular phenotypes. University of Miami serves an ethnically diverse population, over half of which have Hispanic background. Our knowledge about the genetic contribution to eye disease is still evolving. In this study, we compile data from our clinical experience to highlight common genes for eye disorders, as well as phenotypes with limited genetic information.

**Methods:** Patients were referred by ophthalmologists at Bascom Palmer Eye Institute for phenotypes including albinism,
anterior segment defects, retinal disease, myopia with retinal detachment, and optic atrophy. Clinical genetic testing was ordered based on the phenotype, and results were compiled into the database. The results were then categorized based on phenotype.<br />Results: Overall, 76 patients were identified to have a phenotype included in the study. Forty-Seven (62%) patients underwent clinical genetic testing. Diagnostic rates for albinism, retinal disease, and optic atrophy were 100% in our cohort. Causative DNA variants were less commonly identified in anterior segment defects (29%) and myopia with retinal detachment (28%). The most commonly identified genes for anterior segment defects included CYP1B1 and FOXC1.<br /><br />Conclusions: Analysis of a population of patients with eye disease revealed that some ocular phenotypes have a well-understood genetic contribution, such as albinism, retinal disease, and optic atrophy. Other phenotypes are less defined, particularly among the Hispanic population. Our study shows that for phenotypes including anterior segment defects, myopia and retinal detachment, clinical genetic testing may not be sufficient for molecular diagnosis. Further research is necessary to identify additional genetic etiologies for these phenotypes.

C-231 A needs assessment of genetic counseling in Mexico

Other
Submitter: Daiana Bucio,
Presenting Author: Daiana Bucio,
Primary Author: Daiana Bucio, Department of Genetics. Stanford University School of Medicine
Author 2: Kelly Ormond, Department of Genetics. Stanford University School of Medicine
Author 3: Arturo Lopez Pineda, Dept. of Biomedical Data Science. Stanford University SOM
Author 4: Daisy Hernandez, Department of Genetics. Stanford University School of Medicine

Introduction: Mexico is a diverse country with high prevalence of infant mortality due to congenital anomalies, births to mothers over 35, and deaths from early-onset breast cancer. While genetic counseling has expanded globally, Mexico and other countries in Latin America have not adopted it as a separate profession. Given the rapid expansion of genetic testing, understanding the current practices, policies, and needs for genetic counseling in Mexico is crucial to improving healthcare outcomes. <br />
Methods: Semi structured interviews of 19 key-informants from 10 Mexican states were conducted remotely. Interviews focused on seven major topics: genetic counseling, medical genetics, genetic testing, impact of culture and religion on services, genetics education, creating a genetic counseling profession, and establishing a genetic counseling program. Interviews were audio recorded, transcribed, and analyzed using a thematic coding approach. To add context to qualitative results, quantitative data about genetics education in medical programs and geneticists' geographic distribution was gathered and analyzed.<br />
Results: Out of 32 states, 46% of enrolled medical students do not receive medical genetics training and only Mexico City averages at least one medical geneticist per 100,000 people. Barriers to genetic counseling services include: geographic distribution of geneticists, lack of access to
diagnostic tools, patient health literacy and cultural beliefs, and education in medical genetics and genetic counseling. Participants reported generally positive attitudes towards a genetic counseling profession; barriers include physician attitudes towards sharing their patient population and a current shortage of available jobs for geneticists. Conclusions: To create a foundation that can support a genetic counseling profession in Mexico, the clinical significance of medical genetics must be promoted nationwide. Potential approaches include: requiring medical genetics coursework, developing community genetics services, and increasing jobs for medical geneticists.

C-234 Do Labels Matter? Alternative Option Labeling Impacts Decision-Making In Noninvasive Prenatal Screening

Other
Submitter: Camille Fisher, Dell Children's Medical Group

Presenting Author: Camille Fisher, Dell Children's Medical Group

Primary Author: Camille F Fisher, Dell Children's Medical Group

Author 2: Laura E. Birkeland, University of Wisconsin - Madison

Author 3: Catherine A. Reiser, University of Wisconsin - Madison

Author 4: Qianqian Zhao, University of Wisconsin - Madison

Author 5: Christina G.S. Palmer, University of California, Los Angeles

Author 6: Brian J. Zikmund-Fisher, University of Michigan School of Public Health

Author 7: Elizabeth M. Petty, University of Wisconsin - Madison

Prenatal screening should be an informed, autonomous patient choice. Extrinsic factors which influence patient decision-making threaten the ethical basis of prenatal genetic screening. Prior research in the area of medical decision-making has identified that labeling may have unanticipated effects on patient perceptions and decision-making processes. This Internet-administered study explored the impact of option labeling on the noninvasive prenatal screening (NIPS) selections of U.S. adults. Screening options included 1) NIPS for select aneuploidies and 2) combined NIPS for select aneuploidies with prenatal genome sequencing. A total of 1,062 participants were recruited through Amazon Mechanical Turk (MTurk) and randomly assigned to one of three possible label sets reflecting provider-derived and industry-derived labels used in prenatal screening. Label Set A (“Trisomy Screening” and “Sequencing + Trisomy Screening”) presented screening options with technical language meant to reduce contextual information about screening alternatives. Label Set B (“Core Screening” and “Comprehensive Screening”) and Label Set C (“Traditional Screening” and “Global Screening”) drew directly from labels and terms used clinically or derived from industry marketing materials. Multinomial regression analysis showed option labeling had a statistically significant impact on the NIPS selections of study participants.
(p-value = 0.028). However, odds ratio pairwise comparisons between label sets did not demonstrate statistical significance. Outcomes of the Satisfaction with Decision Scale (SWD) indicated labels did not play a role in perceived participant satisfaction with screening selection. The results of this study indicate a need for further evaluation of the impact NIPS labeling has on patient screening decisions in real-world clinical interactions. Clinical providers and testing laboratories offering NIPS should give careful consideration to the labels used for prenatal screening options so as to minimize influence on patient screening selection and decision-making processes.

C-237 Genetic Counselors' Discussion of Parkinson's Disease Risk in Gaucher/Metabolic Clinics

Other
Submitter: Lola Cook Shukla,
Primary Author: Annie Nyberg, Indiana University School of Medicine
Author 2: Jeanine Schulze, Indiana University School of Medicine
Author 3: Leah Wetherill, Indiana University School of Medicine
Author 4: Katherine Sapp, Indiana University School of Medicine
Author 5: Tatiana Foroud, Indiana University School of Medicine
Author 6: Bryan Hainline, Indiana University School of Medicine
Author 7: Lola Cook, Indiana University School of Medicine
Presenting Author: Annie Nyberg,

After a decade of research about the link between Gaucher/GBA mutations and Parkinson’s disease, there is increased discussion about how to address this association in various genetic counseling settings. We evaluated the current knowledge, attitudes, and practice of metabolic genetic counselors regarding the link between Gaucher and Parkinson’s disease. Board-certified or board-eligible genetic counselors who had worked with a patient or family affected by Gaucher disease were invited to participate in an online survey. The majority of respondents possessed basic knowledge about both Gaucher and Parkinson’s disease including their association, although deficits were identified in genotype-phenotype knowledge. Notably, a quarter of genetic counselors had never addressed the link with individuals during a counseling session. Comfort levels with various aspects of the topic varied including discussing the possibility of cognitive impairment/dementia. Common barriers to discussion were: lack of specific information regarding the link and risk figures to use; perception that some GBA mutations are not associated with Parkinson’s disease, concern that timing was not always appropriate (initial consultation versus follow-up visit), and reservation about discussing adult-onset conditions in a pediatric setting. Number of patients seen throughout a career, work setting (university medical center
versus non-university medical center), and comfort discussing Parkinson’s disease correlated with
discussion of the association. In summary, genetic counselors working in this particular setting, and
likely other settings, would benefit from educational tools and practice statements that guide how to
integrate this information into genetic counseling sessions, ultimately improving genetic counseling
about this emerging topic.

A-238 The Clinical Journey of Patients with Riboflavin Transporter Deficiency Type 2

Pediatrics
Submitter: Fatima Emran Amir,

Primary Author: Fatima Emran Amir, Cincinnati Children's Hospital Medical Center

Author 2: Carrie Atzinger, Cincinnati Children's Hospital Medical Center

Author 3: Keith Massey, Cure RTD Foundation

Author 4: John Greinwald, Cincinnati Children's Hospital Medical Center

Author 5: Lisa Hunter, Cincinnati Children's Hospital Medical Center

Author 6: Elizabeth Ulm, Cincinnati Children's Hospital Medical Center

Author 7: Margaret Kettler, Cincinnati Children's Hospital Medical Center

Presenting Author: Fatima Emran Amir, Cincinnati Children's Hospital Medical Center

Riboflavin Transporter Deficiency (RTD), formerly known as Brown-Vialetto-Van Laere (BVVL) syndrome
or Fazio Londe syndrome, is a rare early-onset progressive neurologic disorder. RTD is caused by
pathogenic variants in the SLC52A2 or SLC52A3 genes that cause RTD Type 2 and 3 respectively. RTD
Type 2 can present at differing ages with a phenotypic spectrum of motor, sensory, and cranial nerve
neuropathy, often with ataxia, optic atrophy and respiratory problems. Riboflavin supplementation has
shown to be an effective and readily available treatment. However, patients with RTD Type 2 may often
experience long clinical journeys without a diagnosis or they may receive incorrect diagnoses before
they receive their correct diagnosis of RTD. The purpose of this study is to identify what symptoms,
genetic testing, and healthcare interactions patients with RTD Type 2 have before receiving the
diagnosis. To do so, parents of children with RTD Type 2 (n=10) from the Cure RTD Foundation were
invited to participate in this study. Interviews were conducted to collect information on the patient’s
clinical journey and diagnosis. Descriptive statistics were used to report various aspects of the clinical
journey and diagnosis. The average diagnostic delay for our patients was 27.6 months. Neurologists
were the most common provider seen by patients (90%). The most common symptoms before diagnosis
were gait ataxia, nystagmus, and upper body muscle weakness. Gait ataxia was the most common
symptom within the first year of the clinical journey. Mitochondrial disease was the most common
suspected diagnosis (30%). Despite clinical variability, there are common features in the clinical journey of patients with RTD Type 2. The addition of the SLC52A2 gene to gene panels and the newborn screen should be considered. With readily available treatment, we hope this study leads to earlier diagnoses, earlier treatment, and better outcomes for patients with RTD Type 2.

**Key Words:** Riboflavin Transporter Deficiency, SLC52A2, BVVL, Fazio Londe, clinical journey, genetic testing, diagnostic odyssey

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**A-241 Variable Presentations in Three Children with PURA Syndrome**

*Pediatrics*

Submitter: Campbell Brasington, Carolinas Medical Center

Presenting Author: Campbell Brasington, Carolinas Medical Center

Primary Author: Campbell Brasington, MS, CGC, Carolinas Medical Center

Author 2: Edward Spence, MD, UNC, Division of Genetics and Metabolism

Author 3: Berrin Monteleone, MD, Carolinas Medical Center, Clinical Genetics

Author 4: Laurie Demmer, MD, Carolinas Medical Center, Clinical Genetics

Author 5: Shelley Dills, MS, CGC, Carolinas Medical Center, Clinical Genetics

Author 6: Tamara Haygarth, MS, CGC, Carolinas Medical Center, Clinical Genetics

Author 7: Dana Mittag, MS, CGC, Carolinas Medical Center, Clinical Genetics

Recently, a new syndrome has been described due to sequence changes and deletions within the PURA gene or deletions of 5q31.3 that include the PURA gene. The PURA syndrome is a neurodevelopmental encephalopathy that includes global developmental delay, hypotonia, feeding difficulties, seizures, and apnea. We present three cases who have been diagnosed through our clinic within the past year with variable presentations. The first was a 6-year-old with a pathogenic c.697_699delTTC variant identified on an epilepsy panel who initially presented to our clinic at 6 months of age with distinctive features, hypotonia, microcephaly, and abnormal eye movements. Initial genetic and metabolic work up as well as MRI was negative. He says 1-2 words and developed seizures at 5 years of age. The second is a 2.5-year-old with a de novo pathogenic c.697_699delTTC variant identified on whole exome sequencing who initially presented to our clinic at 7 months of age with significant hypotonia and developmental delays. More recently, she developed nystagmus, dystonic movements, and some mild white matter changes on her MRI. She is nonverbal and she does not have seizures at this time. The third is a 2-month-old with a de novo pathogenic c.1A>G variant identified on rapid whole exome sequencing who presented as an inpatient at one week of age with lethargy, decreased feeding, hypotonia, hypothermia, and abnormal respiration. His MRI was normal. Currently, he continues with some autonomic instability and occasional eye deviations but has not developed seizures. PURA syndrome should be considered in any child with moderate to severe global developmental delay,
hypotonia, hypersomnolence, hypoventilation, hypothermia, seizures, abnormal movements, white matter abnormalities on MRI, or feeding difficulties. While these features overlap many other genetic syndromes, diagnosis of PURA syndrome can be confirmed via an epilepsy gene panel that includes the PURA gene or via whole exome or genome sequencing. <br />

A-244 Clinical diagnosis of Russell-Silver Syndrome resulting from a Beckwith-Wiedemann Syndrome genotype

**Pediatrics**

*Submitter: Ashleigh Hansen, Genetic Counselling Trainee,*

*Presenting Author: Ashleigh Hansen, Genetic Counselling Trainee,*

*Primary Author: Ashleigh Hansen, Biochemistry and Medical Genetics, University of Manitoba*

*Author 2: Dr. Tyler Peikes, Biochemistry and Medical Genetics, University of Manitoba*

*Author 3: Dr. Patrick Frosk, Pediatrics and Child Health, University of Manitoba*

**Introduction:** Chromosome region 11p15.5 contains imprinted genes that are involved in the control of fetal and placental growth. This region is composed of two imprinted domains under the control of imprinting centres ICR1 and ICR2 (KVDMR1). Hypomethylation of paternal ICR1 leads to Russell-Silver Syndrome (RSS) whereas hypermethylation of maternal ICR1 and hypomethylation of maternal ICR2 leads to Beckwith-Wiedemann syndrome (BWS). RSS is characterized by severe intrauterine growth restriction, poor postnatal growth and normal head circumference. Individuals typically present with a characteristic triangular face, short stature, body asymmetry, fifth-finger clinodactyly, and are at an increased risk of developmental delay. In contrast, BWS is characterized by overgrowth and an increased risk for embryonic tumour development. <br />

**Case:** We report a male who presented at 5 years of age with short stature (3rd to 15th percentile), low weight (3rd to 15th percentile), normal head circumference (50th percentile), and mild global developmental delay. He was dysmorphic with a pronounced triangular face, wide spaced teeth and bilateral fifth finger clinodactyly. Pregnancy history was remarkable for cigarette smoking in the first trimester. Birth history was unremarkable and his growth parameters were normal. Family history was unremarkable. Although not entirely indicative of RSS given the normal birth size, molecular testing for RSS was pursued because of the various other suggestive features. <br />

**Discussion:** Molecular testing indicated hypomethylation of the ICR2 locus, a result inconsistent with this clinical presentation. In isolation, these molecular results suggest an opposite phenotype, BWS. Given this discordant phenotype, we hypothesize that a more global abnormality in genomic methylation may be responsible for his failure to thrive and other RSS-like features. Diagnosis of children with discordant results at this locus pose new challenges for appropriate tumour screening and complicate the counselling of affected individuals and families. <br />
A-247 Experience of Youth and Families with Special Healthcare Needs in Transition to Adult Healthcare Services

Pediatrics
Submitter: Kelly Confroy Kemak,
Presenting Author: Kelly Confroy Kemak,
Primary Author: Kelly Confroy Kemak, MS, GC, UNC Greensboro Genetic Counseling Program
Author 2: Randi Culp Stewart, MS, CGC, UNC Greensboro GC Program, Cone Health System
Author 3: Caroline Hacker, MSN, FNP-C, Cone Health System, Tim and Carolyn Rice Clinic for Children
Author 4: Pamela Reitnauer, MD, MPH, PhD, Cone Health System, UNC Greensboro, UNC-CH Medical School

Healthcare transition is the shift from pediatric to adult oriented care. For youth with chronic or genetic conditions, particularly those with intellectual disability or learning delays, the transition process can be complex, and responsibilities often fall upon the family. This study aimed to assess families’ experience with transition including limiting factors, challenges experienced, advice from families and services utilized, as well as the role of genetic counselors in transition. Parents of children, age 18 to 35 years with intellectual disability or learning delays, were recruited to complete an electronic survey via the Angelman Syndrome Foundation or Family Support Network of Greater Greensboro. Thirty-seven participants completed the survey including 29 whose children had a diagnosed genetic condition. Approximately two-thirds of families had completed transition and felt it had been successful. Many families experienced challenges and received little support from the healthcare community. The families who had not transitioned described factors that inhibited the process including reluctance to change providers and lack of appropriate adult services. Respondents highlighted ways in which genetic counselors could be involved in the transition process including providing informational and emotional support and participating in the cultivation of care guidelines on transition. Overall, our findings suggest that families of children with special healthcare needs are often not receiving transition support and have unmet needs. Genetic counselors are positioned to assist families in the process of transition.

Keywords: youth with special health care needs, healthcare transition, transition to adult oriented care, pediatric care to adult medicine

A-250 Parental experience with whole exome sequencing reanalysis and its impact on the diagnostic odyssey

Pediatrics
Presenting Author: Nicole Lucas,
Primary Author: Nicole Dawn Lucas, University of South Carolina
Author 2: Emily Jordon, University of South Carolina
While analyzing the human exome by whole exome sequencing (WES) has provided many individuals with genetic diagnoses, many are still left undiagnosed. Individuals who remain undiagnosed after WES can subsequently undergo WES reanalysis later due to improvements in bioinformatics, software updates, and an increase in known gene-disease associations. This is the first study, to the investigator’s knowledge, which investigates parental perspective of those undergoing the most current genetic testing available. This study recruited parents of undiagnosed individuals who have completed WES and subsequent reanalysis through the Greenwood Genetic Center to investigate their response to and experience with WES reanalysis. Six semi-structured interviews were conducted, recorded, and transcribed verbatim. Transcripts were analyzed using grounded theory and assigned codes to meaningful segments of text. Results showed most participants had lower expectations of reanalysis compared to the initial WES and felt it would not lead to a diagnosis. Most participants responded to nondiagnostic reanalysis results with feelings of disappointment and worry about the future. However, some exhibited a difference in the degree to which they negatively responded. Most participants recognized that reanalysis has been unhelpful for their child but expressed willingness to contribute to science if it will assist future individuals on a diagnostic odyssey. Despite feelings that reanalysis was unhelpful, most participants would consider reanalysis in the future. Considering the apparent comprehensive nature of genomic testing, these results show the need to balance hope and realistic expectations during counseling and consent of WES reanalysis. In addition, participants desired ongoing support from their genetic counselor while undergoing reanalysis.
Almost 750,000 youth with special healthcare needs in the United States transition to adult care annually. Less than half obtain services needed to successfully transition. Adolescents with Neurofibromatosis Type 1 (NF1) can have attention or learning deficits, communication concerns, or need for educational assistance, increasing demand for transition support. Awareness of adolescents’ transition needs or factors influencing transition is lacking.

**Aims**
We gauged transition readiness in adolescents with NF1 and their peers and studied factors influencing transition readiness. We assessed adolescents’ views on transition to adult care and perceptions of factors that influence success. We addressed adolescents’ sense of control of and success in the transition process.

**Methods**
We administered transition scales for adolescents ages 12-17 years with NF1 who use medical services in Utah and a control group. We conducted qualitative interviews with a subset of the NF1 cohort to determine views on predictors of optimal transition and control over the transition process.

**Results**
Individuals with NF1 were less likely to identify how their health will affect them in the future and more likely to have health insurance knowledge. Scores on transition scales were similar between groups. Six key factors influenced scores: age, knowledge of diagnosis and related providers, confidence in independent care as an adult, understanding of health insurance’s purpose and significance, having a plan for adulthood, and consistent medical visits. Adolescents had neutral views on the transition process. Beliefs about control and transition success were tied to greater independence and personal growth, better medical care, processing uncertainty, fitting in, and planning for the future.

**Conclusion**
Adolescents with Neurofibromatosis Type 1 have little difference in transition readiness from typically developing peers. There are specific factors that influence their confidence in successful transition. This data supports a need for a comprehensive cross-clinic transition plan.

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**A-256 Chromosome 3p Inverted Duplication with Terminal Deletion: Second Postnatal Report with Additional Clinical Features**

*Pediatrics*

**Submitter:** Jacquelyn Riley, Cleveland Clinic

**Primary Author:** Jacquelyn Riley, Cleveland Clinic

**Presenting Author:** Jacquelyn Riley, Cleveland Clinic

**Author 2:** Catherine Stefaniuk, DO, Cleveland Clinic Foundation

**Author 3:** Francine Erenberg, MD, Cleveland Clinic Foundation

**Author 4:** Lauren Palange, MS, LGC, Cleveland Clinic Foundation

**Author 5:** Caroline Astbury, PhD, Cleveland Clinic Foundation

**Introduction:** Distal deletions and duplications of 3p, although uncommon, are individually well-characterized chromosome abnormalities. We report an inverted duplication of 3p with an adjacent
terminal 3p deletion. To our knowledge, only one other postnatal patient and two second trimester pregnancies have been reported with this finding. 

Case Report: Our patient, a 16 month-old girl, came to medical attention prenatally due to intrauterine growth restriction and concern for cardiac defect. In the neonatal period, she was diagnosed with a dilated aortic root, atrial/ventricular septal defects, and mitral valve prolapse with mitral regurgitation. Other findings included: hemangiomas of right flank and liver, neutropenia, umbilical hernia, hypotonia, gross motor delay, and myopic astigmatism. Additional physical features were an accessory nipple, adducted thumbs, ptosis, prominent epicanthal folds, and low-set ears. Family history was non-contributory. To evaluate these findings, microarray analysis was pursued and revealed a 5.37 Mb deletion of chromosome bands 3p26.1 to 3p26.3 and a 13.68 Mb duplication of 3p24.3 to 3p26.1. FISH analysis confirmed that the duplication was inverted. Parental FISH studies confirmed de novo occurrence.

Discussion: Upon extensive literature review, this is only the second reported postnatal case of an inverted duplication of chromosome 3p with an adjacent terminal deletion of 3p. Many of our patient’s features are reported in both 3p deletion and 3p duplication syndromes, including congenital heart disease, growth restriction, microcephaly, hypotonia, and developmental delay. Further, this patient has additional features not commonly reported in 3p deletion or duplication patients, such as hemangiomas and neutropenia. The identification of this patient contributes to further understanding of features associated with concurrent deletion and inverted duplication in the short arm of chromosome 3. This report may assist clinicians working with patients who have constellations of similar features or similar cytogenomic abnormalities.

A-259 Investigating the Role of Intragenic YWHAE Copy Number Variations in Neurodevelopmental Disorders

**Pediatrics**

*Submitter: Abby Stevens, Lineagen*

*Presenting Author: Abby Stevens, Lineagen*

*Primary Author: Abby Stevens, MS, Lineagen, Inc*

*Author 2: Hope Twede, BS, Lineagen, Inc*

*Author 3: Rena Vanzo, MS, Lineagen, Inc*

*Author 4: Patricia Rushton, PhD, Lineagen, Inc*

*Author 5: Ankita Patel, PhD, Lineagen, Inc*

The YWHAE gene encodes the 14-3-3ε protein, a critical regulator of neurogenesis and neuronal differentiation. Using a previously developed methodology, we have also identified YWHAE as a critical gene in neurodevelopment. The YWHAE gene is also one of the critical genes involved in 17p13.3 microdeletion and microduplication syndromes. However, to date, there has been only one report in the literature of a deletion in YWHAE alone. This patient presented with seizures, brain abnormalities, and
learning disabilities. We have identified three cases with an intragenic CNV in YWHAE from a cohort of 24,614 individuals presenting with neurodevelopmental concerns. We present the phenotype of these individuals and emphasize the need for further investigations into the role of YWHAE in disease pathology. Case 1: 15kb deletion in YWHAE involving exon 2. This is a 1 year 5 month old male with delayed milestones, expressive language disorder, encephalopathy, convulsions/spells, stereotyped movement disorder, and feeding difficulties. Case 2: 21kb deletion in YWHAE involving exons 2-4. This is a 12 year 9 month old male with 47,XYY who presents with atrial septal defect, verbal and written expression disabilities, executive functioning deficits, and neuropsychiatric issues including anxiety, rigid thinking, and lack of understanding of abstract and inferential language. Case 3: 26kb duplication in YWHAE involving exons 5-6 and a 10q21.1 duplication (interpreted as likely benign). This is a 2 year 6 month old male with autism spectrum disorder (ASD), tactile hypersensitivity, light sensitivity, and sleeping problems. In summary, three affected males demonstrated at least one diagnostic feature of ASD, including verbal deficits, rigid thinking, and stereotyped behaviors. Intragenic CNVs have not been reported in standard control populations. Considering the rarity of such findings, in addition to the role of whole gene CNVs in clinical symptoms, our cohort supports the assertion that YWHAE intragenic CNVs play a role in phenotypic features. However, further research is needed.

A-262 Beyond PKHD1: Reconsidering Genetic Testing for Neonatal Polycystic Kidney Disease

Pediatrics
Submitter: Grace E. Vannoy, Broad Institute
Presenting Author: Grace E. Vannoy, Broad Institute
Primary Author: Grace E. VanNoy, Broad Institute of MIT and Harvard
Author 2: Casie A. Genetti, Boston Children’s Hospital
Author 3: Thomas E. Mullen, Quest Diagnostics
Author 4: Monica H. Wojcik, Boston Children’s Hospital
Author 5: Daniel G. MacArthur, Broad Institute of MIT and Harvard
Author 6: Pankaj B. Agrawal, Harvard Medical School, Boston Children’s Hospital
Author 7: Deborah R. Stein, Harvard Medical School, Boston Children’s Hospital

Introduction: Neonatal polycystic kidney disease (PKD) is a condition typified by numerous renal cysts and enlarged kidneys. Biallelic mutations in PKHD1 account for ~75% of neonatal PKD. Given the early onset and severity of the condition, the other ~25% of cases are also believed to be monogenic; however, genetic testing beyond PKHD1 analysis is not often pursued. Case Report: The proband was a male fetus found at 20 3/7 weeks gestational age (GA) to have bilateral enlarged, cystic kidneys. The
fetus was delivered at 30 6/7w GA due to the development of hydrops and died at delivery. Post-mortem sequencing and del/dup analysis of PKHD1 was negative. A subsequent male fetus of the same parents had echogenic kidneys at 18w GA, and enlarged, cystic kidneys at 23 1/7w GA. The infant was delivered at 37w GA and postnatally confirmed to have enlarged echogenic kidneys with innumerable cysts. The family enrolled in a research protocol and received whole exome sequencing. Both affected children had two PKD1 mutations, a maternal missense variant (c.377C>T, p.Pro126Leu) and a paternal missense variant (c.6656C>T, p.Pro2219Leu). Neither mutation is reported in the literature or public databases; both amino acid residues are highly conserved, and both mutations are predicted by in silico models to be deleterious. There is no history of renal cysts in heterozygous family members. Discussion: A dose-dependent mechanism for cyst development in PKD has been established in mice, with biallelic loss of PKD1 being embryonic lethal. A small number of case reports document neonatal PKD in infants with a pathogenic familial PKD1 mutation in trans with a hypomorphic PKD1 variant from an unaffected parent. We propose the variants in this family are both hypomorphic and in combination reduce protein production sufficiently to cause neonatal PKD. The identification of biallelic PKD1 mutations in the affected children in this family suggests a role for PKD1 in neonatal PKD cases without a molecular diagnosis and the value of testing this gene for family planning and accurate counseling.

B-239 Newborn Screening for X-linked Adrenoleukodystrophy: A Year of Experience from a Genetic Counseling Perspective

Pediatrics
Submitter: Jessica C Barry, Children's Hospital of Philadelphia

Presenting Author: Jessica C Barry, Children's Hospital of Philadelphia

Primary Author: Jessica C. Barry, MS, The Children's Hospital of Philadelphia

Author 2: Kierstin Keller, MS, The Children's Hospital of Philadelphia

Author 3: Amanda B. Pritchard, MD, The Children's Hospital of Philadelphia

Author 4: Andrew C. Edmondson, MD, PhD, The Children's Hospital of Philadelphia

Author 5: Lynne A. Ierardi-Curto, MD, PhD, The Children's Hospital of Philadelphia

Author 6: Can Ficicioglu, MD, PhD, The Children's Hospital of Philadelphia

Background: X-linked adrenoleukodystrophy (X-ALD) is a peroxisomal disorder characterized by the accumulation of very long-chain fatty acids (VLCFA) in the adrenal glands and nervous systems. X-ALD is clinically heterogeneous, primarily affecting males though 50% of female carriers develop neurologic symptoms in late adulthood. Hematopoietic stem cell transplant can treat the severe cerebral form. In April 2017, the state of Pennsylvania began newborn screening (NBS) for X-ALD. Methods: Infants were screened for C26:0 lysophosphatidylcholine (C26:0-LPC) levels on dried blood spot cards. Twice elevated C26:0-LPC levels were reflexed to ABCD1 gene sequencing and patients were referred for
further evaluation. Here we report a retrospective analysis of the neonates with abnormal X-ALD NBS referred to the Children’s Hospital of Philadelphia (CHOP).<br />

Results: Between April 2017-2018, 8 neonates were referred to CHOP for abnormal X-ALD NBS. A pathogenic ABCD1 variant was identified in 3 infants: 2 females with older brothers were found to have de novo mutations; 1 male had a maternal uncle with X-ALD. A maternally inherited ABCD1 variant of uncertain significance (VUS) was identified in 1 female and 2 males; the males are now monitored by our X-ALD protocol. One pedigree identified a maternal aunt with an atypical multiple sclerosis and several at-risk males (testing pending). Two patients had negative ABCD1 sequencing: 1 male with multiple medical problems and consanguineous parents found to have homozygous PEX12 mutations; 1 female born at 33 week gestation with normal VLCFA and low plasmalogens due to prematurity.<br />

Conclusions: The addition of X-ALD to NBS identified 3 affected males no being monitored by X-ALD protocol. Screening for X-linked conditions unveils at-risk relatives: unscreened male siblings, older extended relatives at risk for milder forms of the disease. As VLCFA levels do not predict disease onset or severity and there is no intrafamilial or genotypic correlation, counseling at-risk family members presents a challenging prospect for genetic counselors.

B-242 The Relationship Between 47,XXY (Klinefelter syndrome), Autism Spectrum Traits (AST), and Early Hormonal Therapy (EHT)

**Pediatrics**

*Submitter: Carole Samango-Sprouse, Ed.D., The Focus Foundation*

*Primary Author: Selena Chea, The Focus Foundation*

*Author 2: Dr. Carole Samango-Sprouse, The Focus Foundation*

*Author 3: Teresa Sadeghin, The Focus Foundation*

*Author 4: Dr. Andrea Gropman, Children's National Health System*

*Presenting Author: Selena Chea, The Focus Foundation*

Background: 47,XXY is the most frequently occurring X&Y chromosomal variation (1:660), yet 75% of cases remain unidentified in their lifetime. The social-cognitive phenotype of these boys includes language-based learning disorders, speech & motor delays, and executive dysfunction. ASD has been reported to be increased in this population, but this research has been confounded by many salient factors. This study investigated the incidence of AST within the social-cognitive pathway and the effects of EHT on these traits in boys with 47,XXY.<br />

Methods: 74 boys with 47,XXY between the ages of 2-7 years underwent neurodevelopmental evaluations, including the Gilliam Autism Rating Scale, 2nd Edition (GARS-2); Social Responsiveness Scale, 2nd Edition (SRS-2); and Behavior Rating Inventory of Executive Function-Preschool (BRIEF-P). 22 boys (30%) with 47,XXY received EHT, while 52 (70%) did not. EHT was administered based on patients’ pediatric endocrinologist’s assessment of phallus size compared to neurotypical boys of the same age.<br />

Results: On the GARS-2, boys in the EHT
group showed significant improvement in their social interaction compared to the non-EHT group (P=.026). There was also a significant difference in the probability of ASD between the two groups (P=.038), where the non-EHT group had a 30.1% likelihood for ASD traits compared to 13.6% in the EHT group. Positive effects of EHT were seen in the social cognition domain of the SRS-2 (P=.041) for the treated group. On the BRIEF-P, boys in the EHT group had greater emotional control (P=.029) and flexibility (P=.019).<br /><br />Conclusions: This study provides further evidence that this subset of boys with 47,XXY present with an increased risk for disturbances on the social-pragmatic pathway within ASD. The etiology of this vulnerability is unknown but could be derived from family history of ASD, parental origin of the additive X, timing of EHT, and/or other unknown factors. This origin of the vulnerability warrants further investigation to identify those infants at greatest risks who then need more specialized support.

B-245 c.103+56_34 dup Allele in Hunter Disease may be a Pseudodeficiency Variant: from Genetic Testing and Genetic Counseling of Maternal Families Members

Pediatrics
Submitter: You-Hsin Huang, MacKay Memorial Hospital, Taipei, Taiwan
Primary Author: You-Hsin Huang, MacKay Memorial Hospital, Taipei, Taiwan
Presenting Author: You-Hsin Huang, MacKay Memorial Hospital, Taipei, Taiwan
Author 2: Shuan-Pei Lin, Rare Disease Center, MacKay Memorial Hospital, Taiwan
Author 3: Chuan-Chi Chiang, Chinese Foundation of Health, Newborn Screening Center
Author 4: Min-Ju Chan, Chinese Foundation of Health, Newborn Screening Center

Mucopolysaccharidosis type II (MPS II, Hunter disease) is an X-linked lysosomal storage disease caused by a deficiency of iduronate-2-sulfatase (IDS) responsible for the degradation of glycosaminoglycans (GAGs). Accumulation of GAGs causes progressive damage, which affects patient’s appearance, physical abilities, organ function and mental development. Since August 2015 in Taiwan, we started mass newborn screening (NBS) for Hunter disease by using dried blood spots (DBS) of LC-MS/MS method for measuring IDS enzyme activity. A total of 358,151 newborns were screened, 90 of them were referred to tertiary center for further evaluation, including IDS gene was analyzed. Surprisingly, the c.103+34_56dup variant was identified in 64.4% of the referral cases; average IDS enzyme activity was 3.72±2.31 (NR: 30-53 nmol/4h/mg. protein) and disaccharide units (KS, DS and HS) of urinary GAGs detected by LC-MS/MS were within normal limits. The cases with c.103+34_56dup variant have no any clinical characteristic of Hunter disease after three years of follow-up. Therefore, after pedigree studies and genetic counseling, family members were assessed as the same as newborn babies. 25 maternal family members were enrolled and 9 relatives carried the c.103+34_56dup variant. Four were male and five were female. We found that these maternal male relatives also have low IDS enzyme activity and no specific finding in urinary GAGs, even two were 62 and 90 year old men who have no clinical manifestation. Our report on
maternal family members with c.103+34_56dup variant highlights the importance of genetic counseling and careful elevation among newborns and high-risk family members. In view of the high prevalence of the c.103+34_56dup variant and uncertain clinical significance in Taiwanese newborns, further more comprehensive family studies and long-term follow-up for individuals with this variants may be still necessary.

B-248 NDE1-Related Disorder: A Case Report

Pediatrics

Submitter: Amy Kenney, Children's Hospital of the King's Daughters - Medical Genetics and Metabolism

Presenting Author: Amy Kenney, Children's Hospital of the King's Daughters - Medical Genetics and Metabolism

Primary Author: Amy Kenney, Children's Hospital of The King's Daughters

Author 2: Samantha Vergano, Children's Hospital of The King's Daughters

The NDE1 (nudE neurodevelopment protein 1, OMIM #609449) gene, located on chromosome 16, is critical in cerebral cortical development. Mutations in this gene have been documented to cause lissencephaly, severe brain atrophy, microcephaly, and cognitive disability. Here we present an unusual NDE1 case observed in our clinic. The child was found prenatally to have a paternally inherited 16p13.11 deletion, with a postnatal finding of a maternally inherited pathogenic variant in the NDE1 gene detected through whole exome sequencing. There have been only two publications of a 16p13.11 microdeletion combined with a NDE1 mutation. Our patient serves as another documented case of a rare presentation of an NDE1-Related Disorder, extending the spectrum of severe microcephaly and brain disruption. In addition to brain malformations and developmental delay, our patient is one of the few reported to not have a hypoplastic cerebellum. It is unclear why the cerebellum of our patient was normal in appearance on brain MRI. Our patient is the first to be described with bilateral clubfeet and hearing loss. In addition to expansion of the phenotype, we present this case to emphasize that both prenatal and postnatal testing was vital in completing diagnosis of this patient and providing the family with an accurate recurrence risk. This case highlights the importance of pursuing additional genetic testing when the initial genetic result does not fully explain the patient’s phenotype. Additionally, it highlights the complex and unique role genetic counselors play in helping families navigate and advocate for their children during the diagnostic odyssey.
B-251 Genotype-phenotype correlation—an atypical case of Wolf-Hirschhorn with a typical 4p deletion.

Pediatrics
Submitter: Kari Magnussen, CGC, Randall Children's Hospital
Presenting Author: Kari Magnussen, CGC, Randall Children's Hospital
Primary Author: Kari Magnussen, Randall Children's Hospital
Author 2: Dr. Andrea Petersen,
Author 3: Dr. George Anadiotis,
Author 4: Leslie Durham,

With the ever increasing utilization of molecular testing in patients with non-specific phenotypes, we have gone beyond the simple, phenotype-driven genetic approach to something dramatically more complex. Our understanding of “classic” syndromes is evolving as we uncover unexpected genotypes. Here we discuss a case of a well-described deletion known to underlie Wolf-Hirschhorn syndrome (WHS) in a patient without characteristic features of the disorder. The WHS phenotype includes a “Greek warrior helmet” facial appearance, microcephaly, pre- and postnatal growth delay, intellectual disability, and seizures. Molecularly, patients exhibit a variably-sized deletion on chromosome 4p with a positive correlation between the size of the deletion and phenotypic severity. Specifically, smaller deletions, ranging from 1.9-2.5Mb are associated with milder features, however hallmark clinical characteristics are still expected. We present a non-dysmorphic, normocephalic patient with hypotonia and epilepsy but no growth issues or intellectual disability, in whom microarray uncovered a 3.8Mb deletion on 4p. Not only did our patient not exhibit the hallmark features of WHS, his deletion was on the larger side of the spectrum, thus exhibiting a negative correlation between clinical severity and deletion size. Despite the non-specific clinical features, the molecular diagnosis is clear, conferring a clinical diagnosis on the bases of back-inference from a molecular testing result. Our case is valuable in so far as it adds to the known phenotypic spectrum of WHS. Beyond this, however, it underscores a broader issue with serious implications for genetic counseling—as the rate of incidental findings increase, and phenotypes expand, how do we counsel our patients? More work is needed in this area to find the best solution; in the meantime, we suggest inclusion of a discussion of broad phenotypic variability in every counseling visit.

B-254 De novo heterozygous RAB3GAP1 variant – an exploration of a mild Warburg Micro syndrome case

Pediatrics
Submitter: Hillary Porter, Children’s National Health System
Primary Author: Hillary Porter, Children’s National Health System
Presenting Author: Hillary Porter, Children’s National Health System
Author 2: Natasha Shur, Children’s National Health System

Warburg micro syndrome (WMS) is an autosomal recessive disorder caused by mutations in RAB3GAP1, RAB3GAP2, RAB18, or TBC1D20 genes. WMS is typically characterized by congenital cataracts, hypotonia, brain abnormalities, and severe intellectual disability with increased risk of autism. Many individuals with WMS are described as non-verbal with failure to grow and progressive muscle weakness and spasticity. There are limited clinical reports in the literature related to children with mild presentations. We report a patient with development and learning delays, ADHD, microcephaly, poor weight gain, bilateral cataracts, sacral dimple, history of undescended testes, and dysmorphic features. A de novo heterozygous RAB3GAP1 c.2395G>A (p.E799K) variant was identified via whole exome sequencing. A maternal BCORL c.4925G>A (p.R1642Q) variant associated with X-linked intellectual disability was also identified. Although the typical inheritance pattern for WMS is autosomal recessive, and only one mutation has been identified in the proband, he has many features strongly suggestive of a clinical diagnosis. However, his development is far above previously described patients with WMS. At age 9, he talks in sentences with articulation difficulties, rides a bike, and participates in mainstream classes. He is social with peers and well-adjusted at home without concerns for autism. His case is important to raise awareness that some children with WMS may make great progress. This case also emphasizes the importance of clinical judgement when interpreting complicated molecular results. Possible explanations for only one mutation found may include limited whole exome coverage, a hereto unidentified deletion or duplication on the other allele, a modifying gene, an additional epigenetic change, or a de novo autosomal dominant inheritance mechanism. In the interim, the family reached out to WMS support groups and describes a similar child. As more children with WMS are reported, we believe additional atypical cases will come to our attention.

B-257 Novel mutations and clinical features in two cases of WAC-related intellectual disability diagnosed through whole exome sequencing

Pediatrics

Submitter: Chelsea Roadhouse, MSc, CGC, CCGC, McMaster Children’s Hospital

Presenting Author: Chelsea Roadhouse, MSc, CGC, CCGC, McMaster Children’s Hospital

Primary Author: Chelsea Roadhouse, Department of Pediatrics, McMaster University Medical Centre

Author 2: Malgorzata Nowaczyk, Pathology and Molecular Medicine, McMaster University

Author 3: Gina Cowing, Department of Pediatrics, McMaster University Medical Centre

Author 4: Chumei Li, Department of Pediatrics, McMaster University Medical Centre

Introduction: WAC-related intellectual disability, also referred to as DeSanto-Shinawi syndrome, is a genetic condition caused by mutations in the WAC gene. This gene encodes a protein involved in transcription regulation, and is highly expressed in the brain. The condition is characterized by
intellectual disability, behavioral abnormalities, and dysmorphic features. Most individuals come to medical attention with neonatal hypotonia, feeding problems, respiratory issues, and/or vision problems. To date, 19 cases have been reported in the literature. <br />
Case Reports: We report two unrelated pediatric patients with WAC-related disorder diagnosed via whole exome sequencing (WES). Both males had extensive genetic investigations before the availability of WES as a clinical test. Clinical features observed in our patients that are consistent with previously reported cases include: global developmental delay, behavioral abnormalities, dysmorphic features (deep-set eyes, prominent forehead), mild brachydactyly, prominent fingertip pads, and epilepsy. Additional clinical features not previously reported in WAC-related cases include: frequent skin infections and abnormal frontal hair whorl in Patient A, and tethered cord in Patient B. Both patients had novel de novo heterozygous frameshift mutations predicted to cause loss of normal protein function through protein truncation or nonsense-mediated mRNA decay: Patient A: c.1707dupA; p.H570TfsX23; Patient B: c.1820dupA;p.N607KfsX10. <br />
Discussion: Given the recent recognition of WAC-related intellectual disability as a distinct syndrome, these cases provide an opportunity to further delineate the spectrum of clinical features. Emerging literature has suggested that the location of the mutation in the WAC gene may affect the severity of intellectual disability. Therefore, as more patients are identified, genotype-phenotype correlations may be clarified. Finally, these cases highlight the diagnostic utility of whole exome sequencing in reducing the diagnostic odyssey for patients with intellectual disability.

B-260 Caregiver Perceptions and Quality of Life in Adolescents with Duchenne Muscular Dystrophy

Pediatrics

Submitter: Julia R Stone, MS, University of Pittsburgh

Primary Author: Julia R Stone, MS, University of Pittsburgh

Presenting Author: Julia R Stone, MS, University of Pittsburgh

Author 2: Lauren P. Morgenroth, MS, TRiNDS

Author 3: Robin E. Grubs, MS, PhD, LCGC, University of Pittsburgh

Author 4: John R. Shaffer, PhD, University of Pittsburgh

Author 5: Paula R Clemens, MD, University of Pittsburgh Medical School

Duchenne muscular dystrophy (DMD) is a rare, X-linked neuromuscular disorder characterized by early proximal muscle weakness and progressive loss of muscle function. As research into DMD treatments has grown, there has been increasing interest in assessing quality of life (QoL) for boys and men with DMD. Many early studies on QoL in DMD utilized parent-proxy reports, but recent research has suggested that boys with DMD might perceive their QoL differently than their caregivers. The purpose of this study was to determine if parents of adolescents with DMD perceive their child’s QoL the same as
the boys perceive their own QoL and to determine if specific aspects of DMD (steroid use, loss of ambulation, noninvasive respiratory support, and inability to self-feed) affect these perceptions. This study analyzed data from PedsQLTM 4.0 Generic Core Scale survey and the PedsQLTM 3.0 Neuromuscular Module administered to participants ages 11-17 years old and their caregivers (N=217 pairs) through the Cooperative International Neuromuscular Research Group (CINRG) Duchenne Natural History Study. Participant and caregiver responses were compared directly using paired t-tests. Participants reported higher physical QoL (p<0.003) and lower emotional (p=0.049), social (p<0.001), and school-functioning (p<0.022) QoL compared to their caregivers on the general survey. There was no difference in reported physical QoL on the neuromuscular survey. Interestingly, participants who lost the ability to self-feed reported higher total QoL than participants who maintained that ability (p=0.044). The results indicate that there are differences between adolescent experiences and parent perceptions, and that adolescents with DMD may be coping well with their physical limitations. This study also suggests that the widely-used PedsQLTM 4.0 survey may not appropriately capture physical QoL in adolescents with DMD. There is limited data regarding QoL for adolescents with DMD, and this study provides important information for professionals aiming to assess and improve QoL for these adolescents.

B-263 Assessing Family Perceptions of Diagnostic Terminology for Disorders of Sex Development (DSDs)

Pediatrics

Submitter: Stephanie Wiryaman,

Primary Author: Stephanie Wiryaman,

Presenting Author: Stephanie Wiryaman,

Author 2: Linford Williams, Children's Hospital of Pittsburgh of UMPC

Author 3: Beverly M. Yashar, University of Michigan

Author 4: Lauren Mohnach, CS Mott Children's Hospital, Michigan Medicine

Author 5: J. Thomas Fitzgerald, University of Michigan

Author 6: David E. Sandberg, University of Michigan

Terminology for conditions with atypical chromosomal, gonadal, or anatomic sex development is controversial. The umbrella term, 'disorder of sex development (DSD),' adopted by international consensus in 2006, is viewed negatively by most patient advocacy groups. Previous studies focused on terminology preferences; our goal was to measure the connotative meanings of various terms for patients and parents. To circumvent selection bias associated with recruiting through advocacy groups, we targeted participants receiving care at one interdisciplinary DSD clinic: 14 chart-selected adolescents/young adults (AYA) and 15 of their parents completed the survey (30% response rate). The
semantic differential (SD) was used to assess how AYA and parents perceive their self/child, the specific diagnosis/anatomic phenotype (DP), and the terms 'DSD' and 'Intersex.' Mean scores (range: -100 - +100) were compared using Cohen's d for effect size. The SD comprises 2 subscales: Inner and Outer domains, reflecting distinctions between internal efficacy vs. perceived opinions of others. AYA perceived all 3 medical terms relatively neutrally (x̅: DP=−5.2, DSD=−9.7, Intersex=−3.5) in contrast to positive perceptions of Self (x̅=44.7). Parents' ratings demonstrated similar trends (x̅: DP=−8.8, DSD=−6.1, Intersex=−1.8, Child=50.9). AYA rated DP and DSD more negatively on the Outer SD (x̅: DP=−15.1, DSD=−19.9) than the Inner (x̅: DP=4.9, DSD=0.5), suggesting an impact of perceived stigma. Parents also rated the Outer SD (x̅: DP=−16.4, DSD=−14.6) lower than the Inner (x̅: DP=−1.2, DSD=2.4). Time since diagnosis may affect negative perceptions: AYA diagnosed <10 yrs. ago rated Self (x̅=33.4) and DP (x̅=−13.6) more negatively than diagnosis >10 yrs. ago (x̅: Self=59.7, DP=6.1). Variations within and between families demonstrate the complexity of factors influencing perceptions of self and of medical terminology. This work underscores the importance of identifying the meanings that AYA and their families assign to diagnostic terminology and working together to use terms with shared meanings.

C-240 CDC42: A candidate gene for neurodevelopmental disorders

Pediatrics

Submitter: Diana Bertrand, Lineagen, Inc.

Presenting Author: Diana Bertrand, Lineagen, Inc.

Primary Author: Diana Bertrand, Lineagen, Inc

Author 2: Rena Vanzo, Lineagen, Inc

Cell division cycle 42 (CDC42) is a member of the Ras superfamily of signaling molecules and has been proposed as a candidate gene involved in neurodevelopmental conditions. Missense mutations in CDC42 have been reported in individuals with Takenouchi-Kosaki syndrome, characterized by intellectual disability, macrothrombocytopenia, and lymphedema. Additionally, nine different point mutations in the CDC42 gene were found in 15 individuals with clinical features including intellectual disability, facial dysmorphism, cardiac malformations, hearing and vision concerns, and brain malformations. Functional studies performed by Martinelli, et al. showed that mutations in different places along the gene resulted in multiple distinctive phenotypes. Copy number variants (CNVs) involving only the CDC42 gene are rarely reported. We report a case series of five individuals with partial duplications including exons 2-6 of the CDC42 gene. Four of these individuals have autism spectrum disorder; other shared symptoms include delayed milestones and attention deficit-hyperactivity disorder. This series includes a set of boy-girl twins, two brothers, and an unrelated singleton. Parent studies have not been performed, but it can be assumed that these duplications are inherited in the familial cases. Using a methodology developed by Uddin, et al., we identified the CDC42 gene as a critical exon containing gene, meaning it contains at least one exon that is highly expressed in the brain and has low mutation burden in unaffected individuals. Previous work has shown that critical exon containing genes are overrepresented in biological pathways involved in neurodevelopmental disorders and are enriched in
pathogenic CNVs in a neurodevelopmental population compared to controls. While functional studies of these partial duplications have not been performed, our findings implicate CDC42 as a contributor to neurodevelopmental conditions. These cases add new clinical information which may help clarify the role of the CDC42 gene in neurodevelopmental disorders.

C-243 Pediatric Experience of Prenatally Identified 45,X/46,XY Males

Pediatrics
Submitter: Kathryn Curry, St. Luke's Hospital

Presenting Author: Kathryn Curry, St. Luke's Hospital

Primary Author: KT Curry, St. Luke's Children's

Background: The phenotype of 45,X/46,XY can range from typical females with Turner syndrome to phenotypic males. Turner syndrome guidelines state that phenotypic males with 45,X/46,XY are excluded from the Turner Syndrome diagnosis. However reports of Turner-like features in phenotypic males have been reported. Case Presentation: Two phenotypic males were incidentally identified through prenatal genetic screening and diagnostic testing to be 45,X/46,XY. Case 1) Amniocentesis performed due to a possible brain malformation identified at on the 20-week anatomy scan. Only a mosaic marker chromosome Y identified on karyotype. Case 2) Woman with a previous Turner syndrome affected pregnancy sought NIPT and the sex could not be determined. 45,X/46,XY was found on follow up karyotype. Conclusion: 45,X/46,XY phenotypic males are now being identified prenatally instead of in adulthood due to infertility and short stature. The working clinical diagnosis is debated between endocrinologists, the diagnosing genetics team, and the Turner syndrome society. Do they follow under the diagnosis and screenings appropriate for partial XY gonadal dysgenesis (PGD) or mosaic male Turner, or both? We present two cases for discussion.

C-246 Growth Parameters at Birth in Patients with Mucopolysaccharidosis: Large-Scale Newborn Screening Program in Taiwan

Pediatrics
Submitter: You-Hsin Huang, MacKay Memorial Hospital, Taipei, Taiwan

Primary Author: You-Hsin Huang, MacKay Memorial Hospital, Taipei, Taiwan

Presenting Author: You-Hsin Huang, MacKay Memorial Hospital, Taipei, Taiwan

Author 2: Shuan-Pei Lin, Rare Disease Center, MacKay Memorial Hospital, Taiwan

Author 4: Chuan-Chi Chiang, Chinese Foundation of Health, Newborn Screening Center

Author 5: Li-Yuan Wang, Taipei Institute of Pathology, Taipei, Taiwan
Background: Mucopolysaccharidoses (MPSs) are a group of rare inherited metabolic disorders that result from deficiency of specific enzymes responsible for the degradation of glycosaminoglycans (GAGs). An early diagnosis could be achieved by newborn screening (NBS) and NBS programs have been available in Taiwan since August 2015. Previous studies have shown mean birthweight for newborn with MPSs is slightly higher. Here we report the growth parameters at birth in MPSs identified by NBS.

Methods: The large-scale NBS in Taiwan was based on tandem mass spectrometry assessment for α-iduronidase (IDUA) and iduronate-2-sulfatase (IDS) enzyme activity. Since August 2015, a total of 358,151 babies were screened and 5 MPS II patients and 4 MPS I patients were confirmed. The comprehensive growth parameters including gestation age (GA), born birthweight (BW), body length (BL), head circumference (HC), and chest circumference (CC) were collected and analyzed.

Results: Of those MPS I, two were identical twins with missense variants (c.1037T>G; c.1091C>T) and the others were siblings with one intronic splicing (c. 300-3C>G) and one missense variant (c. 1874A>C). All of 5 MPS II babies carried pathogenic variants (c.817C>T; c.1025A>G; c.311A>T; c.1400C>T; c.254C>T). The average IDUA and IDS enzyme activities were 0.89±0.5 μmol/g protein/ hr vs 0.40±0.2 nmol/4h/mg protein, respectively. Mean ± SD of GA was 39.4 ± 0.2 wks, BBW was 2.75 ± 0.2 kg, BL was 47.4 ± 2.3 cm, HC was 32.5 ± 1.3 cm, and CC was 31.6 ± 0.8 cm.

Conclusions: Newborn screening has proven to be effective in identifying the pre-symptomatic infants with MPSs. Our study aims to find out suitable indicators for MPSs at birth for early detection and severity classification. However, we found that the results of growth parameters with MPSs from NBS program are similar to general newborn population. Thus, it remains a challenge to identify reliable early indicator for clinical diagnosis of MPSs.

C-249 Characterizing the Phenotypic Presentation of an International Sample of 48, XXXY and 49,XXXXY, two rare variants of 47, XXY (Klinefelter syndrome) and the Impact of Testosterone Replacement Therapy (TRT)

Pediatrics
Submitter: Carole Samango-Sprouse, Ed.D., The Focus Foundation

Primary Author: Patricia Lasutschinkow, The Focus Foundation

Author 2: Carole Samango-Sprouse, The Focus Foundation; George Washington University; FIU

Author 3: Selena Chea, The Focus Foundation

Author 4: Gretchen Harmon, Nemours Medical Center

Author 5: Francie Mitchell,

Author 6: Michael McLeod,
48,XXXY(48s) and 49,XXXXY(49s) occur in 1:50,000 & 1:85,000-100,000 male births, respectively. They have intellectual, musculoskeletal & endocrine deficits, with 49s being more complex. We characterize the phenotypic profiles with a large international sample of 48, XXXY & 49, XXXXY and report on the influence of TRT.<br />73 males with 49s & 23 males with 48s had a multidisciplinary evaluation in immunology, neurocognition, neurogenetics, physical therapy and speech/language. A subset of boys were treated with TRT. <br />48s & 49s present with an increase of childhood apraxia of speech, immunologic difficulties & motor planning deficiencies. Dysmorphic features included distinct facial features, clinodactyly, cryptorchidism, tremors & radioulnar synostosis. 49s had increased cardiac malformations of CHD, ASD & VSD. 48s and 49s showed significant improvements when TRT was given. In receptive, 48s (TRT) had Standard scores (Ss) of 93.6 vs 81.0 In expressive, 48s (TRT) had Ss of 94.3 vs 83.7. 48s (TRT) had nonverbal IQ of 81.8 vs 71.6. In VMI, 48s (TRT) had Ss of 91 vs 78.2. In visual perception, 48s (TRT) had Ss of 87 vs 73.6. In expressive, 49s (TRT) had Ss of 68.2 vs 55.7. Cognitively, 49s (TRT) had nonverbal IQ of 77.6 vs 76.5. In VMI, 49s (TRT) had Ss of 67.17 vs 64.8. In visual perception 49s (TRT) had Ss of 66.72 vs 65.4. This study reports on a novel international sample of two rare variants of 47, XXY. There was variability between and within groups, demonstrating the large range of capabilities and outcomes. 49s displayed increased and unreported risk of cardiac defects and immunological vulnerability while 48s showed a much more capable developmental profile than previously appreciated. Both groups had improvement in selected developmental domains with TRT. 48s & 49s had dysfunction in planning deficits in speech, motor & executive function similar to but more complex than 47, XXY. Both groups showed an encouraging biological response that requires additional investigations.

C-252 The Psychiatric Impact of Tuberous Sclerosis Complex and Utilization of Mental Health Treatment

Pediatrics
Submitter: Kate Mowrey, The University of Texas Health Science Center at Houston

Presenting Author: Kate Mowrey, The University of Texas Health Science Center at Houston

Primary Author: Kate Mowrey, University of Texas Health Science Center at Houston

Author 2: Myla Ashfaq, MS, CGC, The University of Texas Health Science Center at Houston

Author 3: Laura Farach, MD, FACMG, The University of Texas Health Science Center at Houston

Author 4: Deborah Pearson, PhD, University of Texas Health Science Center at Houston

Author 5: Steve Roberds, PhD, Tuberous Sclerosis Alliance
Tuberous Sclerosis Complex (TSC) is a multi-system, neurocutaneous disorder with a spectrum of TSC-associated neuropsychiatric disorders (TAND). The most common neuropsychiatric manifestations in the pediatric and adult populations are cognitive concerns, depression, and anxiety. While 90% of individuals with TSC have some TAND features, only 20% receive treatment, leading to a 70% treatment gap. There remain significant attitudinal and structural barriers that hinder one’s ability to reach proper mental health care services. This web-based study used validated measures in conjunction with researcher-designed questions to evaluate perception of disease severity, presence of anxiety and depression, as well as the utilization and barriers towards mental health services among adults with TSC. Participants were recruited through the Tuberous Sclerosis Alliance and in UTHealth TSC clinics. Overall, our study population had mild anxiety, minimal depression, and a moderate perception of disease severity. Notably, the difference between the median depression score for men and women was statistically significant with men scoring higher than the females (p = 0.02), meaning that the men in our study were more depressed than the women. Out of 69 respondents, 57% (n = 39) reported receiving mental health treatment at some point over their lifetime. In both the mental health treatment group and non-mental health treatment group, cost was the most often indicated barrier to accessing mental health resources (treatment group, cost: 51%; stigma: 21%) (non-treatment group, cost: 27%; stigma: 20%). Disease severity had a moderate and low-moderate association with anxiety and depression, respectively. Regardless of past utilization, respondents had a positive outlook towards the use of mental health services with the major barrier being cost. For the benefit of the TSC community, a genetic counselor could undertake the responsibility of consistently assessing patients with TSC for TAND, offering appropriate referrals and helping to navigate barriers to receiving care.

C-255 “Familial immune thrombocytopenia” Correctly Identified as Familial Platelet Disorder with Propensity to Acute Myeloid Leukemia due to RUNX1 c.1163C>A (p.S388*)

Pediatrics
Submitter: Kelly Rich,

Presenting Author: Kelly Rich,

Primary Author: Kelly Rich, BS,

Author 2: Sarah H. O’Brien, MD, MSc, Nationwide Children's Hospital

Author 3: Elizabeth A Varga, MS, LGC, Nationwide Children's Hospital

Familial platelet disorder with propensity to acute myeloid leukemia (FPD/AML) is a rare autosomal dominant disorder reported in only 70 families. Often FPD/AML goes undiagnosed due to its rarity and clinical overlap with other inherited or acquired thrombocytopenias. Here we describe a second family with the RUNX1 c.1163C>A pathogenic variant causative for FPD/AML, and discuss challenges and
A 10-year-old female presented to hematology clinic with lifelong thrombocytopenia (108-138 x10^9/L; normal >140) and recent fatigue. She had carried a diagnosis of immune thrombocytopenia (ITP) since age 2, but never required ITP-type therapy. A second opinion was sought by the family due to the patient’s family history. Her father had mild thrombocytopenia first documented at age 36 (100 x10^9/L; normal >140). Her paternal grandmother had been given a diagnosis of ITP at age 56 (90 x10^9/L; normal >122) with myelodysplastic syndrome (MDS) progressing to AML diagnosed at 61. Both the proband and her paternal grandmother had abnormal platelet aggregation findings not explained by their degree of thrombocytopenia. A custom NGS panel was ordered on the proband, revealing a pathogenic mutation in RUNX1 predicted to result in premature protein termination (p.S388*). Bone marrow aspirate (BMA) and biopsy were obtained, which revealed no dysplastic or clonal changes. This case illustrates the importance of a thorough family history, in conjunction with medical and laboratory records review of relatives, and comprehensive genetic counseling. It is essential to recognize the variable expression typical of FPD/AML; age of presentation ranges from early childhood into the 60s. MDS/AML risk is estimated at 20-60%. Universally accepted management guidelines do not exist, but current recommendations suggest BMA, complete blood count (CBC) and clinical exam, with CBC and clinical exam repeated every 6-12 months, with BMA if there are significant and persistent changes in blood counts. Hematopoietic stem cell transplant is the only curative treatment.

C-258 Is bigger really better? Reviewing the utility of a >2000-gene sequencing panel for developmental disabilities in our pediatric institution.

Pediatrics

Submitter: Sarah Clowes Candadai,

Primary Author: Megan C Sikes, Seattle Children’s Hospital

Author 2: Sarah V Clowes Candadai, Seattle Children's Hospital

Author 3: Kathryn Golden-Grant, Seattle Children's Hospital

Author 4: Kimberly Foss, Seattle Children's Hospital

Presenting Author: Megan C Sikes,

Autism spectrum disorder (ASD) and intellectual disability (ID) are two types of developmental disorders that affect approximately 1-2% and ~0.5-1.5% of minors, respectively. ASD and ID can often be comorbid disorders associated with a wide array of genetic conditions, previously reported to be identifiable by exome sequencing in ~14-33% of cases. Due to these factors, concurrent sequencing of >2000 genes associated with developmental disorders using a trio-based, exome capture approach has become increasingly utilized for children with developmental disorders of suspected genetic etiologies. We reviewed our data for 61 patients who underwent this testing and had clinically interpreted results to examine trends in utility of testing in our pediatric population at Seattle Children's Hospital (SCH). We
used a combination of retrospective chart and billing reviews. The overall diagnostic rate as interpreted by the Board Certified MD or NP in Genetics was 29%. The diagnostic rate was greater for trios (32%, N = 34) than duos (25%, N = 12) or singletons (12%, N = 8) and higher diagnostic rates for patients with ≥6 body systems affected were seen (46%, N = 11), compared to 4-5 (32%, N = 25), ≤3 (18%, N = 17), or ≤2 (17%, N = 6). Overall, results had documented impacts on clinical management of the patient in 33% of cases. The total cost of testing was $130K, the cost to patients was $100 (<1%), the cost to insurance payers was 27K (21%), and the cost to SCH was $103K (79%). Our results mirror those quoted by the reference laboratory. The diagnostic rate and proportion of cases with impacts to management reflect high utility of this test as it’s being used. The financial burden of testing has fallen on the institution with a relatively low reimbursement rate for appropriate testing.

C-261 Making a genetic diagnosis in a level IV neonatal intensive care unit population: How many do we find and how long does it take?

*Pediatrics*

*Submitter: Kayleigh Ann Swaggart, Cincinnati Children's Hospital Medical Center*

*Presenting Author: Kayleigh Ann Swaggart, Cincinnati Children's Hospital Medical Center*

*Primary Author: Kayleigh Ann Swaggart, University of Cincinnati, Cincinnati Children's Hospital*

*Author 2: Leandra Tolusso, Cincinnati Children's Hospital Medical Center*

*Author 3: Daniel Swarr, Cincinnati Children's Hospital Medical Center*

*Author 4: Hua He, Cincinnati Children's Hospital Medical Center*

*Author 5: Brian Dawson, Cincinnati Children's Hospital Medical Center*

*Author 6: Kristen Suhrie, Cincinnati Children's Hospital Medical Center*

In order to determine what genetic diagnosis are made in a level IV Neonatal Intensive Care Unit (NICU) population and to determine how long it takes to make that diagnosis, we performed a retrospective chart review of all patients admitted to a single level IV NICU in 2013 and 2014. A total of 1327 unique patients were admitted during the study period. During the NICU stay and up to two years of age, 478 genetic tests were ordered for 276 (20.8%) patients. A genetic diagnosis was made in 36.3% of patients who had genetic testing. In total, 128 patients (9.6%) received 130 genetic diagnoses by two years of age through genetic testing or other means, including clinical criteria or research testing. Of these neonates, 29 (22.3%) had diagnoses made prenatally or at a referring hospital prior to admission to our NICU. Of the 101 diagnosis made following admission to our NICU, 47 (46.5%) were made during the NICU stay, 34 of which were made during the neonatal period (≤ 28 days) and 54 (53.5%) were made after the NICU stay but before two years of age. We found 86 unique diagnoses in this cohort and 75.6% of them were seen only once in the two year study period. The median day of life at diagnosis was 44.5 days (range 2-624 days). We saw a high incidence of genetic disease in our cohort over that of the general population,
suggesting that genetic disease is an important driver for newborns requiring level IV NICU care. The significant incidence of genetic disease in this population highlights the need for genetic services and genetic counseling in a level IV NICU setting. By integrating these services into our routine care for this population there is the potential to decrease the time to diagnosis and improve care for these unique patients.

Patient reported barriers to genetic counseling for hereditary breast and ovarian cancer risk

**Platform Presentations: Cancer**

*Submitter: April Hermstad, Emory Prevention Research Center*

*Primary Author: April Hermstad, Emory Prevention Research Center*

*Author 2: Christine Stanislaw, Winship Cancer Institute of Emory University*

*Author 3: Christine Tallo, Winship Cancer Institute of Emory University*

*Author 4: Cecelia Bellcross, Emory University*

*Presenting Author: Cecelia Bellcross, Emory University*

A randomized clinical trial was conducted in Emory Healthcare breast imaging centers to identify women at increased risk of hereditary breast/ovarian cancer (HBOC) and to determine the most effective means of referral to maximize uptake of genetic counseling (GC) services. Increased risk was determined using the Breast Cancer Genetics Referral Screening Tool (B-RST™), a validated electronic family history screener designed to identify persons at risk for HBOC. Despite successful identification of more than 600 at-risk individuals, initial GC uptake was low in all three referral groups: 1) self-referral, 2) electronic health record message to ordering provider, and 3) direct patient contact by study staff. To understand barriers to uptake in this setting, and to maximize the number of patients who ultimately received cancer genetic services, we emailed a follow-up survey to 239 qualifying participants who had not scheduled a genetic counseling appointment within three months of their positive B-RST result (group 1) or their last contact with the study (groups 2 & 3). The survey’s purpose was twofold: to remind and educate participants about the benefits of GC, and to identify GC barriers among individuals at increased risk of HBOC. The survey explored numerous psychosocial measures, e.g., cancer worry, risk perception, HBOC knowledge, perceived barriers, benefits of, and attitudes about genetic counseling. The most commonly reported barriers to scheduling were lack of physician recommendation (71%), health insurance concerns (67%) and indecision about GC (66%). However, 52% reported interest in future GC contact. A majority (52%) also indicated they were somewhat or very likely to receive genetic counseling within the next six months. Of 97 survey participants (response rate 40.4%), 15 individuals (15.5%) completed GC following the survey, most within three months. This rate is more than double that of those who did not complete the survey (7.3%), suggesting that the additional point of contact was effective in increasing GC uptake.
Why don’t women respond to risk notification letter following mammography?

Platform Presentations: Cancer
Submitter: Allison Schartman, Indiana University Health

Presenting Author: Allison Schartman, Indiana University Health

Primary Author: Allison F Schartman, Indiana University School of Medicine

Author 2: Gail H. Vance, Indiana University School of Medicine

Author 3: Stephen R. Dlouhy, Indiana University School of Medicine

Author 4: Jennifer L. Ivanovich, Indiana University School of Medicine

Author 5: Kimberly Quaid, Indiana University School of Medicine

Author 6: Todd L. Foster, St. Vincent Health

Author 7: Stephanie A. Cohen, St. Vincent Health

Family history information is often collected from women while undergoing a screening mammogram. A computer software algorithm was implemented within a mammography platform that identifies individuals at-risk for Lynch syndrome based on Amsterdam and revised Bethesda criteria, and generates a risk notification letter. This study aimed to describe how individuals interpret the risk notification letter and determine factors that influenced the decision whether or not to pursue genetic counseling and/or genetic testing after receipt of a risk notification letter. Of 40,277 individuals who had a mammogram over 8 months, 376 were identified at-risk for Lynch syndrome (0.93%) and those who had not previously undergone genetic counseling were sent a risk notification letter (N=365). A survey with closed and open-ended questions was developed and sent to those who received a risk notification letter. A total of 57/365 completed the survey for a 15.6% response rate. Only 4 (7.0%) reported they had genetic counseling following receipt of the risk notification letter. Commonly identified barriers to pursuing a genetic counseling appointment included lack of perceived benefit, lack of awareness and fear of risk, cost and insurance discrimination concerns, lack of referral, and external factors (time illness, etc.). When presented options for what might have made them respond to the risk notification letter, the most commonly selected response was adding information to the letter about benefits to genetic testing (93% highly or somewhat likely), followed by adding information about hereditary cancer syndromes and including personal information about their family history of cancer. This study provides insight to increase genetic counseling uptake in this population.
Information Seeking and Scanning Behaviors in Individuals Scheduled for Cancer Genetics Consultations

Platform Presentations: Cancer
Submitter: Sabrina Nichole DiMaso, MS, DuPage Medical Group

Presenting Author: Sabrina Nichole DiMaso, MS, DuPage Medical Group

Primary Author: Sabrina Nichole DiMaso, The Ohio State University

Author 2: Shelly Hovick, PhD, The Ohio State University

Author 3: Alexandra Ilacqua, MS, LGC, Mount Carmel Health System

Author 4: Leigha Senter-Jamieson, MS, LGC, The Ohio State University

Information seeking (actively searching for information) and scanning (exposure to information in the absence of actual intention to receive it) have been studied in the context of health behaviors, but there are very little data about the impact of information behaviors on the perceptions of individuals presenting for genetic counseling. To investigate, we conducted a cross-sectional survey of patients scheduled for cancer genetic counseling appointments (N=111). The electronic survey instrument was built using constructions of the Planned Risk Information Seeking Model (PRISM), which states that intent to seek information is the result of one’s perceptions of their own knowledge insufficiency, risk perceptions, and attitudes and beliefs toward information seeking. The survey collected information about primary topics of interest and sources of information seeking and scanning, as well as relationships between information behaviors and risk perceptions, perceived knowledge, perceived control, cancer-related worry, and understanding of the genetic counseling process. The majority of participants (84.7%) report information scanning. More than half (54.1%) report information seeking. Those without a personal history of cancer were more likely to seek information than those with a personal history of cancer. The most likely source of information seeking was the Internet. Information seeking was found to be associated with higher perceived knowledge, higher personal control over cancer risk, and better understanding of the genetic counseling process (ps < .05). This data sparks discussion over the effects of information behaviors as well as how information behaviors may be leveraged by genetic counselors in their clinics. Understanding information seeking and scanning behaviors of genetic counseling clients is the first step in understanding client information needs in order to tailor genetic counseling information interventions. This study serves as a pilot for future projects about information behaviors in the context of genetic counseling.

Identification of cancer risk during prenatal genetic counseling sessions: Evaluation of current practice protocols

Platform Presentations: Cancer
Submitter: Jennifer Cech, UC Irvine

Submitter: Jennifer Cech, UC Irvine
At our center, 59% of three-generation pedigrees taken during a prenatal genetic counseling session in 2016 included an incidental finding of any cancer, a 19% increase from 2010. Due to this high prevalence of reported family histories of cancer, prenatal genetic counselors are in a position to identify and refer at-risk patients for comprehensive cancer genetic risk assessment and testing. The aim of this study was to assess current practice protocols of prenatal genetic counselors to understand if there is uniformity in how they evaluate and respond to families with reported cancer history. An online survey of 104 prenatal genetic counselors revealed that the majority of counselors ask about age of diagnosis when cancer is discussed, but only 61% ask about cancer every time they take a three-generation pedigree or use a questionnaire that includes cancer. When presented with sample pedigrees, prenatal counselors responded differently to a high risk of cancer in a maternal vs. a paternal lineage; 24% elected to refer to cancer genetic counseling for a paternal high-risk family compared to 62% for a maternal high-risk pedigree. Counselors with only prenatal experience were more likely to discuss the option of cancer genetic counseling for a low-risk history, whereas those with prior cancer experience were more likely to tell the patient the history was not suggestive of a hereditary cancer predisposition syndrome. This study also determined that practice protocols of prenatal genetic counselors have changed in the last eight years; there was an 11% increase in how often they took a three-generation family history that included cancer in 2010 vs. those same counselors’ responses in 2016. This study highlights the need for a standard practice protocol to guide prenatal genetic counselors on how to evaluate, respond, and relay information regarding cancer genetic risk assessment to prenatal patients.

**Uveal Melanoma Prognostic Genetic Testing: An Emerging Role for Genetic Counselors**

*Platform Presentations: Cancer*

*Submitter: Honey Nagakura, MS, CGC,*

*Presenting Author: Honey Nagakura, MS, CGC,*

*Primary Author: Honey Nagakura, MS, CGC, Integrated Genetics*

*Author 2: Amy Cronister,*

*Author 3: Jaime Jessen,*
Uveal Melanoma (UM) Prognostic Genetic Testing, performed on UM tumor cells, is used to predict the chance of metastatic disease. Genetic tumor results are combined with tumor histology and patient demographics to produce a personalized survivorship prediction. Here we present two cases with different results to illustrate the underlying counseling issues. Both patients were diagnosed with uveal melanoma and had prognostic genetic testing. Patient 1 is a 55-year-old male whose tumor had a largest basal diameter (LBD) of 8mm. Tumor genetic testing revealed disomy 3. GNAQ exon 5 sequencing showed the p.Q209 mutation, confirming that tumor tissue was sampled. Based on this and individual clinical and histomorphological data provided by the referring physician, the patient was given a survivorship prediction of 92-95% in 10 years, compared to the control group of 91%. Patient 2, by comparison, is a 53-year-old female whose tumor had an LBD of 19mm and monosomy 3. Her survivorship prediction was 22-31% in 10 years, compared to the control group of 95%. For both patients, the counseling process included a review of the testing technologies performed, factors incorporated into the survivorship prediction, and disclosure and discussion of the patient’s survivorship prediction for years 3, 5, and 10, compared to controls. The objective for each session was to help the patient understand the implications of the patient’s individualized results, and importantly, to address individual psychosocial needs and concerns.

Genetic counselors have the expertise to disclose UM prognostic genetic testing results and address psychosocial issues. As the applications of tumor testing continue to advance, genetic counselors have a unique opportunity to collaborate with oncologists and other cancer care providers to facilitate patient understanding regarding the results and implications of genetic tumor testing.

Identifying Individuals with Mutations Prior to Cancer Diagnoses using NCCN Criteria: Successful or Not?

**Platform Presentations: Cancer Guidelines and Risk Assessment**

*Submitter: Brian Reys, MS, CGC, UT Southwestern*

*Primary Author: Brian Reys, MS, CGC, UT Southwestern*

*Presenting Author: Brian Reys, MS, CGC, UT Southwestern*

*Author 2: Caitlin Mauer, UT Southwestern Medical Center*

*Author 3: Sara Pirzadeh-Miller, UT Southwestern Medical Center*

*Author 4: Theo Ross, UT Southwestern Medical Center*

Introduction: Early detection and prevention are cornerstones in the efforts to reduce cancer morbidity and mortality. Current guideline goals are to identify high-risk individuals before they develop cancer. NCCN BRCA1/2 genetic testing criteria are widely recognized standards for offering BRCA1/2 testing. This study aims to evaluate the effectiveness of current NCCN criteria in identifying high-risk patients before their cancer diagnoses. 

*Methods:* A retrospective chart review was performed for 650
patients with a personal history of cancer (breast, ovarian, pancreatic, and prostate) seen at UT Southwestern and affiliate hospitals between 2009-2018. All patients tested positive (pathogenic/likely pathogenic) for a breast cancer-associated mutation (ATM, BARD1, BRCA1, BRCA2, BRIP1, CDH1, CHEK2, MRE11A, NBN, NF1, PALB2, PTEN, RAD50, RAD51C, RAD51D, TP53). Review determined if patients met NCCN (v1.2018) BRCA1/2 testing criteria before and after their personal diagnosis of cancer. Patients who met testing criteria for other syndromes were excluded. The study controlled for known mutations in families, past iterations of NCCN guidelines and instances of limited family history. <br />Results: Of patients with BRCA1/BRCA2 mutations, 86/243 (35%) and 60/186 (32%), respectively, met NCCN testing criteria only after their personal diagnosis of cancer. These rates were higher in patients positive for mutations in moderate risk genes: ATM (22/55, 40%), CHEK2 (36/63, 57%) and PALB2 (18/40, 45%). 10 (2%) patients never met NCCN criteria despite their cancer diagnosis, 5 of those being positive for a BRCA1/2 mutation. Overall, 245/650 (38%) of patients did not meet NCCN criteria until after their cancer diagnosis. <br />Conclusion: 38% of patients with known cancer risk-causing mutations would not have met NCCN criteria prior to their diagnosis of cancer. As the field debates the merits of population based testing, this study suggests the current criteria for identifying high-risk patients are not successful at preventing cancers.

Moderate Penetrance Breast Cancer Genes: Surgical Decisions and Bilateral Breast Cancer Risk
Platform Presentations: Cancer Guidelines and Risk Assessment
Submitter: Jordan Berg, UT Southwestern
Presenting Author: Jordan Berg, UT Southwestern
Primary Author: Jordan Berg, UT Southwestern
Author 2: Caitlin Mauer, UT Southwestern
Author 3: Brian Reys, UT Southwestern
Author 4: Sara Pirzadeh-Miller, UT Southwestern
Author 5: Theodora Ross, UT Southwestern

With the onset of panel testing in cancer genetics, more and more patients are diagnosed with mutations in moderate risk breast cancer (BC) genes including ATM, CHEK2, and PALB2. A paucity of data regarding bilateral BC risk exists for these genes and the implications for surgical decisions. Here we determined prevalence of bilateral BC among ATM, CHEK2, and PALB2 carriers and surgical decisions following BC diagnosis and positive genetic testing. <br />Retrospective chart review was performed for women with a personal history of BC who tested positive for a pathogenic mutation in ATM, CHEK2, or PALB2 within the UT Southwestern cancer genetics program between 2013-2017. Cancer diagnoses and treatment plans were analyzed for those that met inclusion criteria. <br />A total of 14,593 patients
underwent genetic counseling/testing. Of 136 patients who met inclusion criteria, 47 ATM, 55 CHEK2, and 38 PALB2 mutations were identified. Nine women (6.6%) had two mutations and four of these were a combination of ATM, CHEK2, or PALB2 mutations. Rates of bilateral BC at time of genetic diagnosis were 12.8% (6/47) for ATM, 16.4% (9/55) for CHEK2, and 13.2% (5/38) for PALB2, as compared to 7.6% (277/3661) among internal control population. Of those with unilateral BC, 86.7% (104/120) had not chosen to undergo prophylactic mastectomy of the remaining breast prior to genetic diagnosis. Of these, 37.8% (14/37) of ATM, 39.5% (15/38) of CHEK2, and 48.3% (14/29) of PALB2 carriers chose prophylactic surgery following genetic diagnosis.<br />
This study shows that prevalence of bilateral BC in ATM, CHEK2, and PALB2 carriers is higher than expected. Despite NCCN guidelines not formally recommending prophylactic bilateral mastectomy based on ATM, CHEK2, and PALB2 mutations alone, 37.8% of BC patients in the cohort elected bilateral mastectomy following positive genetic testing. While further studies are needed to clarify incidence of bilateral BC among ATM, CHEK2, and PALB2 carriers, these data suggest genetic counselors need to be prepared to discuss risks of second primary cancers and surgical planning.

**Triple Negative Breast Cancer – an Indication for Testing Beyond BRCA1/BRCA2**

**Platform Presentations: Cancer Guidelines and Risk Assessment**

**Submitter: Katherine Skora,**

*Primary Author: Katherine A Skora MS MPH CGC, GeneDx*

*Author 2: Kristen J Vogel Postula MS CGC, GeneDx*

*Author 3: Laura M Andolina MS CGC, GeneDx*

*Author 4: Lisa R Susswein MS MHA CGC, GeneDx*

*Author 5: Patricia D Murphy PhD FACMG, GeneDx*

*Author 6: Rachel T Klein MS CGC, GeneDx*

*Author 7: Kathleen S Hruska PhD FACMG, GeneDx*

*Presenting Author: Kristen J. Vogel Postula, MS, CGC, GeneDx*

Background: Triple negative breast cancer (TNBC) is a feature of BRCA1-related breast cancer (BC) and the National Comprehensive Cancer Network (NCCN) recommends BRCA1/BRCA2 (BRCA) testing for women with TNBC diagnosed ≤60, regardless of family history of breast, ovarian, pancreatic or prostate cancer (FHx). It is unclear if this indication is also appropriate for cancer panels. We assessed yield and proportions of BRCA variants between patients meeting only this criterion (TNBC 46-60, no FHx) and those meeting other criteria.<br />
Methods: We retrospectively reviewed personal and family histories of patients referred for cancer panel testing. Individuals had testing for at least ATM, BRCA, CDH1, CHEK2, PALB2, PTEN and TP53, and were excluded if they were male, <18, of Ashkenazi Jewish ancestry
or had ovarian or pancreatic cancer. Chi-square and Fisher’s exact tests were used to compare yields.

Results: Among BC patients, 10.4% (n=24,381) carried at least one pathogenic/likely pathogenic variant (PV), 35.6% of which were in BRCA. Among women with TNBC 46-60 and no FHx (n=426), 7.0% had a PV; 51.6% of PVs were in non-BRCA genes. We compared yields and BRCA proportions to other groups meeting NCCN criteria. For women with BC ≤45, no FHx (n=2,403), 8.6% had a PV (58.6% in non-BRCA). Women with BC ≤50 and a second primary BC, no FHx (n=335), had a 14.3% yield (59.2% in non-BRCA). Finally, women with BC ≤50 with FHx (n=9844), had a 12.7% yield (61.8% in non-BRCA). There was a significant difference in yield between TNBC 46-60 (no FHx) and women with BC≤50 with a second BC (7.0% vs 14.3%, p=0.0011) as well as in comparison to BC≤50 with FHx (7.0% vs 12.7%, p<0.001). The difference between TNBC 46-60 and BC≤45 was not significant (7.0% vs 8.6%, p=0.34).

Conclusions: Per current guidelines, TNBC ≤60 is an indication for only BRCA testing. Guidelines for testing of other genes in these individuals are not available. In women who only met this criterion, over 50% of PVs were in non-BRCA genes. These data support testing women with TNBC ≤60 for a broader spectrum of cancer genes.

Adult-onset neurologic disease risks in carriers of recessive conditions: Current knowledge, practices, and attitudes of genetic counselors providing carrier screening.

Platform Presentations: Counseling/Psychosocial
Submitter: Tara A Jones, MS, Cedars Sinai

Primary Author: Tara A Jones, MS, Cedars Sinai

Presenting Author: Tara A Jones, MS, Cedars Sinai

Author 2: Aishwarya Arjunan, MS, MPH, CGC, Counsyl

Author 3: Jason Rothstein, MPH, Norton & Elaine Sarnoff Center for Jewish Genetics

Author 4: Jeanine Schulze, MS, LCGC, Indiana University School of Medicine

Author 5: Lisa Kinsley, MS, CGC, Northwestern University Feinberg School of Medicine

Author 6: Sharon Aufox, MS, CGC, Northwestern University Feinberg School of Medicine

Carriers of certain autosomal recessive and X-linked recessive conditions are also at risk to develop adult-onset conditions. With the increasing use of expanded universal carrier screening, patients at risk for adult-onset conditions will be identified in the preconception/prenatal period. The current practices and attitudes of preconception/prenatal genetic counselors (PPGCs) regarding risk discussions for adult-onset conditions during pre- and/or post-test counseling sessions are unknown. To address this gap, PPGCs were surveyed regarding their attitudes and practices on counseling patients for adult-onset neurological conditions, using a well-published link in fragile X premutation carriers with a risk to develop tremor/ataxia (FXTAS) and a newer link in affected patients and carriers of Gaucher disease
with a risk to develop Parkinson disease (GBA-PD), as proxies. Between November 10 to December 22, 2017, PPGCs who were members of NSGC and counseled about carrier screening within the past three years were invited to take an online survey. One hundred twenty genetic counselors completed the survey. A majority of counselors reported awareness of the GBA-PD link (n = 78; 65%), though few reported discussing it in preconception/prenatal settings (n = 30; 38.5%). Contrastingly, nearly 100% of respondents reported discussing FXTAS (n = 117) in the same settings. The GBA-PD link was discussed more consistently when disclosing positive GBA results or when the patient/family approached the topic. Main reasons for not discussing the GBA-PD link included: not knowing enough about the link and the lack of professional guidelines. The main reasons for discussing either link included: the presence of peer-reviewed literature regarding the link, respecting a patient’s right-to-know, and, in the case of FXTAS, the presence of guidelines from professional organizations. These results highlight an inconsistency in PPGCs discussions of adult-onset risks with carriers and a need to develop guidelines to help standardize the care and education of these patients.

Effect of Providing Education about Carrier Results via Web versus Genetic Counselor on the Subsequent Therapeutic Relationship

Platform Presentations: Counseling/Psychosocial
Submitter: Lori A. Hamby Erby, National Human Genome Research Institute/Johns Hopkins Bloomberg School of Public Health GCTP

Primary Author: Lori A. Hamby Erby, National Human Genome Research Institute/Johns Hopkins Bloomberg School of Public Health GCTP

Presenting Author: Lori A. Hamby Erby, National Human Genome Research Institute/Johns Hopkins Bloomberg School of Public Health GCTP

Author 2: Tyler Wisniewski, National Human Genome Research Institute

Author 3: Katie Lewis, National Human Genome Research Institute

Author 4: Barbara Biesecker, RTI International

Author 5: Les Biesecker, National Human Genome Research Institute

The expertise of genetic counselors should be targeted to contexts in which clients are most likely to benefit. One possible delivery model involves education via a web platform with follow-up genetic counseling to assist with adaptation to the information. A prior study of carrier results delivery to healthy adults beyond childbearing years examined post-session outcomes and demonstrated noninferiority of web-based results delivery when compared to delivery by a genetic counselor (GC). The counseling tasks in genetic counseling rely on the development of a therapeutic relationship. Psychotherapy research demonstrates that a therapeutic relationship grows stronger when the counselor and client meet multiple times. We examined whether the therapeutic relationship as
assessed by an observer was higher in post-carrier results follow-up genetic counseling sessions when results were previously delivered by the same genetic counselor than when results were delivered via the web. Participants were part of the NIH ClinSeq study. They were first randomized to receive education about their results via a web platform or via a GC and were then further randomized to receive follow-up genetic counseling or not. We rated audio recordings of 73 follow-up genetic counseling sessions using the observer version of the Working Alliance Inventory (WAI-O). Eleven sessions were rated by a second coder, with an inter-rater reliability of 81.1%. T-tests were used to consider differences in WAI-O scores between the two groups who received follow-up counseling. Participants had a mean age of 63 years and were primarily white (93%) and well-educated. The mean therapeutic alliance scores did not differ significantly between the two study arms (education by GC 5.34/7; education by web 5.24/7; t=0.72, p=0.24). Results suggest that the use of a web platform in this specific context did not adversely affect the subsequent therapeutic relationship, but it would be important to consider this in future studies with higher impact genetic test results.

Preimplantation genetic diagnosis in inherited heart diseases: A qualitative study

Platform Presentations: Counseling/Psychosocial
Submitter: Laura Yeates, Centenary Institute and Royal Prince Alfred Hospital

Primary Author: Laura Yeates, Centenary Institute and Royal Prince Alfred Hospital
Presenting Author: Laura Yeates, Centenary Institute and Royal Prince Alfred Hospital

Author 2: Kristie McDonald, Centenary Institute
Author 3: Charlotte Burns, Centenary Institute and Royal Prince Alfred Hospital
Author 4: Christopher Semsarian, Centenary Institute and Royal Prince Alfred Hospital
Author 5: Jodie Ingles, Centenary Institute and Royal Prince Alfred Hospital

Introduction: Preimplantation genetic diagnosis (PGD) is a reproductive technique that ensures a pathogenic variant is not passed to the next generation. PGD is known to cause significant emotional burden. Inherited heart diseases show variable penetrance and clinical heterogeneity, ranging from asymptomatic individuals to heart failure and sudden cardiac death. Here we explore the experiences of PGD in the setting of inherited heart diseases.

Method: Participants were recruited from a specialised multidisciplinary cardiac genetic clinic. Purposive sampling was used. Patients and partners who had previously considered and/or undertaken PGD were invited to participate. A semi-structured interview schedule was developed to explore overall experiences and reasons for PGD uptake. Broad topics included experience of disease, reproductive history, psychosocial and financial considerations. Interviews were recorded, transcribed verbatim and thematic analysis performed.

Results: 14 participants were recruited (12 with an inherited cardiomyopathy, 1 with an inherited arrhythmia and 1 partner). Two broad themes emerged 1. Past experience influencing now: encompassing patients experience of disease, reproductive history and personal beliefs, and 2. Deliberating the decision:
including uncertainty for self and future generations, judgement from others, isolation and financial considerations. Amongst those who chose to undergo PGD (7/14), past experience of a significant cardiac event, such as family history of sudden cardiac death, was an important factor in the decision process.<br />

Conclusion: The decision to undergo PGD in inherited heart disease is complex and influenced by individual experience of disease. We highlight key areas where genetic counselling intervention may assist in PGD decision processes.<br />

Rare Disease Caregiving in America: What Genetic Counselors Need to Know

Platform Presentations: Counseling/Psychosocial

Submitter: Erica Ramos, MS, LCGC,

Presenting Author: Erica Ramos, MS, LCGC,

Primary Author: Erica Ramos,

Author 2: C. Grace Whiting, National Alliance for Caregiving

Author 3: Lisa Weber-Raley, Greenwald & Associates

Author 4: Nicole Boice, Global Genes

An estimated 25-30 million Americans have a rare disease or condition. As the genetic underpinnings of rare disease are elucidated and genetic testing becomes more accessible, more individuals are likely to engage with genetic counselors. Understanding the needs of these patients, families and caregivers is paramount. In fall 2017, the National Alliance for Caregiving, in partnership with Global Genes, conducted a national online quantitative study of 1,406 unpaid caregivers age >=18 living in the United States who provide care to a child or adult with a rare disease or condition. 71% of rare caregivers provide care to someone whose rare disease or condition is genetic. 400 unique rare diseases and conditions were captured with cystic fibrosis (9%), pulmonary arterial hypertension (4%), atypical hemolytic uremic syndrome, Ehlers-Danlos syndrome, and Fabry disease (2% each) among the most often mentioned. 73% of these rare caregivers report that their care recipient consulted with a genetic counselor. Most rare caregivers are immediate relatives, with 59% caring for their own child under 18, 17% caring for their own adult child, and 14% caring for a spouse/partner. 22% cared for multiple individuals with rare disease. Rare caregivers say providing care is emotionally stressful (67%), twice as high as that of general caregivers. 41% report having fair or poor emotional or mental health. 74% of rare caregivers struggle with a sense of loss for what their care recipient’s life would be like without their condition. Only 44% feel their role as a rare caregiver has had a positive impact on their family. 31% of rare caregivers turn to a genetic specialist/counselor for information. Among all rare caregivers, 11% indicate that a genetic counselor is needed and difficult to find. This research suggests rare disease has a broad and lasting impact on caregivers, in both daily life and long-term well-being. As these caregivers are often family, genetic counselors are
Psychometric properties of the Genetic Counselling Outcome Scale (GCOS): A Rasch analysis

Platform Presentations: Counseling/Psychosocial
Submitter: Jehannine C. Austin, PhD, MSc, CGC, CCGC, University of British Columbia

Primary Author: Kennedy Borle,

Author 2: Jehannine Austin,

Author 3: Skye Barbic,

Presenting Author: Kennedy Borle,

Background: In genetic counseling research, the Genetic Counseling Outcome Scale (GCOS) is becoming widely used to measure empowerment. Although the GCOS was developed and validated in a clinical genetics setting, there is little psychometric data about the instrument and Rasch Measurement Theory (RMT) has not been applied. The measurement model underpinning RMT has potential to support the clinical relevance of GCOS scores, thereby advancing an evidence-based approach to measuring empowerment in genetic counseling. Purpose: To use RMT to explore how the scales psychometric properties of the GCOS could be fine-tuned for measuring empowerment in genetic counseling.

Methods: We used retrospective data from a clinic in which the GCOS was routinely administered before (T1) and one-month after (T2) a psychiatric genetic counseling appointment. We tested the psychometric quality of the items using methods guided by RMT. Specifically, we tested the ordering of response option thresholds, fit, spread of the item locations, residual correlations, person separation index (PSI), and stability across time. Results: 235 participants (avg age: 39.4 years (SD=12.1), 82% female) completed the GCOS at T1 and T2. The original 24 items showed poor overall fit to the Rasch model, with 23/24 items showing statistical and graphical evidence of misfit. Fit was improved by collapsing response scale to three categories and removing eight items. The final 16 items showed excellent overall fit to the Rasch model ($\chi^2=119.9$, df=112, $p=0.29$), high reliability ($r_p=0.85$), an ordered response scale structure, and no item bias for gender, age, or ethnicity. The set of items showed strong evidence for picking up genetic counseling related change (mean =0.91 logits).<br />

Conclusions: These data support a set of 16 items to measure a uni-dimensional construct of empowerment in this context. Collectively, the 16-items demonstrated high sensitivity to pick up change over time. Opportunity exists to revisit the original 24-item set to address the anomalies revealed by the RMT analysis and refine the GCOS.
Closing the Disparity Gap: Alternative Service Delivery Models as an Opportunity to Increase Access to Genetic Testing in Underrepresented Groups

**Platform Presentations: Diversity and Access**

*Submitter: Lauren Ryan, MS, LCGC, Color Genomics*

*Presenting Author: Lauren Ryan, MS, LCGC, Color Genomics*

*Primary Author: Lauren Ryan, MS, LCGC, Color Genomics*

*Author 2: Anjali Zimmer, Ph.D., Color Genomics*

*Author 3: Cynthia L. Neben, Ph.D., Color Genomics*

*Author 4: Alicia Y. Zhou, Ph.D., Color Genomics*

**Introduction:** Traditionally, access to genetic counseling and testing has been largely restricted to affluent and urban populations. However, as demand for these services grows, the field is developing alternative service models to accommodate broader populations. Here, we describe the model of testing at one clinical laboratory, Color Genomics, that includes testing through a traditional model, ordered by the client’s own healthcare provider (traditional), and testing of two unique populations: people who received testing as an employee benefit (benefits) and people who self-initiated with an independent provider (independent).

**Methods:** We analyzed 52,752 individuals who underwent testing with a 30-gene NGS panel for hereditary cancer risk. All tests were ordered by a healthcare provider and included access to complimentary, telephone-based genetic counseling.

**Results:** The average age in the benefits cohort was lower compared to independent or traditional cohorts (40.0 vs. 48.6 vs. 51.7 years), as were the rates of personal diagnoses of cancer (3.9% vs. 19.6% vs. 44.8%), highlighting the opportunity to provide genetic information when there is the greatest potential for risk reduction. Benefits had a higher proportion of males (49.3%) compared to independent (19.2%) or traditional (15.9%) cohorts, despite most genes on the panel affecting risk for both sexes. The benefits cohort was more ethnically diverse (43.9% non-Caucasian) compared to independent (25.3%) or traditional (33.9%) cohorts. Positive rates were lower in benefits (5.8%) but similar in independent (10.2%) and traditional (11.7%). Rates of variants of uncertain significance (VUS) were similar (22.0% benefits, 18.3% independent, 20.3% traditional).

**Conclusions:** Taken together, these data support the likelihood of high clinical benefit to broader populations. By adding alternative service delivery models, clinical laboratories such as Color enable self-selection of genetic testing uptake and present opportunities to increase access and diversity in the testing population across age, sex, and ethnicity.

UNDERSTANDING BARRIERS TO GENETIC TESTING FOR SICKLE CELL TRAIT: THE AFRICAN-AMERICAN MALE PERSPECTIVE

**Platform Presentations: Diversity and Access**

*Submitter: Shandrea Da'chelle Foster,*

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Primary Author: Shandrea Da'chelle Foster,

Author 2: Debera Zvejnieks, USC Genetic Counseling Program

Author 3: Yvonne Donald, James R. Clark Memorial Sickle Cell Foundation

Author 4: Christopher Mazoue, USC Orthopedic Surgery

Presenting Author: Shandrea Da'chelle Foster,

Research has shown a reluctance in African-American males to pursue testing for sickle cell trait. Few studies have tried to discern what barriers are contributing to this issue within the African-American male community. Research suggests a lack of knowledge may be the biggest contributing factor. This study hypothesized there would be a significant difference in knowledge of sickle cell trait based on educational level, age, and health beliefs. African-America male participants (N=116), ages 18 and over, completed a questionnaire assessing knowledge, risk perception, health beliefs, barriers, and motivating factors within the context of sickle cell trait. One-way and two-way analysis of variance identified age as an influential factor. Results showed a significant interaction between age and knowledge of sickle cell trait and sickle cell disease (p = .009). Factors including perceived discrimination, perceived risk of sickle cell trait based on parent report, and sentiments on playing sports with sickle cell trait were all influenced by age (all p < 0.05). Health beliefs such as having tattoos or piercings and getting annual check-ups with a primary care physician were also influenced by age (both p < 0.02). The most significant barrier identified was a lack of information about testing options from primary care physicians, while the largest motivating factor for testing was for personal health reasons. Findings from this study could aid genetic counselors with strategies to increase sickle cell trait testing in African-American men. Thereby, increasing awareness of sickle cell trait in the community for informative health and reproductive outlook.

Meeting the needs of Low Health Literacy patients in the Era of Precision Medicine: A Pilot Intervention to Improve Patient-Provider Communication in Cancer Genetic Counseling

Platform Presentations: Diversity and Access
Submitter: Galen Joseph, University of California, San Francisco

Presenting Author: Galen Joseph, University of California, San Francisco

Author 2: Rena Joy Pasick, University of California, San Francisco

Author 3: Dean Schillinger, University of California, San Francisco

Author 4: Claudia Guerra, University of California, San Francisco

Primary Author: Galen Joseph, University of California, San Francisco
Genomic literacy is necessary to realize the promise of Genomic Medicine, particularly in the context of efforts to increase participation of diverse populations in genomics research and clinical practice. We present results of a pilot intervention to improve oral communication between genetic counselors (GCs) and their low health literacy (LHL) patients. The intervention consisted of: communication workshop curriculum development and evaluation; 2-month post-workshop interviews with participating GCs (n=9) about their efforts to apply LHL communication strategies in practice; observations of counseling sessions (n=24) with 2 GC workshop participants and post-counseling patient interviews (n=9). The 4.5-hour workshop presented evidenced-based strategies for effective communication with LHL patients (e.g. Plain Language, Teach-back), and exercises to practice adapting them to the counseling context. GCs reported appreciating the opportunity to refine their communication skills; however, they found techniques like plain talk and teach-back challenging to adopt given their training and communication habits. GCs also raised concerns about achieving informed consent and providing scientifically accurate information when using plain language, but were pleased that reducing the quantity of information they conveyed allowed more time for psychosocial counseling. Observations and patient interviews showed positive outcomes for patients who clearly understood the implications of the test and the next steps, and who expressed satisfaction with the counseling. These findings are the starting point for a RCT that will compare “traditional” genetic counseling with a “modified” protocol incorporating LHL strategies for returning exome sequencing results to diverse patients as part of the CSER2 (Clinical Sequencing Evidence-Generating Research) consortium. If proven beneficial, we will work with GC training programs and practicing GCs to adopt these modified practices to ensure that the benefits of genomics reach all populations and do not exacerbate existing health disparities.

Attitudes and Beliefs of the Amish and Mennonite Communities Towards Medical Photography in the Context of Facial Dysmorphology Novel Analysis

**Platform Presentations: Diversity and Access**

*Submitter: Jillian Lineburg, Arcadia University*

*Presenting Author: Jillian Lineburg, Arcadia University*

*Primary Author: Jillian Lineburg, Arcadia University*

*Author 2: Karlla Brigatti MS, LCGC, The Clinic for Special Children*

*Author 3: Lisa Kessler MS, LCGC, Genetic Counseling Program, Arcadia University*

Recent advances in medical photography pose new ethical questions for the field. Among such advances is Face2Gene, a suite of phenotyping applications using facial recognition analysis to supply possible
diagnoses. The primary aim of this study was to assess attitudes toward medical photography in the Old Order Amish and Mennonite (Plain) communities of Lancaster County within the context of use for phenotyping software. The Plain communities often eschew portrait photography in accordance with their cultural practices of humility and emphasis on community. The secondary aim of this study was to obtain photographs for use in training Face2Gene on two conditions with distinctive physical features. Interviews were conducted with parents of individuals with Cortical Dysplasia- Focal Epilepsy Syndrome (CDFE) and Polyhydramnios, Megalencephaly and Symptomatic Epilepsy (PMSE). Both conditions are found in Plain communities and in the general population. Thirteen individuals participated in a face-to-face interview that explored preferences, comfort, and attitudes about medical photography. Eleven participants consented to medical photography. Responses were recorded, transcribed, and coded for common themes. Four themes emerged: trust, confidentiality, relevance, and values. Trust in medical providers influenced participant preference for methods of medical photography. Participants felt a desire to uphold the privacy of the individual and security of their photographs. Furthermore, there was greater acceptance of photography if it was directly relevant to the patient’s care. Though it competes with other cultural values that speak against photography, altruism emerged as an important motivator for participation in medical photography. Further research about medical photography in the digital age is needed to elucidate preferences, attitudes, and beliefs in other cultures. However, this study contributes to the foundation for future research that would make possible the creation of ethical guidelines and best practices for medical photography.

Geometric Inclusivity: An assessment of current practices in pedigree nomenclature for patients identifying as transgender and gender nonconforming

Platform Presentations: Diversity and Access

Submitter: Liz Sheehan,

Presenting Author: Liz Sheehan,

Primary Author: Liz Sheehan, Brandeis University

Author 2: Gayun Chan-Smutko, Brandeis University

Author 3: Robin Bennett, University of Washington

Author 4: Miles Harris, Mount Sinai Center for Transgender Medicine and Surgery

The healthcare community is attempting to expand its knowledge of lesbian, gay, bisexual, and transgender health; however, much of existing literature and research concentrates on fluidity in sexual orientation rather than gender identity. Both NSGC and the National Comprehensive Cancer Network (NCCN) have differing guidelines for acceptable pedigree symbols to represent transgender patients and minimal recommendations for gender nonconforming (GNC) patients. A key advantage to standardized pedigree nomenclature is consistency in interpretation of the family structure by providers. One potential barrier to uniform representation and consistent care for patients who identify as transgender
or GNC is the inconsistency of accepted pedigree symbols to represent them. We assess the variability of current pedigree symbol practice among genetic counselors and students as well as self-reported confidence in addressing their transgender and GNC patients’ psychosocial needs through a survey distributed through NSGC. Participants felt symbols more closely associated with recommendations set forth by NSGC (41.1%) and NCCN (29.7%) for transgender patients would be most appropriate and emphasized a desire to be affirming of their patient’s gender identity. We found a greater degree of variability in symbols representing a GNC patient, with 19.2% of participants selecting “other” and explaining they were unsure of the best choice. Overall confidence in addressing psychosocial needs was low. Fewer than 10% reported feeling “very confident” meeting psychosocial needs and this was positively correlated with prior education on transgender and GNC healthcare (p<.002). A high interest (99%) in further education demonstrates a recognition of self-education as an effective strategy for increasing awareness and improving competency. Renewed engagement with transgender and GNC communities on educational content as well as affirming approaches to pedigree nomenclature with an eye towards standardization is necessary for appropriate and consistent care.

Challenges to Informed Consent for Exome Sequencing: A Best Worst Scaling Experiment

Platform Presentations: ELSI
Submitter: Rachel Gore, ScM, University of Maryland School of Medicine
Presenting Author: Rachel Gore, ScM, University of Maryland School of Medicine
Primary Author: Rachel Gore, ScM, National Human Genome Research Institute, SBRB Branch
Author 2: John F. P. Bridges, PhD, The Ohio State University, Dept. of Biomedical Informatics
Author 3: Julie S. Cohen, ScM, CGC, Kennedy Krieger Institute
Author 4: Barbara B. Biesecker, MS, PhD, CGC, RTI, International

As exome sequencing expands as a diagnostic tool, patients and providers have voiced concerns about the breadth and scope of potential results. Genetic counselors report perceived challenges to prioritizing complex information during consent sessions. This study aimed to understand how genetic counselors approach the consent process and weigh the relative importance of its components. Best-worst scaling was used to characterize how genetic counselors prioritize essential elements of informed consent specific to exome sequencing. The development of a best-worst scaling experiment was informed by a systematic literature review and two focus groups. Choice sets were created using a balanced incomplete block design, where participants selected the most and least important element of informed consent in each set. Mediation analyses was used to assess whether responses were associated with previous experience ordering exome sequencing, perceived efficacy in consenting patients, and counselors’ tolerance for ambiguity. An online survey was distributed to all full members of the National Society of Genetic Counselors and completed by 342 recipients in a variety of practice specialties. Data
were analyzed using mean best-worst scores to summarize how often each object was selected as most and least important. Ranking of best-worst scores suggests that genetic counselors prioritize collaborative decision-making, assessing patient understanding, and managing expectations for results, with the least emphasis placed on discussing technological complexities. Stratified analyses by paired t-tests found that counselors with more experience ordering exome sequencing, and those reporting higher perceptions of patients’ ability to manage information were significantly more likely to prioritize discussion of variants of uncertain significance (p<0.05). Results convey counselors’ prioritization of individual patient needs for obtaining informed consent for exome sequencing, and that professional characteristics and attitudes may influence preemptive discussion of uncertain results.

Ethical Implications of Laboratory-Sponsored Items and Events for Genetic Counselors: An Exploratory Study

Platform Presentations: ELSI
Submitter: Arielle Flynn,
Primary Author: Arielle Flynn,
Author 2: Alexandria Meyer, Ambry Genetics
Author 3: Taylor Berninger, Augustana-Sanford Genetic Counseling GradProgram; USCDHealth
Author 4: Kate Partynski, St. Joseph Health
Presenting Author: Arielle Flynn, Augustana-Sanford Genetic Counseling Graduate Program

In this exploratory study, we sought to record and analyze the opinions of training and practicing genetic counselors from all specialties with regards to the gift-giving practices of genetics laboratories. In a 28-question survey sent through the NSGC listserv, 704 completed responses were received. Quantitative data was analyzed using descriptive statistics and comparisons with Chi-Square analysis. Respondent demographics appear to reflect NSGC reported demographics. Responses showed a diverse range of opinion and a concerning lack of knowledge regarding rules about accepting gifts within their own institutions and awareness of laws and regulations at any level. Participant knowledge of laws surrounding gift-giving varied; 16.8% reported knowing of laws, 26.4% reported no knowledge of laws, and 56.8% reported being unsure if there are any laws. Factors associated with reported knowledge of the existence of laws include current genetics laboratory employment, whether or not there is a requirement to report gifts, age, years working as a genetic counselor, and opinion on the need for maximum gift values. When asked their perception of gift-giving as a conflict of interest (COI), 56.8% of respondents view gift-giving as a COI and 43.2% do not. Several factors associated with individual opinion regarding this practice as a COI include opinions on the need for maximum gift values and need to report gifts, being required to report gifts, age, gender, and primary practice location. Based on an analysis of responses, we suggest an increase in education events and discussions to promote knowledge regarding legal, employer, and graduate program regulations involving laboratory gifts. We
also suggest implementation of education regarding the history of gift-giving in the medical sphere to give context to discussions surrounding gift-giving from laboratories to genetic counselors.

Outcomes of return of secondary findings among a multi-site study

Platform Presentations: ELSI
Submitter: Barbara Bowles Biesecker, PhD, Senior Health Policy Analyst, Research Triangle Institute, International

Presenting Author: Barbara Bowles Biesecker, PhD, Senior Health Policy Analyst, Research Triangle Institute, International

Primary Author: Barbara Biesecker, Research Triangle Institute, International

Author 2: Ragan Hart, University of Washington

Author 3: Leslie Biesecker, NHGRI, NIH

Author 4: Robert Green, Harvard University

Author 5: David Veenstra, University of Washington

Author 6: Jonathan Berg, University of North Carolina

Author 7: Lucia Hindorff, NHGRI, NIH

Return of secondary findings (SF) from genome sequencing, as recommended by the ACMG, offers patients the opportunity to manage elevated risks from identification of medically actionable variants. The clinical benefits of receiving these results depend on compliance with recommended health care. Genetic counselors consent participants to receipt of SF and help to evaluate those found to have them. Within the NIH Clinical Sequencing Exploratory Research consortium, 18 participants consented to be interviewed, comprising 10 adults and 8 parents of children who underwent sequencing across 9 institutes. An IRB-approved structured interview guide framed assessment of psychological reactions, clinical follow up and communication of results to at-risk relatives. For 15 interviewees, the secondary finding was unexpected. The importance of life context in which the SF was learned proved to be a key theme, notably among parents of an affected child. No participant voiced regret over learning of their SF. Thirteen interviewees pursued follow up with a health care provider; 7 with their primary care provider, and 6 met with a specialist as recommended. All 18 reported their SF to one or more first degree relatives. Eleven responded that no relative underwent testing related to the SF. None of the 18 interviewees reported pursuit of health care services beyond recommendations based on their SF. Rather, there was under compliance with recommended care. Together these findings provide early data that research participants manage secondary findings well, although further studies are needed. Genetic counselors will be essential to ensuring appropriate follow up care and counseling.
Adolescents share their views: a qualitative analysis of adolescents' preferences for learning genomic sequencing results

Platform Presentations: ELSI
Submitter: Josie Pervola,
Primary Author: Josie Pervola, College of Medicine, University of Cincinnati
Author 2: Melanie Myers, Division of Human Genetics, Cincinnati Children's Hospital
Author 3: Michelle McGowan, Cincinnati Children’s Hospital Medical Center, Ethics Center
Author 4: Cynthia A. Prows, Division of Human Genetics, Cincinnati Children's Hospital
Presenting Author: Josie Pervola, College of Medicine, University of Cincinnati

Purpose: The American College of Medical Genetics (ACMG) recommendations for the return of secondary results conflict with long standing recommendations to defer predictive testing for adult onset conditions for minors until the age of majority. The ACMG recommendations do support parents’ choices to opt in or out of secondary analysis for their child for 59 genes; yet there is no consideration of soliciting adolescents’ preferences and choices in these decisions. This study aimed to (1) explore the reasons adolescents choose to learn, or not learn, sequencing results for conditions that are or are not preventable, treatable, have adult-onset, and carrier-status and (2) describe the involvement adolescents want when making testing decisions.

Methods: After independently choosing the type of genomic research results they wanted to learn, adolescents and one of their parents were interviewed to explore the reasoning behind their choices. Interviews were audio-recorded and transcribed. Transcripts were analyzed using a constant comparative method, and deductive and inductive codes were used for thematic analysis. Results: Among 64 adolescents, aged 13-17, the most commonly excluded conditions were those not treatable (n=22, 71%) and not preventable (n=18, 58%). Three major themes emerged from adolescent discussions about why they made their choices: (1) actionability of information, (2) knowledge seeking, and (3) consideration of psychological impact. Reasons expressed among adolescents were similar, but adolescents who chose to exclude results placed greater emphasis on risk; whereas adolescents who chose to learn results paced greater emphasis on benefits. Nearly all adolescents (98%) wanted to be involved in the decision making process, and over half (n=34) wanted to make testing choices independently. Conclusions: Our research contributes empirical evidence to support professional guidelines about adolescents’ engagement and preferences in genetic testing decisions. Key words: adolescents, genomic sequencing results, preferences, predictive testing, qualitative

Moral Distress in Genetic Counseling
Platform Presentations: ELSI
Submitter: Erin Wadman,
Moral distress is the phenomenon whereby health care providers experience the inability to take action or act in morally appropriate ways when encountering a morally compromising situation. The identified correlation of moral distress to burnout and resignation in nursing and other health care fields has led to increasing attention and concern among health care professionals to identify the sources of moral distress, as well as find ways to alleviate it. An online mix-method survey was sent to NSGC members and used to gain information on (1) sources of moral distress, (2) emotions involved, (3) coping strategies, and (4) suggestions to alleviate it. The ProQOL 5 scale was included to measure genetic counselor compassion satisfaction, burnout, and secondary traumatic stress. Two hundred and thirteen genetic counselors completed the survey. Forty-eight percent of respondents experienced moral distress and fourteen sources were identified. The greatest sources were situations involving genetic testing, pregnancy termination, and finances. Those more likely to experience moral distress worked in a prenatal setting (35%), were over the age of 50 (26%) and worked for more than 21 years (24%). Genetic counselors were more likely to talk to a co-worker for support, and seek social support, address the source of the problem, and sustain self through working with patients as coping strategies. Most genetic counselors (16.7%) recommended talking to another genetic counselor to alleviate moral distress. Moral distress did not correlate with genetic counselor burnout, but did correlate with higher levels of secondary traumatic stress (P<.01). Thirty-two percent of genetic counselors considered leaving their specialty and 23% considered leaving their profession based on their experience(s) with moral distress. Our study establishes the existence of moral distress in the genetic counseling field and supports the need for coping strategies and recommendations in order to alleviate future genetic counselor moral distress.
A 32-year-old woman was referred for genetic evaluation and counseling by her PCP because testing performed by a direct to consumer (DTC) genetic testing company identified Y chromosome SNPs. Patient reported lack of menstrual periods, painful/failed gynecologic and sexual encounters. Physical examination revealed fatty breast tissue rather than true mammary development, axillary hair, normal external female genitalia, and pubic hair in a gynecoid pattern. FSH and LSH were consistent with post-menopausal levels and TSH level was normal. Family history was negative for features of an inherited disorder of sexual differentiation (DSD). Transabdominal ultrasound revealed an atrophic uterus and possible atrophic gonads. Cytogenetic analysis was ordered revealing a normal, male karyotype (20/20 cells). NGS panel was ordered and identified a likely pathogenic exon 7 deletion in NR5A1. Pathogenic variants in this gene have been associated with hypospadias, ambiguous genitalia, and rarely full sex reversal in 46,XY individuals. Early menopause has been associated with female carriers, which was consistent with our patient’s maternal family history. The case was complicated by various psychosocial aspects. The patient had a history of anxiety and major depressive disorder. She initiated DTC testing to learn more about her mental health, ancestry, and unique genetic traits. She was unprepared for a DSD diagnosis. She had unstable housing and transportation, limited telephone access, and significant mental health issues which interfered with result disclosure, understanding and coping with results, and subsequent scheduled surgeries. While the DSD diagnosis was beneficial to our patient’s physical health (risk-reducing surgery), it impacted her mental health and gender identity. As the availability of DTC testing grows, more incidental findings will be identified. This case illustrates the role of genetic professionals in confirming DTC testing results, creating a diagnostic plan, and providing psychosocial counseling.

A Pilot Study of CLIA-compliant Secondary Findings in Research Sequencing: Outcomes Amongst Recipients of Positive and Negative Reports

Platform Presentations: Incidental and Unexpected Findings
Submitter: Julie Chevalier Sapp, National Human Genome Research Institute

Presenting Author: Julie Chevalier Sapp, National Human Genome Research Institute

Author 2: Jennifer J. Johnston, Medical Genomics and Metabolic Genetics Branch, NHGRI

Author 3: Kate Driscoll, Medical Genomics and Metabolic Genetics Branch, NHGRI

Author 4: Alexis Heidlebaugh, Social and Behavioral Research Branch, NHGRI

Author 5: Ane Sargardia, Social and Behavioral Research Branch, NHGRI

Author 6: D. Nadine Dogbe, Social and Behavioral Research Branch, NHGRI

Primary Author: Julie C. Sapp, Medical Genomics and Metabolic Genetics Branch, NHGRI
Debate about the return of secondary findings from research exome/genome sequencing remains despite consensus in the clinical realm. This study piloted a process for returning CLIA-validated secondary findings to participants and described the outcomes of receiving such results. We developed a novel, research-clinical translational genomics process for CLIA-validated secondary findings analysis of research exome data and results return by a genetic counselor. Eleven intramural principal investigators at the National Institutes of Health implemented this process in their protocols over a two-year period. Nearly 1,200 individuals were sequenced, 14 positive secondary findings were validated and returned to 18 participants by one of two genetic counselors not involved in the primary protocols. Disclosures were performed primarily by phone, took an average of 55 minutes, and included obtaining a targeted family history and provision of specific referrals to genetic counselors in specialty clinics in the participants' local area. Follow-up interviews were performed with 13 participants after receipt of a positive report. There were no indicators of significant distress from the secondary findings. Eleven participants communicated their results to family members and 9 reported accessing recommended health care services. Further, a sample of 107 participants who received a negative secondary findings report returned via postal mail were surveyed four months after their result. Most demonstrated accurate understanding of the result and expressed reassurance (64%). However, a sizable minority (up to 17%) expressed some confusion regarding the distinction of primary from secondary findings. These findings contradict the assumption that participants will experience psychologic distress and pursue excessive health care utilization after receipt of secondary findings. These outcomes also demonstrate a tractable coupling of clinical and research genomic sequencing and provide evidence for how genetic counselors may play an integral role in large-scale genomics research.

**Proactive Genetic Screening in a primary care setting reveals surprising results**

**Platform Presentations: Incidental and Unexpected Findings**

*Submitter: Allison Janson Hazell, Genetic Counsellor, Medcan Clinic*

*Primary Author: Allison Janson Hazell, Genetic Counsellor, Medcan Clinic*

*Author 2: Jessica Gu, Medcan*

*Author 3: Monica Zarb, Medcan*

*Author 4: Jill Furnival, Medcan*
**Author 5: Lea Velsher, Medcan & North York General Hospital**

**Author 6: James Aw, Medcan**

**Presenting Author: Allison Hazell, Medcan**

Introduction: Advances in genomic research and DNA sequencing technologies have revolutionized our ability to offer large gene panels at reasonable costs. Limited data exist on the true prevalence and penetrance of “rare” actionable genetic conditions in the unselected (or “healthy”) population. Initial studies, largely based on the 2013 ACMG recommendations for the return of incidental findings, suggest that 1 to 9% of individuals harbor pathogenic or likely pathogenic mutations in medically actionable genes. Additionally, evidence continues to support the clinical utility of genetic testing in determining appropriate medical management for these “healthy” individuals.

Purpose: Report on our experience with elective genetic screening and our results to date, including: family history, specific mutations identified, actionable findings, cascade screening, challenges in determining penetrance and screening protocols.

Methods: Medcan, a preventive health and wellness clinic in Toronto, Canada, serves over 20,000 patients annually. In September 2017, we began offering a proactive 139-gene panel (based on ACMG59 with additional actionable genes) through Invitae. The laboratory reports only pathogenic and likely pathogenic variants. Medcan clients are offered our “Proactive Genetic Screening (PGS)” service during their annual health assessment for an additional fee, and meet with a genetic counselor for pre- and post-test counseling.

Results: As of May 8, 2018, 590 clients have undergone PGS and 97 are positive for a health-related risk; an additional 400 clients are anticipated by November 2018. Our positive rate is higher than expected at 16%, and has resulted in changes to screening recommendations for 80% of positive clients. Of the positive cancer- and cardiac-related results, 34% and 25% reported relevant family history, respectively.

Conclusion: Our experience with elective genetic testing in a high volume primary care setting provides insight into expectations and recommendations for the future of genomic screening in the “healthy” population.

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**A Comprehensive Look at the Neurodevelopmental Outcomes and the Effects of Early Hormonal Therapy (EHT) in a Large, Prenatally Diagnosed Population of Boys with 47,XXY (Klinefelter syndrome)**

**Platform Presentations: Incidental and Unexpected Findings**

Submitter: Carole Samango-Sprouse, Ed.D., The Focus Foundation

Primary Author: Carole Samango-Sprouse, Ed.D., The Focus Foundation

Presenting Author: Carole Samango-Sprouse, Ed.D., The Focus Foundation

Author 2: Selena Chea, The Focus Foundation

Author 3: Teresa Sadeghin, The Focus Foundation

Author 4: Dr. Andrea Gropman, Children’s National Health System
There have been significant advances in procedures for early detection and innovations for the care of boys with 47,XXY. This occurs 1:660 and presents with language-based learning disorders, intact spatial cognition, and executive dysfunction. There have been several prospective studies involving large, prenatally diagnosed 47,XXY cohorts from the 1970-80s, but an updated and comprehensive study on these boys is necessary to provide information on the early childhood trajectory and potential effects of EHT.<br />

171 prenatally identified boys with 47,XXY were referred for neurodevelopmental evaluations between 0-3 years of age. This cohort was segregated by EHT status: EHT (n=65) and non-EHT (n=106), and compared across scales of neurodevelopmental domains: Preschool Language Scales (PLS)'s auditory comprehension (AC) & expressive communication (EC); Bayley Scales of Infant Development (BSID)'s mental development index (MDI) & psychomotor development index (PDI); Early Language Milestone Scale (ELM)'s expressive (EL) & receptive (RL) language; and Expressive One Word Picture Vocabulary Test (EOWPVT)'s EL.<br />

The EHT group showed significant differences on the PLS' AC & EC (P<.0001) when compared to the non-EHT. On BSID, treated boys had significantly higher MDIs & PDIs (P<.0001) than untreated. The EHT group also showed significantly improved EL (P=.0017) & RL (P=.0015) on the ELM, and EOWPVT (P=.037).<br />

The number of families who receive a fetal, neonatal, or early childhood diagnosis of 47,XXY is increasing due in large part to the greater use of noninvasive prenatal testing (NIPT). It is critical that providers have a knowledge base that will enhance delivery of current, accurate information. This study provides further support that EHT has potentially positive effects on the neurodevelopment in boys with 47,XXY. Early and targeted interventions are key aspects of counseling that will have the potential to alter the long-term prognosis of boys with 47,XXY. Future study is warranted to elucidate the optimal timing and dosage for treatment during early childhood years.

Counseling Conundrum: Sex Discordance Identification Following Preimplantation Genetic Testing for Aneuploidy (PGT-A) or Noninvasive Prenatal Testing (NIPT) Using SNP-Based Methodologies

Platform Presentations: Incidental and Unexpected Findings

Submitter: Katherine L. Howard, Natera

Primary Author: Katherine L. Howard, Natera

Presenting Author: Katherine L. Howard, Natera

Author 2: Melissa Maisenbacher, Natera, Inc.

Author 3: Katrina Merrion, Natera, Inc.

Author 4: Wendy DiNonno, Natera, Inc.

INTRODUCTION: PGT-A and NIPT determine fetal sex with high accuracy before/during pregnancy. If additional prenatal screening or clinical presentation at birth suggests sex discrepancy, medical follow-up is needed to rule out a disorder of sexual differentiation.<br />

OBJECTIVE: Describe reported cases
and etiologies of sex discrepancy after PGT-A or NIPT.<br />METHODS: Provider reported cases of possible sex discrepancy after PGT-A or NIPT at a single lab were retrospectively reviewed. For PGT-A, genotyping was performed using Illumina Cyto12 SNP-based microarray with informatics. For NIPT, cell-free DNA was isolated and amplified by massively-multiplexed PCR targeting 13,392 SNPs covering chromosomes 13, 18, 21, X and Y. Only cases with complete evaluation to identify a cause for discrepancy were included.<br />RESULTS: Four of 23,297 (0.02%) PGT-A cases and 49 of 1,081,541 (0.005%) NIPT cases had discrepant sex suspected pre/post-delivery. For PGT-A, 2 (50%) resulted from incorrect embryo transfers (biological parental match but not the intended embryo) and 2 (50%) resulted from natural conception around the time of embryo transfer. For NIPT, phlebotomy labeling errors comprised 6 (12.2%); confined placental mosaicism, 10 (20.4%); ultrasound errors, 13 (26.6%); and disorders of sexual development (DSD), 20 (40.8%). DSDs diagnosed include; 5 cases of ovotesticular (chimeric/gonadal dysgenesis), 4 cases of 46,XX (male/ambiguous genitalia; 1 congenital adrenal hyperplasia) and 11 46,XY (female/ambiguous genitalia; 6 with androgen insensitivity syndrome). No discrepancies were due to lab error for PGT-A/NIPT cases.<br />CONCLUSIONS: A SNP-based methodology can eliminate sample swap, natural conception around the time of embryo transfer and vanished twin as causes of discordant sex after PGT-A or NIPT. Other causes of discordant sex can include ultrasound errors, PGT/NIPT result errors, embryo mosaicism, confined placental mosaicism and various DSDs. A thorough investigation can provide reassurance and guide appropriate medical management and counseling about cause and recurrence risk.

Genetic testing of patients with cerebral palsy reveals one-third of cases have a monogenetic cause and a significant recurrence risk

**Platform Presentations: Neuromuscular/Pysciatric**

**Submitter:** Claire Teigen, GeneDx  
**Primary Author:** Claire Teigen, GeneDx  
**Presenting Author:** Claire Teigen, GeneDx  
**Author 2:** Houda Zghal Elloumi, GeneDx  
**Author 3:** Francisca Millan Zamora, GeneDx  
**Author 4:** Julie Scuffins, GeneDx  
**Author 5:** Dianalee McKnight, GeneDx

Cerebral palsy (CP) is a broad diagnostic term encompassing disorders impacting movement and posture caused by changes in the fetal or infantile brain (Rosenbaum et al., 2007). CP is a common clinical diagnosis, with an incidence of 1 in 500 births, and therefore is often found in a family history (Oskoui et al., 2013). However, CP may not be addressed in genetic counseling as it is commonly attributed to complications at birth rather than to a genetic etiology (MacLennan et al., 2018).<br />We aimed to
establish the contribution of genetic causes to CP. Results from exome sequencing (ES) of 1346 patients with CP were retrospectively reviewed. Overall, ES yielded a positive result indicating a genetic etiology in 32.7% of cases (440/1346). Testing of a proband concurrently with parents (ES-trio) had a significantly higher diagnostic yield (35.3%) compared to proband-only testing (23.3%; p<0.005). Positive findings were reported in 225 different genes, indicating the tremendous genetic heterogeneity of CP. Among the positive results, in 65.2% the causative variants were autosomal dominant, 20.7% autosomal recessive, and 13.4% X-linked. ES-trio testing revealed that the majority of patients diagnosed with an AD or XL disorder (71.4%) had de novo variants. These finds indicate a significant recurrence risk in 32% (139/440) of positive cases: 21% (91/440) of probands had biallelic variants, 3% (15/440) had maternally inherited X-linked variants, and 4% (23/440) had an inherited autosomal dominant variant.<br />Overall, a trio-based comprehensive approach to genetic testing for CP can help to identify a genetic etiology in approximately one-third of cases. Such findings can be informative for genetic counseling for families by not only providing an accurate recurrence risk but also information on prognosis, adjusted therapies, and management options. <br />Rosenbaum et al. (2007) Dev Med Child Neurol Suppl 109 :8-14 (PMID: 17370477); Oskoui et al. (2013) Dev Med Child Neurol 55 (6):509-19 (PMID: 23346889); MacLennan et al. (2018) Dev Med Child Neurol 60 (2):209-210 (PMID: 29336076)

Open Communication of Duchenne Muscular Dystrophy Facilitates Disclosure Process by Parents to Unaffected Siblings

Platform Presentations: Neuromuscular/Pysciatric

Submitter: Laura Anne Goodell,

Presenting Author: Laura Anne Goodell,

Primary Author: Laura Anne Goodell, University of Maryland School of Medicine

Author 2: Katharine Bisordi, University of Maryland School of Medicine

Author 3: Elizabeth Ulm, Cincinnati Children’s Hospital Medical Center

Author 4: Rachel Nusbaum, University of Maryland School of Medicine

Duchenne muscular dystrophy (DMD) is a progressive childhood onset neuromuscular disease with no known cure. There is extensive literature about the impact of a diagnosis on the psychosocial well-being of unaffected siblings, with a need for additional research to provide information about optimal ways to disclose this information to unaffected children. We sought to explore the parental experience disclosing a sibling’s diagnosis of DMD to unaffected children who were age 8-17 years old either at the time of their sibling’s diagnosis or presently. Parents were recruited through Maryland Muscular Dystrophy Association, Parent Project Muscular Dystrophy, and Cincinnati Children’s Hospital Medical Center Neuromuscular Center. An existing interview guide, rooted in family communication, was modified to incorporate themes and topics found in literature specific to DMD and disclosure to unaffected siblings. We qualitatively explored these experiences through semi-structured interviews and
performed thematic analysis using a coding system to identify overarching themes and subthemes. Several main themes regarding challenges to the disclosure process emerged. We identified the following themes in procedural aspects of disclosure: lack of provider support, importance of the DMD community, and open and gradual timeline of disclosure. Under emotional experiences, we identified these themes: overwhelming nature, elements of surprise disclosure, and balancing parental and sibling needs. Most questions from unaffected siblings related to procedural elements of care such as treatments and equipment. Additional unanticipated themes emerged that may contribute to the knowledge of family culture surrounding DMD: the complex role of Facebook as a family resource, deferring carrier testing for siblings, and inclusion of DMD in school projects. While the process of disclosure is complicated by a variety of factors such as lack of provider support and overwhelming emotional burden, families highlight the importance of open communication in discussion with unaffected children.

Survey Validation for Screening of Hypermobile Ehlers-Danlos Syndrome

Platform Presentations: Neuromuscular/Psychiatric
Submitter: Megan Quinlan, Cleveland Clinic

Presenting Author: Megan Quinlan, Cleveland Clinic

Primary Author: Megan Quinlan,

Author 2: Lisa Martin, Cincinnati Children's Hospital Medical Center

Author 3: Lisa Berry, Cincinnati Children's Hospital Medical Center

Author 4: Jodie Johnson, Cincinnati Children's Hospital Medical Center

Author 5: Derek Neilson, Cincinnati Children's Hospital Medical Center

Introduction: Hypermobile Ehlers-Danlos Syndrome (hEDS) is the most common inherited connective tissue condition and individuals with the condition experience systemic effects. Although it often runs in families, there is no known genetic etiology for hEDS. Unfortunately, diagnosis for hEDS is based on clinical evaluation making family history studies difficult. To clarify the etiology of hEDS, development and validation of self-administered tools are needed. <br />

Methods: We developed a self-administered survey comprised of photographs and questions capturing the criteria for the 2017 International Classification for hEDS. We invited patients with clinically diagnosed hEDS and their family members to fill out our survey. To validate our survey, we compared our survey estimates of hEDS diagnosis status to retrospective clinical diagnoses by medical record review. Specifically, we compared Beighton scores individual diagnostic features, and overall diagnosis status for individuals with or without hEDS. <br />

Results: Sixty-two participants filled out the survey including 30 patients. Our survey-estimated Beighton scores were consistent with clinical scoring, generally being 1-point lower. The features that were best predictors of hEDS were 2017 Classification Criterion 1 and Criterion 2 Feature C. Specifically, participants with hEDS were more likely to have chronic pain and a positive 5-point questionnaire
Overall, our survey correctly classified 85% (22/26) of participants. Conclusions: With modifications, our survey tool could be used as a screening tool for larger studies assessing relatives’ diagnosis status. Similarly, the survey could be used in a clinical setting to determine which individuals are most likely to meet criteria for a diagnosis of hEDS. Keywords: Hypermobile Ehlers-Danlos Syndrome, Ehlers-Danlos Syndrome Hypermobility Type, hypermobility, survey, screening, inheritance

The role of MTHFR C677T variants in postpartum psychopathology: A prospective study of at-risk women to inform prenatal genetic counseling practice

Platform Presentations: Neuromuscular/Pysciatric
Submitter: Emily Morris, University of British Columbia / Provincial Health Service Authority

Primary Author: Emily Morris, University of British Columbia / Provincial Health Service Authority

Presenting Author: Emily Morris, University of British Columbia / Provincial Health Service Authority

Author 2: Catriona Hippman, University of British Columbia

Author 3: Caitlin Slomp, University of British Columbia

Author 4: Angela Inglis, Provincial Health Services Authority

Author 5: Prescilla Carrion, University of British Columbia

Author 6: Rolan Batallones, University of British Columbia

Author 7: Arianne Albert, Women's Health Research Institute

Author 8: Colin Ross, University of British Columbia

Author 9: Roger Dyer, University of British Columbia

Author 10: Jehannine Austin, University of British Columbia

Background: Postpartum mental illnesses (PPMI) are urgent health concerns, but their etiology is not well understood. Low red blood cell (RBC) folate has been associated with psychiatric disorders, and one study suggested that perinatal folic acid supplementation can improve maternal long-term depression symptomatology. The MTHFR C677T variant influences folate metabolism, and some studies have implicated it in psychiatric disorders, making it a strong candidate gene for PPMI. Objective: To explore the relationship between MTHFR C677T genotype, RBC folate levels, and PPMI (depression, mania, and psychosis) in women with a history of mood or psychotic disorders. Hypothesis: In the first three months postpartum TT homozygous women would have increased symptoms of depression, mania, and psychosis, compared to CC homozygotes. Methods: We recruited a prospective cohort (N=365) of pregnant women (psychiatric history confirmed by the Structured Clinical Interview for the DSM-IV
(SCID-IV)). At 3 times postpartum, we administered the Edinburgh Postnatal Depression Scale (EPDS), Clinician-Administered Rating Scale for Mania (CARS-M) and the Positive and Negative Symptom Scale (PANSS) for psychosis and obtained blood samples to measure RBC folate and determine genotype. We investigated the interaction between RBC folate and genotype on the highest EPDS, and CARS-M scores with linear regression, and the proportion of PANSS above cut-off with logistic regression. Results: There was no significant interaction between RBC folate and MTHFR genotype on highest EPDS (p=0.19), CARS-M (p=0.09), or PANSS (p=0.14). There was also no difference between genotypes for EPDS CARS-M or PANSS (all p>0.05) controlling for RBC folate, and no relationship between RBC folate and any of the scales on its own (all p>0.05). Conclusion: Our data do not support a relationship between MTHFR, folate, and risk for postpartum psychopathology in at-risk women, at least in the context of food fortification/supplement use. These data can inform genetic counseling practice.

CYP2C19 genotype is associated with tolerability and response outcomes in es/citalopram-treated youth with anxiety and/or depressive disorders

Platform Presentations: Neuromuscular/Pysciatic
Submitter: Stacey Aldrich, MS, Washington University in St. Louis
Presenting Author: Stacey Aldrich, MS, Washington University in St. Louis
Primary Author: Stacey Aldrich, University of Cincinnati
Author 2: Ethan Poweleit, Cincinnati Children’s Hospital and Medical Center
Author 3: Cynthia A. Prows, Cincinnati Children’s Hospital Medical Center
Author 4: Lisa J. Martin, Cincinnati Children’s Hospital Medical Center
Author 5: Jeffrey R. Strawn, Cincinnati Children’s Hospital Medical Center
Author 6: Laura B. Ramsey, Cincinnati Children’s Hospital Medical Center

In children and adolescents, antidepressants are commonly used to treat anxiety and depressive disorders, but most pharmacogenetic studies to date have focused on adults when investigating the association between CYP2C19 genotype and treatment outcomes with escitalopram and citalopram (es/citalopram). CYP2C19 encodes the main enzyme responsible for metabolizing the two antidepressants into therapeutically inert metabolites. DNA sequence variants directly impact the enzyme’s efficacy, with variants categorized as no function, normal function or increased function alleles. In adults, slower CYP2C19 metabolizers have higher blood concentrations of es/citalopram at an equivalent dose, while faster CYP2C19 metabolizers have lower blood concentrations. As a result, slower metabolizers may be at higher risk for side effects and faster metabolizers at higher risk for treatment failure. Our retrospective study analyzed electronic medical record data from 263 youth <19 years with anxiety and/or depressive disorders who were prescribed es/citalopram (n=263). Slower CYP2C19 metabolizers experienced more side effects than faster metabolizers during es/citalopram treatment.
A higher percentage of slower metabolizers discontinued es/citalopram compared with normal metabolizers (p<0.01). Meanwhile, faster metabolizers responded more quickly to es/citalopram (p<0.01) and trended toward fewer days spent in inpatient hospitalization (p=0.06). The results highlight a disparity in es/citalopram treatment outcomes when a standardized dosing approach is used without consideration of CYP2C19 genotype in pediatric patients with anxiety and/or depressive disorders. Larger studies are needed to confirm these findings and to assess whether personalizing the dose of es/citalopram based on CYP2C19 genotype enhances treatment outcomes. These results may aid genetic counselors when advising clinicians and families on the implications of CYP2C19 test results in this setting, especially as many pediatric genetic disorders have higher rates of anxiety and depressive disorders.

A Novel Automated Service Delivery Model for Negative NIPT Results in the Era of Technology Enabled Healthcare

**Platform Presentations: Service Delivery**

**Submitter:** Cassidi Dailey Kalejta, Metis Genetics

**Primary Author:** Cassidi Dailey Kalejta, Metis Genetics

**Presenting Author:** Cassidi Dailey Kalejta, Metis Genetics

**Author 2:** Sonja Eubanks Higgins, MS, LCGC, Metis Genetics

**Author 3:** Hilary Kershberg, MS, LCGC, Southern California Permanente Medical Group

**Author 4:** Jeff Greenberg, Southern California Permanente Medical Group

**Author 5:** Monica Alvarado, MS, LCGC, Southern California Permanente Medical Group

**Author 6:** Kerry Cooke, Metis Genetics

**Author 7:** Sucheta Bhatt, MD, Illumina

**Author 8:** Denise Bulpitt, BSN, RN, Metis Genetics

**Author 9:** Jamie Armour, MS, LCGC, Metis Genetics

**Author 10:** Bassem Bejjani, MD, Metis Genetics

**Author 11:** Shawnia Ryan, MS, LCGC, Metis Genetics

**Author 12:** Amanda Elms, Metis Genetics

**Introduction:** As the demand for genetic counselors (GCs) increases, alternatives to traditional service delivery models are needed. Recent studies show, patients increasingly prefer technology enabled healthcare. Patients are relying less on healthcare providers (HCPs) and instead are using various
sources to obtain healthcare information, including non-clinical and online content. We propose an automated method of delivering post-test education and disclosure of negative Non-Invasive Prenatal Testing (NIPT) results to ensure appropriate patient support with clinically accurate information.<br />

Methods: Pregnant women defined as high-risk registered with Genetics Maven (Maven), a proprietary HIPAA-compliant web-based portal, to receive their negative NIPT result through our automated process. When the negative test result was available, patients watched a 2-minute educational video, answered three comprehension questions, and consented to downloading their result only if they wanted to learn the predicted sex of the fetus.<br />

Results: From 04/2017 – 04/2018, 3901 patients viewed the educational video and downloaded their test result. Of these patients, 2 (0.05%) answered 0/3 questions correctly, 32 (0.82%) answered 1/3 questions correctly, 545 (13.97%) answered 2/3 questions correctly, and 3322 (85.16%) answered 3/3 questions correctly. Patients completed the automated process at all hours of the day with 87% downloading their result outside of typical HCP office hours.<br />

Discussion: This data supports the effective communication of negative NIPT results to patients through this automated delivery model. Patients demonstrated a clear understanding of the material presented and, if desired, accessed the educational materials multiple times. Patients engaged at a time of their choosing without an office visit. Further studies could reveal if this automated process of result disclosure combined with clinically accurate video education is equally effective for other genetic tests.

Barriers associated with uptake of genetic counseling and testing in a randomized study of remote genetic services compared to usual care in community practices without genetic providers.

Platform Presentations: Service Delivery
Submitter: Cara Cacioppo, MS, LCGC, University of Pennsylvania Telegenetics Program

Presenting Author: Cara Cacioppo, MS, LCGC, University of Pennsylvania Telegenetics Program

Primary Author: Cara N. Cacioppo, University of Pennsylvania

Author 2: Brian Egleston, Fox Chase Cancer Center

Author 3: Colleen Burke Sands, University of Pennsylvania

Author 4: Syeda Abbas, University of Pennsylvania

Author 5: Linda Patrick-Miller, University of Chicago Medical Center

Author 6: Neeraja Reddy, Mapmygenome

Author 7: Elisabeth McCarty-Wood, University of Pennsylvania

Author 8: Susan M. Domchek, University of Pennsylvania
Background: Providing telegenetic services by phone or real-time videoconference (RVC) for patients at community practices without access to genetic providers could increase access to genetic testing. Uptake of genetic services via telegenetics compared to usual care options has not been reported. Methods: To date, 106 patients at 6 community practices were randomized to remote genetic counseling (35 phone; 31 RVC) and 40 to usual care. Primary outcomes were uptake of genetic counseling and testing at 6 months. We used Fisher's exact tests, T-tests, logistic regressions, and thematic coding for analyses. Results: To date, 79% (52/66) of participants in the remote services arms had pre-test genetic counseling as compared to 5% (2/40) in the usual care arm (p < 0.001). 56% (37/66) in the remote services arm completed genetic testing and 4 genetic carriers were identified as compared to 12.5% (5/40) and 0 carriers in the usual care arm (p < 0.001 for genetic testing uptake). Three common themes emerged around barriers and challenges to accessing genetic services for participants in the usual care arm who have not received genetic testing at six months: lack of information about how to access genetic counseling/testing (23%; 8/35), concerns about insurance coverage/potential cost (14%; 5/35), and competing priorities, (i.e., limited time due to other medical and treatment appointments) (14%; 5/35). Conclusions: These data suggest that offering telegenetic services may increase the uptake of genetic counseling and/or testing and identification of genetic carriers in community practices without access to genetic services. Continued evaluation of the access barriers to genetic services in the community setting is critical to understanding uptake of genetic counseling and testing.

Genetic Education: Patient Satisfaction with a Prenatal Video Tool

Platform Presentations: Service Delivery
Submitter: Joan B. OLIVER, Integrated Genetics

Presenting Author: Joan B. OLIVER, Integrated Genetics

Primary Author: Joan B Oliver, Integrated Genetics

Author 2: Kristi Fissell, Integrated Genetics

Author 3: Lila Dayani, Integrated Genetics

In accordance with the NSGC Genetic Counselor Workforce Working Group goal of “identifying and integrating tools that increase efficiency and productivity of genetic counselors in clinical practice,” a team of genetic counselors from Integrated Genetics created genetic education videos targeted to patients without complex genetic risk factors. These videos were intended to augment a patient’s discussion with providers. They included basic elements of genetic screening and testing options: Video 1 covered prenatal screening and diagnosis of chromosome abnormalities; Video 2 covered carrier screening. Testing options were presented without test brand names. Concepts of inheritance and risk, screening versus diagnosis, and patient-based decisions and autonomy were conveyed via graphics and
narrated by an on-screen genetic counselor. The videos were piloted (Video 1: N=158 viewings; Video 2: N=33 viewings) in OBGYN or perinatology offices. A Likert scale measured 6 aspects of patient feedback. Responses to Video 1 and Video 2 respectively, found: 99%/100% agreed that “information was at a level I could understand;” 98%/100% agreed that “visual images helped me to understand;” 90%/94% agreed that “information helped me make decisions about testing options.” Viewer comments were elicited and revealed that the graphic depictions of complex genetic terminology and education on understanding risk were most helpful; others wanted a shorter video or wanted an individualized risk assessment. Both videos were subsequently modified based on the feedback. Our pilot demonstrated that videos performed at a high level of patient satisfaction, providing evidence that this tool could increase efficiency of GC services and enhance the patient experience. Areas of further study include evaluation of the lower scores related to patient decision-making to determine if content could be added to better facilitate this process.

Leveraging Scalable Genetic Counseling Tactics to Meet the Needs of a Statewide Genomic Screening Initiative

Platform Presentations: Service Delivery
Submitter: Kelly Moreland East, MS, CGC, HudsonAlpha Institute for Biotechnology

Presenting Author: Kelly Moreland East, MS, CGC, HudsonAlpha Institute for Biotechnology
Primary Author: Kelly East, MS, CGC, HudsonAlpha Institute for Biotechnology
Author 2: Ashley Cannon, PhD, MS, CGC, University of Alabama at Birmingham
Author 3: Meagan Cochran, MS, CGC, HudsonAlpha Institute for Biotechnology
Author 4: Anna Hurst, MD, MS, FACMG, University of Alabama at Birmingham
Author 5: Whitley Kelley, MS, CGC, HudsonAlpha Institute for Biotechnology
Author 6: Brandon Shaw, MS, CGC, University of Alabama at Birmingham
Author 7: Kevin Bowling, PhD, HudsonAlpha Institute for Biotechnology
Author 8: Kristina Emmerson, HudsonAlpha Institute for Biotechnology
Author 9: Candice Finnila, PhD, HudsonAlpha Institute for Biotechnology
Author 10: Sara Knight, PhD, University of Alabama at Birmingham
Author 11: Tom May, PhD, HudsonAlpha Institute for Biotechnology
Author 12: Irene Moss, University of Alabama at Birmingham
Author 13:
The Alabama Genomic Health Initiative (AGHI) was launched in 2017, and became one of the first state-wide, state-funded programs to bring genomic testing to a large, unselected population. Through AGHI, Alabama residents have access to a genotype-based screening test aimed at identifying known pathogenic variants in 59 genes found on the ACMG Secondary Findings v2.0 list. As of April 2018, 1,654 people have consented to be a part of the initiative. AGHI is a collaboration between the University of Alabama at Birmingham and the HudsonAlpha Institute for Biotechnology. A team of genetic counselors from both institutions work together to meet the educational and counseling needs of the program. Participants who receive a positive genotyping result confirmed in a CLIA-certified laboratory receive a personal phone call from an AGHI genetic counselor to discuss the result. To date, 1.1% have received a positive result, indicating the presence of a genetic risk factor. Pathogenic variants have been identified in 9 different genes, including APOB, BRCA1, BRCA2, LDLR, MYBPC3, MLH1, MYH7, PKP2, and RYR1. 50% of positive results have been unexpected – meaning there was little personal or family history associated with the risk factor identified. It is critical to attend to the needs of participants receiving a negative result. We have developed a process for quickly assessing personal and family history to guide follow-up after result disclosure. History is gathered during the enrollment process and reviewed by a genetic counselor. Internally developed criteria are used to flag individuals who may benefit from clinical genetics follow-up regardless of genotyping result. Individualized information about the suspicious family history and recommendations for follow-up are included within the AGHI result report. To date, 44% of all AGHI participants have been labeled with a “strong” personal or family history. In the era of cost-effective genomic testing, it is of increasing importance for genetic counselors to develop, evaluate, and share scalable service delivery models.

Cost-Savings and High Patient Satisfaction with Automated Disclosure of NIPT Results

Platform Presentations: Service Delivery
Submitter: Cassidi Dailey Kalejta, Metis Genetics
Primary Author: Cassidi Dailey Kalejta, Metis Genetics
Presenting Author: Cassidi Dailey Kalejta, Metis Genetics
Author 2: Sonja Eubanks Higgins, MS, LCGC, Metis Genetics
Author 3: Hilary Kershberg, MS, LCGC, Southern California Permanente Medical Group
Author 4: Jeff Greenberg, Southern California Permanente Medical Group
Author 5: Monica Alvarado, MS, LCGC, Southern California Permanente Medical Group
Author 6: Kerry Cooke, Metis Genetics
Author 7: Sucheta Bhatt, MD, Illumina
Introduction: Healthcare professionals (HCPs) spend valuable time and resources disclosing Non-Invasive Prenatal Testing (NIPT) results. We developed a novel, automated negative NIPT disclosure process to save HCPs time and provide education and test results to women. <br />Methods: High-risk, pregnant Southern California Permanente Medical Group (SCPMG) women who opted for NIPT (performed by Illumina) received their negative results through the automated process. HCPs provided patients with registration instructions. Registered women received an email indicating their result was available, watched an educational video explaining the negative NIPT result, and answered three comprehension questions. Women downloaded their result if they elected to learn the predicted chromosomal sex of the fetus. They were invited to complete a survey regarding the efficiency, ease, and satisfaction with the disclosure process. Of note, women with positive results were not included. <br />Results: 829 women out of 4429 registered women responded to the survey. The following percentage of women strongly agreed/agreed with: ease of account creation and portal navigation (95%); efficient and convenient result disclosure (93%); felt informed after watching the 2-minute video (95%); and preferred downloading results rather than waiting for their next appointment (97%). On average, SCPMG saved 10-12 minutes/patient. Cost savings for SCPMG is approximately $8.00-$9.00/patient, or $88,500/year for the high-risk population and $354,000 if expanded to the general-risk population. <br />Discussion: Our ongoing study demonstrates high satisfaction and cost-savings with this automated, scalable solution. Women prefer receiving their result electronically versus waiting for their next doctor’s visit. Secure and automated solutions will allow HCPs to focus on women with positive results, which require a higher level of attention and care. Further studies should be performed to validate, confirm, and extend the findings of this study.<br />

Perspectives from the Trenches: An Analysis of How the Workforce is Currently Utilized to Train the Next Generation of Genetic Counselors
Platform Presentations: Training and Workforce
Submitter: Ashley Barnes,
Presenting Author: Ashley Barnes,
Primary Author: Ashley Barnes, Brandeis University
Author 2: Vivian Pan, Kaiser Permanente Research Bank
The demand for qualified individuals to provide genetic services is rapidly increasing, creating an explosion of jobs within the field of genetic counseling. Training additional genetic counselors would help address the emergent demands for genetic services, but the availability of clinical supervision to train students is a rate-limiting factor. This study aimed to evaluate experiences and the perspectives of genetic counselors on the clinical training of genetic counseling students. Four hundred fifteen patient-facing genetic counselors belonging to either the NSGC or ABGC completed an anonymous online survey. Approximately half of participants provided clinical supervision in 2017 and these participants represented 98% of accredited programs in the United States and Canada. The majority of participants (94.3%) perceived the training of additional students as either extremely important or very important. Approximately 55% of participants indicated that they could train additional students per year, with 34.1% of those participants reporting the ability to train an additional 3-5 students yearly. Participants without a genetic counseling program within 60 miles of their clinic were more likely to report that they could train more students. Workload, patient volume, and number of additional professional responsibilities were not found to be associated with participants’ capacity to train more students. Inclusion of telemedicine cases and expansion of internship opportunities outside direct patient care were ranked as the most effective ways to train additional students. These findings illustrate that patient-facing genetic counselors not only endorse the training of additional genetic counseling students, but also have the ability to provide additional clinical supervision. The utilization of clinical sites located further from existing training programs, potentially using telemedicine or travel stipends, as well as the incorporation of internship experiences in industry, research, and laboratories may allow more students to be trained.

Standardized Patients: Enhancing Genetic Counseling Graduate Training

Platform Presentations: Training and Workforce
Submitter: Lisa Jay Kessler, Arcadia University

Presenting Author: Lisa Jay Kessler, Arcadia University

Primary Author: Lisa Jay Kessler, Arcadia University, Genetic Counseling Program

Author 2: Denise LaMarra, Perelman School of Medicine

Author 3: Kathleen D. Valverde, Arcadia University

Accredited genetic counseling programs teach 22 practice-based competencies (PBCs) in four domains. The purpose of this pilot study was to determine the effectiveness of using standardized patients (SPs) to formatively assess interpersonal competencies (domain II). SPs are individuals trained to portray patients in a consistent, measurable way to teach/assess healthcare trainees, and provide opportunities to practice emotionally and medically challenging cases without a clinical supervisor present. SP
methodology has not been studied yet in the context of GC graduate education. Two case scenarios were developed in collaboration with a medical school's SP Program: 1) Whole exome (WES) consenting with a secondary finding result and 2) Huntington disease (HD) testing. Sixteen second-year GC students participated in pre- and post-test sessions for both scenarios. Sessions were video-recorded, monitored by faculty, and evaluated by clinical supervisors. SPs provided verbal feedback and completed communication/interpersonal skills checklists for each trainee. Students completed self-assessments and satisfaction surveys after each session. SPs rated GCs as demonstrating good or very good levels of empathy 100% of the time (WES) and 94% of the time (HD). SPs reported feeling comfortable or very comfortable referring a friend or family member to this counselor 100% of the time in the WES case, and 81% in the HD case. All students indicated the feedback from the SPs was helpful; the average feedback score was 3.38/4 for the WES case and 4/4 for the HD case. Results show that this SP program effectively assessed GC students on their interpersonal and counseling skills. The SPs identified deficiencies that allowed for targeted video review and subsequent tailored feedback from faculty. Preparation with SPs can reduce the dependence on clinical rotations for basic skill development, allowing clinical supervisors time to teach more advanced skills, and increasing their ability to work with additional students to ease the workforce issue.

Exploring the Developmental Process of Genetic Counseling Supervisors

**Platform Presentations: Training and Workforce**

*Submitter: Caitlin Reid,*

*Primary Author: Caitlin Reid,*

*Presenting Author: Caitlin Reid,*

*Author 2: Monica Marvin, University of Michigan*

*Author 3: Beverly Yashar, University of Michigan*

*Author 4: Ian MacFarlane, Elizabethtown College*

With the expansion of genetic counseling (GC) training programs, more counselors are being asked to provide clinical supervision earlier in their career. Formal training opportunities related to this responsibility are limited and the developmental trajectory of novice supervisors’ skills is not well understood. Our goal was to understand novice supervisors’ needs in order to better support their confidence and competence as supervisors. Eligible GC participants were recruited through the American Board of Genetic Counseling, had 1 to 5 years of clinical experience, had supervised at least 2 students and planned to continue supervising. Twenty participants completed semi-structured phone interviews using a novel interview guide that explored preparation for and motivation to supervise, definition and perception of successful supervision, and challenges and related solutions. Transcripts were coded and themes were identified using an inductive approach. All participants were female, less than 34 years old, most worked at a University Medical Hospital (n=13) and had 6 or more supervisors at
their site. A variety of clinical specialties were represented. Participants mean self-rated competency as a supervisor was a 6.8 (standard deviation of 1.5) on a scale of 1 to 10 (not at all competent to completely competent). Most described student feedback as a common tool for self-assessment and skill development. Student feedback was received in varied ways and was most often perceived as positive in nature. Many participants defined “successful supervision” as having a successful relationship with the supervisee, although definitions of successful relationships varied. Additionally, most defined confidence in one’s GC skills as an important prerequisite to confidence as a supervisor. Our findings suggest supporting the development of novice supervisors requires fostering self-efficacy in genetic counseling skills, improving formative and summative forms of student feedback, and developing tools that help novice supervisors self-assess their clinical and supervision skills.

Statewide Assessment of the Utah Genetic Counseling Clinical Workforce

Platform Presentations: Training and Workforce

Submitter: Karin M. Dent, University of Utah Health Sciences Center

Primary Author: Karin M. Dent, University of Utah Health Sciences Center

Presenting Author: Karin M. Dent, University of Utah Health Sciences Center

Author 2: Erin E. Baldwin, ARUP Laboratories; Salt Lake City, UT

Author 3: Marjan Champine, Huntsman Cancer Institute, University of Utah; Salt Lake City

Author 4: Katie Dunn, Humana, Inc.; Louisville, KY

Author 5: Michelle Landon, Myriad Genetics Laboratories; Salt Lake City, UT

Author 6: Heather Sarin, Utah Dept of Health; Salt Lake City, UT

Author 7: Lauren Wallace, Division of Reproductive Genetics, Intermountain Healthcare;

Author 8: Nancy C. Rose, Division of Reproductive Genetics, Intermountain Healthcare;

Author 9: Jenna Christensen, Utah Medical Education Council; Salt Lake City, UT

In 2017, the Governor-appointed Utah Medical Education Council (UMEC) surveyed the Utah (UT) genetic counselor (GC) workforce. The goal was to illustrate the composition and distribution of the active GC workforce and to determine if it can sufficiently meet current and future demands of the state. The UMEC and an advisory committee developed a 29-question survey mailed to all genetic counselors holding a Utah GC license. The survey questions were designed to assess factors such as practice setting, specialty, professional responsibilities, and licensee plans to reduce hours, retire, or otherwise leave the field. Data collection was completed in December 2017 and analyzed by SPSS. The survey response rate was 86%. Of the 147 respondents, 78% practiced in UT. Thirty-seven percent of those lived in and provided services in state; 41% lived outside of UT and provided some
services in state. Fifty-seven percent of the workforce living in UT reported counseling patients. Clinical settings in UT experienced a net GC loss of 3.7% over the last two years due to the workforce moving primarily into non-clinical settings. Of the clinically active GCs, one third of those living in UT reported seeing 5-10 patients per week, while 23% of GCs living outside of UT reported counseling more than 20 patients per week. Although it is unclear if all respondents counseled patients full-time, the results suggest 1.2 clinical GCs per 100,000 UT residents. In order to maintain this ratio, 2.0 additional clinical FTEs will be needed per year as the current workforce continues to transition into non-clinical roles, reduce hours, or retire. While these data reflect current trends in the UT clinical GC workforce, they likely mirror national trends supporting the need for expansion of professional training and the creation of strategic initiatives to reduce the gap between GC clinical service demands and availability.

The Current Landscape of Genetic Counseling (GC) Licensure in the United States

Platform Presentations: Training and Workforce

Submitter: Natalie Vena, Celmatix

Primary Author: Natalie Vena, Celmatix

Presenting Author: Natalie Vena, Celmatix

Author 2: Jennifer Helgeson, Celmatix

Author 3: Elaine A. Sugarman, Celmatix

GC service providers must be appropriately licensed and comply with regulations defined by the states in which patients reside. With the growing use of telegenetics, providers offering nationwide GC services must ensure appropriate licensure coverage. The National Society of Genetic Counselors offers guidance in establishing licensure legislation, but the application and renewal requirements vary greatly among states. Here we describe the current requirements for obtaining and maintaining GC licensure in the US. By May 2018, 22 states had active GC licensure legislation. An application (7 online, 15 paper) must be submitted to the state licensing board with initial application and licensing fees ($40-$400). All states require official documentation of American Board of Genetic Counseling certification. Eighteen states require an official transcript from an Accreditation Council for Genetic Counseling accredited program, 5 require multiple professional recommendations and/or employment verification, and 2 require additional training programs. Four states require supplemental information, such as proof of identity, resume, or liability insurance documentation. Additional incurred costs may include passport photos, notarization, and postage. Fourteen states require background checks, and 9 require fingerprinting. Nine states have fees associated with the background check ($5-$70), with added fingerprinting or Criminal Offender Record Information fees not included. Nineteen states require verification of applicants' existing professional out-of-state licenses, and 13 charge a fee for each request ($4-$50). All states require license renewal ($30-$500), but renewal schedules and continuing education requirements vary. The cost, time, and documentation required to submit, obtain,
and maintain individual state licensure places an increasing burden on providing nationwide GC services. While licensure helps establish competences and ensure public protection, opportunities to simplify the process and support counselors pursuing multiple licenses should be explored.

**Incorporation of Genetic Testing for Familial Hypercholesterolemia Doubles Diagnosis Rate**

**Platform Presentations: Variant Interpretation and Diagnostic Utility**

*Submitter: Emily Brown, MGC, CGC, Johns Hopkins Hospital*

*Presenting Author: Emily Brown, MGC, CGC, Johns Hopkins Hospital*

*Primary Author: Emily Brown, Johns Hopkins University*

*Author 2: Laura Goodell, University of Maryland*

*Author 3: Rebecca McClellan, Johns Hopkins University*

*Author 4: Kathleen Byrne, Johns Hopkins University*

*Author 5: Thorsten Leucker, Johns Hopkins University*

*Author 6: Steven Jones, Johns Hopkins University*

*Author 7: Seth Martin, Johns Hopkins University*

**Introduction**

Familial hypercholesterolemia (FH) is a hereditary condition characterized by elevated LDL-C from birth leading to premature coronary artery disease and physical sequelae of lipid deposition in tissues. Early diagnosis is critical since timely treatment can prevent atherosclerosis and coronary heart disease. Nevertheless, less than 10% of prevalent cases of FH in the United States have been diagnosed. Low rates of diagnosis are attributable in part to affected patients not meeting the stringent clinical diagnostic criteria of the Dutch Lipid Clinic Network (DLCN).

**Methods**

We retrospectively reviewed patients seen in the Advanced Lipids Disorders Clinic at Johns Hopkins Hospital between 2015 and 2018. DLCN criteria were applied to classify each patient, before and after genetic testing, as having Unlikely, Possible, Probable, or Definite FH. Genetic testing included sequencing and deletion duplication analysis of four genes (LDLR, PCSK9, APOB, and LDLRAP1). Variants were classified according to the 2015 ACMG guidelines.

**Results**

The retrospective review identified 108 adult probands who were seen in our clinic for evaluation for FH. Eighteen individuals (17%) were determined to carry a likely pathogenic or pathogenic variant and have heterozygous FH. Nine of these individuals (50%) met criteria for Definite FH on clinical grounds prior to genetic testing. The clinical and family histories, and physical exam features, of the remaining nine patients were not sufficient to provide a definitive diagnosis. Only after a positive genetic test result did these patients meet criteria for Definite FH.

**Conclusions**

Incorporating genetic testing for FH doubled our diagnosis rate when compared to classifying solely on clinical grounds. Affected
individuals may not have originally met DLCN criteria for a variety of reasons including having a mild phenotype or previous treatment which modified their clinical phenotype. Therefore, our data support genetic testing in evaluation for FH, as a diagnosis has important implications for patients and their relatives.

**Clinical utility of clinical whole genome sequencing (cWGS): a review of pilot data from 88 cases**

**Platform Presentations: Variant Interpretation and Diagnostic Utility**

*Submitter: Carolyn Brown, Genetic Counselor, Illumina*

*Presenting Author: Carolyn Brown, Genetic Counselor, Illumina*

*Primary Author: Carolyn M. Brown, Illumina Inc.*

*Author 2: Alka Malhotra, Illumina Inc.*

*Author 3: Krista Bluske, Illumina Inc.*

*Author 4: Aditi Chawla, Illumina Inc.*

*Author 5: Amanda Clause, Illumina Inc.*

*Author 6: Maria Laura Cremona, Illumina Inc.*

*Author 7: Miguel Del Campo, Rady Children's Hospital*

*Author 8: Carolina Galarreta, Rady Children’s Hospital*

*Author 9: R Tanner Hagelstrom, Illumina Inc.*

*Author 10: Marilyn C. Jones, Rady Children's Hospital*

*Author 11: Diane Masser-Frye, Rady Children’s Hospital*

*Author 12: Julia McEachern, Illumina Inc.*

*Author 13: Denise L. Perry, Illumina Inc.*

*Author 14: Keisha Robinson, Illumina Inc.*

*Author 15: Alicia Scocchia, Illumina Inc.*

*Author 16: Erin Thorpe, Illumina Inc.*

*Author 17: Kristen Wigby, Rady Children's Hospital*

*Author 18: John Belmont, Illumina Inc.*
Clinical whole genome sequencing (cWGS) is a test that detects many variant types, including single nucleotide, copy number and mitochondrial variants. cWGS is not yet widely available and data addressing its clinical utility, defined as the ability to inform clinical decision making and, ultimately, to improve outcomes, are limited. To investigate the clinical utility of cWGS, surveys were sent to the ordering providers of 94 probands in Illumina’s iHope program, a philanthropic initiative that provides cWGS to individuals with limited access to genetic testing. 88 surveys have been completed. In 58 (66%) probands, > 1 variant of potential clinical relevance was reported. In 29/58 cases (50%), results prompted changes in management including implementation of condition-specific supportive interventions, specialist referrals, imaging studies or physiological testing. For example, a child with CHRNE-associated congenital myasthenic syndrome was referred to neurology for medication management. In children with Rubenstein-Taybi and Kaufmann syndromes, secondary findings in PMS2 and BRCA2 were identified as affecting future management. In 30 (34%) probands, no variants were reported. In 3/30 (10%) negative cases, results impacted management by prompting specialist referrals or by facilitating the decision to pursue skin biopsy. In 4/30 (13%) cases, a reduced likelihood of genetic disorders promoted exploration of alternate etiologies. Diagnostic, prognostic and recurrence information are not typically considered as elements of clinical utility, but were identified as benefits of cWGS; posttest counseling was informed by cWGS in 52/58 (90%) cases with variants reported and in 4/30 (13%) of negative cases. In summary, pilot data suggest that cWGS contributes to clinical decision making in nearly half of probands and informs genetic counseling in about two thirds. Many of these changes would not have been considered without the information gleaned from cWGS. Ongoing research is needed to understand the effects of these management changes on patient outcomes.
Since exome sequencing (ES) became commercially available, technological advancements and the knowledge of benign and disease-causing variation in novel candidate disease genes have greatly increased. Advancements and gene discovery have established need for periodic reanalysis and reclassification of previous cases. Procedures vary and can include proactive reanalysis and/or provider-driven reanalysis. The reanalysis method most likely to lead to diagnosis following has not been studied. Herein we investigate outcomes of reanalysis amongst varying indications for reanalysis patients with previous ES. Since 2011, 636 cases had at least one completed re-analysis and/or reclassification, with 673 total. 417 were provider-initiated, 256 lab-initiated, 228 upgraded, 39 downgraded and 406 were had no changes in reported classification, (some with changes in individual gene and/or alteration reclassification but resulting in no overall change). Provider initiated reanalysis was less likely to result in a reclassification, regardless of whether updated clinical information was provided (Provider request unchanged 399/417 (95.7%), lab initiated changed 248/256 (96.9%), p<0.0001) and lab driven reanalysis was more likely to result in an upgraded result (210/256 (82.1%), p<0.0001)). The primary reasons for reclassifications were upgrades due to new literature describing new gene-disease relationships, and downgraded alterations due to new population frequency databases (p<0.0001, 0.0049 respectively). Our findings suggest that proactive reanalysis with literature surveillance on alterations and new gene-disease discoveries enhances diagnoses. The comprehensive nature of ES makes it uniquely powerful for identifying novel molecular diagnoses at both first analysis and reanalysis. Data sharing with collaborations to publish data on new disease genes is paramount to aid in new diagnoses. These data emphasizes the importance of counseling patients about the likelihood of result reclassification and navigating the complexity of changes in diagnosis.

Outcomes of 94 Patient-Driven Family Studies for Reclassification of Unselected Variants of Uncertain Significance

Platform Presentations: Variant Interpretation and Diagnostic Utility

Submitter: Ginger Jade Tsai, University of Washington

Presenting Author: Ginger Jade Tsai, University of Washington

Primary Author: Ginger Jade Tsai, University of Washington, Department of Laboratory Medicine

Author 2: John Michael O. Rañola, University of Washington, Department of Laboratory Medicine

Author 3: Christina Smith, University of Washington, Department of Laboratory Medicine

Author 4: Lauren Thomas Garrett, University of Washington, Department of Laboratory Medicine

Author 5: Silvia Casadei, University of Washington, Department of Medicine

Author 6: Brian H. Shirts, University of Washington, Department of Laboratory Medicine
Family studies for reclassification of variants of uncertain significance (VUS) are available for select families at many commercial laboratories, but there are few studies that describe outcomes such as reclassification results and patient satisfaction. In light of growing patient demand for VUS reclassification, we evaluated outcomes of a patient-driven framework that offered familial VUS reclassification analysis to any adult with any clinically ascertained VUS from any laboratory. With guidance from our online tutorial FindMyVariant.org, participants gathered family history information to build pedigrees, coordinated sample collection for relatives, and communicated information between the study and their families. We performed quantitative cosegregation analysis when possible and evaluated variant classifications using Tavtigian’s unified framework, which facilitates combining Bayesian analysis with ACMG/AMP guidelines. 94 families with 114 VUS, predominantly in cancer risk genes, were recruited over two years. Success rates for family member recruitment and VUS reclassification were calculated from the 46 families who had been enrolled for at least one year. A mean of 6.5 relatives per family were invited to participate, and a mean of 4.3 relatives per family returned samples for genotyping. 29 of 56 VUS (52%) in these 46 families were reclassified. In the entire cohort of 94 families, we observed diverse VUS reclassification pathways, including identification of a de novo variant and testing of multiple siblings for a recessive variant in trans with a known pathogenic variant. When quantitative cosegregation analysis was not possible, genotyping of relatives often contributed to reclassification by identifying relatives with phenotypes highly specific for or incompatible with specific classifications. Given access to familial testing and educational materials, motivated families can contribute substantial information to VUS reclassification. Clinical laboratories should consider offering family studies to all patients with VUS.

Variant Interpretation is a Wide-Spread and Valuable Practice Amongst Clinical Genetic Counselors Across Multiple Specialties

**Platform Presentations: Variant Interpretation and Diagnostic Utility**

*Submitter: Karen Wain, Geisinger - Autism & Developmental Medicine Institute*

*Primary Author: Karen Wain, Geisinger - Autism & Developmental Medicine Institute*

*Presenting Author: Karen Wain, Geisinger - Autism & Developmental Medicine Institute*

*Author 2: Danielle R. Azzariti, Laboratory for Molecular Medicine*

*Author 4: Amy Knight Johnson, University of Chicago*

*Author 5: Patti Krautscheid, ARUP Laboratories*

*Author 6: Julianne O'Daniel, University of North Carolina at Chapel Hill*

*Author 7: Deborah Ritter, Baylor College of Medicine*

*Author 8: Juliann M. Savatt, Geisinger - Autism & Developmental Medicine Institute*
Broad-scale genomic technologies are incorporated into clinical care across many specialties, and recent variant interpretation guidelines, databases, and other resources have emerged to address interpretative challenges related to this testing. While variant interpretation (VI) practice has traditionally been the purview of clinical laboratories, clinical genetic counselors (GCs) are increasingly reporting assessing evidence for VI purposes in clinical practice. The aim of this study was to explore the practice of VI by clinical GCs across multiple clinical specialties. An online survey was administered to National Society of Genetic Counselors (NSGC) members via Survey Monkey. GCs providing part- or full-time clinical counseling were eligible. Respondents (n=239, ~9.6% response rate) represented all major clinical specialties. Demographics were generally consistent with the 2018 NSGC Professional Status Survey, though there was a lower rate of prenatal GCs (24.3% vs. 41.%). The majority (68.3%) report reviewing evidence documented by the laboratory in most (>60%) reports received; 45.5% report assessing evidence beyond what is noted in a report. VI is often performed independently (43.8%), and many respondents utilize team discussions (31.3%) or case conferences (30.8%). Most respondents (67.4%) have disagreed with a laboratory interpretation, but this is typically rare or infrequent (96.5%). There were no associations between VI practice and clinical specialty, years practicing, or previous/current laboratory or research roles. Factors that influence the decision to perform VI in clinical practice were 1) when the variant was interpreted as being of uncertain significance (74.9%), 2) the consistency of a reported variant with patient phenotype (70.9%), and 3) the consistency of a variant interpretation with ClinVar/other databases (65.9%). This study confirms that VI activities occur frequently in GC clinical practice across specialties and are an important part of genomic medicine. These results should inform GC educational curricula and scope of practice.

**A-265 Associations between ultrasound soft markers and copy number variants**

**Pre- and Perinatal**

Submitter: Lindsay Ann Bailey, Geisinger Health System

Presenting Author: Lindsay Ann Bailey, Geisinger Health System

Primary Author: Lindsay Bailey, Geisinger Health System

Author 2: Kajal Angras, Geisinger Health System

Author 3: Corinna L Muller, Geisinger Health System

Copy number variants (CNVs) are submicroscopic structural genetic changes that may or may contribute to disease. CNVs may be classified as benign, variants of unknown clinical significance (VUS) or pathogenic. Genetic Counselor and healthcare colleagues are challenged by the uncertain implication of
VUS. Therefore, there is still much that needs to be learned about CNVs and their potential implications on health and development. Despite the challenge with understanding implications with certain CNVs, recent evidence has taken the direction in favor of obtaining microarray analysis to detect the presence of clinically relevant CNVs in a fetus with a normal karyotype in the setting of fetal ultrasound anomalies. However, there is no data to support the use of microarray for identifying an underlying genetic cause when soft markers are detected on ultrasound. Electronic health records were reviewed for the past 7 years within the Geisinger Health System of pregnancies of children with known CNVs. Cases with known prenatally detected and/or postnatally detected CNVs were reviewed to identify presence of soft markers on the second trimester ultrasound. Eight hundred fifty four patients with a prenatally diagnosed soft marker were identified through a data pull, and 156 have a CNV (18.3%) identified on microarray. This data aims to help physicians and genetic counselors determine overall prognosis for the fetus and better counsel patients regarding genetic associations when a soft marker is identified prenatally. In addition, understanding of an association between soft markers and CNVs can facilitate appropriate follow up postnatally.

A-268 Utilization of cffDNA testing in a publicly funded contingent prenatal screening model

Pre- and Perinatal

Submitter: Kara Bellai Dussault,
Presenting Author: Kara Bellai Dussault,
Primary Author: Kara Bellai Dussault, Better Outcomes Registry and Network (BORN)
Author 2: Tianhua Huang, BORN, NYGH
Author 3: Mark Walker, The Ottawa Hospital, BORN
Author 4: Andrea Lanes, OHRI, BORN
Author 5: Nan Okun, Mount Sinai Hospital, BORN
Author 6: Christine Armour, Children's Hospital of Eastern Ontario, BORN
Author 7: Shelley Dougan, Better Outcomes Registry and Network (BORN)

Ontario, Canada offers a publicly-funded contingent model of prenatal screening where cell-free fetal DNA (cffDNA) testing is funded in situations conferring a higher risk for fetal aneuploidy, including positive multiple marker screen (MMS) result, advanced maternal age (AMA, ≥40 years) and nuchal translucency (NT) measurement ≥3.5mm. This study examined the utilization and positive rates for each funded indication in order to inform future funding policy around cffDNA testing implementation in Ontario.<br />This descriptive cohort study is based on secondary analysis of data collected by Ontario’s prescribed maternal and child registry, the Better Outcomes Registry & Network (BORN), to which all
laboratories and hospitals contribute. The study population includes all pregnant women who received cffDNA testing from January 2016 to December 2017. 25,204 cffDNA testing records were collected over the study period. The most common clinical indicators for funded cffDNA testing were: AMA (45%), positive MMS (37%), increased risk for aneuploidy due to other clinical factors (13%), and previous aneuploidy (6%). CffDNA testing ordered subsequent to a high NT measurement had the highest positive rates for trisomy 21 (14%), trisomy 18 (5%), trisomy 13 (2%) and monosomy X (2%). Positive rates for cffDNA tests funded following the identification of soft markers were highest for absent/hypoplastic nasal bone (3%) and increased nuchal fold (1%). The use of certain eligibility criteria could be audited by cross-referencing with other data sources available in the BORN registry. For example, of the cffDNA tests funded for the indication of AMA, 3.5% were actually <40 at EDD, and 22.5% of cffDNA tests funded due to high NT had an NT measurement <3.5mm. Examining the utilization and positive rates for cffDNA testing funded in Ontario for various high-risk indications allows the potential for audit and improvement of adherence to standardized cffDNA screening protocols, and provides a basis for reassessment of the funding model currently in place.

A-271 Non-invasive prenatal testing in Australia: a qualitative exploration of women’s experiences in private and public settings

Pre- and Perinatal
Submitter: Eliza Courtney, MGC, National Cancer Centre Singapore

Presenting Author: Eliza Courtney, MGC, National Cancer Centre Singapore

Author 2: Carol-Anne Verrenkamp, Sydney Medical School – Northern, The University of Sydney

Author 3: Sian Smith, Psychosocial Research Group, Prince of Wales Clinical School

Author 4: Zara Richmond, Department of Medical Genomics, Royal Prince Alfred Hospital

Author 5: Michael J Sinosich, Douglass Hanly Moir Pathology, Sonic Healthcare Ltd

Author 6: Robert Markham, Sydney Medical School – Central, The University of Sydney

Author 7: Jane Fleming, Sydney Medical School – Northern, The University of Sydney

Author 8: Kristine Barlow-Stewart, Sydney Medical School – Northern, The University of Sydney

Primary Author: Eliza Courtney, MGC, Sydney Medical School - Northern, The University of Sydney

PURPOSE
Non-invasive prenatal testing (NIPT) is becoming an increasingly favorable option for Australian women in both public and private healthcare settings, however, there remains a paucity of literature in this area. This qualitative study aimed to explore the decision-making experiences of Australian women who have undergone NIPT in public and private settings.

METHODS
Semi-structured interviews were performed with 21 women who had undergone NIPT (10 from public hospitals and 11 from private obstetric practices) and were recorded, transcribed verbatim and analyzed.
using thematic analysis. RESULTS

Whilst the experience for the vast majority was seemingly positive and most held favorable attitudes towards NIPT, differences did exist between those from private and public settings. Women from the public sample described a more deliberative decision-making process following multiple points of contact with healthcare providers. In contrast, women from the private sample typically had a strong trust relationship with their obstetrician, were already aware of the availability of NIPT and actively requested the test themselves. Across both samples, NIPT was praised for its positive attributes with little acknowledgement of its limitations, whereas the potential risks with invasive testing were repeatedly emphasized. There was a desire for good quality, easily accessible and reader friendly information at an early stage. CONCLUSION

Our findings indicate that healthcare professionals need to be aware of the skewed way in which women appraise test attributes so as to ensure the benefits, risks and limitations are being balanced appropriately in order for informed decision-making. Robust pre-test counseling and the use of decision aids should be central to the delivery of NIPT and the wider prenatal testing paradigm.

A-274 Pregnancy Outcome Information after Receiving an “Aneuploidy Suspected” Screen Result via Non-Invasive Prenatal Screening

Pre- and Perinatal
Submitter: Jordan Dix, LabCorp

Presenting Author: Jordan Dix, LabCorp

Primary Author: Jordan D Dix, MS, CGC, LabCorp

Author 2: Michelle Burch, MS, CGC, LabCorp

Author 3: Amy C Dexter, MS, CGC, LabCorp

Author 4: Emily Walsh, MS, CGC, LabCorp

Author 5: Christine Vaughan, MS, CGC, LabCorp

Author 6: Chevonne D Eversley, PhD, FACMG, LabCorp

Background: Non-invasive prenatal screening (NIPS) first entered the field in 2011. Integrated Genetics began offering its own laboratory developed InformaSeq assay in 2014. InformaSeq has three reporting categories: aneuploidy detected, aneuploidy suspected, and aneuploidy not detected. The “aneuploidy suspected” category, by far, is the most infrequent reporting category; hence, providers tend to have questions regarding the clinical impact of a “suspected” screen result. Here we present Integrated Genetics’ experience with the clinical outcomes of these results. Methods: A database of positive results was maintained by the genetic counselors (GC), and clinical outcome data was collected six weeks post-test or post-delivery when necessary. For the purpose of this study we analyzed follow-up data for “aneuploidy suspected” results reported between 09/07/2014 and 03/31/2017. Results: During the selected time interval, a total of 270,637 samples were reported. Of those, 197 (<0.1%) samples
resulted “aneuploidy suspected” and were included in the database. Seventy-five patients who received “aneuploidy suspected” screen results underwent diagnostic testing via chorionic villus sampling, amniocentesis, or both. For the remaining 122 samples, follow up diagnostic testing information was unavailable; however, six patients in this category reported experiencing a fetal demise. Of interest, 59 of the 75 patients with an “aneuploidy suspected” screen result that sought diagnostic testing received normal fetal results via karyotype or microarray. Discussion: “Aneuploidy suspected” screen results can pose a unique challenge when counseling patients regarding their risks. Current follow up recommendations for “aneuploidy suspected” results are the same as “aneuploidy detected” results which includes the option of diagnostic testing. Given the mixture of abnormal and normal diagnostic test results presented here, further clinical characterization of the “aneuploidy suspected” range may aid in defining recommendations beyond fetal diagnostic testing.

A-277 Cell free DNA testing at 9 weeks: A clinical laboratory experience
Pre- and Perinatal
Submitter: Kimberly Fanelli, Fanel, Integrated Genetics, Integrated Genetics
Presenting Author: Kimberly Fanelli, Fanel, Integrated Genetics, Integrated Genetics
Primary Author: Kimberly Fanelli, MS, CGC, Integrated Genetics
Author 4: Eyad Almasri, MSc, Integrated Genetics
Author 2: Brittany Dyr, MS, CGC, Integrated Genetics
Author 3: Samantha Caldwell, MS, CGC, Integrated Genetics

Cell free DNA (cfDNA) is a well-established test for screening high risk, and more recently average risk pregnancies for common aneuploidies. CfDNA provides patients the earliest information regarding aneuploidy risk during pregnancy, allowing for early prenatal diagnosis to be considered. Here, we describe the laboratory experience and clinical performance of MaterniT®21 PLUS for samples submitted at 9.0-9.9 weeks gestation. Since 2011, over 750,000 maternal blood samples submitted to Sequenom Laboratories for MaterniT®21 PLUS were subjected to DNA extraction, library preparation, and genome-wide massively parallel sequencing as described by Jensen et al. Over 7,000 samples in this cohort were submitted between 9.0-9.9 weeks gestation. Statistical analysis of this patient cohort was performed. For all positive results, outcome data (e.g. cytogenetic/molecular results and/or birth outcomes) is dependent on feedback provided by the ordering provider. Analysis of over 7,000 samples yielded 102 results positive for trisomy 21, trisomy 18 and trisomy 13; an overall positivity rate of 1.44%. Of those 102 results, there was 1 false positive for trisomy 21 and one false positive for trisomy 18 reported to the laboratory. There were no known false positives for trisomy 13. Only 145 samples (2.05%) did not yield a result due to low fetal fraction (1.8%) or technical issues (0.25%); 97.95% of samples received positive or negative test results. The average fetal fraction for all samples was 8.5%. The most common indications for referral included advanced maternal age (~61%),
average risk (~31%) and family/personal history (~4%). Twins and triplets accounted for 249 (3.5%) of samples in this cohort. MaterniT®21 PLUS offers patients reliable screening for fetal aneuploidy, even at 9 weeks gestation. Earlier access to cfDNA results allows patients the opportunity to discuss prenatal diagnosis options with their healthcare provider. These results were compared to data from over 600,000 samples and clinical laboratory experience is comparable.

A-280 Continuing Genetics Education May Increase OB/GYN Referrals to Prenatal Genetic Counseling

Pre- and Perinatal

Submitter: Devin Fendlay,

Presenting Author: Devin Fendlay,

Primary Author: Devin Fendlay, University of Maryland School of Medicine

Author 2: Christine Hertenstein,

Author 3: Austin Janaitis,

Author 4: Amanda Higgs,

In many prenatal settings, OB/GYNs are the providers explaining genetic screening and testing. However, previous research has shown that many OB/GYNs are not comfortable discussing this material. OB/GYNs' lack of confidence in genetic knowledge has been noted in studies as early as 2000, with 65% of OB/GYNs reporting they did not feel confident in their genetic knowledge due to the rapid rate of change in the technology and information. However, many OB/GYNs report not having a genetic counselor available to meet with their patients. The aims of this study were to explore obstetrician-gynecologists' (OB/GYNs') referral behaviors to prenatal genetic counseling, the barriers to referral, and OB/GYNs' attitudes towards alternative service models such as group counseling sessions. An online survey was conducted to which 17 OB/GYNs belonging to one of four professional organizations responded. The majority of respondents were female OB/GYNs working in a university-affiliated practice. Six respondents were certified maternal-fetal-medicine (MFM) specialists and were more likely to report referring patients to genetic counseling to discuss family history of a genetic condition or an abnormal ultrasound finding that may be related to a genetic condition. Increased referrals were also reported by OB/GYNs who have participated in at least one form of continuing genetics education since medical school. No OB/GYNs reported that they routinely refer patients to genetic counseling to discuss medication risks during pregnancy. Lastly, 42.9% of OB/GYNs who do not have a genetic counselor available on the same day as their patient’s appointment report that they would refer patients more often if a counselor was available in person or through telemedicine on the same day as the appointment. This data suggests that continuing genetics education as well as improving access to same-day genetic counseling services will increase referrals to prenatal genetic counselors.
A-286 Serendipitous Detection of Maternal Tetrasomy 9p as a Result of Prenatal Cell-free DNA Screening

Pre- and Perinatal

Submitter: Cheryl E. Harper, Quest Diagnostics

Presenting Author: Cheryl E. Harper, Quest Diagnostics

Author 2: Kristina F. Kahl, MS, LCGC, Quest Diagnostics, San Juan Capistrano, CA

Author 3: Renius Owen, PhD, Senior Scientific Director

Author 4: Ben P. Anderson, MB(ASCP)CM, CGMBS, Quest Diagnostics - San Juan Capistrano, CA

Author 5: Ke Zhang, Quest Diagnostics - San Juan Capistrano, CA

Author 6: Guity Ghaffari, PhD, Quest Diagnostics - San Juan Capistrano, CA

Author 7: JoAnn C. Kelly, PhD, FACMG, Quest Diagnostics, San Juan Capistrano, CA

Author 8: Sandra J. Coe, MS, LCGC, Quest Diagnostics, San Juan Capistrano, CA

Author 9: Felicitas L. Lacbawan, MD, Quest Diagnostics - San Juan Capistrano, CA

Primary Author: Cheryl E. Harper, MS, CGC, Quest Diagnostics, San Juan Capistrano, CA

We present a unique case in which prenatal cell free (cfDNA) screening indicated possible maternal aneuploidy of 9p, leading to the identification of Tetrasomy 9p (T9P) in the pregnant patient. This patient was a 22 year old female at 14 weeks gestation at the time of prenatal cfDNA screening (QNatal Advanced TM). Results showed increased material on chromosome 9p, suggestive of maternal trisomy 9p. Due to the confounding suspected maternal aneuploidy, fetal analysis was unable to be performed and a result was not reported. This finding was discussed with the provider by a genetic counselor at which time maternal and fetal cytogenetic analyses (microarray or conventional studies) were recommended. Additional clinical information was obtained and described the patient as healthy without known history of medical or developmental problems. Subsequent maternal microarray revealed an approximate 68 Mb terminal gain of 2 extra copies of 9p24.3q13, suggestive of a supernumerary isochromosome of 9p (arr[hg19] 9p24.3q13 (203,861,67,983,174) x 4); conventional cytogenetic analysis confirmed mosaicism for an isochromosome 9p (mos 47,XX, +(9)(p100[8]/46,XX [12], consistent with tetrasomy 9p. Fetal studies have not been ordered. T9P generally represents the presence of a supernumerary chromosome involving 9p with 30% of cases having mosaicism. The described phenotype is highly variable, ranging from infants with multiple anomalies often with severe intellectual disability to apparently healthy individuals identified serendipitously. Congenital heart defects, renal anomalies, and microcephaly have been described in T9P. While some anomalies seen in T9P may be detected on fetal ultrasound, neither routine nor cf(DNA) prenatal screening would typically identify T9P. In this case, the suspicion of maternal aneuploidy by prenatal cfDNA screening resulted in
the recognition of maternal T9P that then allowed for further diagnostic testing, genetic counseling, and clinical management to be offered during pregnancy.

A-289 Giant Omphalocele: What is the Genetic Association?

Pre- and Perinatal
Submitter: Mary-Kayt Jones, Arcadia University

Primary Author: Mary-Kayt Jones, Arcadia University

Presenting Author: Mary-Kayt Jones, Arcadia University

Author 2: Erica Schindewolf, Center for Fetal Diagnosis and Treatment - CHOP

Author 3: Kathleen Valverde, Arcadia University

Author 4: Samantha Adams, Children’s Hospital of Philadelphia

Author 5: Enrico Danzer, Children’s Hospital of Philadelphia

Author 6: Holly Hedrick, Children’s Hospital of Philadelphia

The genetic etiology of giant omphalocele (GO) is not well delineated. Previous studies have demonstrated a lower level of aneuploidy for GO than for small omphalocele, largely based on karyotype data. The goal of this study was to determine whether other types of genetic testing identify common anomalies in GO. A retrospective medical record review was performed on confirmed cases of GO, with pre- or postnatal genetic testing from July 2004 to August 2017, seen at the Center for Fetal Diagnosis and Treatment at the Children’s Hospital of Philadelphia. 94 individuals were identified with GO. Data collected included demographic data, size and contents of the omphalocele sac, pre- and postnatal genetic testing reports, clinical outcomes and follow-up. 80 individuals (85%) met inclusion criteria. Descriptive analysis was performed. 80% of our study cohort had two or more genetic tests completed. Karyotype and SNP microarray testing were the most common tests performed. Exome sequencing had been carried out for 3 patients since 2015. 64 of 80 individuals (80%) with GO had normal genetic test results, and 16 individuals (20%) were found to have an abnormal genetic finding that could impact clinical care. In four cases (25%), abnormal results were clearly causative for GO (Trisomy 13, Trisomy 18, Beckwith-Wiedemann syndrome and Teebi Hypertelorism syndrome). Overall, 95% (76/80) of individuals did not have a genetic explanation for their GO while 5% (4/80) had a genetic etiology identified. Pregnancies affected with GO should be offered prenatal diagnostic testing. Karyotype testing provides the highest diagnostic yield for GO, but SNP microarray may detect other clinically relevant findings. Postnatal genetic evaluation should also be offered to determine clinical management and if additional genetic testing is needed such as next-generation sequencing panels or exome. These results can provide useful prognostic information for families with an affected pregnancy regarding outcomes for the fetus, future clinical care for the child and recurrence risk information.
A case of extremely elevated maternal serum alpha-fetoprotein (MSAFP)

Pre- and Perinatal

Submitter: Karen Marchand, Beth Israel Deaconess Medical Center

Presenting Author: Karen Marchand, Beth Israel Deaconess Medical Center

Primary Author: Karen Marchand, MS, LGC, Beth Israel Deaconess Medical Center

Author 2: Barbara M. O'Brien, MD, Beth Israel Deaconess Medical Center

Author 3: Leanna Sudhof, MD, Beth Israel Deaconess Medical Center

Author 4: Nicole Poulos, MS, LGC, Beth Israel Deaconess Medical Center

Author 5: Paula Delerme, MS, LGC, Beth Israel Deaconess Medical Center

Author 6: Lauren Lichten, MS, LGC, Beth Israel Deaconess Medical Center

Author 7: Millie Anne Ferres, MD, Beth Israel Deaconess Medical Center

Introduction:

Alpha feto-protein (AFP) is produced by the liver, ovaries, placenta, and fetus. In the second trimester, assessment of maternal serum AFP (MSAFP) is used to screen for open fetal defects, which are associated with moderately elevated MSAFP. More significant elevation of MSAFP can have alternative maternal or fetal etiologies and portends a poor prognosis. We describe our evaluation process for a patient who had a transient extreme elevation of MSAFP.

Case report:

Our patient is a healthy 36-year-old G2P1 woman who presented for ultrasound and counseling after an extremely high MSAFP of 198.36 MoM (6061.4 ng/ml) at 16w6d (dating confirmed by 1st trimester ultrasound). The differential diagnosis included lab error, fetal anomaly, maternal or fetal malignancy, fetal nephrosis, and placental abnormalities. Ultrasound evaluation of the fetal anatomy, placenta, and maternal ovaries was unremarkable. Repeat MSAFP was done at 18w6d in the form of a quadruple screen and showed MSAFP to be decreased but still very elevated at 32.94 MoM (1331.9 ng/ml). The other analytes were within normal limits. Our patient had normal liver function tests and normal liver ultrasound. Amniocentesis was normal (46,XY karyotype and AFP of 0.9 MoM). Maternal pelvic MRI showed normal ovaries bilaterally with no ascites or adnexal pathology. Repeat MSAFP at 20w3d and 27w1d showed downtrending values (393.6 ng/ml and 158.3 ng/ml). Our patient underwent frequent antenatal surveillance (fetal biometry every 2 weeks, fetal wellbeing ultrasounds weekly 30-34w and twice weekly 34w+). Delivery was by repeat cesarean at term, at which time pelvic washings were obtained (negative). The neonate had APGARs of 8 and 9 and weighed 3465 grams. Placental pathology was unremarkable. The post-partum course was unremarkable with normal MSAFP at 6w post-partum (2.5 ng/ml).

Discussion:

Extreme MSAFP elevation requires thorough evaluation for maternal, placental, and fetal etiologies. While concerning for poor outcome, elevation can be transient with a good outcome for both mother and fetus.
Predictors of carrier screening among genetic counselors are not well-studied. Years of experience as a genetic counselor could influence personal interest in carrier screening. This research studied years of genetic counseling experience and likelihood to pursue carrier screening. Demographic factors, including race, age, sex, and genetic counseling specialty, were also explored as potential predictors of carrier screening. Individuals could participate in this study if they were second-year students or practicing genetic counselors of reproductive age. Participants could never have been pregnant or fathered children. Respondents were asked demographic data, their likelihood to pursue screening, and whether they had already pursued screening. SAS was used for descriptive and association (Chi-square and logistic regression) analyses. 504 individuals participated in this study, with an average age of 28.5 years. Most participants were Caucasian females, 24% were students, and 15% were prenatal counselors. Among genetic counselors, most had practiced for less than five years. About one-third of participants had prior carrier screening. Most participants had screening before practicing for five years. Controlling for age, race, and specialty, participants who had practiced for less than five years were less likely to have had screening. Prenatal genetic counselors were more likely than students (OR = 3.5) and other genetic counselors (OR = 1.8) to have had screening. Among those who had not had screening, participants were less likely to pursue screening if they had less than five years of experience (OR=3.2). Non-Caucasian participants less often said they would likely pursue screening (OR = 0.3). Overall, prenatal counselors and those with fewer years of practice were more likely to have had screening. Among those who had not had screening, interest in screening was higher among more experienced and Caucasian counselors. Future research could explore these associations further and learn what genetic counseling career experiences motivate screening decisions.
How do patients attending prenatal genetic counseling sessions feel about and respond to being asked about personal or family history of mental illness?

**Pre- and Perinatal**

**Primary Author:** Sarah Nimrichter, University of South Carolina

**Presenting Author:** Sarah Nimrichter, University of South Carolina

**Author 2:** Jehannine Austin PhD FCAHS, CGC/CCGC, University of British Columbia

**Author 3:** Ashley Jones, MD, Palmetto Health USC Medical Group

**Author 4:** Victoria Vincent, MS, CGC, Palmetto Health USC Medical Group

**Submitter:** Sarah Nimrichter, MS,

**Introduction:** Genetic counseling (GC) can help people with mental illness (MI) and their families. Though common, MI is rarely a primary referral indication for GC, and stigma inhibits spontaneous MI disclosure by patients. Furthermore, genetic counselors avoid asking patients about MI for fear of causing discomfort. Purpose: We explored patient interest in and comfort with discussing MI during a prenatal GC session and tested hypotheses that: 1) women with a personal and/or family history of MI would be more interested in discussing MI, and 2) women who were interested in discussing MI would have more current symptoms of depression. Methods: Participants were pregnant women receiving routine prenatal screening/testing GC at Palmetto Health USC Medical Group Department of OB/GYN. After their appointment, participants completed a purpose designed questionnaire and the Edinburgh Postnatal Depression Scale (EPDS). Results: Of the 40 participants, 28 (70%, 28/40) were interested in discussing MI. Most of the participants whose counselor asked about MI (26/30) were comfortable with being asked, and 11/13 of those who had a full discussion with their counselor about MI were comfortable with the discussion. Of the participants who were not directly asked, 8/9 would have felt comfortable if asked about MI. No participants indicated they would feel very uncomfortable to be asked about or to discuss MI in their prenatal GC session. There were no significant differences in: level of interest in discussing MI between those who did and did not have a personal or family history of MI (p=.220), or in EPDS scores between those who were interested and those who were not interested in discussing MI (p=0.14). Conclusion: These results suggest that patients are interested in and comfortable with discussing a personal and/or family history of MI with a genetic counselor during prenatal GC. Prenatal genetic counselors should routinely ask about MI while taking the family history and be prepared to discuss information regarding the genetic components of MI.

Exploring Counseling Trends with cell-free DNA (cfDNA) in Genetic Counseling

**Pre- and Perinatal**

**Submitter:** Miranda K Ruben, Indiana State University
Cell-free DNA (cfDNA) has become a utilized prenatal screen for common fetal aneuploidy, sex chromosome identification, and a variety of other genetic conditions since 2011. However, indications for offering cfDNA, terminology used when describing cfDNA, and follow up discussions have yet to be explored.

Methods: Prenatal genetic counselors (GCs) were recruited through the National Society of Genetic Counselors to take an anonymous online survey regarding their experiences, opinions, impressions, and methods for determining eligibility for cfDNA.

Results: There were 85 usable responses to the survey. Results indicate a consensus among genetic counselors offering cfDNA to women who are advanced maternal age, received a positive maternal serum screen, and abnormal ultrasound findings (p<0.001) but were less likely to offer women cfDNA for family history indications. Following a positive cfDNA result, nearly all genetic counselors discussed diagnostic options and follow up ultrasounds, but fewer discussed pregnancy termination (52.7%), adoption (33.0%), maternal serum screening for open neural tube defects (25.3%), and some discussed no further testing (46.0%). More GCs discussed termination than adoption (p=0.008). Terminology for cfDNA varied among genetic counselors (p=0.011) with GCs using cell-free DNA or cell-free fetal DNA (41.7%), non-invasive prenatal testing (41.7%), and non-invasive prenatal screening (12.0%). There was no difference between perceived patient preference for cfDNA vs diagnostic testing following an abnormal ultrasound (p=0.162) while perceived patient preference for cfDNA was found following positive maternal serum screening (p<0.0001).

Conclusion: Although there are obvious trends among GCs for consistently discussing diagnostic testing, other topics appear more variable. This, in addition to variable terminology used, may lead to inconsistencies in care or confusion among patients.
Fetal nasal bone (NB) evaluation in first trimester screening (FTS) improves clinical performance in Down syndrome (DS) detection rates. As NB visualization is often difficult early in the screening window, our Center offers a repeat NB evaluation for patients with “absent” or “uncertain” NB on initial examination.<br />

We completed a retrospective chart review to determine the impact of repeat first trimester NB evaluation for DS risk assessment. Our Center performed 6780 FTS sonograms between 1/1/2015 and 1/1/2018. We identified 589 (9%) patients with absent/uncertain NB, and recorded self-reported race, maternal age, NB visualization on exam 1 and exam 2, and DS risk (“normal” or “abnormal” by laboratory cut-offs).<br />

Of the 377 patients who completed repeat NB exam, 269 (71%) had a present NB on exam 2. African American/Caribbean patients and Caucasian patients comprised 41% (n = 110) and 44% (n = 117) of this cohort, respectively. Compared to African American/Caribbean patients, patients of all other ethnicities combined were more likely to have a present NB on exam 2 (p < .00001). Specifically, 117/141 (83%) of Caucasian and 110/185 (60%) of African American/Caribbean patients had a present NB on exam 2 (p < .00001).<br />

Initial FTS results were abnormal for 38/269 (14%) patients with a present NB on exam 2, and 33/38 (87%) normalized following NB visualization. Twenty-two of these 33 patients were Caucasian. Of the 23 total Caucasian patients with abnormal FTS after exam 1, 22/23 (96%) normalized, whereas 7/11 (64%) of African American/Caribbean patients’ initially abnormal FTS results normalized.<br />

Our data suggest that repeat NB examination is beneficial in refining DS risk assessment. While particularly useful for Caucasians in whom an absent NB confers greater risk, this practice improves the specificity of FTS for all women so recommendations for further aneuploidy screening/testing are provided to truly high-risk patients.<br />

A-307 Exploring Women’s Perceived Support for Abortion Due to Fetal Anomaly: Stigma in the Medical Community<br />

Pre- and Perinatal<br />
Submitter: Jordan Snajczuk,<br />
Presenting Author: Jordan Snajczuk,<br />
Primary Author: Jordan Snajczuk, Virginia Commonwealth University
OBJECTIVE: To explore women’s perceived support from various healthcare providers as they pursued abortion due to fetal anomaly.

METHODS: In this quantitative-qualitative study, we recruited women, ages 18 or older, at gestational ages of 12 weeks or greater, having an abortion procedure due to fetal anomaly. Participants completed a pre-procedure survey to measure acceptance of their decision and perceived support from family/friends and healthcare providers. This data was scored using a Likert scale. After the procedure, semi-structured phone interviews were conducted to explore experiences with obstetricians, maternal fetal medicine specialists, genetic counselors, and the physician who performed the procedure. Interview data was analyzed independently by two members of the research team to identify underlying themes. Data collection concluded after saturation of themes.

RESULTS: From October 2017 to February 2018, 13 women completed the survey and nine completed the phone interview. The majority of women scored as “Supported” or “Strongly Supported” for each type of provider. When providers struggled or failed to discuss abortion as an option, women suggested that this reinforced stigma surrounding abortion. Participants expressed that genetic counselors should be easily accessible and provide resources regarding cost and logistics of the procedure. Participants also desired that healthcare professionals review as much information as possible during the decision-making process, include partners in the process of abortion for fetal anomaly, and consider that abortion is emotionally complex.

CONCLUSION: Our research shows that while participants undergoing abortion for fetal anomaly felt largely supported by healthcare professionals, most voiced feelings of stigmatization. Participants described the key roles desired from genetic counselors, as well as advice for all medical professionals. These findings suggest there is a need for aiding professionals to provide accurate, unbiased information during options counseling.

A-310 Prenatal Genetic Counseling for Marijuana or Opioid Use During Pregnancy

Pre- and Perinatal

Submitter: Naomi Wagner, Boston University School of Medicine

Primary Author: Naomi Wagner, Boston University School of Medicine

Presenting Author: Naomi Wagner, Boston University School of Medicine

Author 2: Shuyi Jiang, Boston University

Author 3: Lisa Demers, MS, CGC, Roche Diagnostics

Author 4: Lillian Torrey Sosa, MS, CGC, Boston University School of Medicine
There have been notable increases in marijuana, heroin, and prescription opioid use in the United States in the past two decades. In line with trends in the general population, prenatal use of marijuana and opioids has increased in recent years. Given these trends as well as evidence for negative pre- and postnatal effects of both marijuana and opioid use during pregnancy, it is imperative for prenatal care providers to be able to counsel their patients about these substances. Prenatal genetic counselors routinely discuss teratogens with their patients, but little is known about current genetic counseling practices for prenatal substance use. The present study explored the experiences and perceptions of prenatal genetic counselors with regard to counseling for marijuana, opioid, alcohol, tobacco, and caffeine use. An anonymous, web-based survey was distributed to members of the National Society of Genetic Counselors, and 135 (8.9%) eligible participants completed the survey. Over a third of respondents noticed some or much more patient-reported use of marijuana and opioids since they began practicing, a trend that was not seen with alcohol, tobacco, or caffeine. There was a significant difference between the respondents’ level of concern for prenatal marijuana use compared to prenatal opioid use (p < 0.001). Of note, 5.2% of the respondents felt extremely concerned about prenatal marijuana use, whereas 62.2% felt extremely concerned about prenatal opioid use. Despite these differences in concern, counseling practices for the two substances were similar. Our results suggest that a majority of prenatal genetic counselors do not consistently ask their patients about either marijuana or opioid use. Importantly, less than half of the respondents reported feeling completely knowledgeable about the risks of using marijuana or opioids during pregnancy. As drug use trends and policies evolve, addressing gaps in genetic counselors’ knowledge and re-evaluating counseling practices for substance use during pregnancy will be critical.

**A-313 Approach to encourage expectant couples in Japan to understand about living with children with Down syndrome**

**Pre- and Perinatal**

*Submitter: Motoko Watanabe, Ochanomizu University*

*Presenting Author: Motoko Watanabe, Ochanomizu University*

*Primary Author: Motoko Watanabe, Ochanomizu University*

*Author 2: Mari Matsuo, Tokyo Women’s Medical University*

*Author 3: Masaki Ogawa, Tokyo Women’s Medical University*

*Author 4: Hidehiko Miyake, Ochanomizu University*

*Author 5: Toshiyuki Yamamoto, Tokyo Women’s Medical University*

Noninvasive prenatal testing (NIPT) was first introduced as a clinical service for Japanese clients in April 2013 as part of genetic counseling research. Because the research project will be completed this year, the situation concerning NIPT in Japan is expected to change, for example, through an increase in the
number of clinics offering NIPT. In genetic counseling research, medical staff members have reported difficulty explaining Down syndrome to expectant couples and encouraging understanding about the condition. We held an open symposium to try to encourage understanding of NIPT and people with targeted chromosomal abnormalities for expectant couples. The symposium was composed of two parts: one provided by medical staff members and one by an individual with Down syndrome and three families with individuals with Down syndrome. They talked about financial support, social activities, and caring for children in daily life, and they shared their thoughts about prenatal testing. The individual with Down syndrome talked about his life and thoughts about prenatal testing. After the symposium, a questionnaire survey was administered to 78 participants (response rate = 59%; 46/78). A total of 65% of the participants were medical staff members, and 35% were members of the general population, including expectant couples. All participants reported being satisfied with the symposium, 93% reported an increased understanding about Down syndrome, and 91% reported being eager to know more about Down syndrome. The results showed extremely high satisfaction with the symposium and suggest that it led to the acquisition of knowledge and motivation to know more about Down syndrome. However, there were fewer attendees from the general population, including expectant couples, at the symposium, compared with medical staff members. There is a need motivate and encourage the general population to attend such symposiums.

B-266 Assessing Fertility Concerns and Reproductive Health Knowledge in Adult Males with Cystic Fibrosis

Pre- and Perinatal
Submitter: Eileen E Barr, Arcadia University

Presenting Author: Eileen E Barr, Arcadia University

Author 4: Denis Hadjiliadis, University of Pennsylvania

Author 5: Daniel Dorgan, University of Pennsylvania

Primary Author: Eileen Barr, Arcadia University

Author 2: Rebecca Mueller, University of Pennsylvania

Author 3: Kathleen Valverde, Arcadia University

Author 6: Kelsey Spielman, University of Pennsylvania

INTRO: Cystic fibrosis (CF) has guidelines for disease management, but recommendations for timing and content of conversations about sexual and reproductive health (SRH) vary. As life expectancy for CF has increased, SRH is increasingly relevant. Men with CF are almost always infertile, though assisted reproductive technology (ART) can enable biological fatherhood. PURPOSE: This study aimed to evaluate knowledge, experiences and attitudes towards infertility, ART, and SRH to provide insight for a larger study to develop guidelines to meet needs of CF males. METHODS: A piloted survey was electronically
sent to all adult males with CF cared for by Penn Medicine Adult CF Program. The survey consisted of 33 close-ended questions and 4 supplementary open-ended responses. Close-ended responses were analyzed with descriptive statistics and chi-square tests; open-ended responses were coded thematically by the first author. RESULTS: 53 participants responded, a response rate of 35.3%. All subjects reported knowing CF impacts male fertility. The median age (+SD) subjects recalled first learning this was 16 (+6.4 years). 29 (54.7%) learned from a healthcare provider and 9 (16.9%) from parents. 11 participants (20.8%) wished they learned sooner, majority (10) of whom learned after 16 years (p<0.001). Upon learning, 29 (54.7%) wondered if there were still options to have children, and 20 (37.7%) wondered if it could be fixed. 22 (41.5%) have visited a fertility specialist. CONCLUSION: Majority of adult men with CF are aware of the infertility but knowledge regarding ART options and uptake remains limited. Further, these data suggests a preference to learn this information by age 16, which should be confirmed in larger studies. In addition, the data provides insight to the range of emotions and questions experienced. As one subject wrote, boys with CF should learn in “early adolescence, so that he has plenty of opportunities to ask pertinent questions as they arise or become relevant in his life.” ACKNOWLEDGEMENTS: Funding was supported by the NSGC CF SIG research scholarship.

B-269 Going against the guidelines: patient decisions following preimplantation genetic testing

Pre- and Perinatal
Submitter: Jillian Carroll,

Primary Author: Jillian M Carroll, MA, MS, CGC, Integrated Genetics

Author 2: Ellen L Schlenker, MS, LCGC, Integrated Genetics

Author 3: Kristi Fissell, MS, CGC, Integrated Genetics

Presenting Author: Jillian M Carroll, MA, MS, CGC, Integrated Genetics

The Society for Assisted Reproductive Technologies recently documented the continued and “steady increase” of the use of assisted reproductive technologies (ART) with over 70,000 babies born in 2016. At the same time, the use of preimplantation genetic testing (PGT) for aneuploidy screening (PGT-A) and for specific single gene testing (PGT-M) has also become more mainstream. A 2007 ASRM committee opinion on PGT recommended that patients undergoing PGT-M have genetic counseling and confirmatory testing while patients undergoing PGT-A receive education and discussion of screening and diagnostic options. The purpose of this study is to evaluate prenatal testing decisions in prenatal patients who have undergone PGT.<br /><br />The study population included 137 patients who received genetic counseling in a pregnancy conceived using ART with PGT from 2015-2017. Overall, 85.4% of patients (n=117) had PGT-A testing, 7.3% of patients (n=10) had PGT-M, and 7.3% of patients (n=10) had both. Regardless of the type of PGT, patients overwhelmingly declined diagnostic confirmation of their preimplantation results. 15.4% of patients with PGT-A elected to undergo diagnostic testing while none of the PGT-M pursued diagnostic testing. 10% of the patients who used
both PGT-A and PGT-M pursued diagnostic testing. There was no statistically significant difference regarding the uptake in these groups. Of note, in the patients who elected diagnostic testing, 63.2% had abnormal ultrasound findings and 10.5% had positive screening, suggesting that factors beyond their PGT influenced decision making.<br /><br />This study reveals that the vast majority of PGT patients choose not to pursue diagnostic testing, despite the recommendations for confirmatory testing following PGT-M. This is in line with an overall shift away from prenatal diagnostic testing. Given this tendency, it is even more important that patients receive genetic counseling to discuss the inherent limitations of PGT and the testing options during pregnancy.

### B-272 Genetic counseling for carrier screening and prenatal diagnosis involving a Tay-Sachs disease variant of uncertain significance and possible pseudodeficiency allele in the East Asian population

**Pre- and Perinatal**

**Submitter: Jordan Dix, LabCorp**

**Presenting Author: Jordan Dix, LabCorp**

**Primary Author: Jordan D Dix, MS, CGC, LabCorp**

**Author 2: Suzette M Huguenin, PhD, FACMG, LabCorp**

**Author 3: Charles J Macri, MD, Medical Faculty Associates at George Washington University**

**Author 4: Jill S. Fonda Allen, MS, CGC, Medical Faculty Associates at George Washington University**

**Introduction:** Tay-Sachs disease results from a deficiency of the enzyme beta-hexosaminidase A (HexA) and can be diagnosed biochemically via enzyme analysis or molecularly with the identification of two pathogenic variants in the HEXA gene. HEXA pseudodeficiency alleles exist that affect enzyme testing but do not cause Tay-Sachs disease. For individuals of Ashkenazi Jewish descent, the carrier risk of Tay-Sachs disease is approximately 1 in 27, compared to 1 in 250 to 1 in 300 in the general population. Due to the decreased a priori carrier risk, carrier screening in low risk populations can be significantly more complex and time consuming than screening in at-risk populations. Case Report: We present a case where carrier screening in the Chinese partner of a Tay-Sachs carrier led to identification of a molecular variant of uncertain significance (VUS). The couple presented for genetic counseling at 11.7 weeks gestation in conjunction with routine first trimester screening. The patient was of Ashkenazi Jewish ancestry and was found to be a carrier of Tay-Sachs disease by both HexA enzyme analysis in leukocytes and DNA analysis. Her partner, of Chinese ancestry, was screened, resulting in conflicting enzyme activity interpretations for serum, leukocytes, and plasma. Full gene sequencing of HEXA identified a VUS, c.548T>A (p.L183H), in the partner. Fetal diagnostic testing was pursued and molecular analysis on amniocytes revealed that the fetus inherited the maternal 1278insTATC pathogenic variant while the paternal c.548T>A VUS was not detected. Postnatal enzyme analysis of the infant was in the unaffected range. Discussion: Collective data indicates that this VUS is common in the East Asian population and
may be a pseudodeficiency allele, although more data is needed to make any conclusions. Genetic counseling and interpretation of prenatal testing was complex in this case. We discuss these issues in the context of current guidelines and the increasing use and availability of genomic techniques.

**B-275 Public interest in carrier screening in the Brazilian population**

*Pre- and Perinatal*

*Submitter: Marina Dutra-Clarke,*

*Presenting Author: Marina Dutra-Clarke,*

*Primary Author: Marina Dutra-Clarke, UC Irvine Medical Center*

*Author 2: Maureen Bocian, MD, FACMG, UC Irvine Medical Center*

*Author 3: Kathryn Steinhaus-French, MS, LCGC, UC Irvine Medical Center*

*Author 4: Kathryn Osann, PhD, UC Irvine School of Medicine*

Brazil has a particularly heterogeneous population comprised of indigenous, European, and African ancestral roots, that have contributed to risks to be a carrier for certain autosomal recessive genetic disorders, such as sickle-cell disease, alpha and beta thalassemia, cystic fibrosis, and Tay-Sachs disease (in the Ashkenazi Jewish Brazilian population). The risks to be a carrier for these conditions justify the need to implement population carrier screening because there is currently no preconception or prenatal population carrier screening program in Brazil. An anonymous online survey was distributed to Brazilians using social media platforms, such as Facebook and Reddit. A total of 353 eligible participants responded. This study explored topics including knowledge of the disorders for which Brazilians are at-risk, perception of risk for these disorders, knowledge of autosomal recessive inheritance, and interest in carrier screening. The mean knowledge score for autosomal recessive inheritance and what it means to be a “carrier” was 53% in this cohort. Participants expressed high interest in carrier screening, regardless of demographic background. 78% of participants expressed high interest in carrier screening and 91% expressed high interest specifically in carrier screening for life-threatening disorders if treatment was available. Participants significantly preferred the option of carrier screening prior to getting pregnant as opposed to during pregnancy or waiting for newborn screening. Additionally, 86% of participants were interested in carrier screening for conditions that are not included in newborn screening. Challenges to implementing a screening program include the shortage of genetics-trained professionals, particularly outside of the South and Southeast regions, inadequate genetics education for medical students, and the lack of infrastructure for research centers and diagnostic laboratories. This study demonstrates interest and a need for Brazil to expand their genetic testing services to include preconception and prenatal carrier screening.
B-278 Third trimester cell free DNA: A clinical laboratory experience
Pre- and Perinatal
Submitter: Kimberly Fanelli, Fanel, Integrated Genetics, Integrated Genetics

Presenting Author: Kimberly Fanelli, Fanel, Integrated Genetics, Integrated Genetics

Author 4: Eyad Almasri, MSc, Integrated Genetics

Primary Author: Kimberly Fanelli, MS, CGC, Integrated Genetics

Author 2: Brittany Dyr, MS, CGC, Integrated Genetics

Author 3: Samantha Caldwell, MS, CGC, Integrated Genetics

Cell free DNA (cfDNA) is a well-established test for screening high risk, and more recently average risk pregnancies for common aneuploidies. Outside of fetal ultrasound, cfDNA is the only aneuploidy screening option available to women after 21 weeks gestation. Although no samples ≥ 27 weeks were part of the initial validation study cohort, late gestational age was not expected to influence test results based on known methodology and performance characteristics. Here, we describe the laboratory experience and clinical performance of MaterniT®21 PLUS for samples submitted in the third trimester.

Since 2011, over 750,000 maternal blood samples submitted to Sequenom Laboratories for MaterniT®21 PLUS were subjected to DNA extraction, library preparation, and genome-wide massively parallel sequencing as described by Jensen et al. Over 9,000 samples in this cohort were submitted at ≥27 weeks. Statistical analysis of this patient cohort was performed. For all positive results, outcome data (e.g. cytogenetic/molecular results and/or birth outcomes) is dependent on feedback provided by the ordering provider.

Analysis of over 9,000 samples yielded 231 results positive for trisomy 21, trisomy 18 and trisomy 13; an overall positivity rate of 2.57%. Of those 231 results, 2 false positives for trisomy 13 were reported to the laboratory and no false positives for trisomy 21 or trisomy 18. Only 62 samples (0.67%) did not yield a result due to low fetal fraction (0.06%) or technical issues (0.60%); 99.33% of samples received positive or negative test results. The average fetal fraction was 18.89% and the average gestational age 30.7 weeks. The most common indications for referral included ultrasound abnormalities (~47%), advanced maternal age (~23%) and average risk (~12%). Twins and triplets accounted for 235 (2.5%) samples in this cohort.

MaterniT®21 PLUS offers patients reliable screening for fetal aneuploidy in late gestational age, when screening options are limited. These results were compared to data from over 600,000 samples and third trimester experience is comparable.

B-281 Current Genetic Counseling Practice Following Positive Non-Invasive Prenatal Testing For Sex Chromosome Abnormalities
Pre- and Perinatal
Submitter: Lauren Fleddermann,
The purpose of this study was to describe current prenatal and pediatric genetic counseling practice following a non-invasive prenatal testing (NIPT) result positive for a sex chromosome abnormality (SCA). Screening for SCAs can be confounded by natural loss of the X chromosome from maternal cells during aging, confined placental mosaicism, and undiagnosed maternal sex chromosome abnormality. Furthermore, with the exception of 45,X, individuals with SCA usually have no ultrasound or postnatal findings. This makes follow-up for unresolved positive NIPT necessary; however, there are currently no clinical guidelines. This study used a prospective anonymous questionnaire to survey 176 prenatal and pediatric genetic counselors. The majority of pediatric (>70%) and prenatal (>80%) respondents were somewhat or extremely comfortable counseling patients about SCAs. However, prenatal respondents in the field for <5 years were significantly less comfortable counseling about every condition except 45,X (p<0.02). A majority of prenatal counselors always offered diagnostic testing (>88%) and anatomy ultrasound (~90%), but the percent consistently offering maternal karyotype (22-52%) and postnatal evaluation (28-87%) varied. Maternal karyotype was offered more often when NIPT was positive for 45,X or 47,XXX and patients had normal diagnostic testing (p<0.023) or declined testing (p<0.019). Postnatal evaluation was more likely to be recommended when diagnostic testing was declined (p<0.01). A majority of pediatric counselors always offered the child a karyotype postnatally (>72%) but the percent offering maternal karyotype (6-46%) varied widely. With the current inconsistencies, many newborns with undiagnosed SCAs who could benefit from growth hormone therapy, early intervention, and/or targeted surveillance may be missed. There is a need for professional guidelines to help improve clinical care for patients with NIPT results positive for SCAs.
The National Society of Genetic Counselors (NSGC) provides guidelines for genetic counselors to follow during counseling sessions. Prenatal counselors are advised to offer the options of parenting, termination, and adoption to patients with a positive prenatal diagnosis. In previous research, it was found that the option of termination was being offered at a higher frequency than the option of adoption. This study investigated factors that could play a role in a prenatal genetic counselor’s decision to offer the option of adoption to patients in a prenatal genetic counseling session. A survey of 13 questions was sent out through the NSGC Listserv. Eligible participants were board certified or board eligible prenatal genetic counselors that were currently providing prenatal counseling or have done so in the past. Analysis of data from 98 participants revealed a significant relationship between offering the option of adoption and the participants’ education about adoption, clinical rotation experience, years practicing, and number of high-risk patients. Additional findings include a relationship between participant education about adoption and the number of years since graduating, as well as participant education and the level of restriction on obtaining an abortion in each state. Results are discussed in terms of their implications for improving genetic counseling graduate program curriculum and prenatal genetic counseling sessions for patients.

B-287 The Patient Perspective of the Informed Consent Process For Non-invasive Prenatal Screening

Pre- and Perinatal
Submitter: Megan Horn, Insight Medical Genetics
Presenting Author: Megan Horn, Insight Medical Genetics
Primary Author: Megan Horn, Insight Medical Genetics
Author 2: Anne Matthews, Case Western Reserve University
Author 3: Aaron Goldenberg, Case Western Reserve University
Author 4: Larisa Rippel, University Hospitals Cleveland Medical Center

Purpose: The purpose of this study was to assess and analyze the informed consent process (ICP) for Noninvasive Prenatal Screening (NIPS) in different office settings from the patient perspective in order to aid healthcare providers to better serve their patients.<br />
Methods: Participants were recruited from obstetrician (OB) and genetic counseling (GC) sites to complete a 30-minute semi-structured telephone interview. Participants were women of advanced maternal age who decided to utilize NIPS in their current pregnancy. Interviews were recorded and transcribed verbatim. A constant comparative method was used to analyze the data and inductively derive themes.<br />
Results: Ten interviews were completed; six participants were recruited by GCs and 4 were recruited by OBs. Five themes were
identified: 1) optional screening, 2) thoroughness, 3) time, 4) reasons to screen, and 5) documentation. All participants expressed that they felt that this screening was optional. All participants expressed personal reasons to pursue prenatal screening. Participants differed in the amount of information they recalled discussing with their provider and the amount of time their provider spent with them. <br/>

Conclusion: GC participants recalled discussing more recommended NIPS pretest counseling points with their provider than OB participants. This study indicates there could be differences in the ICP given by different provider groups.<br/>

B-290 An Exploration of the Involvement of Genetic Counselors in the Delivery of Aneuploidy Screening and Testing
Pre- and Perinatal
Submitter: Qian (Lorraine) Lei,

Presenting Author: Qian (Lorraine) Lei,

Primary Author: Qian Lei, Brandeis University

Author 2: Lauren Lichten, Brandeis University

Author 3: Barbara M. O’Brien, Beth Israel Deaconess Medical Center

Author 4: Chelsea Mandigo, Massachusetts General Hospital

There is a shortage of certified genetic counselors to keep up with the publics’ growing demand for genetic counseling services. This is especially a concern for the field of prenatal genetic counseling because of the introduction of non-invasive prenatal screening via cell-free DNA (cffDNA) analysis and the 2016 American College of Obstetricians and Gynecologists (ACOG) practice guideline that suggests cffDNA should be offered as an available screening option for all women. The purpose of this study is to assess prenatal genetic counselors’ involvement in offering aneuploidy screening and testing. An anonymous survey was distributed to the NSGC listserv and was completed by 193 prenatal genetic counselors. Only 29.7% of the 136 respondents stated that they do follow the ACOG guideline. Barriers for implementing the ACOG guideline reported by participants included: busy work schedule, adding additional time to counseling sessions, limited insurance coverage, and poor pre-test counseling by other health care providers. Although 14.7% of respondents mentioned busy work schedules as a barrier, participants reported seeing an average of 4.4 patients daily and a Quantitative Workload Inventory was an average of 16, indicating a reasonable workload. Overall, participants indicated genetic counselors are the most appropriate provider to consent patients for both screening and diagnostic aneuploidy tests regardless of indication. Participants who indicated that their non-genetics providers have received education on aneuploidy testing found it to be more appropriate for them to consent patients for cffDNA in two circumstances: AMA and isolated echogenic intracardiac foci (p<0.05). This study suggests that prenatal genetic counselors are not yet offering cffDNA to all women and few are utilizing alternative service delivery to increase workplace efficiency. To accommodate the demand for
prenatal genetic counseling services it is important for prenatal genetic counselors to focus on education for non-genetics providers and incorporate more alternative service delivery.

B-293 Factors Influencing Decision Making About Prenatal Screening and Testing in Parents of Children with Down Syndrome

Pre- and Perinatal
Cassidy Measner


Pre- and Perinatal
Submitter: Sharon F. Molinari, LabCorp
Presenting Author: Sharon F. Molinari, LabCorp
Primary Author: Sharon Molinari, MS, CGC, Laboratory Corporation of America
Author 2: Jenny Shafer, MS, CGC, Laboratory Corporation of America
Author 3: Christine Riordan, MS, CGC, Laboratory Corporation of America
Author 5: Stuart Schwartz, PhD, FACMG, Laboratory Corporation of America
Author 6: Katie Rudd, PhD, FACMG, Laboratory Corporation of America
Author 7: Justin Schleede, PhD, FACMG, Laboratory Corporation of America
Author 4: Laura Kline, MS, CGC, Laboratory Corporation of America

One of the most common structural chromosome abnormalities detected prenatally is a deletion of 22q11.21 associated with DiGeorge/Velo-cardio-Facial (VCF) syndrome. Historically, this has been identified using fluorescent in situ hybridization (FISH) and the primary indication for testing was fetuses presenting with a major heart defect detected by ultrasound. With the advent of microarray analysis, this deletion has been identified in fetuses presenting with ultrasound findings other than heart defects and has been detected in conjunction with other unexpected microarray abnormalities. For example, patient 1 underwent an amniocentesis at 19.4 weeks gestation due to bilateral clubfeet and an echogenic intracardiac focus on ultrasound. Microarray analysis revealed a 2.88 Mb deletion of the 22q11.21 region and an 888 kb deletion of the 16p11.2 region associated with autism. Patient 2 underwent an amniocentesis due to ultrasound findings of Tetralogy of Fallot and a clubfoot. Microarray
analysis revealed a 2.88 Mb deletion of the 22q11.21 region and a 498 kb deletion of the 2p16.3 region, including part of the NRXN1 gene associated with neurodevelopmental problems. A review of 50,000 prenatal microarray analyses over 7 years revealed 254 cases with 22q11.2 deletion results. Analysis of this data revealed that 7.5% of the samples also had a second microarray abnormality detected and approximately 38% of the fetuses tested did not have a prenatally detected heart defect. Specifically looking at the trends for the last year, 25% of cases had a second microarray abnormality and >50% with a deletion did not have a heart defect. Many of these additional microarray abnormalities detected would have an impact on not only the current pregnancy but on future pregnancies. These findings suggest that the referral pattern has changed for microarrays, increasing the probability of a second microarray anomaly in patients with VCF and emphasize the importance of counseling patients about the possibility of additional findings.

B-299 Confirmed Trisomy 18 in a fetus who was conceived via In Vitro Fertilization with Pre-implantation genetic screening for aneuploidy

Pre- and Perinatal
Submitter: Caitlin O'Brien, Rutgers University
Presenting Author: Caitlin O'Brien, Rutgers University
Primary Author: Caitlin O'Brien, Rutgers University
Author 2: Elena Ashkinadze M.S, CGC, Rutgers- Robert Wood Johnson Medical School

The patient was a 39-year-old G2P1001 of Asian Indian decent whose first child, along with the current pregnancy were conceived via IVF. Infertility was attributed to male factor. Her spouse was 38 years old at the time of the meeting. The embryos had been cryopreserved when she was 37. Her first pregnancy resulted in a healthy female. For this cycle, five embryos were thawed, three made it for biopsy and complete chromosome screening (CCS) also known as preimplantation genetic screening (PGS). Only one embryo was predicted to be normal 46, XX, was transferred and resulted in a singleton gestation. The patient was referred for prenatal genetic counseling at 12 weeks of gestation because of abnormal ultrasound findings of increased NT of 5mm and a suspected omphalocele. The patient was counseled that these findings were suggestive of trisomy 18; however, because the patient had CCS, trisomy 18 was much less likely. Rather, she was presented with a deferential that included the 6-10% risk for a microarray abnormality [1], a single gene disorder or an isolated ventral wall defect.<br />

Additionally, Beckwith Wiedemann Syndrome, with about 50% of cases being caused by imprinting defects [2], was considered because of the increased chance of imprinting disorders with pregnancies conceived through IVF with PGS [3]. The patient opted to have chorionic villus sampling (CVS) and FISH analysis revealed a trisomy 18, female karyotype (47,XX,+18).<br />

The patient was counseled regarding the natural history of trisomy 18 and opted for termination of pregnancy. Cultured cells from the CVS were sent to the lab which had performed the CCS. It was subsequently confirmed that the correct embryo was transferred and the misdiagnosis by PGS was due to embryo mosaicism. This case
illustrates the importance of informing patients of the limitations of PGS/CCS. Patients who undergo IVF with PGS should still be counseled regarding the same screening and testing options as other women their age and the case of fetal anomalies, diagnostic testing for fetal aneuploidy should still be offered.

B-302 A novel prenatal report of post-zygotic rescue of partial monosomy: antenatal diagnostic work-up unveils homologue-templated deletion correction in a structurally normal fetus

Pre- and Perinatal

Submitter: Katelynn G. Sagaser, MS, CGC, Johns Hopkins University School of Medicine

Presenting Author: Katelynn G. Sagaser, MS, CGC, Johns Hopkins University School of Medicine

Primary Author: Katelynn G. Sagaser, MS, CGC, Division of MFM, Johns Hopkins University School of Medicine

Author 2: Karin J. Blakemore, MD, Division of MFM, Johns Hopkins University School of Medicine

Author 3: Judith P. Rossiter, MD, Dept. of OB/GYN, University of MD St. Joseph Medical Center

Author 4: Samantha Caldwell, MS, CGC, Sequenom Laboratories

A 33-year-old G7P1051 presented for genetic counseling due to non-reportable informaSeq® cell free DNA (cfDNA) results. Following genetic counseling, the patient elected simultaneous MaterniT®21 PLUS cfDNA screening, SNP-chromosomal microarray analysis (CMA) by amniocentesis, and blood karyotype. Maternal karyotype was normal (46,XX). MaterniT®21 PLUS reported a 56.75 Mb deletion of 13q21.1-q34. CMA revealed normal chromosomal dosage with a 57.4 Mb long contiguous stretch of homozygosity (LCSH) of 13q21.1q34. The remainder of the CMA had no homozygosity; the parents denied consanguinity. Parental microsatellite testing confirmed maternal segmental uniparental isodisomy of 13q21.1q34, and a sequencing panel of the 13 known autosomal recessive disease genes in this region was negative on amniotic fluid DNA. All prenatal sonograms were normal, and the patient declined fetal blood sampling for evaluation of additional cell lines. She spontaneously delivered a healthy male at 38 weeks, and we performed a SNP-CMA on placental samples obtained at delivery. Placental CMA confirmed the 57.5 Mb mosaic terminal deletion and allelic mosaicism of 13q21.1q34, with the deletion present in ~37% of cells.<br />

To our knowledge, this is the first report of homologue-templated deletion correction in a human brought forth by a prenatal diagnostic odyssey. The mosaic presence of the 13q21.1q34 deletion and 13q21.1q34 LCSH on placental CMA, together with the non-mosaic 13q21.1q34 LCSH on amniotic fluid, suggest that the zygote’s deletion persisted in part of the placenta but corrected by copying its normal homologue in certain cell lines. This complex, post-zygotic rescue mechanism has significant implications for prenatal genetic counseling due to risks for autosomal recessive diseases as well as phenotypes related to an occult cell line with the deletion within the fetus. This case, furthermore, highlights the utility of SNP-CMA on amniocentesis for copy number and UPD evaluation in the setting of non-reportable and/or partial monosomy cfDNA results.<br />
B-305 Customizable Non-Invasive Prenatal Testing for Single Gene Disorders using cell free DNA

Pre- and Perinatal
Submitter: Christina M Settler, Progenity

Presenting Author: Christina M Settler, Progenity

Primary Author: Christina Settler, Progenity

Author 2: Jamie Zdrodowski, Progenity

Author 3: Katarina Klusman, Progenity

Author 4: Julie Kim, Progenity

Author 5: Adele Kruger, Progenity

Author 6: Ronald Beaubien, Progenity

Author 7: Jeff Buis, Progenity

Author 8: Natalie Kiesling, Progenity

The ability to predict the fetal genotype of an at-risk pregnancy utilizing cell-free DNA (cfDNA) has been a request of patients and clinicians since the introduction of cfDNA screening for fetal aneuploidy in 2011. We have developed a novel platform for non-invasive prenatal testing of single gene disorders by cfDNA from a maternal blood sample. Here we present the results from a series of pregnant women who were carrying at-risk pregnancies. Blood was collected from pregnant patients at ≥ 10 weeks gestational age in Streck BCT® and transported overnight to the Progenity lab. Plasma was separated and cell-free DNA extracted using an internally developed bead based method. The relative quantity of fetal DNA in the sample was obtained through testing a portion of the cell-free DNA using a NGS method. The BIORAD QX200 Droplet Digital PCR system was used to perform a variant-specific probe based assay on the remainder of the cell-free DNA sample, producing the cell-free DNA allele ratio. The total fetal DNA contribution, cell-free DNA allele ratio, and other run based metrics were used to calculate the fetal status (Affected vs. Unaffected) and the associated probability. The ten pregnant women included in this study were all carrying at-risk pregnancies identified through carrier testing. In each case, variant-specific assays were custom developed and the expected fetal disease status was determined. When available, biological samples were collected from the resultant neonate, and in all cases the fetal disease status was concordant with the neonate genotype. We have developed a highly accurate platform for the noninvasive prenatal detection of monogenic diseases, capable of interrogating variants with different modes of inheritance, including compound heterozygous and autosomal recessive mutations. The customized assay provides families with fast and accurate
information about the status of a single gene disorder during pregnancy, allowing them to make well-informed decisions about prenatal diagnostic testing and pregnancy management.

B-308 Investigating Patient Misconceptions Regarding Cell-Free DNA: Beyond the "Gender Test"

Pre- and Perinatal
Submitter: Stephanie Spaulding,

Presenting Author: Stephanie Spaulding,

Primary Author: Stephanie Spaulding, Master of Genetic Counseling Training Program, University of

Author 2: Kyla Patek, Maternal Fetal Medicine, Virginia Hospital Center

Author 3: Katherine R. Forster, The Johns Hopkins Center for Fetal Therapy, Department of Gy

Author 4: Jenna Plamondon, Department of Obstetrics, Gynecology, and Reproductive Scien

Patient misconceptions regarding cell-free DNA (cfDNA; also referred to as non-invasive prenatal testing, NIPT, or NIPS) have been anecdotally shared between genetic counselors since its inception. As cfDNA becomes more widely available, genetic counselors and other healthcare providers have expressed concerns regarding the routinization of implementation and its effect on patients’ informed decision making. Previous studies have identified patient confusion regarding implications of cfDNA and other prenatal screening results. However, there is little research on techniques to address and rectify these misconceptions. Using an anonymous online survey, we identified several counseling interventions that prenatal genetic counselors report as successful when discussing patient confusion surrounding cfDNA, including restating the correct information, reframing a patient’s statement to provide correction, and asking the patient directly about the source of their confusion. The survey, completed by 79 prenatal genetic counselors, also confirmed patient misconceptions that were reported in prior studies, such as confusion surrounding the implications of positive and negative cfDNA results. Overall, prenatal genetic counselors encounter many patient misconceptions about cfDNA in their practice, which is likely a pervasive issue that is present for all prenatal care providers. Genetic counselors are uniquely suited within the prenatal field to correct patient misconceptions in order to best facilitate appropriate informed consent.

B-311 Positive cell-free DNA screening for sex chromosome aneuploidy: clinical experience and description of outcomes

Pre- and Perinatal
Submitter: Lauren Ahles Wallace, Intermountain Healthcare

Presenting Author: Lauren Ahles Wallace, Intermountain Healthcare
Objective: To describe our experience with the clinical accuracy and parental decision making for positive cell-free DNA (cfDNA) screen results for sex chromosome aneuploidy (SCA).  

Methods: This is a retrospective study of patients with positive cfDNA screen results for SCA from 2013-2018 in a single healthcare system. Patients were identified through a genetic test result database and were assessed for screening indication, performing laboratory, presence of abnormal ultrasound findings, and prenatal/postnatal chromosome results. 

Results: Forty-eight patients were identified including 32 (67%) positive for Turner Syndrome (TS) and 16 (33%) positive for a SC trisomy (7 Klinefelter, 6 trisomy X, and 3 XYY syndrome cases). At present, 42 (88%) have delivered with two patients lost to follow up. Twenty-eight of 40 patients (70%) pursued confirmatory testing. Ten patients—eight TS cases and two SC trisomy cases—pursued prenatal diagnosis, 17 pursued newborn testing, and one patient had testing on POCs. Abnormal karyotypes were identified in 6/19 (32%) TS cases and 7/9 (78%) SC trisomy cases. Mosaic or partial deletion/duplication results were found in 5/28 (18%). Of the 12 patients who did not pursue confirmatory testing, eight had abnormal fetal ultrasound findings. Maternal karyotype was also mosaic in one TS case (45,X[17]/46,XX[33]). 

Conclusion: Parents are more likely to pursue prenatal diagnosis following a screen positive Turner Syndrome cfDNA result but are less likely to pursue confirmatory testing in the setting of abnormal fetal ultrasound findings. Diagnostic testing should always be offered following a positive cfDNA result for SCA as false positives are common and identification of complex karyotypes may alter counseling.

B-314 Factors associated with obtaining results upon repeat cell-free DNA testing in samples redrawn due to insufficient fetal fraction

Pre- and Perinatal
Submitter: Karen White,

Primary Author: Karen White, Ariosa Diagnostics Inc., Roche Sequencing Solutions Inc.

Author 2: Yunwei Wang, Ariosa Diagnostics Inc., Roche Sequencing Solutions Inc.

Author 3: Kelly Chen, Ariosa Diagnostics Inc., Roche Sequencing Solutions Inc.

Author 4: Maximilian Schmid, Ariosa Diagnostics Inc., Roche Sequencing Solutions Inc.

Presenting Author: Kelly Chen, Ariosa Diagnostics Inc., Roche Sequencing Solutions Inc.

Objective: To investigate factors associated with obtaining results on repeat cell-free DNA (cfDNA) testing for fetal trisomy after an initial sample with no result due to insufficient fetal fraction.

Methods: A consecutive series of 428,707 clinical laboratory samples was queried to identify
patients with multiple samples drawn within a 90-day period for the Harmony® prenatal test. For patients whose first sample was reported to have less than 4% fetal fraction, maternal demographics, gestational age, timing of sampling and repeat test outcome were reviewed. A logistic regression model was built to determine the probability of obtaining a result upon repeat testing. Results 2,906 unique pregnancies were identified for study. Average maternal weight was 211 pounds; average gestational age at initial draw was 12.3 weeks. Overall, 53 percent of pregnancies obtained a result on the second draw. Twin and IVF pregnancies did not yield a statistically different proportion of results than singleton and non-IVF pregnancies. Obtaining a result after redraw was associated with maternal weight, elapsed time between draws, and gestational age at the time of repeat sampling but not maternal age or gestational age at initial draw. The odds ratio of obtaining a result was 1.04 (95% CI 1.031 to 1.051) for elapsed time between draws and 0.994 (95% CI 0.993 to 0.996) for maternal weight. This means a 4% increase in odds of a result per day waited, holding maternal weight fixed and a 0.6% decrease in odds of a result for per pound weight, holding time between draws fixed. Conclusions Modeling based on this large dataset can help inform clinical decisions by estimating the probability of obtaining a result with a repeat test after an initial cfDNA test sample has insufficient fetal fraction. Delaying the collection of a repeat sample increases the probability of obtaining a result; however, this increase must be weighed against potentially limiting patient options due to advancing gestational age.

C-264 Prenatal Diagnosis of 47,XX,+der(14)t(14;17)(q11.2; p12): a child of a balanced translocation carrier and a 3:1 segregation

Pre- and Perinatal
Submitter: Hannah Schuster Anderson, ARUP Laboratories

Primary Author: Hannah Schuster Anderson, ARUP Laboratories

Presenting Author: Hannah Schuster Anderson, ARUP Laboratories

Author 2: Lauren Wallace, Intermountain Healthcare

Author 3: Robert Andres, Intermountain Healthcare

Author 4: Nancy Rose, Intermountain Healthcare

Author 5: Michelle Bosworth, ARUP

Author 6: Danielle LaGrave, ARUP

Approximately 5% of couples experiencing recurrent pregnancy loss carry a balanced translocation. Explanations of the possible gametes formed by carriers of balanced translocations are commonly oversimplified, describing the results of alternate segregation and adjacent-1 segregation (2:2 segregation). While this most common occurrence, it behooves genetic counselors to describe potential gametes more accurately and convey factors influencing the likelihood of each possibility. A routine 20-
week anatomy noted cystic hygroma, agenesis of the corpus callosum, cerebellar hypoplasia, and a possible complex heart defect. After genetic counseling, the patient elected a genetic amniocentesis and cytogenetic SNP microarray analysis. The fetal microarray demonstrated duplication of 17p13.3p12 (15.7 Mb and 303 genes) and 14q11.2 (1.0 Mb and 36 genes). Due to the concern for an unbalanced translocation, a karyotype was requested. The fetal karyotype result was 47,XX,+der(14)t(14;17)(q11.2;p12). This nomenclature describes a female fetus with 46 chromosomes plus an additional derivative chromosome 14; resulting from a parent who carries a balanced 14;17 translocation, and of 3:1 segregation. This demonstrates the utility of fetal microarray analysis in the context of multiple congenital anomalies. The derivative chromosome is similar in appearance to chromosome 21, and may have been misidentified if karyotype alone had been ordered. The use of microarray was consistent with the American College of Obstetrics and Gynecology recommendation on this technology stating this test is appropriate for any fetus undergoing invasive testing who has one or more major structural anomalies. Additionally, Shaffer et al 2012 has identified an increased detection rate of 23.8% of microarray over karyotype when cerebellar hypoplasia is noted on prenatal ultrasound with additional anatomical findings. In addition, this case highlights the importance of complete counseling regarding possible gametes of balanced translocation carriers in the prenatal genetic testing setting.<br />

C-267 Clinical Impact and Cost Effectiveness of a 176 Condition Expanded Carrier Screen
Pre- and Perinatal
Submitter: Kyle A Beauchamp, Counsyl

Presenting Author: Kyle A Beauchamp, Counsyl

Primary Author: Kyle Beauchamp PhD, Counsyl

Author 2: Kenny Wong, Counsyl

Author 3: Katie Katie Johansen Taber, Counsyl

Author 4: Gabriel Lazarin, Counsyl

Author 5: Eric Evans, Counsyl

Author 6: Jim Goldberg, Counsyl

Author 7: Dale Muzzey, Counsyl

Introduction<br />

Expanded carrier screening (ECS) for heritable conditions is now considered an acceptable practice by the American College of Obstetricians and Gynecologists, yet the health economics of ECS remains poorly understood.<br />

Methods<br />

The clinical impact and cost-effectiveness of a 176-condition ECS panel were investigated using a decision tree model comparing
minimal screening against ECS. Disease incidences were modeled using carrier statistics from >40,000 anonymized ECS patients, while cost and life-years-lost data were aggregated from the literature and a cost-of-care database. Model robustness was evaluated using one-way and probabilistic sensitivity analyses.

**Results**

Approximately 300 pregnancies per 100,000 are predicted to be affected by a panel condition; these conditions are costly (e.g., $1,000,000 in lifetime costs per affected child) and impact mortality (e.g., 30 undiscounted life years lost per affected child). A decision tree model predicts that, relative to minimal screening, ECS reduces the rate of affected births by 200 per 100,000. Using life years as the clinical outcome of interest, ECS is cost-effective when compared to minimal screening.

**Conclusions**

ECS is predicted to substantially reduce the population burden of Mendelian disease. These benefits are robust to reasonable perturbations of model parameters and cost-effective when compared to other medical interventions.

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**C-270 Uptake of carrier screening among male reproductive partners of prenatal and preconception patients: a retrospective review**

Pre- and Perinatal

Submitter: Meagan E Choates, MS, CGC, UTHealth

Presenting Author: Meagan E Choates, MS, CGC, UTHealth

Primary Author: Meagan E. Choates, The University of Texas Health Science Center at Houston

Author 2: Blair K. Stevens, The University of Texas Health Science Center at Houston

Author 3: Lauren Murphy, The University of Texas Health Science Center at Houston

Author 4: Claire N. Singletary, The University of Texas Health Science Center at Houston

Author 5: Chelsea Wagner, The University of Texas Health Science Center at Houston

Author 6: Theresa Wittman, The University of Texas Health Science Center at Houston

The American College of Obstetricians and Gynecologists (ACOG) recommends that carrier screening should be offered to all women who are pregnant or considering a pregnancy to enable them to make informed decisions regarding family planning. If an individual is identified as a carrier of an autosomal recessive condition, screening should be offered to the individual’s reproductive partner. While many studies have explored predictors of patients’ uptake of carrier screening, very little research exists that describes the uptake of their partners. As most conditions included on carrier screening panels are autosomal recessive, the partner’s carrier status is an essential component in determining a couple’s reproductive risk. Our study thus aimed to describe the uptake of carrier screening by male partners of patients identified to carry an autosomal recessive genetic disorder. A retrospective database review was performed of carrier screening cases seen at the University of Texas Health Maternal-Fetal Medicine clinics between October 2017 and April 2018 (#HSC MS 18 0351). Descriptive statistics were used on the data set. Within this period, 2776 patients were seen, of which 522 either elected routine
carrier screening or presented as a known carrier. From this group, the overall uptake of carrier screening by male partners was 11.7% (n=61), and was only 25.9% (n = 96/370) specifically among patients who were identified as or known to be carriers. A majority of male partners (60.54%) had their carrier screening performed only after their partner was identified as a carrier, with an average delay of 14.5 days between result disclosure and subsequent uptake of screening. Uptake was higher when routine carrier screening results returned as abnormal (n = 42/108, 38.9%) compared to those who presented to genetic counseling as a known carrier (n = 54/262, 20.6%). This study supports the need for further research to better understand the factors that influence or prevent uptake of carrier screening in this population, which may enable more effective patient counseling.

C-273 Exploring Positive Diagnostic Results after Receiving “Aneuploidy Suspected” Screen Results via Non-Invasive Prenatal Screening

Pre- and Perinatal
Submitter: Jordan Dix, LabCorp

Primary Author: Jordan D Dix, MS, CGC, LabCorp

Author 2: Michelle Burch, MS, CGC, LabCorp

Author 3: Amy C Dexter, MS, CGC, LabCorp

Author 4: Emily Walsh, MS, CGC, LabCorp

Author 5: Christine Vaughan, MS, CGC, LabCorp

Author 6: Chevonne D Eversley, PhD, FACMG, LabCorp

Presenting Author: Amy C Dexter, MS, CGC, LabCorp

Background: Prenatal risk assessment by means of non-invasive prenatal screening (NIPS) has become a vastly utilized screening method in recent years. Different labs offering this testing utilize various reporting strategies. Integrated Genetics’ informaSeq screens for trisomy 13, 18, and 21, as well as sex chromosome aneuploidies, with three reporting categories for the autosomal chromosomes: aneuploidy detected, aneuploidy not detected, or aneuploidy suspected. To date, little information is available regarding the outcomes of “aneuploidy suspected” screen results. Here we discuss our experience concerning “aneuploidy suspected” screen results with available follow-up abnormal fetal karyotypes.

Methods: Screen positive informaSeq results were tracked and genetic counselors followed up on these results six weeks post-test or post-delivery, if needed, to gather clinical information including diagnostic testing results, ultrasound findings, and pregnancy outcomes. Results: A total of 16 patients were reported to have abnormal fetal karyotype results after receiving an “aneuploidy suspected” informaSeq screen result. Seven resulted as an entire gain of the chromosome suspected, confined placental mosaicism was confirmed in two cases, one was the result of an isochromosome, and two other cases identified mosaicism. The remaining four cases with abnormal fetal karyotypes were positive for a
chromosomal aneuploidy other than the reported “suspected” chromosome. Discussion: While NIPS has proven to be a highly accurate screening method, these outcomes underscore the importance of confirmatory diagnostic testing.

C-276 Aneuploidy Screening in the Antenatal Testing Unit at Boston Medical Center: Assessing the Context of Decision-Making around Non-Invasive Screening Options

Pre- and Perinatal
Submitter: Jessica Mary Fallon, Boston University Genetic Counseling Program

Primary Author: Jessica Mary Fallon, Boston University Genetic Counseling Program
Presenting Author: Jessica Mary Fallon, Boston University Genetic Counseling Program
Author 2: Christina Yarrington, MD, FACOG, Boston Medical Center, Boston University
Author 3: Philip D. Connors, MS, CGC, Boston Medical Center, Boston University

Objective: This pilot study aimed to assess the decision-making process of women offered cell-free DNA (cfDNA) screening whose pregnancies were deemed to be at an elevated risk for aneuploidy. The goal was to better understand this process by examining factors related to personal feelings, previous exposure to genetics in healthcare, access to transportation, religion and religiosity, and influence of family, friends, and community.

Methods: Semi-structured, in-person interviews were conducted with English speaking women who met the above criteria immediately after their appointment with a genetic counselor where they had been offered cfDNA screening. Interviews were transcribed, coded, and analyzed by the Study PI using grounded theory methodology to identify significant themes.

Results: The participants reported that they were most concerned with being prepared for adverse pregnancy outcomes. The study found that neither the influences of the genetic counseling appointment, their religion, or their immediate families would outweigh their personal opinions in decisions surrounding their pregnancies or healthcare decisions in general.

Conclusions: This research examined pre-selected personal aspects of the decision-making process in the context of the participants’ pregnancies and analyzed how their support systems and the type of information available about their pregnancy influenced that decision-making.

C-279 How many carriers are being missed? A comparison of traditional carrier screening methodologies and whole gene comprehensive methodologies for cystic fibrosis and spinal muscular atrophy.

Pre- and Perinatal
Submitter: Heather Fecteau, NxGen Mdx

Presenting Author: Heather Fecteau, NxGen Mdx
Current recommendations by the ACOG include offering cystic fibrosis and spinal muscular atrophy (SMA) carrier screening to all women of reproductive age, regardless of race or ethnicity, before conception or early in pregnancy. Prior studies have shown that classic methodologies of carrier screening include using genotyping for cystic fibrosis and SMN1 copy number analysis for SMA perform poorly in pan-ethnic American population. To address this concern, NxGen MDx has designed cystic fibrosis and SMA assays that include whole gene analysis. We investigated our patient population to determine what percentage of carriers would have been missed by traditional carrier screening methodologies. A retrospective review was performed on all NxGen MDx patients reported to carriers of pathogenic variants in the CFTR and SMN1 genes. Variants that would be detected using four common genotyping panels done by NGS were compared to variants that were detected using whole gene NGS of the CFTR gene. All variants found with whole gene NGS were classified based on ACMG guidelines, and only likely disease-contributing mutations were reported. Analysis for SMA carriers detected using SMN1 gene copy number assays was compared to comprehensive SMA screening that includes both SMN1 gene copy number analysis as well as SMN1 whole gene sequencing. We found 1,068 carriers for cystic fibrosis using NxGen MDx whole gene NGS with ACMG guideline variation curation. Compared to traditional genotyping technology of the CFTR gene, 34% of patients would have been missed. There were 1,472 carriers for SMA in our patient population. Using MLPA or qPCR alone, 25% of possible silent carriers and point mutation carries for SMA would have been missed. NxGen MDx’s whole gene sequencing of CFTR and comprehensive SMA carrier screening greatly improves detection rates in patients for two of the most common genetic conditions. By capturing more carriers for cystic fibrosis and SMA, patients are given access to additional reproductive options and family planning discussions with their healthcare providers.

C-282 Cell Free DNA for Sex Chromosome Anomalies, Copy Number Variants, and Single Gene Disorders: The Experiences of Prenatal Genetic Counselors

Pre- and Perinatal
Submitter: Katrina Flynn,

Presenting Author: Katrina Flynn,

Primary Author: Katrina Gail Flynn,
Non-invasive prenatal screening (NIPS) using cell free DNA (cfDNA) technology first emerged as a screening tool for Down syndrome in high-risk patients. NIPS technology now allows for prenatal screening for sex chromosome anomalies (SCAs), copy number variants (CNVs) and single gene disorders and is being offered to patients outside the high-risk category. ACOG and ACMG recommendations for the use of SCA and CNV screening differ and neither group has published guidelines for single gene screening. This study surveyed prenatal genetic counselors to understand how they and their practices are currently utilizing these screening tests and discussing them with patients. Counselors were also asked about their opinions on the current and future uses and utility of cfDNA screening. Of the 95 respondents, 43% reported that screening for SCAs is offered to all patients in their clinics, while in 48% cfDNA is most often offered to women at high risk due to either advanced maternal age, abnormal ultrasound findings or a positive serum screen. Currently, CNV screening is most often offered only in special circumstances (48%) such as in the presence of abnormal ultrasound findings or a known family history, while 26% of practices offer CNV screening routinely when offering cfDNA and 25% percent do not currently offer CNV screening at all. Single gene screening is currently being offered in 36% of their clinics primarily for special circumstances such as suggestive ultrasound findings or advanced paternal age. We found consensus among counselors on important issues to discuss with patients and considerations to make about the future of cfDNA. Our results underscore the importance of developing professional guidelines and accumulating data on the positive predictive value and clinical utility of cfDNA screening for CNVs and single gene disorders. Prenatal genetic counselors must thoughtfully balance the available technology with clinical relevance and patient benefit.
Perinatal palliative care (PPC) is a clinical program that provides holistic care to critically ill fetuses and infants alongside psychosocial support to their family members. Genetic counselors are often consulted to explain prenatal or infantile conditions that are life-limiting or life-threatening. The function of the genetic counselor is to provide both education about a condition and supportive resources for their clients. Referral to a PPC program is one way a counselor may provide support. Therefore, being knowledgeable about the medical and psychosocial services offered by PPC programs is important. A recent study found that 11.4% of genetic counselors feel uncomfortable referring to these programs due to a lack of familiarity with PPC. This study aims to increase genetic counselor knowledge about PPC programs through the creation of educational resource materials for genetic counseling training programs accredited by the Accreditation Council for Genetic Counseling (ACGC). A Qualtrics survey was developed and administered to ACGC accredited program leadership to assess PPC education within the curricula, clinical internships, and supplementary activities. Additionally, program directors were asked if programs would benefit from creation of resource material. Survey data shows 85% of responding programs provide education about PPC, and 90% of respondents support creation of educational resource materials. Using the results of the survey to direct content and format of resource material, three documents were created: 1) A series of case studies were created that may also be used as roleplays, 2) An annotated bibliography directing users to articles, books, videos, and websites to increase PPC knowledge, and 3) A PowerPoint covering relevant topics in PPC. This study is designed to impact public health through strengthening the educational experiences of genetic counseling students, which will make them more comfortable with referring clients to PPC services.

C-288 Clinical Utility of Preconception Expanded Carrier Screening

Pre- and Perinatal
Submitter: Katie Johansen Taber, PhD, Counsyl

Presenting Author: Katie Johansen Taber, PhD, Counsyl

Primary Author: Katherine Johansen Taber, PhD, Counsyl

Author 2: Gabriel Lazarin, MS, CGC, Counsyl

Author 3: Kyle Beauchamp, PhD, Counsyl

Author 4: Aishwarya Arjunan, MS, CGC, MPH, Counsyl

Author 5: Dale Muzzey, PhD, Counsyl

Author 6: Kenny Wong, MS, CGC, Counsyl

Author 7: Jim Goldberg, MD, Counsyl

Introduction: When provided during the preconception period, expanded carrier screening (ECS) facilitates reproductive management, such as in vitro fertilization (IVF) with preimplantation genetic
diagnosis (PGD). However, studies exploring reproductive decision-making of at-risk couples have been limited by small sample sizes. Here, we describe the impact of ECS results on planned and actual pregnancy management in the largest sample studied to date of at-risk couples (ARCs) screened preconceptionally. <br />

Methods: Couples who elected ECS and found to be at high risk of having a pregnancy affected by at least one of 176 genetic conditions were invited to complete a survey about the impact of ECS results on planned and actual pregnancy management. <br />

Results: Two hundred and thirty-five ARCs identified preconceptionally completed the survey. Seventy-seven percent reported that they were altering or planning to alter pregnancy management to reduce the risk of having an affected pregnancy, including IVF with PGD, use of donated gametes, adoption, avoidance of pregnancy altogether, and prenatal diagnosis if/when they became pregnant. Subsequent to preconception ECS, nearly half of ARCs had at least one pregnancy by the time the survey was administered, resulting in 126 pregnancies informed by ECS; 40% of these pregnancies were achieved through IVF with PGD. Prenatal diagnosis was pursued in approximately one-third of pregnancies, with 30% of pregnancies found to be affected; approximately three-quarters of affected pregnancies were terminated. In couples who chose not to pursue prenatal diagnosis, common reasons cited were to avoid risk to the pregnancy, a perception that it was not necessary because the couple had undergone IVF with PGD, a perception that the risk of an affected pregnancy was low, and that it “would not make a difference” in the management of the pregnancy. <br />

Conclusions: In a majority of ARCs surveyed, preconception ECS results impacted reproductive decision-making and led to altered pregnancy management that reduced the risk of an affected pregnancy.

C-291 Whole exome sequencing reveals novel USP9X mutation in female fetus with isolated agenesis of the corpus callosum

Pre- and Perinatal
Submitter: Jerica Lenberg,

Primary Author: Jerica L. Lenberg, Augustana University

Author 2: Dolores H. Pretorius, University of California San Diego

Author 3: Eric S. Rupe, University of California San Diego

Author 4: Marilyn C. Jones, University of California San Diego

Author 5: Gladys A. Ramos, University of California San Diego

Author 6: Tara S. Andreasen, University of California San Diego

Presenting Author: Jerica L. Lenberg, Augustana University

Variants in the ubiquitin-specific protease 9X (USP9X) gene have been associated with X-linked syndromic intellectual disability. USP9X is required for neural cell migration and brain development in early embryogenesis. In males, hypomorphic mutations cause syndromic intellectual disability while
females are typically unaffected carriers. However, loss-of-function variants presumed lethal to males have recently been identified to cause a recognizable pattern of malformation and intellectual disability in females. A case series showed 62% of described females with loss-of-function variants in USP9X have a hypoplastic corpus callosum in addition to other congenital malformations. We describe a female fetus with isolated complete agenesis of the corpus callosum detected at 29w6d weeks gestation after the family requested a non-routine ultrasound. Carrier screening, family history, and TORCH titers were negative. The family desired elective termination and chromosomal microarray which was negative. Further testing was desired and whole exome sequencing was performed. A novel likely pathogenic variant in USP9X was detected. This result significantly altered the prognosis and management of the subsequent pregnancy. This case further establishes the spectrum of phenotypes associated with USP9X mutations, as only roughly 20 females have been described to date. Additionally, this case supports the use of prenatal whole exome sequencing, and suggests an emerging role of whole exome sequencing for structural anomalies detected by ultrasound following negative microarray.

C-294 Understanding Preconception Couples’ Perceived Use of Information from Expanded Carrier Screening

Pre- and Perinatal
Submitter: Ashlie Miller,
Presenting Author: Ashlie Miller,
Author 2: Amanda Gammon, Huntsman Cancer Institute
Author 3: Laila Andoni, Lineagen
Primary Author: Ashlie Miller,

Background: Since the shift from single gene carrier screening to expanded carrier screening (ECS) in 2009, there have been several studies involving ECS. However, there have been no studies to our knowledge analyzing how preconception couples plan to utilize information from ECS. <br />
Objective: The main aim of this paper was to prospectively assess what preconception couples would do with information from ECS. <br />
Methods: Surveyed both partners of 48 married preconception couples (n=96) before and after they read and discussed with their partner a recreated news article about ECS. As part of a larger survey, we asked an open-ended question to learn what the participants would do with the ECS information. <br />
Results: The three most common self-reported reasons for how participants would use information from ECS are for mental preparation and knowledge of carrier status (n=64/96), family planning (n=20/96), and tailoring future medical management (n=14/96). Our results also capture common misconceptions about ECS, such as screening for preventable diseases (n=11/96), identifying future health problems for that individual (n=10/96), and providing detailed information about their children’s future health (n=8/96). <br />
Conclusions: More widely accessible education regarding ECS and its limitations are important as the field continues to shift from single gene testing to ECS.
Platform Presentations: Cancer Guidelines and Risk Assessment

Platform Presentations: Cancer Guidelines and Risk Assessment

Platform Presentations: Cancer Guidelines and Risk Assessment

Platform Presentations: Counseling/Psychosocial

Platform Presentations: Counseling/Psychosocial

Platform Presentations: Counseling/Psychosocial

Platform Presentations: Counseling/Psychosocial

Platform Presentations: Counseling/Psychosocial

Platform Presentations: Diversity and Access
Platform Presentations: Diversity and Access

Platform Presentations: Diversity and Access

Platform Presentations: Diversity and Access

Platform Presentations: Variant Interpretation and Diagnostic Utility

Platform Presentations: Variant Interpretation and Diagnostic Utility

Platform Presentations: Variant Interpretation and Diagnostic Utility

Platform Presentations: Variant Interpretation and Diagnostic Utility

Platform Presentations: Variant Interpretation and Diagnostic Utility

Platform Presentations: Training and Workforce
Platform Presentations: ELSI

Platform Presentations: ELSI

Platform Presentations: ELSI

Platform Presentations: ELSI

Platform Presentations: ELSI

Platform Presentations: Cancer

Platform Presentations: Cancer

Platform Presentations: Cancer

Platform Presentations: Cancer
C-297 Does eating placenta help with postpartum mood, energy, and breastfeeding? A matched cohort study of postpartum placentophagy outcomes to inform prenatal genetic counseling

Pre- and Perinatal

Submitter: Emily Morris, University of British Columbia / Provincial Health Service Authority

Primary Author: Emily Morris, University of British Columbia / Provincial Health Service Authority

Presenting Author: Emily Morris, University of British Columbia / Provincial Health Service Authority

Author 2: Caitlin Slomp, University of British Columbia

Author 3: Catriona Hippman, University of British Columbia

Author 4: Angela Inglis, Provincial Health Services Authority

Author 5: Prescilla Carrion, University of British Columbia

Author 6: Rolan Batallones, University of British Columbia

Author 7: Heather Andrighetti,

Author 8: Jehannine Austin, University of British Columbia

Background: Postpartum placentophagy (via encapsulation, or raw/cooked ingestion) is gaining popularity due to a variety of purported benefits to mood, energy, lactation, and overall nutrition. However, empiric studies investigating the effects of postpartum placentophagy on these variables are scarce. Objective: To investigate the impact of postpartum placentophagy on depressive symptoms, energy levels, need for pharmaceutical lactation support, and plasma vitamin B12 levels in women. Hypotheses: In the postpartum, women who consumed their placenta will have: 1) less depressive symptoms, 2) more energy, 3) higher B12 levels, and 4) less pharmaceutical lactation support than women who do not consume their placenta. Methods: A cohort of postpartum women who consumed their placentas (P) were identified from participants in a larger prospective longitudinal study investigating perinatal psychopathology. Using a pseudo-randomization technique, each P participant was matched 4:1 (when possible) with a non-placentophagy control (C) from the same larger study based on: psychiatric diagnosis, postpartum psychotropic medication use, vitamin supplementation, household income, and age. We used data from 3 postpartum time points and Mann-Whitney U tests to investigate differences between the highest Edinburgh Postnatal Depression Scale (EPDS) score, lowest daytime energy score measured by the Sleep-Wake Inventory (SWAI), and lowest B12 between P and C cohorts, and Fisher’s exact test to compare postpartum use of domperidone (used to promote lactation).
between P and C cohorts. Results: We identified 28 P women and matched them to 110 controls. There were no significant differences in EPDS scores (p=.282, \( r^2=.008 \)) SWAI scores (p=.389, \( r^2=.001 \)), B12 levels (p=.685, \( r^2=.006 \)), or domperidone use (p=1.0) between P and C cohorts. Conclusion: This - the largest study to date of the outcomes of placentophagy - does not support claims that postpartum placentophagy improves mood, energy, lactation, or plasma B12 levels. These results provide data to inform prenatal genetic counseling.

C-300 Prenatal Detection of a Cryptic Derivative Chromosome: Association of Ultrasound Findings with an Imprinted Region

Pre- and Perinatal

Submitter: Christine Riordan (Hall), LabCorp

Presenting Author: Christine Riordan (Hall), LabCorp

Author 2: Jennifer Shafer, MS, CGC, LabCorp

Author 3: Sharon Molinari, MS, CGC, LabCorp

Author 4: Laura A. Kline, MS, CGC, LabCorp

Author 5: Stuart Schwartz, PhD, FACMG, LabCorp

Author 6: Peter Papenhausen, PhD, FACMG, LabCorp

Primary Author: Christine M. Riordan, MS, CGC, LabCorp

Microarray analysis has become part of the routine diagnostic process in cases of prenatal ultrasound anomalies. While often these analyses yield normal results, limiting counseling options for these families, it is important to note that array can provide some critical, yet unexpected findings. We present two cases of how microarray findings were not only able to provide an explanation for the ultrasound observations, but also had important reproductive counseling implications. An amniocentesis at 36 weeks gestation with a unilateral right side ventriculomegaly and a small omphalocele on ultrasound had normal chromosome results. Microarray analysis revealed a 1.6 Mb terminal deletion of 6q27->6qter (reported in patients with brain anomalies) and a 5.26 Mb terminal duplication of 11pter->11p15.4. This 11p duplication, containing an imprinted region could be associated with either Beckwith-Wiedemann syndrome (BWS) or Russell-Silver syndrome (RS). These findings suggest a cryptic derivative chromosome possibly arising from a parental balanced rearrangement. Parental fluorescent in situ hybridization (FISH) analysis revealed a paternal 6;11 translocation. A chorionic villus sampling (CVS) was submitted from a 13.4 weeks gestation with a cystic hygroma and hydrops by ultrasound. Microarray analysis revealed a 1.38 Mb terminal deletion of 5q35->5qter (reported in Soto syndrome patients) and a 4.51 Mb terminal duplication of 11pter->11p15.4. Again the 11p duplication, containing an imprinted region, would be associated with either BWS or RS. These findings also suggested a cryptic derivative chromosome. Parental FISH analysis
revealed a paternal 5;11 translocation. Routine chromosome analysis was not adequate to detect these anomalies. The array results correlate with the clinical presentation, providing a prenatal diagnosis and enhancing pregnancy management and delivery options. Most importantly, these array findings also convey information about risk for future pregnancies since in both cases a parental translocation was discovered.

C-303 Prenatal diagnosis of the 15q11.2 microdeletion: challenges for genetic counseling and parental decision making

Pre- and Perinatal
Submitter: Katelynn G. Sagaser, MS, CGC, Johns Hopkins University School of Medicine

Primary Author: Katelynn G. Sagaser, MS, CGC, Division of MFM, Johns Hopkins University School of Medicine

Author 2: Katherine R. Forster, MS, CGC, Fetal Therapy, Johns Hopkins University School of Medicine

Author 3: Kristen A. Leppert, MGC, CGC, Division of MFM, Johns Hopkins University School of Medicine

Author 4: Karin Blakemore, MD, Division of MFM, Johns Hopkins University School of Medicine

Author 5: Angie C. Jelin, MD, Division of MFM, Johns Hopkins University School of Medicine

Author 6: Christine Hertenstein, MGC, CGC, Division of MFM, Johns Hopkins University School of Medicine

Author 7: Cathleen S. Lawson, MS, CGC, Division of MFM, Johns Hopkins University School of Medicine

Author 8: Virginia Corson, MS, CGC, Division of MFM, Johns Hopkins University School of Medicine

Presenting Author: Katherine Rock Forster, Johns Hopkins University

Current guidelines recommend that patients undergoing prenatal diagnosis be offered analysis through karyotype or CMA (ACOG 2016). All patients pursuing prenatal diagnosis at our Center between 1/1/2016 and 5/1/2018 were offered both tests, and 171 patients elected CMA. We identified three cases (1.75%) of 15q11.2 deletion syndrome (OMIM #615656). Case 1: A 40-year-old G2P1001 with a sonographically normal-appearing fetus (predicted as 46,XX by PGS) requested CMA on villi. CMA revealed a maternally-inherited 425 kb deletion of 15q11.2, and the patient underwent D&E. A clubfoot was noted on products of conception. Case 2: A 39-year-old G1P0 elected CVS for a nuchal translucency measuring 9.1 mm. CMA revealed a maternally-inherited 513 kb deletion of 15q11.2. The patient spontaneously delivered at 24 weeks gestation, and the infant was later molecularly diagnosed with Noonan syndrome. Case 3: A 33-year-old G2P0010 underwent amniocentesis due to an increased nuchal fold. CMA revealed a 476 kb deletion of 15q11.2. Following pregnancy termination, mild dysmorphic features and left clubfoot were noted on exam. Parental CMAs and fetal autopsy are pending. The 15q11.2 microdeletion is detected in 0.6-1.3% of the
developmentally delayed population and is associated with an increased risk for neuropsychiatric/neurobehavioral abnormalities (Cafferkey et al. 2014, Abdelmoity et al. 2012). Our prenatal case series suggests that this microdeletion may be encountered with relative frequency on prenatal CMA. As the estimated disease penetrance is only 10% (Rosenfeld et al. 2013), this deletion presents distinct challenges in prenatal decision-making, particularly in the setting of a “normal” parent with the same deletion. With rapid advances in genomic technology, prognostic interpretation of results such as the 15q11.2 microdeletion, which confer only a susceptibility to disease phenotype, pose significant challenges for pregnant patients and genetic counselors alike.

\[ C-306 \text{ 2q12.2q13 Microdeletion Segregating in a Family with Agenesis of the Corpus Callosum} \]

**Pre- and Perinatal**

*Submitter: Laurie Maria Simone, Rutgers University*

*Primary Author: Laurie Maria Simone, Rutgers University*

*Presenting Author: Laurie Maria Simone, Rutgers University*

*Author 2: Elena Ashkinadze, Rutgers- Robert Wood Johnson Medical School*

A G1P0 33-year-old patient was referred for prenatal genetic counseling at 20 weeks gestation due to an increased nuchal fold and inability to visualize the cavum septi pellucidum. She and her 37-year-old spouse are both of Ashkenazi Jewish descent. Pre-pregnancy carrier screening revealed that she is compound heterozygous for the Factor XI deficiency; spouse was not found to be a carrier. Her spouse is a Gaucher carrier; her screen was negative for the common mutations. Her spouse has a history of learning disability, dyslexia, obsessive compulsive disorder and anxiety. He previously had karyotype analysis, revealing that he has a 46,XY,inv(2),(p11.2q13), a reported benign polymorphism. The patient had a level II ultrasound prompting a fetal MRI which confirmed agenesis of the corpus callosum (ACC). She opted for an amniocentesis, which confirmed a male fetus who inherited the paternal chromosome 2 inversion. Fetal microarray analysis revealed a 5.25 MB interstitial deletion on chromosome 2 at the linear position: arr[hg19] 2q12.2q13(107,002,746-112,255,454)x1. Paternal microarray analysis confirmed that the microdeletion was paternally inherited. Subsequent brain MRI of the father revealed complete ACC. Paternal grandparents were negative for the microdeletion, indicating it was de novo. The size and gene content within the deleted region indicate the possibility of clinical significance; yet, no cases with the same breakpoints were found in the literature. Cases of a smaller overlapping deletion have been associated with a developmental delay syndrome, but no cases of ACC were reported. To our knowledge, this is the first reported case of this microdeletion segregating in a family, especially notable is the co-occurrence with ACC. Thus, we suspect there may be a gene in this region associated with ACC. The patient and her spouse were counseled that it is speculative that the microdeletion is causal and will have a 50% risk for recurrence in future pregnancies.
C-309 Making Sense of Patients’ Decision Making and Needs Within the Context of Noninvasive Prenatal Testing

Pre- and Perinatal
Submitter: Lauren Turner,
Presenting Author: Lauren Turner,
Primary Author: Lauren Turner, University of Michigan
Author 2: R. Beth Dugan, University of Michigan - Michigan Medicine
Author 3: Beverly Yashar, University of Michigan
Author 4: Monica Marvin, University of Michigan

Noninvasive prenatal testing (NIPT) screens for fetal chromosomal abnormalities, and though not diagnostic, offers superior sensitivity compared to previous prenatal screening methodologies. While confirmation of positive NIPT results via invasive diagnostic testing is recommended by professional societies, a subset of patients with positive NIPT results decline diagnostic testing and continue their pregnancies. We completed semi-structured interviews to explore the decision-making factors, experiences, and needs of 10 women who declined diagnostic testing and continued their pregnancies following a positive NIPT result. Six participants had positive results for trisomy 21, four had positive trisomy 18 results, and while not part of the inclusion criteria, all participants had abnormal ultrasound findings. Transcripts were coded using grounded theory and identified critical decision making factors, emotional states during the pregnancy, experiences with healthcare providers, and emotional and educational needs (both met and unmet). We found that participants (10/10) cognitively understood their NIPT results are not definitive, but practically interpreted the results as diagnostic. None expressed decisional regret about their testing choices. Participants shared many experiences and needs reported by patients who have undergone invasive diagnostic testing, and described using their NIPT results for both short and long-term planning. However, most participants (8/10) described holding on to the hope that the NIPT may be wrong and expressed a need for their providers to understand and respect this hope. This is a novel need that has not been identified by those who undergo diagnostic testing and suggests a need for a nuanced approach to counseling and management distinct from those with positive diagnostic testing results. Our results highlight an important area where genetic counselors can serve as patient advocates towards the provision of care that is sensitive and responsive to individual patient needs.

C-312 Whose Y is it anyway? Transplants and NIPT II
Pre- and Perinatal
Submitter: Jenna Wardrop, Sequenom
Primary Author: Jenna Wardrop, Sequenom
Noninvasive prenatal testing (NIPT) for fetal aneuploidies by massively parallel sequencing has emerged as a powerful tool in the management of high-risk pregnancies. Fetal sex discrepancies between NIPT and ultrasound can be due to a number of well-documented reasons—including maternal transplant history. Here we discuss 11 select examples of fetal sex discrepancies and/or abnormally strong male results, which were later revealed to be due to a maternal transplant.

Maternal blood samples submitted to Sequenom Laboratories® for MaterniT®21 PLUS or MaterniT® GENOME testing were subjected to DNA extraction, library preparation, and genome-wide massively parallel sequencing.

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Fetal sex discrepancies between ultrasound and NIPT are a rare but known limitation. These discrepancies can be explained by a co-twin loss (or vanishing twin/second sac), fetal sex reversal syndromes/chromosome abnormalities, maternal chromosome abnormalities, and history of transplant. Fetal sex discordance may not always prompt fetal or neonatal karyotyping, but it should be considered in certain circumstances. Data from this cohort suggests not all tissues/organs equally contribute cfDNA to maternal plasma and can mimic fetal data/placental contribution. Inquiring about history of maternal transplant is an important part of pre-test counseling and NIPT fetal sex interpretation. Prenatal screening requires a multifaceted approach.
Cascade screening (CS) provides life-saving information to relatives of people with hereditary cancer or cardiac syndromes; yet many relatives do not learn of their risk. The purpose of this cross-sectional, mixed methods study was to assess how genetic counselors (GCs) facilitate CS. Eligible participants were cancer and cardiac GCs. The study instrument was a novel survey developed using themes identified in a prior qualitative study of CS practices and review of the literature. A draft survey was reviewed by GCs and a survey design unit staff member; a revised draft was piloted by 3 GCs. The final version included mostly multiple choice questions with three open-ended questions. The web-based survey was distributed via email through the National Society of Genetic Counselors (NSGC) Student Research program. Of the 1057 estimated eligible GCs, 247 completed the survey (23.3% response rate). A majority (72.6%) were cancer GCs with 74.5% having 1-5 years of genetic counseling experience. Fifty percent of participants indicated they always discuss CS pre-test and 89.1% discuss it post-test. Participants spent an average of 9.63 minutes discussing CS post-test (SD=5.32). Participants were asked how often they use 22 specific strategies to facilitate CS, using a Likert scale response (1= rarely, 5= almost always); means and standard deviations were generated. The most commonly used strategies were encouraging patients to share (M=4.78, SD=0.51), educating about basic genetics (M= 4.75, SD=0.61), and discussing risks for family members (M=4.61, SD=0.76). The least used strategy was following up to see who had shared (M=1.82, SD=0.98). GCs used an average of 7.85 strategies almost always (SD=3.4, Mode= 8). The number of strategies used was weakly but significantly correlated with time spent discussing CS post-test (r=0.177; p<.011). This study provides a look at how GCs currently facilitate CS. It sets the stage for future studies that could investigate ways GCs can improve the rate of CS.

A-319 Analysis of the Genetic Counseling Job Market - the Future is Bright

Professional Issues
Submitter: Kaitlyn D Burns,
Presenting Author: Kaitlyn D Burns,
Primary Author: Kaitlyn Burns, Augustana-Sanford Genetic Counseling Graduate Program
Author 2: Amy Swanson, Northwestern University Genetic Counseling Graduate Program
Author 3: Jennifer Hoskovec, McGovern Medical School, UTHealth
Author 4: Jennifer Leonhard, Sanford Health
Author 5: Susan Hahn, Quest Diagnostics
Author 6: Quinn Stein, Augustana-Sanford Genetic Counseling Graduate Program
Genetic counseling careers continue to evolve, yet there is a lack of information about hiring trends in the genetic counseling profession. The National Society of Genetic Counselors (NSGC) Professional Status Survey (PSS) captures a valuable biennial snapshot of the workforce. We aimed to better characterize the current job market. We analyzed job advertisements from the NSGC Job Connections and the American Board of Genetic Counseling (ABGC) eBlasts for the years 2014 to 2016 in order to measure frequency of job roles, qualifications, settings, specialties, and type. For the three year period, there were 1594 advertisements representing 1875 unique openings posted by NSGC and 297 advertisements representing 373 openings posted by ABGC. Descriptive statistics were generated and trends were investigated by comparing and contrasting these findings with the National Society of Genetic Counselors (NSGC) Professional Status Survey (PSS). We found that jobs containing a role that “counsels patients” increased as a percentage each year if advertised by NSGC but decreased each year as a percentage when advertised through ABGC. The percentage of jobs posted by NSGC and ABGC in cancer, pediatrics, and prenatal were proportionally less than what was reported in the 2016 PSS. When analyzing job specialties, there were variegated new roles found in job advertisements that had not been documented in previous PSS responses such as ophthalmology counseling or variant curation. A small increase in roles for temporary, contract or fellowship positions was seen, along with small increases in positions that are off-site or remote. Differences in job openings and PSS responses may be due to experienced genetic counselors leaving more traditional roles for new roles and increased utilization of genetic counselors. Analysis of these trends provides vital information for a rapidly evolving field to ensure genetic counselors, prospective students, healthcare systems, and industries are adequately prepared for the job opportunities and the changing landscape of the profession.

A-322 Participant satisfaction with a prospective genetic counselor volunteer and professional development program.

**Professional Issues**

*Submitter: Julia Platt, Stanford Healthcare*

*Presenting Author: Julia Platt, Stanford Healthcare*

*Primary Author: Athena Ganetsos, Stanford Center for Inherited Cardiovascular Disease*

*Author 2: Tia Moscarello, Stanford Center for Inherited Cardiovascular Disease*

*Author 3: Chloe Reuter, Stanford Center for Inherited Cardiovascular Disease*

*Author 4: Jennefer Kohler, Undiagnosed Diseases Network*

*Author 5: Mitchel Pariani, Stanford Center for Inherited Cardiovascular Disease*

*Author 6: Colleen Caleshu, Stanford Center for Inherited Cardiovascular Disease*

*Author 7: Julia Platt, Stanford Center for Inherited Cardiovascular Disease*
Introduction

Despite increasing demand for genetic counselors, prospective genetic counselors seeking to gain exposure to the field have few opportunities for clinical exposure. There even fewer mentorship resources for ongoing professional development of aspiring genetic counselors.

Purpose

To assess the level of satisfaction and perceived value to prospective genetic counselor career development of a volunteer program that integrates traditional shadowing and clinic support duties with a structured professional development program.

Methods

Four prospective genetic counseling students participated in a 12-month-long program at the Stanford Center for Inherited Cardiovascular Disease. Participation consisted of 8-12 hours of volunteer service, clinical observation, and professional development activities weekly. Participants assess program outcomes by completing an exit survey, including Likert-scale questions and open ended questions on factors that influenced their level of satisfaction.

Results

Mean overall satisfaction with the program (1 = strongly dissatisfied; 5 = strongly satisfied) was 4.75. Factors that had the most influence on overall satisfaction were opportunities to shadow (n = 4) and variety of volunteer experiences (n = 3). Agreement with the statement “volunteering helped prepare me for the next stage in my career” (1 = strongly disagree; 5 = strongly agree) was mean 5.00. Agreement with the statement "volunteering helped me to stay actively engaged in my learning and other preparatory activities" was mean 4.75. Agreement with "volunteering improved my ability to apply genetics knowledge to clinical situations" was mean 4.75. Agreement with "volunteering improved my understanding of psychosocial interactions" was mean 4.50.

Conclusions

A volunteer program which integrates traditional clinic support duties with a structured professional development program is associated with a high level of satisfaction and is seen as valuable to career development for prospective genetic counseling students.

A-325 Perceived Role of Clinical Experience in Industry Positions: A Qualitative Study with Industry Genetic Counselors

Professional Issues

Submitter: Janine Kakishita, CSU Stanislaus

Presenting Author: Janine Kakishita, CSU Stanislaus

Primary Author: Janine Elizabeth Kakishita,

Author 2: Carolyn Brown, MSc, CGC, CCGC, Illumina

Author 3: Stephanie Woo,

Author 4: Tina Hambuch, PhD, FACMG, Invitae

Author 5: Janey Youngblom, PhD, MS, CSU Stanislaus

Introduction

The genetic counseling field is expanding to include roles in industry, which often require prior clinical experience.

Purpose

In this exploratory study, interviews were
conducted to gather insights into how industry genetic counselors apply their clinical experience and how genetic counselors without clinical work experience adapt to industry positions.

Methods

Thirty-one industry genetic counselors were interviewed, including nineteen clinically-experienced genetic counselors and twelve genetic counselors without clinical experience. Interviews were transcribed, coded, and analyzed using a thematic approach.

Results

Industry genetic counselors with prior clinical experience perceived their experience gave them credibility in their position. Those without clinical experience sometimes preferred they had clinical experience, specifically related to the subject knowledge of their positions but they do not feel hindered by the absence of it. These genetic counselors often rely on their colleagues for clinical input when needed.

Conclusion

Industry genetic counselors with clinical experience perceive a benefit from having clinical experience including claiming credibility of being a previous clinical counselor with their clients and colleagues as well as always keeping the patient at the forefront of their work. Genetic counselors with clinical experience can perceive how their experience is useful, but don’t consider it necessary. Genetic counselors without clinical experience do not feel hindered in their positions but can recognize where clinical experience would be utilized in their positions including having disease specific knowledge. When needing advice or input on their work, the genetic counselors without clinical experience interact more with their colleagues for clinical-knowledge based input. New graduates considering a career in industry are encouraged to seek clinical experience first by those with clinical experience as well as to reach out to genetic counselors in industry positions to get a better idea of what these position

A-328 Genetic Counselors’ Implementation of Self-Care and Self-Awareness

Professional Issues

Submitter: Lauren Elizabeth Loffredo,

Primary Author: Lauren Loffredo, MS, University of North Carolina Greensboro

Author 2: Christy Stanley, MS, CGC, Wake Forest University School of Medicine

Author 3: Deborah Wells, MS, CGC, Duke Perinatal Consultants of Burlington

Author 4: Lauren Doyle, MGC, CGC, University of North Carolina Greensboro

Presenting Author: Lauren Elizabeth Loffredo,

Self-care and self-awareness practices have been recognized for their positive effect in decreasing compassion fatigue and burnout (Newell & MacNeil 2010; Alkema et al. 2008; Gentry 2002). Both compassion fatigue and burnout are known concerns for the genetic counseling community (Johnstone et al. 2016; Lee et al. 2015; Benoit et al. 2007) and are influencing factors as counselors choose to leave the clinical setting for laboratory positions (NSGC 2016; Dickerson et al. 2015; Injeyan et al. 2011). The present study investigated the self-care (SC) and self-awareness (SA) practices of 277 practicing genetic counselors by distribution of an online self-designed survey to active members of the National Society of
Genetic Counselors. Self-care and self-awareness practices were commonly implemented by respondents and were reported to improve the counselors’ ability to cope with the emotional impact of the career (SC 95.3%, SA 90.6%). The importance of these practices was investigated along with the availability and benefit of both graduate and professional level training in these practices. Though most respondents found self-care and self-awareness practices to be somewhat if not very important for the wellbeing of genetic counselors (SC 95.3%, SA 97.5%), training in these practices was infrequently available. The majority of respondents indicated that graduate level (SC 65.7%, SA 77.1%) and professional level (SC 64.3%, SA 66.1%) training would be helpful. Based on study findings, implications and future research recommendations are provided.

A-331 Genetic Counselor Interactions with Genetic Testing Industry: Prevalence and Perceptions

Professional Issues
Submitter: Erin P Carmany,
Primary Author: Chandler L. Stimach, Wayne State University
Author 2: Erin P. Carmany, Wayne State University
Presenting Author: Chandler L. Stimach, Wayne State University

Studies show there is a high prevalence of interaction between healthcare professionals and commercial industry. There is currently no literature on the prevalence of interactions between the genetic testing industry (GTI) and genetic counselors (GCs) nor how GCs perceive the impact of these interactions on clinical care. The purpose of this study is to quantify GCs’ interactions with the GTI, to analyze perceptions of how these interactions influence clinical care and if GCs feel these interactions are conflicts of interest (COI). A novel cross-sectional online survey was sent to full members of NSGC. In addition to demographic information, we asked if respondents had any of 12 GTI interactions, followed by 5-item Likert-scale questions asking how much they agreed (score=1) or disagreed (score=5) that each interaction influenced their own practice, could influence a colleagues’ practice and if they felt it was a COI. Overall, 99% (376/381) reported having at least two types of interactions with GTI. Meeting with GTI sales representatives, receiving gifts valued under $100, attending sponsored educational events and sponsored meals were the most commonly reported interactions (89-93.5%). The reported prevalence was less than 10% for all others. Patient-facing respondents rated meeting with GTI representatives as most influential on practice (M=2.76) and receiving gifts valued under $100 as least (M=4.44). Respondents agreed most often that holding stock/options in the GTI (M=1.49) was a COI and attending sponsored educational events (M=4.00) and meeting with GTI representatives (M =4.02) least often. This study showed for the first time that, like other healthcare fields, there is a high prevalence of interaction between GCs and the GTI. These results also show that GCs do recognize potential GTI influences but do not necessarily feel all GTI interactions are COI. With the overall high prevalence of
certain GC and GTI interactions, continued education and awareness is needed to appreciate and manage the complexities of GC and GTI relationships.

**A-334 Bridging the Gap: The Role of Genetic Counselors in Cord Blood Banking and Stem Cell Therapy**

**Professional Issues**

*Submitter: Jessica Zoladz, MS, LCGC, Natera*

*Presenting Author: Jessica Zoladz, MS, LCGC, Natera*

*Primary Author: Jessica Zoladz, Natera, Inc.*

*Author 2: Heather Harris, CBR Systems, Inc*

*Author 3: Michelle McDougle, CBR Systems, Inc.*

*Author 4: Melissa Maisenbacher, Natera, Inc.*

**Introduction**

Since the first cord blood (CB) transplant in 1988, CB stem cells have been used to treat genetic disorders, cancers, hemoglobinopathies, immune and metabolic disorders. Recently, the number of clinical trials using CB stem cells in regenerative medicine have expanded. Although families have been privately banking CB for over 20 years, genetic counselors (GCs) have had limited roles in the industry. As stem cell therapies advance and more families consider stem cell banking and therapeutic options, the role of GCs both in clinical discussions and the CB/stem cell industry is critical.

**Case for expanding the role of GCs**

Stem cell therapy using multiple cell types, including CB, is currently in various stages of clinical use/research. Due to the complexity of this evolving landscape, families may benefit from guidance on CB storage and clinical options. Patient-centered counseling approaches offered by GCs can fill this need. GCs in the stem cell industry and various sub-specialties have the opportunity to educate patients about public/private banking options, counsel high-risk families about current and future uses of stem cells, identify potential stem cell transplant or infusion recipients with metabolic disease, immunodeficiency, autism, or cerebral palsy, and care for patients with cancers cured by transplant. GCs may also implement education tools, review family history, deliver test results, coordinate clinical trial consent/enrollment, and facilitate genetic testing (i.e. HLA, PGT-M).<br />

**Discussion**

With the growth of the private CB industry, evolution of the public banking system, and expansion of stem cell clinical trials, there is an increasing need to assist families in navigating this complex environment and support informed decision-making. GCs are proficient in communicating complicated information and in facilitating patient-centered decision-making. Moreover, GCs can accurately communicate the ethical implications pertaining to stem cell research/therapy. These attributes position GCs as an integral part of CB and stem cell industries.
B-317 Genetic Counselors’ Comfort and Knowledge of Cancer Risk Assessment for Transgender Patients

**Professional Issues**  
Submitter: Tala Berro,  
Primary Author: Tala Berro,  
Presenting Author: Tala Berro,  
Author 2: Kim Zayhowski, Stanford University  
Author 3: Tessa Field, Spark Therapeutics  
Author 4: Nadine Channaoui, Department of Veterans Affairs  
Author 5: Jilliane Sotelo, Dana Farber Cancer Institute

Transgender individuals are often their own health advocates, especially if seeking hormone therapies and gender-affirmation surgeries. While there is literature in the genetic counseling field that explores the relationship between genetic counselors and lesbian, gay, and bisexual patients, there is a gap in research that directly addressing transgender patients’ needs. This study assessed cancer genetic counselors’ education, knowledge, and comfort with transgender health issues. A survey evaluated comfort with relevant vocabulary terms and performance on open-ended written case vignettes to approximate how cancer genetic counselors would facilitate conversations with transgender patients about cancer risks. Mean performance on the case vignettes was 78.5% (SD=4.9%). A majority of participants endorsed wanting more education on transgender implications for cancer risk assessment with some participants reporting their discomfort asking about gender pronouns. The study found a lack of consensus on discussing breast cancer screening based on estrogen therapy, pedigree symbol use, and testing of a minor prior to hormone therapy. This is one of the first studies to highlight the educational needs specific to genetic counseling to ensure individualized care for transgender patients.

B-320 Genetic Counselors’ Perceptions of Workplace Respect and its Influence on Professional Decision-making

**Professional Issues**  
Submitter: Lindsay Derby,  
Presenting Author: Lindsay Derby,  
Primary Author: Lindsay Constance Derby, Boston University School of Medicine  
Author 2: Kathleen Berentsen Swenson, Boston University School of Medicine  
Author 3: Tabitha Poorvu, Boston Children’s Hospital
Genetic counselors are dynamic professionals that work in healthcare, policy, industry, research, and a variety of other roles. Based on the 2016 Professional Status Survey, one in four genetic counselors report being dissatisfied with respect from healthcare providers, and one in five from business professionals. A lack of respect in healthcare professions has been shown to have negative consequences on job satisfaction, performance, retention, and patient outcomes. Herein, this exploratory study presents a quantitative analysis on the extent to which genetic counselors value respect and are satisfied with the level of respect they receive in their role, as well as the role of respect in job mobility and professional decision-making. A survey exploring respect value and satisfaction was distributed to practicing genetic counselors that were members of the National Society of Genetic Counselors. Respect from supervisors was reported to be “Extremely important” or “Very important,” in 99% of respondents, and 87% of respondents were “Extremely satisfied” or “Slightly satisfied” with this level of respect. Similarly, 93% of genetic counselors found respect from colleagues to be “Extremely important” or “Very important,” and 91% of respondents indicated they were “Extremely satisfied” or “Slightly satisfied” with respect from colleagues. Non-clinical genetic counselors reported significantly higher satisfaction with the degree of respect from supervisors than clinical genetic counselors (p=0.0196). Furthermore, genetic counselors with additional graduate degrees such as PhD or MPH reported lower satisfaction with respect from supervisors. Results show that professional respect contributes greatly to genetic counselor job retention and movement, with 81% of genetic counselors who have not changed positions in the last two years citing respect as a reason for doing so. Similarly, 76% of genetic counselors indicated respect played a role in their decision to leave their previous position. Practice implications and future directions are further explored.

B-323 Genetic Counselors’ Preparedness for Incidental Findings from Non-Invasive Prenatal Testing

**Professional Issues**

*Submitter: Paige Hazelton,*

*Presenting Author: Paige Hazelton,*

*Primary Author: Paige Elizabeth Hazelton, Cincinnati Children’s Hospital*

*Author 2: Janel Case,*

*Author 3: Sarah Yarnall, Cooper Genomics*

The use of non-invasive prenatal testing (NIPT) for aneuploidy screening has increased dramatically in the last five years due to its high sensitivity and specificity. However, testing cell free fetal DNA (cffDNA) opens the door to maternal incidental findings. This study aims to assess genetic counselors’ preparedness to respond to such incidental findings by surveying prenatal genetic counselors about their experiences with these cases. Surprisingly, 62% of the prenatal genetic counselors (89/143) in this study have encountered incidental findings in their practice, and many shared accounts of unique cases. In addition, participants were asked to respond to three hypothetical scenarios: an incidental finding of
maternal mosaicism for Turner syndrome (45, XO) for which 83% of respondents felt “very prepared” to manage; an incidental finding of a maternal microdeletion, for which 72% of respondents felt “very prepared”; and an incidental finding of maternal malignancy, for which only 48% of respondents felt “very prepared” to handle. There was a statistically significant difference between the first two scenarios and the third, with participants feeling least prepared to manage an incidental finding of maternal malignancy. Participants were also surveyed about their interactions with testing labs, with 34% of respondents stating they had received results informally from the lab, and of those, 70% relayed those results to patients. Overall, genetic counselors felt prepared to counsel patients on incidental findings of maternal mosaicism and maternal microdeletions, yet unprepared to counsel patients on an incidental finding suggestive of maternal malignancy.  

B-326 An exploration of clinical genetic counselors’ interactions with commercial genetic testing laboratories

Professional Issues
Submitter: Kara Christine Klemp, Saint Louis University

Presenting Author: Kara Christine Klemp, Saint Louis University

Primary Author: Kara Christine Klemp, Boston University / Saint Louis University

Author 2: Kira (Apse) Dies, Boston Children’s Hospital

Author 3: Kristin (Sedgwick) Price, Counsyl, Inc.

Author 4: Lauren Lichten, Brandeis University Genetic Counseling Program

The purpose of this study was to explore genetic counselor perceptions of interactions between clinical genetic counselors and commercial genetic testing laboratories. Purposive subject recruitment was conducted via e-mail advertisement to the National Society of Genetic Counselors (NSGC) listserv. Participants who qualified for the study were genetic counselors who work in a clinical setting at least 50% of the time, are involved in ordering or recommending genetic testing products, and attended the 2017 NSGC Annual Conference. Participants were interviewed by telephone using a semi-structured interview guide. The interviews were audio recorded and transcribed. Transcripts were coded and analyzed utilizing grounded theory methodology. In total, 22 clinical genetic counselors were interviewed. Three main themes emerged: (i) education-based interactions are perceived to lack the potential for conflict of interest (COI) because of the clinically beneficial information that they provide; (ii) interactions without educational benefits are perceived as being more likely to create COI; and (iii) despite identifying COI as a potential impact of non-educational interactions, personal ordering practices are perceived as being free of marketing influence. Participants identified interactions with commercial laboratories as necessary aspects of clinical practice. They articulated that they were able to provide improved patient care and conduct informed ordering after receiving educational information at events such as sponsored presentations. Thus, education-based interactions were not perceived to have
the potential for COI. However, interactions that lack an educational component were viewed as outliers, more likely to cause bias by failing to provide participants with educational benefit. Despite the majority of participants identifying interactions that have the potential to create COI, they felt that their personal ordering practices remained uninfluenced. Participant responses in this study indicate a need for improved education and training on the subject of COI.

B-329 From Paper to Practice: Genetic Counseling of Consanguineous Couples

Professional Issues
Submitter: Chau Q Nguyen,
Presenting Author: Chau Q Nguyen,
Primary Author: Chau Q. Nguyen, MS, Arcadia University
Author 2: Sue Moyer Harasink, MS, LGC, St. Christopher's Pediatric Associates
Author 3: Laura J. Conway, PhD, LGC, Arcadia University

Consanguineous couples have an increased risk to have a child with an autosomal recessive condition or congenital anomaly. Consanguinity is common in some cultures but has a negative association in most of the US. Counseling for consanguinity is complex, balancing risk discussion with cultural sensitivity. The National Society of Genetic Counselors (NSGC) has published practice guidelines regarding consanguinity. This study used an online survey to explore genetic counselors’ knowledge and perception of the NSGC guidelines. The survey included true/false questions derived from the guidelines to assess knowledge, Likert scale questions to assess agreement with the guidelines, and open ended questions to identify other areas of need and how they may be addressed. 177 of 180 responses were usable. The majority of participants 60% (n=105/175) were aware of the guidelines prior to partaking in the study. Participants had an average 88.1% correct response rate to knowledge based questions. Most participants answered, “strongly or moderately agreed” to 7/9 recommendations in the guidelines. Participants most often disagreed with specific testing recommendations, including whether consanguinity alone should be considered as a basis for genetic testing (59.6%, n=93/156) or whether consanguinity should be considered when evaluating anomalies found in a fetus (55.5%, n=86/155). Responses to challenges in caring for consanguineous couples included addressing cultural differences, stigma, guilt and shame. 82 respondents provided input about potential useful resources to increase counseling skills, including educational webinars, lectures, patient handouts and quick fact sheets. When asked about recommended changes to the current guidelines, 29.8% (n=17/57) discussed updating guidelines to reflect new technology and 61% (n=35/57) described no changes. These data suggest that the current NSGC recommendations regarding consanguinity are useful, and that further improvements and resources in counseling education could be of benefit for practicing genetic counselors.
Development of a tool to measure genetic counselor workload capacity in the laboratory setting

Professional Issues
Submitter: Elizabeth Ulm, Cincinnati Children's Hospital Medical Center
Presenting Author: Elizabeth Ulm, Cincinnati Children's Hospital Medical Center
Primary Author: Elizabeth Ulm, Cincinnati Children's Hospital Medical Center
Author 2: Hannah Mianzo, Cincinnati Children's Hospital Medical Center
Author 3: Chinmayee B. Nagaraj, Cincinnati Children's Hospital Medical Center
Author 4: Sanjukta Tawde, Cincinnati Children's Hospital Medical Center
Author 5: Emily Wakefield, Cincinnati Children's Hospital Medical Center

With the expansion of non-clinical genetic counseling roles and settings, our laboratory genetic counseling team identified a need to define workload capacity and productivity. The goal of this project was to quantify workload on an average day across multiple roles, for potential applicability towards demonstrating productivity in off-site settings and/or evaluating genetic counselor (GC) staffing needs.

We developed a seven-question electronic survey administered through SurveyMonkey for each GC to complete at the end of each day for four weeks. As daily GC roles vary, the survey documented the role performed (on-call/customer service, report-writing, lab projects, clinic), perception of work volume, number of reports written and complexity, whether the GC completed required daily on-call tasks or whether these were delegated to a GC assistant or another GC, and participation in other lab projects outside of daily roles. Considering a work week of forty hours and our team’s allotment of 149.6 GC-hours per week assigned to laboratory tasks (3.74 FTE total), 79.6% of laboratory GC time was accounted for over four weeks by the survey. Daily data collected by the survey included number of reports written (average: 7, range: 0 – 24 reports); time spent writing reports based on complexity (average: 2.5 hours, range: 15 min – 5 hours); and time spent on non-report-related or client service-related roles (meetings, process improvement projects, education, projects related to new test launches) (average: 1.44 hours, range: 0 – 7.25 hours). These data demonstrate that a daily survey is a flexible tool for assessing daily workload capacity for the team. In the rapidly evolving genetic testing field, these metrics will enable us to estimate the potential impact of changes to our workload and productivity due to test launches or laboratory process changes. This will allow us to objectively assess and predict future genetic counselor staffing needs. This tool can also be used as a guide for other GCs to develop similar capacity measures within their own work settings.
C-318 Perceived Stress and Job Satisfaction: A Comparison of Laboratory and Clinical Genetic Counselors

Professional Issues
Submitter: Brittany Marie Brassell,
Primary Author: Brittany Marie Brassell,
Presenting Author: Brittany Marie Brassell,
Author 2: Elyse B. Mitchell, Mayo Clinic
Author 3: Christine M. Koellner, Mayo Clinic

Genetic counseling can be a stressful, but often extremely rewarding field. Previous literature has found that the overall level of satisfaction in the genetic counseling profession is quite high, but that laboratory or “non-clinical” genetic counselors tend to have an even higher level of satisfaction than clinical genetic counselors (NSGC 2016). The purpose of this investigational study was to further examine satisfaction level and to determine if perceived stress levels differ between the two groups.

Four hundred and nineteen genetic counselors qualified for and took part in an online survey regarding their levels of perceived stress and job satisfaction using the Perceived Stress Scale (PSS) (Cohen, Kamarck, & Mermelstein, 1983) and the Minnesota Satisfaction Questionnaire (MSQ) (Vocational Psychology Research, 1977). Analysis revealed that laboratory genetic counselors have a higher level of job satisfaction and a lower level of perceived stress than clinical counselors, with a negative correlation between the two variables (statistically significant at the 0.01 level, \( r = -.521, p \leq .01 \)). A principle components analysis was performed on potential stressors and aspects of job satisfaction and significant themes were found within each. These themes account for some, but not all of the difference in perceived stress and job satisfaction that was found to exist between laboratory and clinical genetic counselors. The findings of this study give important insight into specific factors that are playing a role in the differences between these two groups. It also points to interventions or research that can be implemented to improve well-being, job performance, and career satisfaction within the field.

C-321 Exploring Genetic Counseling Information Needs & Information Seeking Behaviors

Professional Issues
Submitter: Amy E Donahue, MLIS,
Primary Author: Amy E Donahue, University of Wisconsin School of Medicine and Public Health
Author 2: Elizabeth M. Petty, University of Wisconsin School of Medicine and Public Health
Author 3: April L. Hall, Waisman Center, University of Wisconsin-Madison

Presenting Author: Amy E Donahue, University of Wisconsin School of Medicine and Public Health
Genetic counseling is a unique, rapidly growing field with increasingly diverse practice settings. It spans the information-dense world of genomics, precision medicine, and multiple clinical specialties. Given this context, it is notable that few published studies exist within genetic counseling field on information needs and behaviors. Meanwhile, a substantial body of research exists on this topic for other healthcare professionals, providing support for service provision and resource acquisition. The purpose of this cross-sectional study was to explore genetic counseling information needs and behaviors, including parallels with other healthcare professionals and differences between genetic counseling students, genetic counselors, and within various professional subgroups of genetic counselors. An online survey asked respondents how often they used specific resources; in what situations would they need more information; and what barriers they faced obtaining information. The results suggest commonalities with other healthcare providers, such as frequent use of colleagues as an information source. The results also demonstrated new observations, including differences among resources used and barriers faced between different genetic counseling subgroups. These results elucidate gaps and opportunities in more efficient use and provision of information with the potential to impact genetic counseling workflows.

C-324 Defining the role of a genetic counselor within comprehensive care teams: perspectives of the provider team and patients

Professional Issues
Submitter: Paul Edward Hudson, The Ohio State University Genetic Counseling Program

Primary Author: Paul Edward Hudson, The Ohio State University Genetic Counseling Program

Presenting Author: Paul Edward Hudson, The Ohio State University Genetic Counseling Program

Author 2: Kristin Zajo, Nationwide Children's Hospital

Author 3: Cynthia A. Gerhardt, Nationwide Children's Hospital

Author 4: Elizabeth Varga, Nationwide Children's Hospital

Background: As genetic and genomic testing is increasingly integrated into medical care across a variety of specialties, the genetic counselor (GC) has emerged as a key member of multidisciplinary (MD) teams. Prior research has demonstrated the importance of role clarification when new subspecialties are introduced to these teams given that differences in the expectations of team member may hinder the development of newly introduced professions. This study aims to assess patient and provider perceptions of the GC’s role in four pediatric clinics and how GC skills may be optimally utilized.

Methods: Accreditation Council for Genetic Counseling (ACGC) competencies were used to develop patient and provider surveys. Team members working in four pediatric hematology/oncology clinics were recruited to complete a 48-question survey assessing their perception of a GC’s role in clinic. Patients > 18 years or their guardians were recruited to complete a similar 49-question survey. Roles were grouped into three categories; data were analyzed using descriptive statistics, Kruskal-Wallis and chi-squared tests. Results: Providers (N = 25) perceived most GC roles as shared between GCs and other
team members (54.0%) and fewer roles as primarily a GC’s responsibility (37.2%). Providers perceived roles related to genetic expertise and coordination of care to be primarily the role of a GC significantly more often than roles related to psychosocial skills \((p < 0.0001)\). Patients/caregivers \((N = 70)\) perceived genetic-centric roles as significantly more important than roles related to coordination of care \((p = 0.0326)\) and psychosocial skills \((p < 0.0001)\). Conclusions: GCs in a pediatric setting may maximize their potential in MD clinic by functioning as a genetic expert that assumes critical care coordination responsibilities related to genetic testing, with less emphasis on psychosocial roles. Further communication between providers and GCs may clarify expectations and amend differences in provider perceptions and the current GC-reported division of responsibilities in clinic.

**C-327 FACTORS INFLUENCING RISK OF BURNOUT IN GENETIC COUNSELORS**

**Professional Issues**

*Submitter: Emily M Lancaster, University of Oklahoma Health Sciences Center*

*Presenting Author: Emily M Lancaster, University of Oklahoma Health Sciences Center*

*Primary Author: Emily Lancaster,*

*Author 2: Erin Youngs, MS, LCGC, University of Oklahoma Health Sciences Center*

*Author 3: Stephen Gillaspy, PhD, University of Oklahoma Health Sciences Center*

*Author 4: Susan Hassed, PhD, LCGC, University of Oklahoma Health Sciences Center*

Genetic counselors have been found to experience burnout, which is characterized by feelings of exhaustion, disengagement, and decreased personal accomplishment. Research on causes of burnout for genetic counselors is incomplete. This study sought to examine the role genetic counseling specialty, preventative actions, and demographic information may have in mediating burnout risk for genetic counselors. An online survey was sent out through the National Society of Genetic Counselors listserv. Questions included demographic questions, specialty of practice, the Oldenburg Burnout Inventory which measures disengagement and exhaustion to assess risk of burnout, and qualitative questions for greater understanding of significance. A significant influence of disengagement and exhaustion was the genetic counselors’ self-report. This included self-report of burnout, of spending an appropriate amount of time at work, and satisfaction with patient load. Influential preventative actions found in this study were increased recognition from other professionals relating to genetic counseling skills and professional contributions, use of self-care, and improved work-life balance; these may all be helpful to lessen burnout in the profession.

**C-330 How is The NSGC Definition of Genetic Counseling Being Used?**

**Professional Issues**

*Submitter: Robert G. Resta, Hereditary Cancer Clinic/Swedish Cancer Institute*
Background: In 2006, we, as members of an NSGC task force, proposed a definition of genetic counseling practice. Because the practice of genetic counseling has evolved since then, we questioned whether this definition was still useful. As a proxy for relevance, we investigated whether the published definition is being used in genetic counseling research and training.

Methods: Because there are no standardized measures for determining the utility of a professional practice definition, we measured utilization two ways: 1) Standard citation sources (PubMed Central, Google Scholar, ResearchGate, CrossRef) were reviewed to determine how often the definition was included in scientific publications. 2) A sample of Program Directors of US and international genetic counseling training programs were surveyed about whether and how they incorporate the definition into curricula.

Results: As of May 4, 2018, the definition was cited in 61 references in PubMed Central, 465 references in Google scholar, 342 references in ResearchGate, and 276 references in CrossRef (99th percentile for citations in the Journal of Genetic Counseling). Differences in citation numbers reflect differences in core publications in each database, methodology in surveying publications, and goals of each citation service. The number of citations has increased over the past 5 years compared to the first five years after publication and has been cited in a wide range of journals and texts. Ten US and 10 international graduate program directors in genetic counseling responded to our request for information. All incorporate the definition into students’ training in the first year, and many continue to do so throughout the curricula.

Conclusion: The NGSC genetic counseling definition has been widely used in research and training of genetic counselors. We were unable to find criticism of the definition. Given the dynamic role of genetic counselors, this definition should be regularly re-evaluated to assess its continued utility.

C-333 Academic Appointment For Genetic Counselors: Opportunities, Challenges and Career trajectories

Professional Issues
Submitter: Yiru Chen Zhao,

Primary Author: Yiru C Zhao, Brandeis University
Beyond the NSGC professional status survey, there is little information about the career paths for genetic counselors who hold academic appointments. There is also a gap in knowledge among genetic counselors in general about the qualifications, job responsibilities, and challenges associated with an academic appointment. This exploratory study aims to provide insights into the various career trajectories for genetic counselors holding an academic appointment. One hundred and nineteen genetic counselors with a current academic appointment completed the survey. The majority of the academic appointments were through the School of Medicine at University Medical Centers. Assistant professor (42%) and instructor (40%) were the most commonly reported titles. Over 42% of the participants were affiliated with a genetic counseling program, and they spent more time on teaching and mentoring students, but less time on clinical care than those not affiliated with a genetic counseling program. The requirements for current position reported by at least 40% of the participants included ABGC or equivalent certification, letters of recommendation, teaching experience, publication history and minimum of 3-5 years' practice. The opportunity for career advancement, level of autonomy and teaching were the most reported factors driving genetic counselors to pursue an academic appointment. Overall job satisfaction rate was high among all the participants but those affiliated with a genetic counseling program were more likely to be satisfied. The reported challenges of an academic position included lack of institutional recognition, lack of a career track that allowed for promotion and poorly defined criteria for hiring and promotion, all of which need to be addressed at an institutional level. These findings suggest that genetic counselors find an academic appointment rewarding because of the opportunities to teach, mentor students and conduct research, but that obstacles to career advancement within the academic setting will require changes at the institutional level.

A-340 The Relationship Between Age-of-Onset and the Behavioral Phenotypic Manifestations in Huntington's Disease

Psychiatry/Neurology
Submitter: Megha Ranganathan, student, The Ohio State University

Presenting Author: Megha Ranganathan, student, The Ohio State University

Primary Author: Megha Ranganathan, The Ohio State University

Author 2: Jonathan A. Race, The Ohio State University

Author 3: Dawn C. Allain, The Ohio State University
Objective: The purpose of this study is to characterize behavioral manifestations of the Huntington’s disease (HD) phenotype as associated with age-of-onset (AOO) of clinical diagnosis.

Background: The relationship between behavioral symptoms and AOO of clinical diagnosis in HD has not been fully explored.

Methods: Participants were subjects with manifest HD registered in the Enroll-HD database (as of 2017). The major initial symptom type at disease onset - motor, cognitive, or behavioral and severity of behavioral symptoms at disease presentation were compared in individuals with early onset HD (AOO <30 yrs), early-adult onset HD (AOO 30-59 yrs), and late-adult onset HD (AOO ≥60 yrs). Information on the Clinical Characteristics form and short version of the Problem Behaviors Assessment (PBA-s) was used to assess symptom presence and severity at disease onset. Descriptive statistics, chi-square tests, and multinomial logistic regression models were used for analysis.

Results: A total of 4,469 individuals were eligible for the study. Of individuals in the early onset cohort, 126 (26%) had behavioral symptoms as the presenting symptom compared to 678 (19%) individuals in the early-adult onset cohort and 56 (11%) in the late-adult onset cohort (p<.0001). A one year increase in AOO was associated with a 5.6% decrease in the odds of behavioral symptoms being the presenting symptom at disease onset (p<.0001) and a 5.5% decrease in the odds of presentation with severe behavioral symptoms of any type, particularly disorientation and delusions.

Conclusions: Individuals with earlier onset HD may be more likely to present with behavioral symptoms at disease onset than later-onset individuals. A better understanding of the relationship between AOO and the behavioral phenotype of HD will be helpful in developing therapies that aim to treat symptom specific disease presentations. These findings may influence how risk assessments are made by genetic counselors for individuals at risk for HD. The observations in this study offer important insight into future avenues of research.

B-335 22q and mental health: Development of a resource about the psychiatric manifestations of 22q11.2 deletion syndrome

Psychiatry/Neurology

Submitter: Emily Morris, University of British Columbia / Provincial Health Service Authority

Primary Author: Stephanie Chieffo, Alberta Health Services

Author 2: Caitlin Slomp, University of British Columbia

Author 3: Emily Morris, University of British Columbia

Presenting Author: Caitlin Slomp,

BACKGROUND: Individuals with 22q11.2 deletion syndrome (22qDS) have an increased chance of developing various psychiatric disorders and up to 25-30% will develop schizophrenia. Early intervention
improves outcomes for individuals with mental illness, but parents report gathering information about the psychiatric risks of 22qDS from non-medical sources (i.e. the internet) rather than from a healthcare practitioner. We sought to develop a resource, using input of parents of children with 22qDS, to address the need for publicly available, reliable information about the psychiatric features of 22qDS. 

**METHODS:** Parents of individuals with 22qDS who had received psychiatric genetic counseling in Vancouver, BC were invited to participate in a cognitive interview. Participants were asked to verbalize their thoughts and feelings about what information they found helpful and/or important regarding the psychiatric aspects of 22qDS, and to provide guidance on how to modify a generic mental health resource booklet that they had received after psychiatric genetic counseling to be specific and more relevant to 22qDS. Interviews were conducted via telephone, recorded and transcribed and analysed for themes. 

**RESULTS:** Six parents participated in the interviews. Data that emerged from the cognitive interviews fell into three categories: the value of the information provided; modifications to the generic booklet that could be included in the 22qDS resource; and new additions to include in the 22qDS resource. Participant input was directly incorporated into the development of the resource, supplemented by a literature review. Features of the booklet informed by participant feedback included modification of the “jar model” (a visual representation of multifactorial inheritance) and tools to recognize and manage mental illness. 

**CONCLUSION:** We developed a novel print and online resource regarding the risk of psychiatric disorders in 22qDS, informed by parental interviews. The resource will be quantitatively evaluated by a larger group of parents before public distribution.

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**B-338 Compound heterozygous variants in SHQ1 in sisters with extrapyramidal movement disorder**

*Psychiatry/Neurology*

**Submitter:** Angela Krutish,

**Presenting Author:** Angela Krutish,

**Primary Author:** Angela Krutish, Biochemistry and Medical Genetics, University of Manitoba

**Author 2:** Dr. Kristin Kernohan, CHEO Research Institute

**Author 6:** Care4Rare Canada Consortium, CHEO Research Institute

**Author 7:** Dr. Samantha E. Marin, Pediatrics and Child Health, University of Manitoba

**Author 8:** Dr. Marc R. Del Bigio, Pathology, University of Manitoba

**Author 9:** Dr. Patrick Frosk, Pediatrics and Child Health, University of Manitoba

**Author 3:** Xiaomin Dong, Murdoch Children’s Research Institute

**Author 4:** Dr. John Christodoulou, Murdoch Children’s Research Institute

**Author 5:** Dr. Zornitza Stark, Murdoch Children’s Research Institute
SHQ1 participates in rRNA processing through the assembly of H/ACA-box ribonucleoproteins. Compound heterozygous variants in SHQ1 were previously reported in a patient with a severe neurological presentation suggestive of Hoyeraal-Hreidarsson syndrome. Biallelic mutations in SHQ1 have yet to be characterized. We report two non-dysmorphic sisters who presented in infancy with motor developmental delay, including poor head control, intermittent stiffening of the arms and legs, occasional arching, and inability to sit without support. The patients are of German Mennonite, Ukrainian, and Polish descent. At age two, both sisters developed intractable extrapyramidal movement disorders, presenting as choreoathetosis and dystonia. They also exhibited anxiety, self-injurious behaviors, occasional seizures, and autonomic dysfunction. Cerebrospinal fluid analysis on both patients showed very low dopamine metabolites. The older sister died at age ten years. Autopsy revealed a small brain (5th %ile), neuron loss in the CA1 sectors of the hippocampi, and regional Purkinje neuron loss, the latter two likely secondary to seizures. Related to the motor and biochemical features, neurons of the substantia nigra were substantially smaller than in controls and lacked pigment. Microglial nodules indicated ongoing loss of neurons. Exome sequencing in the patients revealed compound heterozygous variants in SHQ1: a frameshift deletion (p.Asp277SerfsTer27) and a missense variant in a highly conserved residue (p.Glu292Lys). The former has an allele frequency of 0.001 in the European population, while the latter has not been reported. Two Australian brothers with dystonia were also found to carry compound heterozygous variants in SHQ1, one of which is p.Asp277SerfsTer27. Accordingly, these variants offer a promising explanation for the inability of brainstem neurons to produce dopamine and the severe clinical presentation in our patients. An animal model is currently under development to better elucidate the biological significance of these variants.

B-341 Parental Perspective Identification and Genetic Reframing of ADHD Etiology

Psychiatry/Neurology

Submitter: Zachary Michael Salvati,

Primary Author: Zachary M Salvati, MS,

Author 2: Jehannine Austin, PhD, MSc, CGC/CCGC, University of British Columbia

Author 3: Gene Hallford, PhD, University of Oklahoma Health Sciences Center

Author 4: Erin Youngs, MS, LCGC, University of Oklahoma Health Sciences Center

Author 5: Stephen Gillaspy, PhD, University of Oklahoma Health Sciences Center

Author 6: Susan Hassed, PhD, LCGC, University of Oklahoma Health Sciences Center

Presenting Author: Zachary Salvati, MS,

Parental Perspective Identification and Genetic Reframing of ADHD Etiology<br />
Zachary M. Salvati, Gene Hallford, Erin Youngs, Stephen Gillaspy, Jehannine Austin, and Susan Hassed<br />

Background: Attention Deficit Hyperactivity Disorder (ADHD) is an etiologically complex and heterogeneous condition
characterized by inattentiveness, hyperactivity, and impulsivity that interferes with everyday functioning and/or development in two or more environments. Little is known about how parents of children with ADHD think about the cause of the condition or about their interest in genetic counseling. Purpose: To recruit a cohort of parents of children with ADHD to explore: causal attributions for ADHD, the impact of information about etiology of ADHD provided through video education (VE), and interest in psychiatric genetic counseling (PGC). Methods: Online surveys were distributed to parents who had one or more children with ADHD. Genetic counseling outcome scale (GCOS-24) scores were compared before and after the VE intervention; and the causal attribution scale (CAS) was used to determine baseline causal attributions for ADHD.<br />Results: 62 participants completed baseline questionnaires and 29 completed this and the post-VE questionnaire. Overall, participants attributed a greater percentage of ADHD etiology to genetic factors rather than environment, and ethnic minorities with higher education were significantly less confident in their answers (p = 0.027). VE was beneficial to some participants; e.g. they mentioned “reduced stigmatization & understanding” and “better[ing] the outcomes”. However, change in scale score on the GCOS was not significant (p = 0.109). After the VE intervention, 14 participants indicated they would like to talk to a health professional about the implications of genetic contributions to ADHD. Conclusion: Our data suggest that VE may hold some potential benefit for parents of children with ADHD. Larger studies are warranted.<br />

B-344 Exploring Genetic Counselors’ Practices and Attitudes Towards Patients Facing Substance Use Disorders

**Psychiatry/Neurology**

**Submitter: Allie White,**

**Presenting Author: Allie White,**

**Author 2: Gretchen Schneider, MS, LCGC, Brandeis University**

**Author 3: Fayth Kalb, MS, CGC, Ann & Robert H. Lurie Children’s Hospital of Chicago**

**Author 4: Amy Sommer, LICSW, Jewish Family & Children’s Service**

**Primary Author: Alexandra White, MS, Brandeis University**

Substance use disorders (SUDs) are highly prevalent and heritable psychiatric conditions yet little data exists on the practice of genetic counseling for SUDs. Studies on genetic counseling for other psychiatric disorders suggest this practice can promote patient empowerment and decrease a personal sense of stigma. This study aimed to characterize genetic counselors’ encounters with SUDs in clinical practice and identify obstacles to effective genetic counseling for patients facing a history of SUD. Currently practicing genetic counselors in patient-facing roles were asked to complete an anonymous online survey and 220 responded. The average respondent reported that when a history of SUD arises in a session, they “often” include it in the patient’s pedigree, “sometimes” offer psychosocial counseling or discuss the hereditary nature of SUD, and “rarely” provide risk assessment or resources/referrals. A
large portion of respondents (41.2%) received SUD training in graduate school while only 10% reported such training post-graduation. When presented with hypothetical patients with SUD, those with training were more likely to offer certain elements of genetic counseling, particularly a discussion of the inheritance of SUD. In utilizing the Social Distance Scale (SDS) to examine stigma towards individuals with SUD, we found that the average respondent desired social distance from these individuals in intimate relationships and that having personal and/or professional exposure to SUD did not significantly influence scores on the SDS. Our results indicate that genetic counselors are likely to offer elements of genetic counseling to patients with a history of SUD in the hypothetical but are not currently offering these services in their clinical practice. As understanding of the genetics of SUD and the demand for psychiatric genetic counseling services rise, it is imperative that improvements in practical, experiential SUD training continue.<br />

Keywords: substance use disorders, substance use disorder training, stigma, genetic counseling

C-336 22q11.2 Deletion Syndrome: Psychiatrist Self-Report of Knowledge of Mental Health Implications and Willingness to Act in Providing Clinical Services

Psychiatry/Neurology
Submitter: Natalie Lynn Dykzeul, Virginia Commonwealth University
Primary Author: Natalie Lynn Dykzeul, Virginia Commonwealth University
Presenting Author: Natalie Lynn Dykzeul, Virginia Commonwealth University
Author 2: Rachel Gannaway, MS, CGC, Virginia Commonwealth University
Author 3: Jennifer Lent, MS, CGC, Virginia Commonwealth University
Author 4: Judy Silberg, PhD, Virginia Commonwealth University
Author 5: Ruth Trivelpiece, MEd, CCC-SLP, Virginia Commonwealth University

In the human population, 22q11.2 deletion syndrome is a genetic disorder that is associated with a multi-system presentation which includes a significantly increased risk for psychiatric illness. Recent research has shown that patients with 22q11.2 deletion syndrome benefit from regular management and treatment by a psychiatrist or mental health professional. Active clinical psychiatrists were surveyed to evaluate their knowledge of this increased risk, to assess if specific education or clinical exposures impacted their level of knowledge, and to determine their willingness to provide services to this patient population. The data from this exploratory study revealed that psychiatrists, if they have heard of this syndrome at all, have a low-level of understanding of the psychiatric risk, genetic etiology, and natural history of 22q11.2 deletion syndrome. Further, this study indicates that providers’ knowledge is the result of clinical experience rather than formal education or training. Of the responses to the survey, 31% of providers report a history of providing treatment for this genetic syndrome. This data demonstrates that psychiatrists are unfamiliar with this disease and that there is a need for formal
C-339 Perspectives on Spinraza (Nusinersen) Treatment (POST) Study: Views of Individuals and Parents of Children Diagnosed with Spinal Muscular Atrophy

**Psychiatry/Neurology**

*Submitter: Michelle Pacione,*

*Presenting Author: Michelle Pacione,*

*Primary Author: Michelle Pacione, Stanford School of Medicine*

*Author 2: Carly Siskind, Stanford Health Care*

*Author 3: John Day, Stanford Health Care*

*Author 4: Holly Tabor, Stanford Center for Biomedical Ethics*

**Introduction:** Spinal muscular atrophy (SMA) is a genetic disorder characterized by muscle loss. In December 2016 the FDA approved the first and only treatment drug for SMA: Spinraza (nusinersen). Although this new miracle drug brings optimism and hope, there are no published data on the perceptions of individuals with SMA about the benefits, risks, and challenges associated with treatment. This qualitative interview study sought to characterize the perspectives of patients/families with SMA about this new innovative treatment for a previously untreatable and often fatal condition.<br />

**Methods:** Individuals and families were recruited via advertisements on ten Facebook group pages related to SMA and through Stanford’s neurology research registry. Participants were asked to fill out a demographic questionnaire and participate in a semi-structured interview via voice conferencing. Interview questions focused on: 1) experiences with SMA, 2) opinions on Spinraza treatment, and 3) factors they considered in their decision process regarding treatment.<br />

**Results:** Fourteen people were interviewed: ten adults with SMA (ages 27-47) and four parents of children with SMA. Participants ranged in their views/status about Spinraza treatment: four were uninterested, five were still deciding whether to pursue treatment, three were in the process of pursuing treatment, and two were currently getting injections. Participants described several key factors influencing their treatment decisions, including: concerns about risk factors and side effects, high cost, insurance coverage, time involvement, and lack of data about efficacy. <br />

**Conclusions:** The decision to pursue or not to pursue Spinraza was based on access, needs, values, and perceived quality of life. Individuals are heavily weighing the benefits and risks of treatment primarily based on testimonials posted to social media accounts. Practitioners need to more effectively disseminate information about this drug and others in the pipeline and help patients to make informed, value-based treatment decisions.
Introduction: Neurogenetic counselors (NGCs) specialize in neurology genetic counseling (GC). Despite encompassing approximately 8% of the GC workforce, evidence suggests that NGCs are underutilized in neurology practice and the current number of practicing NGCs is insufficient to meet patient care needs. With the expansion of genetic services throughout medicine, NGCs are uniquely positioned to help patients and the neurologists involved in their care. However, little is known about how NGCs practice in clinical, research and industry settings. Purpose: The aim of this study is to describe the current scope of practice of all NGCs. Methods: The study’s survey was designed through literature review and input from NGCs. The survey was piloted and modified, then sent to the NSGC Neurology Special Interest Group and the NSGC membership. Survey results were analyzed using descriptive statistics in Excel. Results: Seventy-four surveys were completed by 40 clinical NGCs (cNGC), 17 research NGCs (rNGC) and 23 industry NGCs (iNGC); respondents could choose multiple areas of practice. The median number of years in neurology was three and the median graduation year was 2009. The median salary was $90,000. NGCs were involved in professional activities, including authoring manuscripts (respondents authored at least 268 peer-reviewed papers). Of the cNGCs, 55% billed for their services, with an average charge of $226 per 96040 unit. Most cNGCs performed their own result variant interpretation. Of the rNGC, 59% performed variant interpretation. Almost all rNGC had direct patient contact and coordinated genetic testing. Most rNGC were involved in grant writing. The iNGC traveled for conferences and to meet with clients. Most wrote test results and performed variant interpretation. Conclusions: This is the first in-depth look at NGC practice, and demonstrates the impact and value of NGCs in clinic, research and industry. The results of this study clearly define the various roles of NGCs and can guide clinics, research groups and industry as they create new roles for NGCs.
Identifying genetic diagnoses for neurological conditions with a considerable hereditary component, such as autism spectrum disorder (ASD), intellectual disability, and epilepsy, is critical to providing proper medical management for these patients and their families. However, patients with these conditions often do not receive appropriate genetic testing. Relatedly, three of the four genetic testing guidelines for ASD and intellectual disability published by the Child Neurology Society and American Academy of Neurology have not been updated to recommend chromosome microarray. To address improper utilization of genetic testing, more information is needed about the practices of the providers most often involved in ordering genetic testing for this patient population: genetic counselors, geneticists, and pediatric neurologists. This study was conducted with an electronic survey addressing the general testing practices of the 251 respondents, first-tier testing they would order for a patient with common neurological conditions, and the respondents’ confidence in their ability to facilitate appropriate genetic testing. Significant variance was noted between testing strategies selected by pediatric neurologists and those of geneticists and genetic counselors for all conditions. Remarkably, 27% of pediatric neurologists reported they would order a karyotype for a patient with autism and intellectual disability. Pediatric neurologists also reported significantly lower confidence with most components of ordering genetic testing and up to 75% responded that they would benefit from further education regarding proper utilization of genetic testing. These results propose that continued integration of genetic counselors into pediatric neurology clinics may improve utilization of genetic testing while reducing the burden on child neurologists. Furthermore, there is a clear need for additional genetics training in neurology and updated collaborative guidelines regarding genetic testing for common pediatric genetic conditions.
A-346 Accuracy and performance of a digital identification tool for hereditary cancer in a largely unaffected population

Public Health
Submitter: Leslie Bucheit, Counsyl

Presenting Author: Leslie Bucheit, Counsyl

Primary Author: Leslie A Bucheit, Counsyl

Author 2: Katherine Johansen Taber, Counsyl

Author 3: Kaylene Ready, Counsyl

Background: Studies estimate that <20% of women with a history of breast cancer (BC) or ovarian cancer (OC) receive recommended genetic counseling and testing (GC/T); estimates are lower for at-risk unaffected women. To facilitate identification (ID) of patients at risk for hereditary cancer, Counsyl developed a digital ID tool that enables patient-driven personal and/or family history (PFHx) reporting prior to or during clinical visits. The digital ID tool automatically matches reported histories to National Comprehensive Cancer Network (NCCN) genetic testing criteria. This study aimed to validate the digital ID tool’s accuracy and report performance in an unaffected population.

Methods: Third-party 3-generation pedigrees were retrospectively reviewed by a certified genetic counselor (CGC) to determine if PFHx met NCCN criteria. Pedigrees could have multiple PFHx cancer events that could meet several NCCN criteria. Events were analyzed independently and in combination by lineage and were sorted into high risk (meets criteria) and low risk (does not meet criteria) groups. After grouping, events were randomized and entered into the digital ID tool to determine its concordance with CGC sorting.

Results: 197 pedigrees that included 765 events were analyzed. 382/382 (100%) high risk and 381/383 (99%) low risk events identified by the digital ID tool were concordant with CGC sorting. The digital ID tool had a calculated accuracy of 99.74% (99.06-99.97% CI), reflecting the rate at which it reached the same recommendation for GC/T as did CGC sorting. Of 313 high-risk events in family history of unaffected probands, 274 (88%) were BRCA-related. Three criteria accounted for >50%: history of OC (24%); BC under age 45 (19%); >3 relatives with BC, pancreatic, or prostate cancers (11%). Remaining unaffected high risk events met other BRCA (35%) or Lynch syndrome (12%) criteria.

Conclusion: The digital ID tool accurately matches histories to NCCN criteria similarly to CGC review. Its use may expand accurate identification of at-risk unaffected patients for GC/T.

A-349 Newborn screens from start to finish: One institutions 10-year experience of abnormal newborn screens for Very Long Chain Acyl-CoA Dehydrogenase deficiency

Public Health
Submitter: Melanie Goodman,

Primary Author: Melanie Goodman,
Newborn screening (NBS) enables presymptomatic diagnosis for treatable disorders. The Texas NBS program screens for over 30 conditions, mostly inborn errors of metabolism (IEMs) in over 380,000 babies annually. Children's Health/UT Southwestern, a major referral center for the Texas NBS, established a genetic counselor-driven program to evaluate babies whose screens suggested an IEM. Here we report a 10-year cohort of over 2,600 babies with abnormal newborn screens. We created a database to integrate demographic and screening data with follow-up testing and time to diagnosis. This report focuses on Very Long Chain Acyl-CoA Dehydrogenase deficiency (VLCADD), which presents a set of diagnostic challenges. Our cohort of 2,600 cases were categorized by condition and diagnostic outcome to determine local positive predictive values (PPV). For VLCADD, 332 flagged screens led to 38 presumptive diagnoses, generating a PPV of 11.45%. Overall, PPVs for various IEMs on the screen ranged from 3% to 57%. We also examined the predictive value of acylcarnitine quantitation for VLCADD diagnosis, and found a lack of correlation between C14 and C14:1 levels on the first screen and the ultimate VLCADD status. Finally, we determined the time to definitive diagnosis or exclusion for each IEM on the screening panel. For VLCADD, we noted a reduction from 99 days to 45 days after the state laboratory initiated reflex ACADVL sequencing in children with abnormal acylcarnitines on the screen. The complexity of NBS diagnostics, particularly the lengthy, multi-modality follow-up tests in disorders like VLCADD and the need for effective communication with the primary care physician, emphasizes the critical role of a genetic counseling team in the diagnostic process.
Purpose: The U.S. Centers for Disease Control and Prevention considers BRCA-related Hereditary Breast and Ovarian Cancer Syndrome (HBOC) and Lynch Syndrome (LS) tier 1 genomic screening conditions due to significant potential for positive impact on public health. Population-based screening (PBS) for inherited cancer, defined here as germline genetic screening of adults independent of personal or family history of cancer, may be the next cancer prevention strategy as genomic medicine advances and testing cost decreases. However, genetic counselors’ (GC) attitudes towards offering PBS for inherited cancer have not been directly studied. This study aims to define GC perspectives of PBS for HBOC and LS.<br />Methods: An online survey was distributed to 3,609 members of the NSGC to assess attitudes towards PBS for HBOC and LS. Descriptive and chi-squared analyses were performed. <br />Results: A total of 367 surveys were analyzed. Attitudes towards PBS among GCs varied: 50.3% felt PBS should not be offered for HBOC or LS; 28.5% and 30.4% felt PBS should be offered for HBOC or LS, respectively; the remainder felt unsure. The majority of GCs (93.3%) felt that the current healthcare system is unprepared for integration of PBS, although >50% believed PBS should be integrated within ten years. Attitudes towards offering PBS were impacted by work setting, cancer specialization, and perceived preparedness (p< 0.05). Working in a non-medical setting or cancer specialty was positively correlated with agreement towards offering PBS (p<0.01). The most common perceived barriers to integration of PBS were shortage of GCs and the need for education of non-genetics providers. <br />Conclusion: The majority of GCs do not feel or are unsure that PBS should be integrated into healthcare at this time. Infrastructural barriers and educational gaps of non-genetics providers need to be addressed before the integration of PBS. Future research may focus on validating educational tools and using alternative service delivery models to integrate PBS in an evidence-based manner.

B-350 Progress of Newborn Screening Educational Materials
Public Health
Submitter: Amy Elizabeth Siemon, Student,
Primary Author: Amy Elizabeth Siemon, Student,
Presenting Author: Amy Elizabeth Siemon, Student,
Author 2: Aaron Goldenberg , Case Western Reserve University
Author 3: Kimberly Wallis, University Hospitals Cleveland Medical Center
Author 4: Anne L. Matthews, Case Western Reserve University

Newborn screening (NBS) is a state run public health initiative designed to identify infants with possible life threatening illnesses. NBS relies on parents’ compliance with follow up diagnostic testing after receiving a positive newborn screen. Research has shown parents who are more knowledgeable about NBS are more satisfied with the program and have decreased stress and anxiety when receiving abnormal results. One form of parental education is written material, either educational brochures or
websites. This study conducted an analysis of all 51 U.S programs’ NBS educational materials, which allowed for comparisons with previously published data to identify the progress of developing effective educational materials. Tools utilized to evaluate 134 educational materials included the Flesh Reading Ease tool to calculate readability, a researcher-developed content checklist based on the literature to evaluate for the inclusion of 19 key messages, and the Patient Education Material Assessment Tool to analyze user-friendliness. On average the educational materials were written at a 10-12th grade level. User-friendliness was overall high, with exception of use of visual aids. On average there were 11.43 out of 19 key messages included in each educational material. The most commonly included messages were benefits of screening, reasons for screening, screening procedures, how to contact the program and where to find additional information. The least included messages were risk of pain/infection from the heel stick, importance of screening for public health, cost/coverage of screening, and how screening is conducted in special circumstances. Genetic counseling was mentioned in a small percentage of materials, but not included as one of the published 19 key messages of the content checklist. While results show there has been progress made towards user-friendliness and key messages being included, improvements can still be made in readability and use of visual aids for NBS educational materials.

C-348 Evaluation of Parents' Experiences when a Child Receives a Positive Newborn Screening Result for Mucopolysaccharidosis type I (MPS I)

Public Health

Submitter: Kathryn Marie DeLong, UNC Greensboro

Presenting Author: Kathryn Marie DeLong, UNC Greensboro

Primary Author: Kathryn DeLong, MS, UNC Greensboro Genetic Counseling Program

Author 2: Kristin Clinard, MS, CGC, Division of Genetics and Metabolism, UNC Dept of Pediatrics

Author 3: Cynthia Powell, MD, The University of North Carolina at Chapel Hill

Author 4: Randi Culp Stewart, MS, CGC, UNC Greensboro Genetic Counseling Program/Cone Health System

Newborn screening (NBS) aims to prevent death and disability through early detection, diagnosis, and intervention of a variety of conditions. Mucopolysaccharidosis type I (MPS I) has been added to the list of recommended conditions to be screened for in the United States. While receiving a positive screening result can be stressful and confusing for parents, exploration of parent experiences following a positive NBS for MPS I is lacking. In order to improve parent support and inform recommendations for delivering abnormal NBS results for MPS I, parents of children who screened positive for MPS I on NBS were interviewed to explore their experiences with the follow-up process. Recruitment occurred via the North Carolina MPS I Pilot Study and National MPS Society. Seven parents were interviewed including two whose children received a confirmed diagnosis of MPS I. Two authors utilized qualitative computer assisted analysis to code transcribed interviews. Themes were identified and organized into domains of
disclosure of NBS results, knowledge and education, psychosocial impact and recommendations for follow-up. Parents experienced a range of emotions, mostly negative in nature, which were attributed to lack of prior parent education regarding NBS and lack of provider knowledge of MPS I. These findings provide guidance and potential recommendations for NBS programs and follow-up protocols. This study highlights the need for better communication and overall awareness of NBS in effort to minimize additional anxiety and confusion for parents of children who screen positive for MPS I. Genetic counselors are well suited to bridge this gap of communication and provided further education.

A-352 A prospective survey of aortic disease biorepository participants’ preferences for method of return of research genetic results

Research Issues
Submitter: Jamie Love-Nichols,

Presenting Author: Jamie Love-Nichols,

Primary Author: Jamie Love-Nichols, University of Michigan

Author 2: Wendy Uhlmann, University Of Michigan

Author 3: Patricia Arscott, University Of Michigan

Author 5: Cristen Willer, University of Michigan

Author 6: J. Scott Roberts, University of Michigan

Author 4: Whitney Hornsby, University of Michigan

There is emerging consensus that when appropriate, actionable research genetic results should be returned to participants. Research is limited on the most acceptable modalities for return of results (RoR), leaving researchers and institutions without guidance on best practices. To address this need at Michigan Medicine, biorepository participants with aortopathy (n=225, 79% male, mean age = 61 years) were asked their preferences for mode of research results delivery. A majority of participants (>63.4%) were accepting of any means of return; however, a substantial minority did not use a patient portal (11.1%), email (9.3%) or found technological means unacceptable (7.4% for patient portal, 27.3% for email). In-person appointment and letter were most preferred, with email significantly less acceptable to participants than other modalities (F(4,1076) =10.69, p<<0.0001). Over 90% of participants reported that any of the professionals —their primary care provider (PCP), a genetics specialist, their cardiovascular specialist, or a member of the research team—were acceptable to return results to them. 99% of participants found their cardiovascular specialist acceptable, and participants significantly preferred their cardiovascular specialist over a member of the research team or their PCP (F(3,851) =6.86, p=0.00014). Genetics specialists were not significantly preferred for RoR to other professionals. In sum, we found that participants were supportive of different modes of result communication and accepting of disclosure by different types of providers. These findings have implications for the
The development of RoR practices when results warrant disclosure to participants. Task shifting of results disclosure to non-genetics professionals and use of less expensive approaches such as telephone disclosure could help expand the reach of RoR practices as genomics research advances.

**B-353 A Roadmap for Precision Medicine Research Recruitment: Empirical Assessment of the Public’s Willingness to Participate & Implications for Recruitment Strategy**

**Research Issues**

*Submitter: Kelsey Elizabeth Moriarty,*

*Primary Author: Kelsey Elizabeth Moriarty,*

*Presenting Author: Kelsey Elizabeth Moriarty,*

*Author 2: Susan M. Wolf, JD, University of Minnesota*

*Author 3: Patricia McCarthy Veach, PhD, LP, University of Minnesota*

*Author 4: Bonnie LeRoy, MS, CGC, University of Minnesota*

*Author 5: Ian MacFarlane, PhD, Elizabethtown College*

*Author 6: Heather Zierhut, PhD, MS, CGC, University of Minnesota*

**Background:** Precision medicine research studies require large participant cohorts; however, previous genomic studies have shown difficulty with recruitment and the need for new recruitment strategies. **Objective:** This survey study describes the public’s familiarity with precision medicine as well as their opinions of and willingness to participate in precision medicine research. The study was undertaken to gain knowledge about factors impacting recruitment. **Methods:** An electronic 75-question survey was administered to adult participants at the 2017 Minnesota State Fair. Participants were asked about their familiarity with, attitudes towards, perceptions of, and willingness to participate in precision medicine research. **Results:** Of 942 total respondents, few had heard the term “precision medicine” (18%) and familiarity came mostly from the media (43%). Fifty-six percent expressed hypothetical willingness to participate in a broad precision medicine study. Significant predictors of willingness were: comfort with unrestricted research (OR=2.15 [1.77-2.60]); perceiving precision medicine research as beneficial, trustworthy, and confidential (OR=1.84 [1.51-2.24]); having a graduate degree (OR=1.57 [1.03-2.38]); comfort with participation without a doctor recommendation and without family participation (OR=1.52 [1.26-1.83]); and familiarity with precision/personalized medicine (OR=1.21 [1.12-1.31]). Hypothetical willingness to participate in precision medicine research increased to 78%-85% of participants when specific medical conditions such as cancer, heart disease, and depression were described. **Discussion:** Based on these results, we suggest a two-wave process to maximize recruitment. The first wave will recruit individuals who perceive precision medicine research as beneficial and are willing to participate without detailed information about the study. The second wave will recruit participants who want more
specifics before agreeing to participate. Including the specific medical condition of planned research, and media advertisements may help.

C-351 Use of a GeneMatcher Platform to Facilitate Connections between Laboratories, Clinicians, and Researchers Interested in Candidate Genes

Research Issues
Submitter: Megan T. Cho,

Primary Author: Laura Fisher, Sarah Lawrence College

Author 2: Halie Holmes, Sarah Lawrence College

Author 3: Cara Forster, GeneDx

Author 4: Sandra Yang, GeneDx

Author 5: Erin Torti, GeneDx

Author 6: Kirsty McWalter, GeneDx

Author 7: Megan Cho, Sarah Lawrence College; GeneDx

Presenting Author: Laura Fisher, Sarah Lawrence College

An increase in exome and genome sequencing utilization has resulted in a need for a system to share information when investigating candidate genes about which little is known. GeneMatcher is a free website platform that connects individuals who are interested in sharing information about the same candidate gene in order to clarify clinical significance. This study assessed the outcomes of discussions in GeneMatcher from the perspective of one clinical diagnostic laboratory with a long history of participation. Data were examined during an eight-month retrospective time period (November 2016-June 2017) and a four-week prospective time period (October 2017). As part of routine laboratory processes, emails received from external requestors through GeneMatcher were responded to by genetic counselors in order to mutually compare basic information as relevant (e.g. type of variant, inheritance, general clinical presentation). Each request was then categorized as a ‘collaboration’ (a joint research effort), ‘one-off’ (overlap warranting further comparison), or ‘not pursuing’ (no similarities between requestor and laboratory cases). The ordering clinicians of cases categorized as a collaboration or one-off were contacted to see if they would like to discuss further with the requestor; if so, they were introduced through email. In the retrospective dataset, 544 requests were discussed, of which 146 resulted in collaborations (26.8%) leading to four publications, 135 in one-offs (24.8%), and 263 were not pursued (48.4%). In the prospective dataset, 98 requests were discussed, of which 24 were collaborations (24.5%) leading to nine publications, 31 were one-offs (31.6%), and 43 were not pursued (43.9%). Overall, over half (53.1%) of the discussions resulted in the laboratory reaching out to ordering clinicians to continue conversations, ultimately resulting in data sharing that may impact patient care.
The results of this study support the benefits of facilitating collaborative discussions to further knowledge and research about candidate genes.

C-354 Feasibility, acceptability, and face validity of a novel, brief, web-based simulation tool for assessing genetic counseling communication

Research Issues
Submitter: Michael Setzer, ScM, MedStar Washington Hospital Center

Presenting Author: Michael Setzer, ScM, MedStar Washington Hospital Center

Primary Author: Michael Setzer,

Author 2: Debra Roter, Johns Hopkins School of Public Health

Author 3: Kendra Schaa, University of Iowa

Author 4: Barbara Bernhardt, University of Pennsylvania Center for Translational Medicine

Objective: Communication has been shown to provide an important role in the healthcare setting and has been linked to various patient outcomes. However, further research is still needed to elucidate the connection between process and outcomes. Current methods in studying genetic counseling communication have logistical and financial barriers. This study was meant to explore the feasibility, utility, and validity of a web-based platform to study genetic counseling communication in order to help ameliorate these barriers.

Methods: Two web-based simulations were created (one prenatal and one cancer). Genetic counselors participated in the study by interacting with one of the two video-based clients; their responses to the simulated client were recorded using a secure telephone voicemail service. Survey questions were included at the end of the simulation to examine genetic counselors’ reactions to the exercise.

Results: Seventy-two genetic counselors completed the survey regarding the web-tool and provided feedback. Participants believed the web tool accurately captured how they communicate in real life (86% agreeing) and provided a realistic client (91% agreeing). There was no significant difference between scenarios ($p > 0.05$). Participants believed that they gave less information than in a typical session (91% agreeing). Themes regarding challenges included the lack of interactivity and inability of the simulated client to directly respond.

Conclusion: This web tool shows promise for use in future genetic counseling communication studies, with the tool having technical feasibility and basic face validity.

A-358 Expansion of a Laboratory Utilization Management Program; the importance of clinical genetic counselors practicing with their LUM "hat" on

Utilization Management
Submitter: Shelly Weiss, Ann & Robert H. Lurie Children's Hospital
Laboratory utilization management (LUM) is a growing specialty that has evolved to optimize appropriate testing and ordering practices. A genetic testing LUM program at Ann & Robert H. Lurie Children’s Hospital of Chicago currently staffs 3 genetic counselors, two of which also provide clinical genetic counseling services to the neurology and hematology/oncology departments. Two additional counselors serve the cardiology and epilepsy departments. These counselors do not have LUM specific training or work within the institution’s LUM program. This study is a quantitative, comparative, and retrospective review of 1420 send-out genetic testing orders prior to LUM clinical service (January 1, 2014 – July 31, 2016) and 727 orders after (September 2016 – December 2017). We hypothesized that with increased LUM presence, rates of cancelation and modification of orders would (1) show an overall decrease and (2) this decrease would be greater for departments in which an LUM trained counselor provided genetic services. Chi-squared analysis performed between the two data sets demonstrated a statistically significant decrease from 19% to 12% (X2=21.974, p<0.05) overall. In addition, modification rates differed between departments with and without an LUM trained counselor (4.7% and 1.5%), though results were not statistically significant (p>0.05). These results suggest that expansion of the LUM team as well as the provision of counselors to high volume ordering non-genetics specialties improved the utilization of genetic testing at our institution. Additionally, these results highlight the benefit of training pediatric clinical genetic counselors in LUM practices to extend the success of the LUM program to additional departments. Future studies could investigate effectiveness of intervention strategies to reduce order modification and incorporate use of counselors with LUM training to aid the institution’s LUM initiative.
Introduction
PreventionGenetics strives to practice utilization management (UM) strategies to save healthcare costs. Historically, our main UM approach was sequencing followed by reflexive del/dup testing via aCGH. With the recent validation of Copy Number Variant (CNV) detection through Next Generation Sequencing (NGS), one test methodology enables the detection of both sequence variants and CNVs and we hypothesized that this would significantly reduce the overall amount of healthcare dollars spent.

Methods
We analyzed the amount billed for aCGH for the 280-gene Comprehensive Inherited Retinal Dystrophy (IRD) panel prior to (Jan - Oct 2017 - phase I) and after (Nov 2017 to Apr 2018 - phase II) the implementation of CNV detection.

Results
Phase I: 63% of clients initially ordered both sequencing and aCGH testing. Our UM policy of reflexing to del/dup only when necessary resulted in 54% of those orders being cancelled. This UM strategy resulted in an overall cost savings of >$63,000.

Phase II: The incorporation of CNV analysis decreased the percentage of clients who initially requested del/dup through aCGH testing to 24%. Those who opted to reflex to aCGH did so to assess for smaller del/dups that may not have been initially detected via NGS, with < 2 genes being the typical order, compared to up to 174 genes in phase I.

Incorporating CNV detection into the NGS panel resulted in significant savings of healthcare dollars. In phase I, 21% of the amounts invoiced for the comprehensive IRD panel were for del/dup studies, compared to only 1.2% in phase II.

Discussion
While internal UM strategies of reflexing to del/dup only when necessary resulted in significant savings for clients and patients in 2017, the incorporation of CNV analysis through sequencing further increased cost savings. We extrapolate that the availability of CNV analysis in all of 2017 would have resulted in over $100,000 of healthcare dollars saved for the comprehensive IRD panel. The implementation of CNV detection via NGS data adds another layer to UM practices at PreventionGenetics.

C-357 Perimortem Genetic Testing in a Children’s Hospital: A case for policy development

Utilization Management
Submitter: Darci Lise Sternen, MS, Seattle Children’s Hospital and PLUGS

Presenting Author: Darci Lise Sternen, MS, Seattle Children’s Hospital and PLUGS

Primary Author: Darci L Sternen, MS, LCGC, Seattle Children’s Hospital, Dept of Laboratories and PLUGS

Author 2: Jessie H Conta, MS, LCGC, Seattle Children’s Hospital, Dept of Laboratories and PLUGS

Author 3: Shannon M Stasi, MS, LCGC, Seattle Children’s Hospital, Dept of Laboratories and PLUGS
Genetic testing in the perimortem period, immediately before or after patient death, involves unique ethical and logistical issues in pediatric hospitals. Genetic testing may be necessary to confirm an underlying diagnosis and inform genetic counseling, yet not meet the institution’s medical necessity criteria because it will not change medical care for that child. This case describes one patient’s perimortem genetic test coordination that led to hospital policy creation for a consistent and fair perimortem genetic testing process. A 6 month old ex-premature infant with history of meconium ileus and respiratory failure requiring continuous mechanical ventilation had negative immunoreactive trypsinogen screening, 2 normal fecal elastases, and a normal CFTR 106 mutation panel. She developed severe hypoxic ischemic injury and expired. Providers contracted with family prior to the baby’s death that CFTR full gene sequencing and del/dup would be coordinated with a postmortem specimen for recurrence risk counseling. This test order was initially denied by the lab stewardship committee because it did not meet hospital medical necessity criteria and the anticipated yield was negligible given clinical history and previous testing. Genetic testing was ultimately sent out after escalation to hospital leadership, to preserve family confidence and trust in the hospital. No CFTR pathogenic variants were identified. Subsequently a perimortem testing policy was developed, with input from lab and clinical teams. Genetic testing is approved when medically necessary for the child’s care or to guide informative medically necessary testing of presymptomatic relatives at high risk for the genetic condition. Genetic testing that has other genetic counseling benefits to a family may be performed but the family is financially responsible for the cost. DNA banking and autopsy should be offered. A fund is being established to help subsidize family costs for DNA banking and genetic testing that is rational but does not meet hospital medical necessity criteria.