531 Glaucoma: Frequency, Risk Factors, and Care
Thursday, May 11, 2017 11:30 AM–1:15 PM
Room 309 Paper Session
Program #/Board # Range: 5607–5613
Organizing Section: Clinical/Epidemiologic Research

Program Number: 5607
Presentation Time: 11:30 AM–11:45 AM
Unexpectedly High Prevalence of Glaucoma in Germany: Results from the Gutenberg Health Study
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Purpose: To determine the prevalence of open-angle glaucoma (OAG) according to the ISGEO classification in an adult European cohort.
Methods: The Gutenberg Health Study (GHS) is a population-based, prospective, observational cohort study in the Rhine-Main Region in mid-western Germany with a total of 15,010 participants. In this study, the first 5,000 subjects with an age range between 35 and 74 years were included. At baseline, participants underwent a standardized protocol with a general cardiovascular and ophthalmic examination, which included slitlamp biomicroscopy, non-contact tonometry, fundus photography, central corneal thickness measurement and visual field testing. Optic disc pictures were obtained by a non-mydriatic fundus camera (Visucam™) and analyzed using the Visupac™ software. The prevalence was determined in two steps. First, the ISGEO classification was applied using "hypernormal subjects" (normal visual function) as reference. In the second analysis, we additionally considered the disc area (DA) dependency of the vertical cup-to-disc ratio by a quantile regression.
Results: The overall prevalence of definite OAG in our sample was 1.6% (n=79). The disc area adjusted prevalence was 1.5% (n=74). The prevalence gradually increased in both models with every age decade (0.8% to 2.4%, respectively). In both models none of the glaucoma cases had a small optic disc (<1.6 mm^2). For medium and large optic discs there was a significant prevalence difference, whether disc area was considered or not. The prevalence in medium optic discs was 1.2% vs. 1.8% and in large optic discs 5.7% vs. 2.5%, respectively, applying the non-adjusted vs. the DA adjusted classification.
Conclusions: Prevalence of definite glaucoma was higher than in most other Caucasian population-based cohorts, although our sample was the youngest cohort so far. In addition, our analysis underlined the crucial influence of optic disc size in determining the diagnosis of glaucoma.
Commercial Relationships: Rene Hoehn, None; **Stefan Nickels**, None; **Alexander K. Schuster**, None; **Philipp S. Wild**, None; **Thomas Münzel**, None; **Karl J. Lackner**, None; **Maria Blettner**, None; **Manfred E. Beutel**, None; **Norbert Pfeiffer**, None

Program Number: 5608
Presentation Time: 11:45 AM–12:00 PM
The Incidence of Glaucoma over 5, 10 and 15 years. The Blue Mountains Eye Study
Paul R. Healey, Shweta Kaushik, Anne Lee, Andrew J. White, Paul Mitchell. Ophthalmology, University of Sydney, Sydney, NSW, Australia.
Purpose: To describe the incidence and associations of open-angle glaucoma in a well defined cohort of older Australians followed for 15 years.
Methods: The Blue Mountains Eye Study is a population–based cohort study which examined 3654 persons aged over 49 years at baseline (82% of those eligible), 2335 after 5 years (BMES2: 75% of survivors), 1952 (BMES3: 76% of survivors) after 10 years and 1149 (BMES4: 56% of survivors) at 15 years. Glaucoma was diagnosed at all four examinations when typical glaucomatous visual field defects (assessed from Humphrey 30–2 fields) matched optic disc cupping with neuro–retinal rim thinning graded from stereo–photographs masked as to other findings and after exmination which included gonioscopy. Incident glaucoma was classified as definite or probable based on completeness of data. Glaucoma incidence was calculated using Kaplan–Meier methods. Discrete multivariate logistic models were used to assess the risk of incident glaucoma according to various baseline ocular and systemic factors, including age, gender and family history.
Results: Between baseline and 10 years 82 participants developed glaucoma, an incidence of 3.4%. Between 10 and 15 years a further 33 developed definite glaucoma, an incidence of 3.2%. The periodic and cumulative incidence of glaucoma increased strongly with age. The association with female gender weakened over time. Age-adjusted prevalence did not vary significantly over time.
The other systemic baseline predictor of incident glaucoma was recall of glaucoma family history (two-fold relative risk). No significant associations were found with smoking, thyroid disease, diabetes or migraine in multivariate modelling.
Baseline ocular risk factors associated with incident glaucoma included higher intraocular pressure (and ocular hypertension), higher vertical cup-disc ratio, the presence of an optic disc neural rim notch, optic disc haemorrhage, parapapillary atrophy type beta and higher myopia.
Conclusions: The incidence of glaucoma continues to increase over time due to population ageing. There is no evidence of a cohort effect. Over long periods, the strongest baseline predictors of glaucoma are optic disc characteristics rather than systemic factors.
Commercial Relationships: Paul R. Healey, None; **Shweta Kaushik**, None; **Anne Lee**, None; **Andrew J. White**, None; **Paul Mitchell**, None
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Program Number: 5609
Presentation Time: 12:00 PM–12:15 PM
Association between self-reported phosphodiesterase inhibitor use and glaucoma in a representative sample of the US population
Stephanie Chen[1], Kuldev Singh[1], Shan Lin[2]. [1]Ophthalmology, Stanford University School of Medicine, Stanford, CA; [2]Ophthalmology, UCSF, San Francisco, CA.
Purpose: While optic neuropathy due to decreased ocular blood flow is a known cause of glaucoma, it is unclear what role systemic phosphodiesterase inhibitors (PDEi) play. We performed a retrospective, cross-sectional study of a nationally representative sample of the US population to investigate the relationship between

the most commonly used PDEi, sildenafil and theophylline, and self-reported glaucoma.

Methods: We used the National Health and Nutrition Examination Survey 2005-2008 cycles for this observational study. 7,042 participants, age ≥40 years, responded to a survey item on glaucoma status and were included in the analysis. Multivariate logistic regression models were constructed to evaluate the association between ≥1 year of self-reported PDEi use and prevalent glaucoma. Regressions were adjusted for potential confounding variables, including demographics and general health conditions. Sample weights were used to ensure generalizability of results.

Results: 482 respondents self-reported a diagnosis of glaucoma (Table 1), of which 11 used sildenafil and 18 used theophylline for ≥1 year. Covariates significantly associated with higher odds of glaucoma in univariate analyses included older age, black race, former smoking status, diabetes, hyperlipidemia, myocardial infarction, and stroke (Table 2). In regression analyses adjusted only for age and gender, sildenafil (OR=5.14, CI: 1.17-22.60, p=0.031) and theophylline (OR=3.63, CI: 1.78-7.41, p=0.001) were significantly associated with self-reported glaucoma. These associations held after further adjustment with demographics and general health conditions for both sildenafil (OR=4.59, CI: 1.21-17.40, p=0.026) and theophylline (OR=2.91, CI: 1.44-5.85, p=0.004).

Conclusions: At least 1-year use of sildenafil or theophylline may be associated with self-reported glaucoma, perhaps by diverting blood flow away from the optic nerve.

	Self-Reported Glaucoma		
Characteristic	No (n=6,560)	Yes (n=482)	*P* Value
Age, mean (SD), y	56.54 (12.01)	66.86 (12.11)	<0.001
Gender (%)			
Female	52.95	52.38	0.868
Race/Ethnicity (%)			
Non-Hispanic White	75.88	72.46	0.002
Mexican/Hispanic	8.79	6.73	
Black	10.14	16.67	
Other	5.18	4.15	
Education (%)			
<High school graduate	19.00	27.51	<0.001
High school graduate/some college	53.86	57.03	
College graduate and beyond	27.14	15.46	
Annual household income (%)			
<$35,000	32.81	47.19	<0.001
≥$35,000 to <$65,000	25.74	31.24	
≥$65,000	41.45	21.57	
Smoking status (%)			
Never	49.43	45.71	<0.001
Former	29.85	41.97	
Current	20.72	12.32	
Diabetes (%)	11.08	23.00	<0.001
Hypertension (%)	84.83	86.18	0.618
Hyperlipidemia (%)	47.81	58.85	<0.001
Myocardial infarction (%)	5.02	9.80	0.003
Stroke (%)	4.34	10.21	0.010

Table 1. Demographics and General Health Characteristics of Participants Based On Self-Reported Glaucoma Status

Characteristic	OR	CI (low)	CI (high)	*P* value
Sildenafil use (≥1 year of use)				
Crude†	5.14	1.17	22.60	0.031
Adjusted‡	4.59	1.21	17.40	0.026
Theophylline use (≥1 year of use)				
Crude†	3.63	1.78	7.41	0.001
Adjusted‡	2.91	1.44	5.85	0.004
*Covariates**				
Age	1.07	1.05	1.08	<0.001
Female sex	0.98	0.74	1.29	0.868
Race/Ethnicity				
White	--	--	--	--
Mexican/Hispanic	0.80	0.59	1.09	0.149
Black	1.72	1.34	2.21	<0.001
Other	0.84	0.42	1.67	0.606
Education				
<High school graduate	--	--	--	--
High school graduate or some college	0.73	0.56	0.96	0.023
College graduate and beyond	0.39	0.29	0.53	<0.001
Annual household income				
<$35,000	--	--	--	--
≥$35,000 to <$65,000	0.84	0.66	1.07	0.156
≥$65,000	0.36	0.25	0.52	<0.001
Smoking status				
Never	--	--	--	--
Former	1.52	1.22	1.89	<0.001
Current	0.64	0.41	1.02	0.059
Diabetes	2.40	1.97	2.91	<0.001
Hypertension	1.11	0.71	1.76	0.629
Hyperlipidemia	1.56	1.31	1.86	<0.001
Myocardial infarction	2.06	1.42	2.98	<0.001
Stroke	2.50	1.43	4.39	0.002

Table 2. Logistic Regression Models for Self-Reported Glaucoma and Risk Factors

† Crude models adjusted only for age and female sex

‡ Adjusted models adjusted for demographics and general health comorbidities

* Univariate regressions performed for each covariate

Odds ratios (OR) are reported with 95% confidence intervals (CI) with two-sided *p*-values <0.05 deemed statistically significant

Commercial Relationships: Stephanie Chen, None; **Kuldev Singh**, None; **Shan Lin**, Iridex (C), Allergan (C)

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Program Number: 5610

Presentation Time: 12:15 PM–12:30 PM

Similarities in POAG genetic risk factors between subjects of African and European ancestries

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Purpose: Primary open-angle glaucoma (POAG) is a highly heritable disease and genome-wide association studies (GWAS) have already identified several loci that predispose to it. Although POAG is more common in African ancestry subjects, little is known about the genetic risk in this group. Previous studies in subjects of African ancestry generally could not replicate known, primarily European-driven genetic associations. The purpose of this study is to evaluate the role of known genetic variants associated with POAG in subjects of African descent.

Methods: Replication of known POAG GWAS loci was sought in two panels, of African (321 cases and 217 controls) and European descent (306 cases and 297 controls) respectively. Each panel had more than 70% power to replicate associations at nominal level for MAF>0.1 and OR>1.5.

Correlation of observed effect sizes with those of previously published literature as well as genomic risk score associations with

the POAG status were used to estimate similarities in genomic architecture of POAG risk.
Results: There was a nominal replication for the CDKN2B-AS (p=0.038) and the ARHGEF12 locus (p=0.007) in Africans, but despite sufficient power, not at the TMCO1 locus. The published GWAS effect sizes were correlated with those observed in the African (r=0.54, p=0.01) and the European panel (r=0.66, p=0.0008). Effect sizes of POAG GWAS loci observed in our African panel were a function of the determinants of statistical power, such as the originally published effect size (p=0.002) and MAF in Africans (p=0.02). Genetic risk scores built on estimates derived from POAG GWAS were marginally associated with POAG in our African panel (p=0.06) and unsurprisingly stronger in the European panel (p=0.0001), and together with sex and age, explained 7 and 10% of POAG variance in the respective populations.
Conclusions: Genetic effects observed in European populations were similar to those observed in African cohorts. In the latter, statistically significant replication in some cases may be complicated by differences in LD patterns across populations of different ancestry and by the generally lower MAFs observed for POAG loci. Because known POAG loci tend to have a much lower MAF in subjects of African descent, there is an even larger heritability gap in this ethnic group compared to others, which needs to be addressed by future studies.
Commercial Relationships: Pirro G. Hysi; **Abhishek Nag**, None; **Christopher J. Hammond**, None

Program Number: 5611
Presentation Time: 12:30 PM–12:45 PM
***Genetics in Glaucoma patients of African descent study (GIGA):* Genetic African ancestry is associated with central corneal thickness and intraocular pressure in primary open-angle glaucoma patients**
Pieter W. Bonnemaijer[1], Colin Cook[2], Abhishek Nag[3, 4], Christopher J. Hammond[3, 4], Cornelia van Duijn[5], Hans G. Lemij[6], Caroline Klaver[1, 7], Alberta A. Thiadens[1]. [1]Ophthalmology & Epidemiology, Erasmus MC, Rotterdam, Netherlands; [2]Ophthalmology, University of Cape Town, Cape Town, South Africa; [3]Twin Research and Genetic Epidemiology, King's College London, London, United Kingdom; [4]Ophthalmology, King's College London, London, United Kingdom; [5]Epidemiology, Erasmus MC, Rotterdam, Netherlands; [6]Glaucoma service, the Rotterdam Eye Hospital, Rotterdam, Netherlands; [7]Ophthalmology, Radboud UMC, Nijmegen, Netherlands.
Purpose: To unravel the relationship between African ancestry, central corneal thickness (CCT), and intraocular pressure (IOP) by estimating the genetic African ancestry(GAA) proportion in primary open-angle glaucoma (POAG) patients and controls from an admixed South African Coloured (SAC) and a South African Black (SAB) population.
Methods: In this case-control study, 254 self-reported SAC and 158 self-reported SAB participants were recruited from an university clinic in Cape Town, South Africa. All participants were genotyped on the Illumina HumanOmniExpress beadchip or HumanOmni2.5Exome beadchip. ADMIXTURE was used to infer participant's GAA among 86632 SNP's. Linear and logistic regression models were used to assess the relation between GAA, POAG, CCT and IOP.
Results: The median proportion GAA was 60% (IQR=70.3) in the study population. Participants with a higher proportion GAA presented with a significantly thinner CCT (P<0.001; β= -4.09 μm per 10% increase in GAA). The effect of GAA on CCT was marginally different among POAG patients vs controls (P=0.066). POAG patients with a higher percentage GAA showed a significantly higher IOP (P=0.034, β=0.49 mmHg per 10% increase in GAA). In POAG patients, the CCT was significantly thinner compared to controls after adjusting for age and gender (P=0.016; OR=1.071 per 10 μm decrease in CCT). In a stratified analysis in participants with a greater than the median GAA, we did not observe any association with CCT and POAG (P=0.550; OR=1.030 per 10 μm decrease in CCT).
Conclusions: This study demonstrated that a higher proportion of GAA was associated with a thinner CCT and a higher IOP in POAG patients. Regardless of genetic ethnicity, a thinner CCT was associated with POAG when adjusted for gender and age. Remarkably, at higher proportions of GAA, the difference in CCT between POAG and controls was reduced. A stratified analysis showed that the association between CCT and POAG was mainly driven by participants with little GAA. This suggests that a thinner CCT is not associated with POAG in Africans and that assessing the CCT in Sub-Saharan Africans may not be of significantly added value in POAG screening.
Commercial Relationships: Pieter W. Bonnemaijer; **Colin Cook**, None; **Abhishek Nag**, None; **Christopher J. Hammond**, None; **Cornelia van Duijn**, None; **Hans G. Lemij**, None; **Caroline Klaver**, None; **Alberta A. Thiadens**, None
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Program Number: 5612
Presentation Time: 12:45 PM–1:00 PM
Screening for Primary Angle Closure Disease in resource constraint region
Nikhil S. Choudhari[1], Prem Anand Chandran[1], Harsha Rao[1], Ganesh Jonnadula[1, 2], Uday Addepalli[1, 2], Sirisha Senthil[1], Chandrasekhar Garudadri[1]. [1]VST Glaucoma centre, L. V. Prasad Eye Institute, Hyderabad, India, Hyderabad, India; [2]University of New South Wales, Sydney, NSW, Australia.
Purpose: Primary angle closure disease is quite often asymptomatic, reportedly more blinding than primary open angle glaucoma (POAG) and more prevalent in resource constraint regions. This study was designed to assess the performance of ocular biometry and van Herick (VH) grading assessed by teleophthalmology in identifying a gonioscopically occludable angle and to determine whether combining test results can improve the prediction of a gonioscopically occludable angle.
Methods: This observational, cross-sectional study was carried out at a primary eye care centre. Slit lamp photography and ultrasound biometry was performed by a trained vision technician. A masked ophthalmologist graded digital slit lamp photographs of the peripheral anterior chamber depth (ACD) by VH system. Eyes having VH grades 2 or less were classified to have narrow angles. Gonioscopy was performed using Sussman 4 mirror lens by one of the two experienced study optometrists. The agreement between a glaucoma specialist and each of the study optometrists for gonioscopy was good [kappa (k): 0.92 and 0.84] in a prior study.
Results: We included 1965 eyes of 1029 adult subjects. The intra-observer agreement in grading 100 randomly selected slit lamp photographs by VH grading (k: 0.76) was better than the inter-observer agreement (k: 0.56). The angle was occludable by gonioscopy in 101 (5.1%) eyes. The diagnostic accuracy of ACD at lowest quartile cut off was the highest [Sensitivity (Sn), Specificity

(Sp), positive (PPV) and negative predictive value (NPV)] being 73.3%, 77.9%, 15.2 and 98.2, respectively. Similarly, Sn, Sp, PPV and NPV of VH classification were 52.5%, 92.8%, 28.2 and 97.3, respectively. Combination of biometric parameters (ACD and axial length at lowest quartile cut off; lens thickness at highest quartile cut off) and VH classification achieved Sp and PPV of 92.2% and 57.6, respectively. On the other hand, negative result of any of the biometric parameter at the above cut offs or VH classification achieved Sn and NPV of 92.1% and 99.1, respectively.
Conclusions: In isolation, van Herick test and ocular biometry demonstrated limited ability to screen for primary angle closure disease. However, test combination is a simple and inexpensive strategy to screen for angle closure disease in a resource constraint region with a downside of 42.4% false positive rate and 7.9% false negative rate at 5.1% prevalence of gonioscopically occludable angles.
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Program Number: 5613
Presentation Time: 1:00 PM–1:15 PM
Exfoliation Syndrome - The Maccabi Glaucoma Study
Tzukit Zehavi-Dorin[1], Louis R. Pasquale[2], Hani Levkovitch-Verbin[1]. [1]Goldschleger Eye Institute, Sheba Medical Center, Tel-Hashomer, Israel; [2]Department of Ophthalmology, Harvard Medical School, Massachusetts Eye and Ear Infirmary, Boston, MA.
Purpose: To investigate exfoliation syndrome (XFS) epidemiology and its association with systemic diseases and solar exposure related diseases including skin cancer, pterygium and actinic keratosis.
Methods: This is a population-based, retrospective, case control study, conducted using the electronic medical database of Maccabi Health Services, the second largest HMO in Israel, insuring 25% of the total population with a nationwide distribution. Study population included Maccabi members from January 2003 to April 2016. The study group included patients diagnosed with XFS with or without glaucoma, according to ICD-9 and CPT codes. The control group was age, sex and ancestry matched and included patients without XFS that were examined by an ophthalmologist within the last 12 months.
Results: We have identified 16,393 patients with XFS, in whom 40.3% (n=6613) had exfoliation glaucoma. The control group included 14,101 patients. Mean age was 78.3 years old and 75.8 for the XFS and control group, respectively. XFS was significantly associated with higher rate of hospitalizations (5 hospitalizations on average in the XFS group (SD± 5.3) and 3.3 in the controls (SD± 4), $p< 0.0001$) and significantly higher mortality (22.2% in XFS vs 2.3% in the controls, $p< 0.0001$). XFS was associated with cardiovascular diseases including hypertension (77.7% vs 74.5% in the controls, $p<0.0001$), myocardial infarction (10.4% vs 8.4% in the controls, $p< 0.0001$%), and congestive heart failure (9.2% vs 5% in the controls, $p< 0.0001$). However, diabetes mellitus was less frequent in the XFS group (32.5% vs 40.8%, $p < 0.0001$). Overall cancer diagnoses were more common in the XFS group (28.16% vs 26.74%, $p < 0.0001$), yet skin cancer (including melanoma, basal cell carcinoma or squamous cell carcinoma) was not associated with XFS (11.8% in the XFS group vs 15.1% in the controls).
Cataract was significantly more common in XFS patients (82.7% vs 59.2%, $p< 0.0001$). Pterygium and actinic keratosis were not associated with XFS.
Conclusions: These data support strong associations between systemic disease and XFS with significantly higher mortality in these patients.
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