I. Opening Session

Dr. Michelle Bosquet Enlow opened the meeting and the participants introduced themselves. Tabitha Hendershot welcomed everyone to the meeting and thanked all the participants for their work on their presentations. Dr. Bosquet Enlow reviewed the meeting goals: to discuss the recommendations made in the Working Group (WG) members’ presentations and select measures and protocols to send to the research community for outreach.

II. NHGRI – Overview of PhenX

Dr. Erin Ramos provided an overview of the program from the National Human Genome Research Institute’s (NHGRI’s) perspective and their strategic plans. Dr. Ramos expressed a need for high quality phenotypic data that use standard methods and data standards to make research data sets more impactful. PhenX was launched in 2007 by NHGRI in response to a need from the scientific community for standard measures. Now PhenX is a trans-NIH effort with half the project funding coming from other NIH Institutes and Centers (ICs). The NHGRI is starting their strategic planning process for the next decade (October 2020 launch date) and wants to position themselves at the forefront of genomic medicine. Dr. Ramos explained that they cannot accomplish the goals in the strategic plan without standard measures and the work of the PhenX project.

III. Review Scope

<table>
<thead>
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<th>Action Items</th>
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<tr>
<td>Prepare data sheets</td>
<td>RTI with help from WG members</td>
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<tr>
<td>Identify secondary reviewers for data sheets</td>
<td>Michelle Bosquet with help from RTI</td>
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<td>Identify protocols for exposures</td>
<td>Dr. Wright</td>
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<tr>
<td>Identify protocols for Household Stability &amp; Caregiving Quality</td>
<td>Dr. Bosquet Enlow &amp; Dr. Sheridan</td>
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<td>Identify protocol for sleep in children under 6</td>
<td>Dr. Chung</td>
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Lisa Cox presented the scope elements and whether there are existing measures in the PhenX Toolkit that are related to pediatrics. She reviewed the criteria from the PhenX Steering Committee (SC) for selecting protocols and provided considerations for selecting protocols.

Ms. Cox then provided an overview of the day and reviewed the goals to select 15-18 measures and associated protocols to send for community outreach. Once measures are selected, RTI will prepare data sheets with input from the WG and send the measurement protocols to community outreach and feedback. RTI will schedule a post-outreach meeting to review before submitting the WG’s final recommendations to the PhenX SC.

IV. Working Group Member Presentations

a. Dr. Michelle Bosquet Enlow

   i. **Measure: Caregiver mental health**
      1. Definition: psychological health of child’s caregiver
      2. Can be assessed using general mental health measures (not specific to caregivers). However, there are some special mental health considerations during pregnancy and in the post-partum period
      3. Existing measures in PhenX Toolkit
         a. Many tools addressing adult mental health
         b. Clinical/diagnostic interview SCID-5
         c. DSM-5 level 1 cross-cutting symptom measure
         d. General symptom scales
         e. Specific disorder symptom scales (depression, anxiety, ptsd, other MH disorders)
         f. Caregiver specific measures – Edinburgh postnatal depression scales (EPDS), specific to pregnancy and postpartum period
      4. Missing elements
         a. Minimal coverage of mental health in pregnancy/postpartum, particularly anxiety
         b. Absence of questionnaires that provide adequate coverage of range of mental health difficulties/psychopathology domains (comorbidity common, clinical interviews are high burden and some too general)
      5. Recommendations
         a. Anxiety in pregnancy – best measure is mixture of pregnancy related anxiety scale, pregnancy outcome questionnaire
         b. Questionnaires assessing broad psychopathology
            i. Adult self-report/adult behavior checklist
            ii. SCL-90 (90 items)
            iii. SDQ17+ (25 items in 5 scales)
            iv. Request suggestions of well validated published instruments that measure prenatal anxiety
            v. Add ASR/ABCL to the toolkit Adult Self-Report/Adult Behavior Checklist, note that its proprietary
            vi. No strong reason to add “competing” measures for
c. Feedback
   i. Dr. Sheridan agrees adding ARS makes sense and is recommending something similar for child health
   ii. Discussion about Edinburgh Postnatal Depression Scale (EPDS). Dr. Wright explains it is the most widely used – in 84 studies. It was originally developed as a unidimensional scale and it can vary widely across ethnic populations. Dr. Bosquet Enlow agreed. Dr. Wright believes there should be some mention of EPDS because it is so widely used and because it specifically addresses mental health in the perinatal period. Dr. Stroustrup agrees and adds there will be a lot of available data because it’s widely used in clinical studies. Dr. Ramos agreed it would be good to add the context for a researcher. Dr. Bosquet Enlow agreed that the WG could prioritize 1-2 key notes for researchers about use and scoring of this protocol.
   iii. When there are multiple existing protocols for the same construct, Ms. Maiese and Dr. Ramos agreed it would be useful to have guidance and annotations for researchers about when protocols are most appropriate. PhenX currently has some specific instructions in the EPDS. Ms. Hendershot agreed this feedback is always useful.

d. Final recommendations
   i. Send a question to outreach community about a measurement protocol to assess perinatal and post-natal anxiety.
   ii. Broad psychopathology protocol – add ARS/ABCL as a new instrument.

ii. Measure: Daycare
   1. Defined as child’s experience with daycare
   2. Existing measures in PhenX
      a. Daycare/preschool attendance
         i. expert review panel provided revised protocol but haven’t been validated yet
         ii. only assessed amount of time and associated with physical health outcomes
   3. Missing elements
      a. Doesn’t assess experiences that influence development or stress on family
   4. Filling gaps
      a. Childhood Care and Programs Section of the National Education Survey, 2016
      b. Environment rating Scales – assesses quality of childcare environment, unlikely to be used widely
      c. Measures from NICHD Study of Early Child Care and Youth Development (SECCYD) – used in large longitudinal study on effects of early care on developmental outcomes
   5. Recommendations
a. Daycare/preschool experiences, Protocol Source: SECCYD Phase I and Phase II forms  
i. Include relevant sections from this measure, create separate forms for daycare and pre-school  
ii. Possibly create different forms for type of care  
iii. Not recommending SECCYD interviews with care providers or observational methods

6. Discussion
a. Dr. Chung asked about assessments taking familial context into account (e.g., two-person household; marital status; work outside the home). Dr. Bousquet reported there are aspects that address financial strain and how happy a parent is with care. She is not sure if it addresses family composition. She recommends it be linked with other questionnaires that address demographics. Ms. Hendershot added there is an "essential measures" section of data sheet so measures can be linked together.
b. Ms. Hendershot asked the source of the data. Dr. Bosquet Enlow responded the parent.
c. Dr. Sagiv asked about the age difference between daycare/preschool and if that was addressed. Dr. Bosquet Enlow said it depends on the kind of preschool program, but age seems flexible.
d. Dr. Ramos was concerned about pulling out sections of a validated questionnaire. Dr. Bosquet Enlow said she thinks it would be ok because the type of question is more descriptive rather than part of a scored questionnaire, so the risk of disruption of the psychometrics is low.

iii. Measure: Household Composition
   1. Defined as individuals living in a child’s home
   2. Existing measures
      a. Household roster relationships in general Social Survey  
      b. Number of rooms in Primary Residence from American Housing Survey protocol  
      d. Family interpersonal relationships from Family and Environment Scale
   3. Missing elements
      a. No single measure that captures all relevant constructs  
      b. Some measures not written from perspective of child/caregiver
   4. Filling gaps
      a. Caregiver Relationship & Family Household Composition from ECHO  
         b. Mother and Home Questionnaire from ALSPAC
   5. Recommendations
      a. Add Household Roster Relationships Pediatric, Protocol source: Household Roster-Relationships from PhenX Toolkit, modified  
         i. Modify form to make child-centric
ii. Add annotation to modify British language (e.g., lives in a flat) and note that household roster should be given to primary caregiver when used for child development research and can be given more than one time in all households where the child resides.

b. Modify Current Marital Status, Protocol Source National Survey of Family Growth, to make neutral for same-sex couples

c. Home Environment, Protocol Source: Mother and Home” Questionnaire from ALSPAC
   i. Changing British wording, using sections form “Mother and home” use measures that address both composition and stability

6. Feedback
   a. Ms. Cox stated an SC rule for the Toolkit is to not modify any text in any instruments. The WG can propose alternatives for British text but can’t edit a protocol to make more child-centric or otherwise. Another option would be to identify an alternate protocol.

   b. Concern about confusion with relationship to the child in household roster. Ms. Cox found that one column of the household roster does ask for relationships. Dr. Sheridan is less concerned about this, but Dr. Bosquet Enlow reminded researchers the interviewee is the householder, not a caregiver. Consensus from the WG was to annotate the existing Toolkit measure saying the interview can be given to primary caregiver when used in child development studies.

7. Final recommendation
   a. Annotate existing Household Roster measure with guidance to interview the primary caregiver.

iv. Measure: Household stability
   1. Defined as predictability and consistency of child’s environment
   2. Existing measures
      a. Annual Family Income – from National Health Interview Survey (NHIS) Family questionnaire, 2007
      b. Family Conflict (Intimate Relationship)
         i. Revised conflicts tactic scale (CTS-2)
      c. Parent-child conflict scale
         i. Conflict Tactics Scales: Parent-Child Version (CTS PC)
         ii. Could have an error in toolkit instructions because they say child can answer but not supported by literature. Dr. Sheridan added this could be an error leftover from an older version.
      d. Family control and Organization from the Family Environment Scale (FES)
   3. Missing elements
      a. Limited direct assessment of/from child
      b. No single measure of construct “household stability”
   4. Filling the gaps
a. Income, Assistance, Financial Strain Questions (ECHO) – nine questions, but the sources are not identified.

b. “Mother and Home” Questionnaire from ALSPAC
   i. Sections relevant for stability (physical qualities, problems with pests, home quality, neighborhood), household composition, work & finances, but the level of detail may be excessive.

c. PROMIS Family Relationships has four and eight-item versions

d. Home Observation for Measurement of the Environment (HOME) is a proprietary protocol and more likely to assess the quality of the home.

5. Recommendations
   a. Home Environment, protocol source: “Mother and Home” Questionnaire from ALSPAC
      i. Recommends editing sections as suggested for household composition and these measures would be combined

6. Feedback
   a. Differing conceptualizations of household stability were expressed by WG members. Dr. Sheridan thinks of whether household is in stable place with members moving in and out. Are the household members the same across time? ALSPAC covers some of this, but other tools address other aspects of stability like violence. Income stability is important but should be measured separately. Dr. Wright also thinks it is important to incorporate temporality because development and change occurs so quickly at young ages. Dr. Chung added that timing and development are important but there is a distinction between dynamism and toxicity; they are not necessarily the same. Dr. Wright agrees but documenting the number of moves is still important because that is a significant predictor of health outcomes, and others agreed. Ms. Hendershot noted that the WG could recommend that there is value in having the protocol administered over multiple points in time.

7. Final Recommendation
   a. Dr. Stroustrup will provide the ECHO measures for home and school locations.
   b. Dr. Sheridan will investigate further for a protocol related to household composition change

b. Dr. Margaret Sheridan

   i. **Measure: Mental health (non-ADHD/ASD)**
      1. Assessment of current tools in PhenX
         a. Good coverage of mental health with specific screeners
         b. The Strengths and Difficulties Questionnaire (SDQ) is only “general” psychopathology measure – widely used, but lacks good clinical cutoffs
      2. For a “General” Mental health measure
         a. Child Behavior Checklist (CBCL) or Behavior Assessment System for Children (BASC)
         b. DSM-5 Parent/Guardian-rated cross-cutting symptom measure,
child age 6-17 (don’t see child version in PhenX Toolkit but should be)
c. DSM-5 Cross-cutting symptom measure for Children (don’t see child version in PhenX Toolkit but should be)

3. Diagnostic Structured Interview
   a. Kiddie Schedule for Affective disorders and Schizophrenia (KSADS) (Child-version of SCID)
   b. Mini-Interview Neuropsychiatric Interview (MINI)
   c. Diagnostic Structure Interview for Children (DISC)
   d. Preschool Age Psychiatric Assessment (PAPA; CAPA)

4. Recommendation
   a. Adding CBCL or BASC – consistent with Dr. Bosquet Enlow’s recommendation to add ADCL
   b. Add KSADS to existing SCID protocol
   c. No preschool version of structured interview, so add structured interview for preschool age (possibly DIPA)

5. Discussion
   a. Discussion of tools for preschool-aged children. Dr. Bosquet Enlow agrees not to recommend PAPA/CAPA. WG could look at DAWBA which allows parents to complete online and receive probability of diagnosis. Dr. Sheridan agrees, but since SCIDS is already in toolkit, can simply add KSADS to existing protocol but for children. All agree it is important to have at least one clinical interview. DIPA could also replace PAPA for preschool-age children. Ms. Hendershot pointed out that these protocols require more than 15 minutes to administer. The burden threshold for PhenX is 15 minutes in an unaffected individual. The WG is only allowed 2-3 high burden protocols.
   b. Dr. Sagiv asks if tools address symptomatology. Dr. Sheridan confirms they do. Dr. Sagiv would recommend linking it with the DSM-5 but there may be value in asking if child has ever received a diagnosis like a question from NHANES.
   c. Age for tools. Dr. Sheridan said tools are used for children starting at 5-7 years. Dr. Bosquet Enlow suggested finding tools for younger children.

6. Final Decision
   a. Add CBCL or BASC
   b. Add KSADS to existing SCID protocol

ii. Measure: Childhood Adversity
   1. A cumulative risk approach is best for measuring childhood adversity, it is common and good at predicting who needs help.
   2. Existing Tools in PhenX
      a. Cumulative Risk
         i. Adverse Life Events Scale (children or adults)
         ii. Life stressor checklist (adults)
         iii. Stressful life events screening questionnaire
         iv. Dimensional Model of Adversity and Psychopathology
b. Threat
   i. Conflict Tactic Scale – Parent/Child version (CTS PC)
   ii. Child Trauma questionnaire (CTQ)
   iii. Childhood Experience of Care and Abuse (CECA)
   iv. Maltreatment and Abuse Chronology of Exposure Scale
   v. Lifetime Trauma and Victimization History Instrument
   vi. Child Abuse Potential Inventory

c. Domestic violence
   i. Conflict Tactic Scale – Revised (CTS-2)

d. Violence
   i. Violence exposure scale for children (revised (VEX-R))
   ii. National survey of child’s exposure to violence
   iii. Juvenile victimization questionnaire 2nd revision
   iv. General victimization scale
   v. Wouldn’t add anything else but could add recommendations for when to use different tools.
      1. Dr. Wright and Dr. Ramos agreed this would be helpful if the WG could take this on.

e. Community violence
   i. Screen for Adolescent violence Exposure (SAVE)
   ii. Neighborhood Safety

f. Deprivation
   i. Neglect
      1. Multidimensional Neglectful Behavior Scale – Child Report
      2. CTS, CTQ, CECA all have neglect subscales
   ii. Cognitive home environment
      1. StimQ (infant, toddler, preschool versions)
   iii. Suggestions:
      1. HOME Interview
      2. HOME questionnaire
         a. Language needs to be updated for it is out of date and the protocol does not include social media.


g. Typical Family function
   i. Family environment
      1. Well documented in PhenX
   ii. School Environment
   iii. Trauma Screens
      1. Several screens in PhenX
   iv. Discrimination Scale – one in PhenX
      1. Suggest adding Heightened vigilance scale – not many designed for kids

3. Feedback
   a. Temporal dimension. Dr. Wright said that the Pregnancy WG also thought about adversity exposure and the effects on the lifecourse. It should be captured better in the Toolkit and this is a good opportunity for this WG to think about how to do that.
b. Categorization of existing tools. Dr. Sheridan thinks it would be useful to include information framing adversity and how various protocol fit in and what the different tools are best used for.

c. Updating HOME language. Ms. Cox asked if standard exist for updated HOME interview. Dr. Sheridan responded that many researchers use an updated version, but no one has published a validated version.

d. Two Family Control and Organization subscales of the Family Environment Scale (FES) are in the Toolkit and may include aspects covered in the Confusion, Hubbub, and Order Scale (CHAOS). Dr Bosquet Enlow and Dr. Stroustrup thought the organization and maintenance section of FES may cover same aspects of CHAOS. Dr. Sheridan looked over FES and confirmed CHAOS is different and valuable enough to propose as its own measure.

4. Final Recommendations

a. Add HOME Interview – with caveat that language needs updating, and this can be indicated in the “specific instructions” section of the data sheet.

b. Add Discrimination Scale – Heightened vigilance scale

c. Consider adding family chaos/unpredictability scale protocol: CHAOS after reviewing the FES in the Toolkit.

c. Dr. Roz Wright

i. Presentation on physical and chemical environmental factors

ii. Biomonitoring over childhood to facilitate determination of chemical exposure during period of rapid development and high plasticity
   1. Evidence of linkages between environmental and chemical exposures and health outcomes
   2. 85-95% of disease derived from environment or GxE interaction
   3. Exposome – shift towards comprehensive exposure assessment over life course

iii. Existing measures
   1. Brominated flame retardants (serum, breastmilk)
   2. PCBs (serum, milk), Persistent Pesticides
   3. Trace metals (Cd, Tb, Mn, Hg, Se), can measure up to 20 trace metals in one analyte
   4. Phenolic compounds (BPA, triclosan, triblocarbon), Parabens
   5. Phthalates
   6. Perfluorinated compounds
   7. Serum Cotinine

iv. Combination of effects
   1. Considerations – mixture of exposures during critical developmental periods

v. Missing elements
   1. Repeated measures, emerging measures providing highly temporally resolved exposure data (geomarkers, hair, teeth)
   2. Protocol appropriately designed to minimize contamination of biological
samples, e.g., laser ablation of hair.

3. Use teeth to retrospectively assess chemicals, well developed protocols to collect teeth in the mail, and it’s non-invasive because children shed teeth naturally.

4. Monitoring mechanisms – what’s validated?
   a. Bracelets to monitor external exposome
   b. Skin patches to monitor Interstitial fluid
      i. Dr. McDonald asked what the matrix is that absorbs the fluid. Dr. Wright was unsure but will share the paper from the Mt. Sinai investigator once it is published.
   c. Dried Blood Spots from Newborn Screening programs for use in other environmental screening

vi. Recommendations
   1. Protocol for banking maternal/child hair
      a. Can collect maternal hair close to delivery to measure exposure of 1 month for every cm of hair
      b. Human Health Environment (HHEAR) network data coordinating center and six lab cores are funded by the National Institute on Environmental Health Sciences (NIEHS). They have expertise in developmental biology and do consultations on integrity of sample and quality control.
      c. ECHO has video tape trainings – could incorporate those into the Toolkit
   2. Use of teeth banking to measure trace elements, organic chemicals
   3. Add protocols for newer devices like bracelets and patch

vii. Feedback
   1. Use of addresses for environmental exposure data. Dr. McDonald said the National Library of Medicine doesn’t have data linked to individuals. It has established 45,000 LOINC codes for laboratory data collection.
   2. Use of Dried Blood Spots (DBS). Dr. McDonald explained DBS samples are available in many places and can be used for up to 30 years. Dr. Wright agreed this is an important data source but use of the data varies by state law.
   3. Urine Collection protocols. Dr. Stroustrup asked if protocols exist for collection of urine from incontinent individuals. Dr. Wright responded these protocols are being developed for ECHO and she will share them as they become available to harmonize with PhenX.
   4. Wearables. Ms. Hendershot and Dr. Ramos expressed that NHGRI is very interested in wearables but asked if they are validated and ready to be included. It is also difficult because NIH-funded materials cannot promote specific products over others but can reference standards. Dr. Ramos would like to see this pursued. Dr. Sagiv said that pesticide monitoring is being done in California.
   5. Geocoding: Dr. Bosquet Enlow suggested getting addresses for geocoding would also be helpful. Dr. Sheridan agreed that capturing moves lends itself to analyzing environmental exposure. Dr. Ramos asked if whether collecting zip codes creates HIPPA issues. Dr. Wright said that ECHO is addressing the personal health information (PHI) issue.
   6. Video Tutorials. Dr. Wright shared that ECHO includes video tutorials for some measures. Dr. Ramos said this would be a great addition to the
 Toolkit.

viii. Final Recommendations

1. Update protocols for urine and hair collection to include protocols for collecting samples in incontinent and child populations – annotate the minimal sample size required
2. Include protocol for teeth – Dr. Wright to identify specific protocol
3. Add protocols for newer devices like bracelets and patches – Dr. Wright to identify specific protocols

d. Dr. Annemarie Stroustrup

i. Measure: Cognitive, neurodevelopment milestones

1. Tools often overlap between cognition and behavior
2. Considerations: most are direct assessment, which are more objective but almost all tools are long and costly. The assessment can be affected by the child’s timidity, as well as the skill of the person conducting the test with the child.
3. Existing measures
   a. Executive function
      i. Behavior Rating Inventory of Executive Function (BRIEF) ages 2-5, 5-18
      ii. Trail making test (TMT) direct assessment for children 9-14
      iii. Overall this is well covered
   b. Early childhood measures
      i. Mullen Scales of Early Learning (ages birth to 68 months)
   c. Intelligence Scale
      i. Age appropriate Wechsler intelligence scales
   d. Pediatric school performance
      i. 4 questions from the Education-School Questionnaire from Pediatric hydroxyurea Phase 3 clinical trial
   e. Early childhood speech and language
      i. Ages and stages questionnaire

4. Gaps
   a. Not many missing
   b. Many other commonly used tools but no reason to add additional tools
   c. NIH Toolbox has several cognitive assessment measures that are easy to deliver and being used in ECHO. They are shorter, and require less training, but only age 3 and up.

5. Recommendations
   a. Could leave as is
   b. Discuss utility of adding additional scales

6. Feedback
   a. Utility of NIH Toolbox. Dr. McDonald and Dr. Stroustrup explained that the Toolbox has newer modules on an iPad, don’t require a trained interviewer, but are proprietary because the interface is maintained by Northwestern University. Dr. Sheridan agreed she likes to use them in conjunction with the gold standard, but we should consider their sensitivity because they are shorter. Dr.
Stroustrup agreed, and it depends on the research questions. For some purposes, they may be sufficient and better suited. Ms. Hendershot wanted to clarify how they are different from current measures in the Toolkit to not confuse users. Dr. Stroustrup explained there are clear distinctions in length and they don’t need trained examiners. Dr. Wright also indicated that the Toolbox modules are also in Spanish. Dr. Ramos says the institute is always looking for ways to leverage other NIH-funded tools. Dr. Bosquet Enlow added that ECHO will be using it, and this may be a good time to add it to anticipate where the research field is moving. With regards to fee, Dr. Ramos wanted to clarify how ECHO covers it. Dr. Wright confirmed ECHO covers the fee, but we could approach Northwestern University about its inclusion in the Toolkit and try to work out an agreement.

7. Final Decision
   a. Agreed to add NIH Toolbox protocols
   b. Need to be specific about which tools in the Toolbox we should recommend and for which measures

ii. Measure: Neonatal abstinence syndrome (NAS)
   1. Clinical syndrome from the abrupt discontinuation of fetal exposure to addictive substances
   2. Existing measures
      a. No existing measures of NAS
   3. Missing elements
      a. Assessment of NAS
   4. Filling the gaps
      a. Finnegan Neonatal Abstinence Severity Score (NASS)
      b. Modified Finnegan Neonatal Abstinence Severity Score (mNASS) – shorter and used extensively in clinical settings, but not as widely validated.
      c. Neonatal Drug Withdrawal Scoring System aka Lipsitz
      d. Neonatal Narcotic Withdrawal Index (NNWI) – only methadone
      e. Neonatal Withdrawal Inventory (NWI)
      f. Withdrawal Assessment Tool – 1 – used for withdrawal of hospital-administered drugs
   5. Recommendations
      a. mNASS – widely used and widely considered gold standard. It is scored by a nurse every five hours. If the baby’s score is 15 or greater, medications begin.
      b. Neonatal Withdrawal Inventory (NWI) – shorter than mNASS with good performance
      c. Continue review for emerging measures (like NASCORE currently in validation study)
   6. Feedback
      a. Dr. Chung wanted to know what obstetric groups decided. Dr. Wright reported that the Pregnancy WG addressed alcohol and tobacco but not opioids.
      b. Dr. Stroustrup added she focused on hospital use tools because this assessment would always be done in a hospital setting.
c. Emerging tools. Dr. Stroustrup mentioned since so much research being done is this domain, there are emerging tools currently being validated. Dr. Sagiv wanted to understand the protocols in the Toolkit are updated and replaced as newer tools become available. Ms. Hendershot reported that new tools can be reviewed and there is also an expert review panel that looks at current content and makes suggestions.

d. ECHO use. Dr. Wright asked what ECHO is doing in regard to this. Dr. Stroustrup reported ECHO is going to get data from Finnegan (NASS & mNASS) through medical record abstraction.

e. High Burden. Ms. Hendershot asked if this is considered high burden. Dr. Stroustrup reported assessment itself is short and easy but needs to be done every 4 hours.

f. Age constraints. Dr. Sagiv asked if there are age constraints. Dr. Stroustrup reported there are recommendations to screen the infant for 5 days if there is a known exposure. Then, there is a separate paper explaining the protocol for treatment.

7. Final Decision
   a. Add mNASS

iii. Measure: Measures tied to opiate epidemic
   1. Defined as testing methods for drugs and abuse
   2. Existing measures
      a. Lab-based urine drug analysis – detects several kinds and classes of drugs
      b. On-site urine drug screen
      c. Common drugs are already included in toolkit
   3. Missing elements
      a. Need to update for incontinent individuals
         i. Will need to find study that has protocol for urine analysis for infants
      b. Not CLIA compliant
   4. Filling the gaps
      a. Lab-based protocol can be updated to collect bagged urine – verify minimum volume of urine (infants unlikely to produce required 90 mL of urine)
      b. Verify that on-site protocol can use bagged urine
      c. Consider implications for child protection involvement
   5. Feedback
      a. Implications for child protection. Dr. Sagiv mentioned this will also be an issue for the childhood adversity measures. Dr. Bosquet added that this is a state legal and IRB issue. Ms. Hendershot added that for the Toolkit, we operate with the assumption that investigators know and understand specific IRB, ethical, and legal considerations, but we can add specific instructions if needed. Dr. Chung agreed, saying medical/legal implications will be specific to measures and investigators should and will probably have that conversation at a higher level before choosing a protocol. Dr. Ramos added that there is also a general guidance page for the PhenX Toolkit. It may be worth a brief note that investigators
should consider any ethical and/or legal implications.

6. Final Decision
   a. Look for existing lab-based protocol to collect bagged urine and verify minimum volume of urine needed for a specimen.
   b. Verify that on-site protocol can use bagged urine and annotate the existing protocol.

e. Dr. Sharon Sagiv (with input from Melissa Parisi)
   i. Measure: ADHD
      1. Considerations – heterogenous, symptom presentation and severity vary, often co-morbid with other conditions
      2. Existing measures
         a. Protocol #121502 ADHD Symptoms – Child
         b. Other protocols that measure ADHD symptomatology
         c. SWAN
         d. Conner’s ADHD/DSM-5 scale
            i. More widely recognized but not free, very similar to SWAN
         e. ECHO uses SDQ
            i. In Toolkit but not under ADHD

3. Missing elements
   a. Parent report
   b. Pediatric medical record
   c. Structured Clinical Interview for DSM 5 Disorders clinician version – adolescents and child

4. Recommendations
   a. ADHD Symptomatology
      i. Either keep existing SWAN or propose others (like Conner’s)
   b. Include ADHD diagnosis measure
      i. Include question from NHANES asking if physician or other health professional has diagnosed the child
      ii. Structured interview (KSADS)
      iii. Medical record abstraction of ADHD diagnosis
         1. Existing protocol for medical record abstraction in PhenX but they’re within protocols for other specific data points
   c. ADHD treatment
      i. Adding question about ADHD treatment
      ii. Medical record abstraction of ADHD treatment

ii. Measure: Autism Spectrum Disorders (ASD)
   1. Diagnosis usually occurs after screening at well-child visits following DSM-5 criteria
   2. Considerations – very heterogeneous, often co-morbid with other conditions
   3. Existing measures
      a. Symptoms of autism spectrum disorders
         i. Childhood autism spectrum test (CAST)
         ii. Autism spectrum quotient for adolescents
   4. Missing elements
a. Better characterization of ASD symptomatology
b. ASD diagnosis

5. Recommendations
   a. Symptoms
      i. Social Responsiveness Scale, Version 2 (SRS-2)
   b. ASD diagnosis measure
      i. - Gold standard is ADOS, ASD is covered in KSADS
         1. KSADS is enough

iii. Measure: Externalizing Behavior
   1. Include attentional problems, manifest in outward “acting out” behavior like aggression, conduct problems, predictor of conduct disorder and criminality
   2. Existing measures
      a. Internalizing, externalizing, and substance use disorders screener
         i. Global appraisal of Individual Needs-short screener (GAIN-SS)
      b. Disinhibiting Behaviors – Impulsivity
         i. UPPS Impulsive behavior scale for Children
      c. Disruptive behavior
         i. Disruptive behavior disorders ration scale (DBDRS)
      d. Broad psychopathology
         i. Strengths and difficulties Questionnaire (SDQ)
      e. Aggression and hostility
         i. Buss-Perry
      f. Lack of prosocial emotions
         i. Preschool parent report
         ii. Preschool teacher report
      g. Inhibitory control
         i. STOP-IT
      h. Sustained and Selective Attention
         i. Conner’s Continuous Performance (CPT 3)
         1. Also measures impulsivity

3. Missing elements
   a. Aggression in children under 12
   b. Impulse control in children under 7

4. Recommendations
   a. Include BASC-3 or CBCL – this could replace some of existing measures in the Toolkit (like SDQ)
      i. But SDQ is shorter and free: it doesn't include a number of externalizing behaviors
   b. Continuous Performance Test for Children (CPT) under 7
      i. Conner’s Kiddie CPT covers ages 4-7
      ii. CPT for older children is in Toolkit already

5. Feedback
   a. Dr. Bosquet Enlow added that elements of BASC are also included in BRIEF-P for younger children. BRIEF-P is already included in the Toolkit
f. Dr. Richard Chung
   i. A lot of good content for adolescents, one thing that is lacking is positive outlook on development, identifying positive development – this is true of things outside PhenX as well

ii. Measure: Bullying
   1. Intentional, repetitive harm perpetrated between children/youth
   2. Existing measures
      a. Not currently in PhenX
   3. Missing
      a. Bullying would be useful to assess
      b. Assessing resilience or a related concept may also be useful
         i. Psychological Resilience 251401 included in PhenX – Brief Resilience Scale but only for adults 18 and over
   4. Filling the gaps
      a. Olweus Bullying Questionnaire (OBQ) – most widely used, 11-17 years old, costs $1
      b. Healthy pathways (included in ECHO)
      c. Resilience
         i. Child and Youth Resilience Measure (CYRM)
         ii. Connor-Davidson Resilience Scale (CD-RISC)
   5. Recommendations
      a. If we want to include bullying, recommend OBQ
      b. Healthy Pathways is viable alternative if fee of $1 disqualifies the OBQ
      c. Consider including strong child-focused resilience measure such as CYRM
   6. Feedback
      a. Scope of OBQ. Dr. Bosquet Enlow asked if it included digital bullying. Dr. Chung needs to confirm.
      b. Definition of resilience. Dr. Bosquet Enlow asked what kind of resilience is being measured by OBQ. Dr. Chung reported that CYRM touches more on external resources and exposures.
      c. Dr. Sheridan noted here is only one resilience scale in PhenX. Dr. Chung responded that this scale only applies to adults. Dr. Sheridan agrees this presents a significant gap. Dr. Wright agreed adding resilience for this age group is a good addition.
      d. Overlap. Dr. Sheridan asked if this overlaps with externalizing behavior. Dr. Chung reported that currently there is no specific measure for bullying, but some other measures include questions that touch on bullying.
      e. Ms. Cox suggested including CYRM under adult resilience protocol as alternative for younger age group. All members agreed.
   7. Final Decision
      a. Consider OBQ for bullying
      b. Add CYRM (child protocol) to existing resilience measure

iii. Measure: Child Lifestyle (diet, eating behaviors, physical activity, sleep)
1. Health habits and other lifestyle components
2. Sleep, diet and physical activity are broad subjects and may deserve their own protocols
3. Most protocols come from obesity work
4. Existing measures
   a. Diet
      i. Breastfeeding
      ii. Dietary Screener Questionnaire (DSQ) from NHANES
      iii. Is somewhat limited
   b. Physical Activity
      i. Sitting-sedentary and others
      ii. More robust coverage of physical activity in Toolkit
   c. Media use
      i. Media use 750701
      ii. Inadequate coverage of sleep and media in Toolkit
5. Filling gaps
   a. Lack of global health attitudes or behaviors protocols
   b. Sleep
      i. PROMIS sleep disturbance – included in ECHO
      ii. PROMIS sleep impairment – included in ECHO
   c. Composite health behaviors and attitudes
      i. FLASHE (NCI) teen report and parent report versions
   d. Media
      i. Pew Internet and American Life Project – not proprietary but hard to find
      ii. Rosen Media and Technology Usage and Attitudes Scale
6. Recommendations
   a. Media use is important and is critical gap
      i. Suggest the Pew Internet and American Life Project because it is updated regularly. Need to look further at which elements to include in PhenX.
7. Feedback
   a. Constructs for media. Dr. Sagiv agrees media is important consideration and wonders what constructs to include for media. Dr. Chung responded that current tools in PhenX look at quality and quantity of media, but more research is needed on Pew Internet survey. Dr. Stroustrup added to look at how often the Pew survey is updated. If they continually update it themselves, this could be a big benefit for PhenX.
   b. Sleep. Dr. Sheridan thinks a measure for sleep for little kids is very important. Dr. Wright added that it’s the most common complaint heard by pediatricians. Dr. Chung added there are currently no normative health behaviors questionnaires for sleep. Ms. Cox found a few sleep questionnaires for kids currently in PhenX, but group agreed to take time to assess what is there for children. Dr. Stroustrup added existing tools don’t address very young children.
8. Final Decision
   a. Add FLASHE as composite health behaviors and attitude measure
   b. Add media measure and do more research on Pew Internet
survey.
   c. Add Sleep measure and Dr. Chung will identify protocol.

iv. Measure: School Environment
   1. Characterization of the learning and social environment of schools as a key influence on social, cognitive, and emotional development
   2. Existing measures
      a. School Social Environment 211001 for 12-18 yo
      b. School Risk and Protective Factors 540501 from Communities that Care (CTC) Youth Survey – SAMHSA
   3. Missing elements
      a. Lack of global school environment measures for younger children
   4. Filling the gaps
      a. Positive Peer Interaction Survey for ages 3-12 from NIH Toolbox
      b. PROMIS peer relationships short form (ages 8-17)
   5. Recommendations
      a. Both NIH Toolbox and PROMIS tools are commonly used and would be good options, PROMIS slightly better – add as alternate measures (young child and older child/teen)
   6. Feedback
      a. Dr. Sagiv noted that BASQ has a social skills component, but it’s completed by a teacher. She wondered how it compares to the Toolbox questionnaire. Dr. Chung wasn’t sure, but his sense is BASQ is more comprehensive. Dr. Bosquet Enlow added it may be good to have the Toolbox protocol as an alternative for people who don’t want to complete the whole BASQ.
      b. Cost. Dr. Bosquet Enlow noted that both PROMIS and Toolbox questionnaires are freely available. While the PROMIS has more content, the NIH Toolbox covers children as young as 3, which is very important because few tools are available for that age. Dr. Sheridan agreed.
      c. Other school environment measures. Dr. Sheridan noted the PhenX Toolkit covers many other measures related to school environment like safety, physical space, etc. but peer relations would be a good addition. Dr. Bosquet Enlow agreed.
      d. Dr. Bosquet Enlow – peer relations on its own is a good measure
      e. Ms. Hendershot – we could consider including the NIH toolbox questionnaire to cover the younger ages.
   7. Final Decision
      a. Add measure for peer relations from the NIH Toolbox.

v. Measure: School
   1. Characterization of school experiences and or performance beyond early childhood/preschool including school participation and performance
   2. Existing measures
      a. Pediatric School Performance
         i. BABY HUG
   3. Missing elements
      a. Limited in breadth and depth
b. Attendance in preschool is likely more variable and consequential

4. Filling the gaps
   a. Healthy Pathways – Academic Performance protocols with parent and child self-report, used in ECHO; five items in past four weeks.

5. Recommendations
   a. Suggest measure of school achievement/performance rather than attendance participation
   b. Healthy Pathways is an accepted and usable protocol

6. Feedback
   a. Ages. Dr. Wright asked what ages it covers. Dr. Chung reported it was used in a study with grades 4-6. He needs to check exact age ranges.
   b. School achievement. Dr. Sheridan agreed that a school achievement measure would be useful.
   c. Address and environmental concerns. Dr. Wright asked if we ask to report address of schools and daycare as these would be important to help gather information related to safety and environmental exposures. Dr. Stroustrup reported ECHO discussed school address, but she is unsure what their final decision was. Dr. Bosquet Enlow asked if something similar to the household stability/moves tool exists for schools. It would likely require creating a new tool, which is not in line with PhenX rules. Ms. Cox identified a Parkinson’s protocol that includes residence history, and Dr. Wright agreed that may be a good place to start. Dr. Bosquet Enlow and Dr. Sheridan will review existing tools from large studies to see if they can find something to capture household stability, moves, and schools with addresses for this purpose.

7. Final Decision
   a. Add school achievement measure with Healthy Pathways

V. Finalize Measures/Protocols – Consensus Decisions

<table>
<thead>
<tr>
<th>New Measurement Protocol</th>
<th>Recommendation</th>
<th>Discussion</th>
<th>Decision</th>
<th>Primary Reviewer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neonatal Abstinence</td>
<td>mNASS or NWI</td>
<td>mNASS is more widely used and exists in EHRs</td>
<td>mNASS</td>
<td>Dr. Stroustrup</td>
</tr>
<tr>
<td>Family Chaos/Unpredictability</td>
<td>CHAOS scale, observation, or FES</td>
<td>Dr. Sheridan recommends CHAOS because doesn't require observation. FES does not cover same measures.</td>
<td>CHAOS*</td>
<td>Dr. Sheridan</td>
</tr>
<tr>
<td>Cognitive Status</td>
<td>NIH Toolbox</td>
<td>Dr. Bosquet Enlow suggests choosing with modules to</td>
<td>Dr. Stroustrup to report</td>
<td>Dr. Stroustrup</td>
</tr>
<tr>
<td>Cognitive Stimulation</td>
<td>HOME Interview and HOME questionnaire</td>
<td>Dr. Sheridan thinks this is important gap in toolkit but need to address language and usability issue. Ms. Hendershot and Ms. Maiiese suggest finding other large studies using an updated version to use in toolkit. Dr. Sheridan can easily find that and will follow up.</td>
<td>Updated HOME</td>
<td>Dr. Sheridan</td>
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<tr>
<td>Home Environment</td>
<td>Mother and Home questionnaire – ALSPAC or household roster</td>
<td>Still need to address people coming in and out of the home. Dr. Stroustrup said ECHO has some form that ask for residence history. Dr. Sheridan will email other researchers to see if she can find a tool that fits what the WG is looking for</td>
<td>Househol d roster with note to be completed by primary caregiver. Dr. Sheridan will continue looking for tools that better fit</td>
<td>Dr. Sheridan</td>
</tr>
<tr>
<td>Household stability</td>
<td>Household roster</td>
<td>Want a tool that captures residence</td>
<td></td>
<td>Dr. Bosquet Enlow &amp; Dr.</td>
</tr>
<tr>
<td>PhenX: consensus measures for Phenotypes and Exposures</td>
<td></td>
<td></td>
<td>Sheridan</td>
<td></td>
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<tr>
<td><strong>Exposures</strong></td>
<td>Tooth collection</td>
<td>Dr. Wright to identify protocols</td>
<td>Dr. Wright</td>
<td></td>
</tr>
<tr>
<td><strong>Exposures</strong></td>
<td>Wearables – patch</td>
<td>Dr. Wright to identify protocols</td>
<td>Dr. Wright</td>
<td></td>
</tr>
<tr>
<td><strong>Exposures</strong></td>
<td>Wearables - bracelet</td>
<td>Dr. Chung asked if this would require recommending a particular product. Dr. Wright said there is need to think through this further because we can't recommend specific products. Ms. Hendershot added that the steering committee is also talking about next domains and including wearables and genomic medicine.</td>
<td>Dr. Wright to identify protocols</td>
<td>Dr. Wright</td>
</tr>
<tr>
<td><strong>ADHD Diagnosis</strong></td>
<td>KSADS or single item question form NHANES</td>
<td>Include KSADS because can embed under SCID</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>ADHD Treatment</strong></td>
<td>KSADS or single item question form NHANES</td>
<td>KSADS probably covers treatment, but Dr. Sheridan worried it wouldn't be accurate because medications change all the time.</td>
<td>*Low priority</td>
<td>Dr. Sagiv</td>
</tr>
<tr>
<td><strong>Behavioral Inventory for Children</strong></td>
<td>BASC-3 or CBCL</td>
<td>Dr. Sheridan started by saying CBCL scoring system is more cumbersome. It's a question of weighing common</td>
<td>CBCL</td>
<td>Dr. Sheridan</td>
</tr>
</tbody>
</table>
usage vs usability. ECHO chose to go with CBCL because more people use it.

<table>
<thead>
<tr>
<th>ASD Symptoms</th>
<th>SRS-2</th>
<th>All in agreement</th>
<th>SRS-2</th>
<th>Dr. Sagiv</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASD Diagnosis</td>
<td>ADOS or KSADS</td>
<td>Dr. Sagiv and Dr. Sheridan noted only way to be officially diagnosed is with ADOS, but KSADS is good alternative and already being added under the SCID. Currently SCID is listed as “clinically administered psychiatric survey” so it won’t be listed as diagnostic tool.</td>
<td>Include KSADS under SCID</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Bullying</th>
<th>OBQ</th>
<th>OBQ</th>
<th>Dr. Chung</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adolescent Behaviors and Attitudes</td>
<td>FLASHE</td>
<td>FLASHE</td>
<td>Dr. Chung</td>
</tr>
<tr>
<td>Sleep (children under 6)</td>
<td>Need to identify protocols for children under 6</td>
<td></td>
<td>Dr. Chung</td>
</tr>
<tr>
<td>Peer Relationships</td>
<td>NIH Toolbox or PROMIS</td>
<td>They address the same things but for different age groups</td>
<td>Include both under same measure as they address different age groups</td>
</tr>
<tr>
<td>Media</td>
<td>Pew Internet and American Life Project or Rosen Media and Tech use Attitudes Scale</td>
<td>More research is needed to look at the survey</td>
<td></td>
</tr>
</tbody>
</table>

b. Other considerations
   i. Dr. Bosquet Enlow mentioned that we suggested a measure for cognitive stimulation but not emotional support from the perspective of the child. Dr. Sagiv said there is an emotional support component in the HOME tool, but Dr. Bosquet Enlow said it is not adequate. Dr. Sheridan suggested the Alabama Parenting
scale and that a few other family functioning scales exist that are caregiver reported, but we can look into this further.

c. Overall
   i. Ms. Cox noted that the WG is in a good place with 20 measures and some already noted as low priority since the group can send up to 18 to outreach. There are a few outstanding protocols to identify.
   ii. Assignment of measures that need protocols identified
      1. Exposures: Dr. Wright will identify protocols for teeth and wearables
      2. Household stability: Dr. Bosquet Enlow and Dr. Sheridan will identify protocol
      3. Sleep in children under 6: Dr. Chung will identify protocol

VI. Next Steps and Wrap Up

a. Clean up

RTI will clean up the list of recommendations and send to the WG for review. RTI will follow up by email for secondary reviewers for all data sheets. Primary reviewer will be the person who originally submitted and presented the protocol at the in-person meeting. Primary reviewers can also reach out to people to ask to be secondary reviewer.

b. Data Sheet Preparation

Jen Beverly presented the timeline. Datasheets will be developed for each measure from December 2018 – January 2019. Datasheets will be sent for community outreach in February 2019. Datasheets will be finalized in March – April 2019. Ms. Beverly also presented the datasheet template to the group.

c. Outreach

Prior to outreach, RTI will send email to owners of proposed protocols seeking approval for use in PhenX Toolkit & follow up as needed

d. Upcoming Conferences/publications

Potential conferences include ACMG and AAP. Dr. Stroustrup attends PAS meeting every year. RTI can support any presentations or publications as necessary.

Pediatrics and JAMA Peds are good journals to target.

VII. Closing Remarks

Ms. Cox noted that the meeting was very productive with great discussion. Dr. Bosquet Enlow closed the meeting thanking all members and wishing everyone a Happy Thanksgiving.