Abstracts
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Intraocular Pressure in an Urban Malay Population: The Singapore Malay Eye Study (SiMES)

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OBJECTIVE: To describe the distribution and factors associated with intraocular pressure (IOP) in Malay adults in Singapore.

METHODS: A population-based, cross-sectional study of 3,280 (78.7% response rate) Malays aged 40-80 years was carried out in Singapore. The population of Malay people living in the southwestern part of Singapore was selected using an age-stratified random sampling procedure. Participants had a standardized interview, clinical examination and imaging of the lens and retina at a central study clinic. IOP was measured from the Goldmann applanation tonometer before pupil dilation.

RESULTS: Data on IOP were available from 3,258 right eyes and 3,259 left eyes. IOP was normally distributed with a mean of 15.4 mm Hg (95% confidence interval [CI], 15.3 to 15.5) in right eyes and 15.3 mm Hg (95% CI, 15.2 to 15.5) in left eyes. Mean IOP (right eye) was not associated with age (15.2, 15.6, 15.6, and 15.1 mm Hg, among participants aged 40-49, 50-59, 60-69, and 70-80 years, respectively, p=0.85). IOP was significantly higher in women than men (mean of 15.7 vs 15.0 mm Hg, $p < 0.001$). IOP was significantly and positively correlated with systolic blood pressure (Pearson correlation coefficient 0.19, $p < 0.001$), diastolic blood pressure (0.14, $p < 0.001$), random glucose (0.14, $p < 0.001$) and glycosylated hemoglobin levels (0.10, $p < 0.001$), and central corneal thickness (0.19, $p <0.001$). IOP was

negatively correlated with spherical equivalent refraction (−0.04, p=0.01) but not axial length (−0.01, p=0.54) or anterior chamber depth (−0.01, p=0.46). In linear regression models adjusting for age and gender, IOP increased by 0.21 mm Hg (95% CI, 0.17 to 0.24) for each 10 μm increase in central corneal thickness.

CONCLUSIONS: This study provides population-based data on the distribution and determinants of IOP in an urban adult Malay population in Singapore. IOP was associated with higher blood pressure, hyperglycemia, and increased central corneal thickness.

SOURCE OF SUPPORT: National Medical Research Council Grants No 0796/2003 and Biomedical Research Council Grant No 501/1/25-5

NOTES

Factors Associated with Intraocular Pressure (IOP) Prior to and During Nine Years of Treatment in the Collaborative Initial Glaucoma Treatment Study (CIGTS)

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OBJECTIVES: To evaluate, both at the time of initial glaucoma diagnosis and while under prolonged IOP-reducing treatment, the effects of demographic and clinical factors on IOP.

METHODS: In a controlled clinical trial, 607 patients with newly diagnosed, open-angle glaucoma were enrolled at 14 clinical centers, randomized to initial surgery or medications, and followed at 6-month intervals. Predictive factors associated with level of IOP at baseline and predictive of IOP during follow-up were evaluated by means of linear mixed modeling.

RESULTS: The mean IOP at baseline was 27.5 mm Hg (SD, 5.6 mm Hg). Factors that were associated with baseline IOP included age, sex, type of glaucoma, pupillary response, and clinical center. IOP was lower at older ages and in females, higher in patients with pseudoexfoliative glaucoma, and higher in patients who had a pupillary defect. During the first nine years of follow-up, dramatic treatment effects on IOP were seen from both surgery and medications, but the extent of IOP reduction was consistently greater in the surgery group (over the 2 to 9 year follow-up period, mean IOP of 17.2 mm Hg for medicine, 15.2 mm Hg for surgery). Among the significant associations with IOP during follow-up was modification of the treatment effect by smoking

status; non-smokers treated surgically had significantly lower IOP than smokers treated surgically (14.6 vs. 16.7 mmHg, respectively; P=0.004). Higher baseline IOP was predictive of higher follow-up IOP (P < 0.0001).

CONCLUSIONS: Measurement of IOP over an extended time on treatment has yielded insight not only into the impact that treatment has on IOP, but also into effects that demographic, environmental, and clinical factors have on IOP. Evidence from the CIGTS indicates that person-level factors make important contributions to IOP control during treatment.

SOURCES OF SUPPORT: National Eye Institute, National Institutes of Health, U.S. Department of Health and Human Services (EY015860) and an unrestricted grant from Allergan, Inc.

NOTES

Detection and Prognostic Significance of Optic Disc Hemorrhages Observed During the Ocular Hypertension Treatment Study

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OBJECTIVES: To assess the incidence of optic disc hemorrhages in the Ocular Hypertension Treatment Study (OHTS) detected at the Optic Disc Reading Center (ODRC) and to determine whether optic disc hemorrhages predicted the development of primary open-angle glaucoma (POAG).

METHODS: Both eyes of participants were assessed for optic disc hemorrhages by annual review of stereoscopic disc photographs at the ODRC.

RESULTS: Data from 3,236 eyes of 1,618 participants with at least one set of follow-up photographs were analyzed. Median follow-up was 96.3 months. Stereophotography confirmed that glaucomatous optic disc hemorrhages were present in 128 eyes of 123 participants prior to diagnosis of POAG. The occurrence of a disc hemorrhage increased the risk of POAG developing in the same eye 6-fold in a univariate analysis, ($p < 0.001$; 95% confidence interval 3.6 - 10.1), and 3.7-fold in a multivariate analysis that included baseline factors predictive of POAG ($p < 0.001$; 95% confidence interval 2.1 - 6.6). The 96-month cumulative incidence of POAG in the eyes without optic disc hemorrhage was 5.2% compared to 13.6% in the eyes with optic disc hemorrhage. The median time from optic disc hemorrhage to a POAG endpoint was 13 months.

CONCLUSIONS: The occurrence of an optic disc hemorrhage was associated with an increased risk of developing a POAG endpoint in participants in the Ocular Hypertension Treatment Study. However, the majority of eyes (86.7%) in which a disc hemorrhage developed have not had a POAG endpoint to date.

SOURCES OF SUPPORT: National Eye Institute, National Institutes of Health, U.S. Department of Health and Human Services (EY09341 and EY09307); Merck Research Laboratories, and Research to Prevent Blindness.

NOTES

Glaucoma and the Intake of Antioxidants Among Older Women: The Study of Osteoporotic Fractures

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OBJECTIVE: Past studies have shown that antioxidant intake may protect the optic nerve and improve trabecular meshwork function. The purpose of this research is to evaluate the association between the presence of glaucoma and the intake of antioxidants from food among participants in the Study of Osteoporotic Fractures.

METHODS: In a random sample of 1,155 (out of 5,482) women ages 67 and older, glaucoma specialists diagnosed glaucoma by assessing optic nerve head photographs and 76-point suprathreshold screening visual fields. Intake of antioxidants from food was calculated based on responses to the Block Food Frequency Questionnaire. In this cross-sectional analysis, the relationship between a diagnosis of glaucoma and antioxidants from food, including Vitamins A, B1, B2, B6, C and E, and alpha- and beta-carotenes, was investigated using logistic regression models.

RESULTS: Among 1,155 women, 8.3% (96) were diagnosed with glaucoma in at least one eye. After adjusting for study site, age, race/ethnicity, education, smoking status, alcohol consumption, walks for exercise, body mass index, self-rated health status, presence of self-reported diabetes and hypertension, and presence of clinically diagnosed late age-related macular degeneration, women with a daily

consumption of at least 2 mg of Vitamin B2 (riboflavin) obtained from natural food sources had decreased odds of glaucoma [OR=0.42; 95% CI=0.19, 0.91] compared with those who consumed less than 1 mg. Women with a greater daily intake of retinol equivalents of Vitamin A from food tended to have reduced odds of glaucoma [OR=0.50; 95% CI=0.24, 1.03; p=0.060] as well as women with greater daily intake of alpha-carotene [OR=0.63; 95% CI=0.37, 1.08; p=0.090].

CONCLUSIONS: A higher intake of antioxidants as part of daily food intake may be associated with a decreased risk of glaucoma. Prospective studies are needed to investigate the relationship between the risk of glaucoma and antioxidants in the diet. Increasing total dietary antioxidant intake could be a promising means of glaucoma prevention.

SOURCES OF SUPPORT: National Institutes of Health, U.S. Department of Health and Human Services (AG05407, AR35582, AG05394, AR35584, AR35583); Research to Prevent Blindness; Gerald Oppenheimer Foundation – Prevention of Eye Diseases.

NOTES

Glaucoma Progression Factors After Extended Follow-Up of Patients in the Early Manifest Glaucoma Trial (EMGT)

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OBJECTIVES:. To determine factors influencing glaucoma progression among all patients at the end of the Early Manifest Glaucoma Trial (EMGT), and to evaluate separately those patients with higher and lower baseline intraocular pressure (median split=21 mm Hg).

METHODS: The EMGT included 255 early open-angle glaucoma patients evenly randomized to argon laser trabeculoplasty plus betaxolol or no immediate treatment and examined every 3 months for up to 11 years. In the EMGT, glaucoma progression was assessed from perimetric and photographic disc criteria. Progression factors were evaluated by Cox proportional hazard analyses, expressed by hazard ratios (HR) and 95% confidence intervals (CI).

RESULTS: When follow-up ended (median = 8 years), glaucoma had progressed among 67% of all patients. Early treatment continued to reduce progression risk considerably (HR=0.53, CI: 0.39 - 0.72); results were similar for patients with higher and lower baseline IOP (HR=0.41 and 0.55). Baseline predictors continued to be higher baseline IOP, exfoliation, bilateral disease, and older age (HR: 1.51 to 2.12; $p < 0.01$), as previously reported. New baseline predictive factors were lower ocular systolic perfusion pressure in all patients (≤160 mm Hg; HR=1.42, CI: 1.04 - 1.94), cardiovascular disease history (HR=2.75, CI: 1.44 - 5.26) in patients with higher baseline IOP; and lower systolic

blood pressure (≤125 mm Hg; HR=0.46, CI: 0.21 - 1.02) in patients with lower baseline IOP. Post-baseline predictors in all patients were follow-up IOP levels (HR=1.12-1.13 per mm Hg higher) and the presence of disc hemorrhages at study examinations (HR=1.02 per percent higher frequency). A new predictor was central corneal thickness (HR=1.25, CI: 1.01 - 1.55 per 40 μm lower), a result observed in patients with higher baseline IOP (HR=1.42, CI: 1.05 - 1.92), but not lower baseline IOP, with significant interaction between IOP and central corneal thickness.

CONCLUSIONS: Treatment and follow-up IOP continued to be highly influential on glaucoma progression at the end of the EMGT, regardless of baseline IOP, as was older age, bilaterality, exfoliation, and baseline IOP. With extended follow-up, new predictors included lower systolic perfusion pressure, lower systolic blood pressure, and cardiovascular history, suggesting a vascular role in glaucoma progression. Another new factor was thinner central corneal thickness in patients with higher baseline IOP.

SOURCES OF SUPPORT: National Eye Institute, National Institutes of Health, U.S. Department of Health and Human Services, and Swedish Research Council.

NOTES

Comparison of Methods to Evaluate Risk Factors for Alternative Cataract Types

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OBJECTIVE: Comparisons of associations of risk factors with the development of cataract in different areas of the lens can elucidate etiology, but such comparisons are complicated because people often develop two or all three of cortical, nuclear sclerotic and posterior subcapsular cataract.

METHODS: We compared three approaches to estimate effects of risk factors on different cataract types: separate proportional hazards analysis of each type; a polytomous logistic regression model with a separate category for people who develop multiple types; and competing risks proportional hazards models with simultaneous estimation of effects of risk factors on each type through use of data augmentation. These three approaches are illustrated with prospective data on the types of cataract that developed among 20,599 participants in the Physicians' Health Study who were followed for a median of 13 years.

RESULTS: During follow-up, cataract that reduced visual acuity developed in 1,923 men; two types of cataract developed in 43%, and all three types developed in an additional 12%. Separate survival analyses of each type of cataract provide estimated effects of interest but do not readily allow for testing and estimation of possibly common effects of a risk factor across types. Polytomous logistic regression permits evaluation of common effects, but does not readily accommodate variable length of follow-up of subjects and cannot estimate the effects of risk factors on

specific cataract types for people in whose eyes more than one type developed. Competing risks survival analysis allows for variable length of follow-up, can use age as the time scale to provide a better description of the different age relationships with risk of each type, and gives tests and estimates of common effects of risk factors across types.

CONCLUSIONS: All approaches can be implemented in available software packages such as SAS, but the competing risks survival approach offers advantages in terms of testing and estimation of common effects, allowance for variable follow-up, options for the time scale, and handling multiple events per person.

SOURCE OF SUPPORT: National Eye Institute, National Institutes of Health, U.S. Department of Health and Human Services (EY12269).

NOTES

A Population-Based Eye Survey of Older Adults from a Low-Income Urban Area of São Paulo, Brazil: Prevalence of Visual Impairment and Blindness

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OBJECTIVE: To assess the prevalence of visual impairment and blindness in older adults in a low-income urban area of São Paulo, Brazil.

METHODS: A random selection of census sector clusters was used to identify a population sample in Ermelino Matarazzo, Vila Jacui, and São Miguel districts in the east zone of São Paulo city. Eligible subjects 50 years of age and older in the 22 selected clusters were enumerated through a door-to-door household survey and invited to examination sites for visual acuity testing and eye examinations from July 2004 to December 2005. The principal cause of reduced central vision was identified for eyes that had visual acuity 20/40 or worse. Presenting and best-corrected visual acuity were the main outcome measures.

RESULTS: A total of 4,224 eligible persons in 2,870 households were enumerated, and 3,678 (87.1%) were examined. The prevalence of presenting and best-corrected visual acuity worse than 20/200 in both eyes was 1.51% (95% confidence interval [CI]: 1.20-1.82) and 1.07% (95% CI: 0.79-1.35), respectively. Presenting blindness was associated with increasing age and lack of schooling. Cataract (29.2%), retinal disorders (22.3%), and glaucoma

(7.6%) were the three major causes of blindness. Refractive error (36.4%), cataract (31.8%), and retinal disorders (10.7%) represented most of the causes of visual impairment.

CONCLUSIONS: Blindness, particularly blindness because of cataract, is a significant problem among this urban low-income adult Brazilian population. Because of a rapidly aging population, Brazilian health authorities need to target prevention of blindness programs to an increasing number of elderly people, with a special emphasis on those with little or no education.

SOURCES OF SUPPORT: WHO/NEI to Institute of Vision (PBD.3/15, B7/181/49); FAPESP (São Paulo, SP, Brazil), grant # 04/06670-9; CNPq (Brasilia, DF, Brazil); FADA (São Paulo, SP, Brazil).

NOTES

Cataract Risk Among Patients with the Acquired Immune Deficiency Syndrome (AIDS)

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INTRODUCTION: Recently, cataract was observed to be the second leading cause of incident vision loss in the Longitudinal Study of Ocular Complications of AIDS (LSOCA). We report the incidence and the risk factors for cataract in this cohort.

METHODS: The LSOCA cohort consists of patients with AIDS ages ≥13 years enrolled at 19 U.S. academic AIDS ophthalmology centers. Cataract prevalence and incidence in phakic eyes of patients were assessed. Cataract was diagnosed by study-certified ophthalmologists when they identified lens opacity on biomicroscopy and best-corrected visual acuity worse than 20/40 was attributed to cataract.

RESULTS: Among 1,689 patients (3,378 eyes) enrolled between 2 September 1998 and 18 August 2005, 30 (30 eyes) had cataract and 79 (108 eyes) were pseudophakic or aphakic at the time of enrollment. The prevalence of cataract or pseudophakia was approximately 20-fold higher in the 40-49 year and approximately 2-fold higher in the 50-59 year age groups than in the population-based Proyecto VER study, which defined 'cataract' similarly. The crude incidence of cataract was 1.68 per 100 eye-years. Pre-existing CMV retinitis was associated strongly with cataract (adjusted OR = 11.1, 95% CI: 6.99-17.5). Increasing age (adjusted OR = 6.79 for age ≥60 vs age ≤30) and hypertension (adjusted OR = 1.94) also were significant risk

factors. Time-dependent analysis indicated cataract risk tended to be higher in the lowest CD4+ category (adjusted OR = 2.13 for 0-49 vs. >200 cells/μL, 95% CI: 1.14-4.00, overall p=0.13). Gender, race, education, risk factors for HIV infection, time since AIDS diagnosis, Karnofsky score, diabetes, hyperlipidemia, use of highly active antiretroviral therapy, presence of opportunistic infections (other than CMV retinitis), anemia, and HIV load were not associated with cataract in the multiple regression model.

CONCLUSIONS: Cataract occurs more frequently among patients with AIDS than in the general population. Cytomegalovirus retinitis was the factor most strongly associated with cataract in this group.

SOURCE OF SUPPORT: National Eye Institute and National Center for Research Resources, National Institutes of Health, U.S. Department of Health and Human Services (multiple awards); Research to Prevent Blindness, and the Paul and Evanina Mackall Foundation.

NOTES

The Role of Mortality in Explaining Differences in Cataract Surgery Utilization Between African-Americans and Caucasians. The Salisbury Eye Evaluation (SEE) Project

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OBJECTIVE: African-Americans are less likely to undergo cataract surgery than Caucasians of the same age and gender. Visual function and cataract severity do not fully account for the disparity. Our aim was to characterize the extent to which racial differences are explained by different frequencies of mortality and to determine whether ages at which surgeries are performed differ among those who access surgery.

METHODS: Individuals between 65 and 80 years of age were followed for 8 years in a population-based study (the SEE project). Cataract severity was assessed from lens photographs. Dates of cataract surgery and mortality were collected prospectively. Participants who had cataract surgery prior to enrollment or visual impairment due to other causes were excluded. Statistical approach: Competing events of age at first-eye surgery and age at death while surgery-free were modeled jointly. To allow for removals from the risk set of surgery due to deaths while surgery-free, a mixture model of two Weibull distributions was used.

RESULTS: 1,862 participants were followed for 8,515 person-years; median age at baseline was 72 years and 518 (28%) were African-Americans. During follow-up, 309 (23%) Caucasians had cataract surgery and 260 (19%) died surgery-free; the corresponding numbers for African-

Americans were 79 (15%) and 127 (25%). The model estimated that 52% of Caucasians and 37% of African-Americans would undergo surgery during their lifetime at a median age of 77 years; those who died before accessing the service (48% Caucasian, 63% African-American) would do so at a median age of 79 and 78 years. Stratified analysis by baseline severity showed more pronounced racial differences in lifetime surgery utilization for the subgroup with severe cataract.

CONCLUSIONS: Among those with severe cataract at baseline, higher mortality among African-Americans explained racial disparities in cataract surgery utilization. Among those without severe cataract at baseline, there was less disparity in the frequency of cataract surgery but African-Americans were operated at older ages.

SOURCE OF SUPPORT: National Institute of Aging, National Institutes of Health, U.S. Department of Health and Human Services (AG25131).

NOTES

Relationship Between Visual Function and Driving Concerns in the Collaborative Initial Glaucoma Treatment Study (CIGTS)

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OBJECTIVE: To examine the association between patient-reported driving concerns and clinical outcomes among participants in the Collaborative Initial Glaucoma Treatment Study (CIGTS).

METHODS: In a controlled clinical trial, 607 newly diagnosed open angle glaucoma patients from 14 clinical centers were randomized to either initial medical therapy or initial trabeculectomy. At the 54-month follow-up examination, patients received clinical evaluations and completed quality of life questionnaires by telephone. Concerns with driving were assessed by the Visual Activities Questionnaire (VAQ) and the National Eye Institute Visual Function Questionnaire (NEI-VFQ).

RESULTS: Of the 510 patients with 54-month data, 410 (80%) were current drivers. Over 50% of drivers reported at least some problems with glare (i.e., headlights from oncoming cars) while 22% had some problems with peripheral vision (i.e., trouble seeing cars in the next lane). Over 50% of drivers reported at least "a little" difficulty with night driving, with older participants and women reporting more difficulty. No differences in driving concerns were found by treatment assignment. In multivariable modeling, controlling for age, race, gender, and treatment, those individuals with more substantial visual field damage (> 10 points CIGTS visual field score) were significantly more

likely to report specific driving problems regarding glare, peripheral vision, and visual processing speed, and to have greater difficulty with night driving (all $p < 0.05$). Patients with 20/50 or worse visual acuity reported more frequent problems with almost all visual tasks related to driving than those with better visual acuity (all $p < 0.05$).

CONCLUSIONS: It is recommended that physicians regularly query patients with glaucoma about driving concerns as those with worse visual field and visual acuity report greater difficulty with specific tasks important to safe driving.

SOURCE OF SUPPORT: National Eye Institute, National Institutes of Health, U.S. Department of Health and Human Services (R03 EY015700).

NOTES

Impact of Vision and Cognition on Brake Reaction Speed, a Measure of Driving Performance: Salisbury Eye Evaluation Driving Study (SEEDS)

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OBJECTIVES: Concern for driving safety has prompted research into understanding factors related to performance. Brake reaction speed (BRS), the speed with which persons react to a sudden change in driving conditions, is a measure of performance. Our aim is to determine the visual, cognitive, and physical factors predicting BRS in a population sample of 1,425 older drivers.

METHODS: The Maryland Department of Motor Vehicles roster of persons aged 67-87, residing in Salisbury, Maryland, was used for recruitment of the study population. Procedures included: habitual binocular visual acuity using ETDRS charts, contrast sensitivity using a Pelli-Robson chart, visual fields assessed with 81 points screening Humphrey field at a single intensity threshold, and a questionnaire to ascertain medical conditions. Cognitive status was assessed using a standard battery for attention, memory, visuo-spatial and scanning, and executive function. BRS was assessed using a computer-driven device that measured separately the initial reaction speed (IRS) (from light change to red until moving foot) and physical response speed (PRS) (moving foot from accelerator to full depression). Five trial times were averaged, and time was converted to speed.

RESULTS: The median brake reaction time varied from 384 to 5688 milliseconds. Age, gender, and cognition predicted total BRS, a non-informative result as there are two distinct parts to the task. Once separated, decrease in IRS was associated with low scores on cognitive factors and missing points on the visual field. A decrease in PRS was associated with having three or more physical complaints related to legs and feet and poorer vision search. Vision was not related to PRS.

CONCLUSION: We have demonstrated the importance of segregating the speeds for the two tasks involved in brake reaction. Only the initial reaction speed depends on vision. Persons in good physical condition may perform poorly on brake reaction tests if either their vision or cognition is compromised.

SOURCE OF SUPPORT: National Institute of Aging, National Institutes of Health, U.S. Department of Health and Human Services (AG16906).

NOTES

Glaucoma and Mobility Performance: The Salisbury Eye Evaluation Project

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OBJECTIVE: To determine the impact of glaucoma on mobility in a population-based cohort.

METHODS: Persons examined as part of a population-based eye disease study performed a series of tasks including walking an obstacle course, climbing stairs, performing tandem stands, and walking a 4-meter course. Persons with glaucoma were compared to those without glaucoma to identify differences in mobility. The main outcome measures were speed to complete the obstacle course, number of bumps, ability to perform tandem stands, walking and stair climbing speeds.

RESULTS: In an analysis adjusting for age, race and gender, walking speed through the obstacle course was 2.4 meters/minute slower for persons with bilateral glaucoma and the log rate ratio of bumps was 0.5 times higher in those with bilateral glaucoma compared to those with no glaucoma ($p < 0.05$ for both). Walking and stair climbing speeds were also slower, and balance was worse in individuals with bilateral glaucoma, but these were not statistically significant relative to those of individuals without glaucoma. None of the associations were statistically significant when comparing persons with unilateral glaucoma to normals. These findings remained after adjusting for other potentially confounding factors including visual acuity, body mass index, height (since taller people were more likely to hit hanging plants), MiniMental

State Exam score, grip strength, arthritis, depressive symptoms, comorbidities, and the use of mobility aids.

CONCLUSIONS: Bilateral glaucoma reduced mobility performance as measured in multiple ways in this population-based study of community-dwelling individuals. Persons with bilateral glaucoma completed the walking course more slowly and had more bumps even after adjusting for use of a mobility aid, comorbidities, and visual acuity. After adjusting for all other factors, persons with bilateral glaucoma walked on average 2.4 meters less per minute through the course than those without glaucoma.

SOURCES OF SUPPORT: National Institute on Aging (AG10184) and National Eye Institute (EY01765), National Institutes of Health, U.S. Department of Health and Human Services.

NOTES

Visual Impairment and Suicide Mortality: National Health Interview Survey (NHIS) 1986-1996

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OBJECTIVE: To examine the relationship between reported visual impairment and suicide mortality.

METHODS: The National Health Interview Survey (NHIS) is a population-based, annual survey of the U.S. non-institutionalized civilian population. Mortality linkage through 2002 of 137,479 adult participants aged 18 years and older from the 1986 to 1996 NHIS was analyzed with respect to reported visual impairment using Cox regression models.

RESULTS: The average follow-up was 11.0 years; 200 suicide deaths were identified. After controlling for survey design, age, sex, and race, participants with visual impairment were at increased risk of suicide death relative to participants without visual impairment (hazard ratio: 1.75; 95% confidence interval [CI]: [1.05–2.90]). Further control for self-rated health lowered, but did not eliminate, the association between visual impairment and suicide (hazard ratio: 1.62; 95% CI: [0.97-2.68]).

CONCLUSION: Our population-based findings provide evidence confirming previous case reports and case-control studies which indicate that visual impairment is associated with an increased risk of suicide mortality.

SOURCE OF SUPPORT: National Eye Institute, National Institutes of Health, U.S. Department of Health and Human Services (R03 EY016481)

NOTES

Quantitative Trait Linkage Analysis of Ocular Refraction in African-American and Caucasian-American Populations

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OBJECTIVE: The development of refractive error is mediated by environmental and genetic factors. We performed regression–based quantitative trait locus (QTL) linkage analyses on African-American and Caucasian-American families to identify genomic regions responsible for ocular refraction.

METHODS: We recruited 493 African-American and 270 Caucasian-American individuals in 96 and 35 families, respectively, to participate in the Myopia Family Study. Ascertainment criteria were designed to enrich the sample for myopia. Genotyping with 387 polymorphic microsatellite markers was performed on 398 African-American and 189 Caucasian-American participants by the Center for Inherited Disease Research. The mean spherical equivalent (SE) refractive error was −2.87 D (SD=3.58) in the African-American sample and −2.90 D (SD=3.15) in the Caucasian-American group. Myopia of at least 1 D was present in 267 (67%) and 136 (71%) of genotyped African-American and Caucasian-American participants, respectively. Multipoint, regression-based linkage analyses were carried-out on logarithmic transformations of the mean SE refraction. Analyses were performed separately for the African-American and Caucasian-American populations using the statistical package Merlin–regress, assuming an underlying -

population mean refraction of 0 D, a variance of 9, and a heritability of 0.6.

RESULTS: The maximum linkage signal for the African-American population was seen at 47 cM on chromosome 7 (LOD=5.8). There was no evidence of genetic heterogeneity due to population admixture at this locus in the African-American sample. In the Caucasian-American group, the maximum linkage peak (LOD=4.3) was obtained at 141 cM on chromosome 12. There was no significant overlap of the LOD score profiles at the most highly linked regions between the African-American and Caucasian-American populations.

CONCLUSIONS: We identified two separate QTLs for ocular refraction in African-American and Caucasian-American populations. Our results suggest that different QTLs may be responsible for mediating myopisation in African-American versus Caucasian-American populations.

SOURCE OF SUPPORT: Not provided**.**

NOTES

Estrogen Receptor Alpha and Matrix Metalloproteinase 2 Polymorphisms and Age-Related Macular Degeneration (AMD) in Older Women: The Study of Osteoporotic Fractures

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OBJECTIVE: To determine whether single nucleotide polymorphisms (SNPs) in the estrogen receptor alpha (ESR1) and matrix metalloproteinase 2 (MMP2) genes are associated with age-related macular degeneration (AMD) in older women.

METHODS: Subjects comprised a random sample of Caucasian women age 75 years and older who attended the year 10 clinic visit of the Study of Osteoporotic Fractures (n=906). Fundus photographs were graded for AMD using a modification of the Wisconsin Age-Related Maculopathy Grading System. Subjects were genotyped for three ESR1 SNPs (rs2234693, rs9340799, and rs1801132) and two MMP2 SNPs (rs243865 and rs2287074) by linear array. Comparisons of allele frequencies among subjects with no, early, and late AMD were made with likelihood ratio tests. Logistic regression was used to control for confounders and explore interactions. Comparisons of complete-case models to multiply-imputed models were made to assess the effect of missing covariate data.

RESULTS: AMD prevalence was 46% for early and 4% for late. The MMP2 rs2287074 SNP was associated with AMD. The G allele was present in 70%, 50%, and 53% of subjects with late, early, and no AMD, respectively ($p < 0.02$). GG vs. AA homozygotes had higher risk of any AMD (OR=1.46; 95% CI: 0.99-2.15), particularly among women who never had used postmenopausal hormone therapy (ET/HT) (OR=2.36; 95% CI: 1.30-4.30); without surgical menopause (OR=1.65; 95% CI; 1.09-2.49); who were younger at menopause (<50 yrs., OR=1.74; 95% CI: 1.04-2.90); and with lower BMD (≤0.72 g/cm2, OR=2.06; 95% CI: 1.20-3.55). There were less than multiplicative joint effects for GG genotype and ET/HT use (OR interaction=0.44, p=.04). The G allele was associated with higher risk of late AMD (OR=8.24; 95% CI: 1.11-61.30); however the estimate is imprecise due to few late AMD cases (n=33).

CONCLUSIONS: A SNP in the MMP2 gene (rs2287074) may be associated with AMD in older Caucasian women, particularly among certain subgroups. Whether this SNP has a direct role in AMD pathogenesis or is merely linked to loci with a functional role should be further elucidated.

SOURCES OF SUPPORT: National Institutes of Health, U.S. Department of Health and Human Services (EY07026, AG05407, AR35582, AG05394, AR35584, AR35583, and AG08415).

NOTES

Joint Effects of LOC387715 Polymorphism with Smoking, Inflammatory Markers, or Hemostatic Factors on the Risk of Age-Related Maculopathy

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OBJECTIVE: To assess potential joint effects on the presence of age-related maculopathy (ARM) by the LOC387715 polymorphism with smoking, inflammatory markers, or hemostatic factors.

METHODS: A population-based, nested case-control sample from the Blue Mountains Eye Study included 188 ARM cases (150 early, 38 late) and 399 controls matched for age, gender, and smoking history. Subjects were genotyped for the LOC387715 Ala69Ser polymorphism (rs# 10490924) by PCR-RFLP. ARM was graded using the Wisconsin ARM photographic grading system. Smoking history was self-reported. Serum high-sensitivity C-reactive protein (hsCRP), interleukin-6 (IL-6), intercellular adhesion molecule-1 (ICAM-1), fibrinogen, homocysteine, plasminogen activator inhibitor-1 (PAI-1), von Willebrand factor (vWF), and white cell count (WCC) were measured. Joint effects on ARM were assessed using logistic regression models adjusting for age and smoking history.

RESULTS: Joint effects on likelihood of early or late ARM were demonstrated for the LOC387715 Ala69Ser G/T and T/T polymorphisms with the following markers: hsCRP (odds ratio [OR]] = 1.2 for the highest tertile with G/G genotype, OR = 1.6 for the two lower tertiles with G/T and T/T genotypes, and OR = 2.2 for the highest tertile with G/T

and T/T genotypes compared to the two lower tertiles of hsCRP with G/G genotype, IL-6 (corresponding ORs = 1.1, 1.6, and 2.2), ICAM-1 (corresponding ORs = 1.0, 1.5 and 2.3) and PAI_1 (corresponding ORs= 1.3, 1.7 and 2.3), but not with fibrinogen, homocysteine, vWF, and WCC. Findings were similar for early and late ARM separately. Current smoking with G/T and T/T genotypes had a strong joint effect on late ARM risk compared to never or past smoking with G/G genotype (OR = 1.2 for current smoking with G/G genotype, OR = 1.8 for never or past smoking with G/T and T/T genotypes, and OR = 6.1 for current smoking with G/T and T/T genotypes).

CONCLUSIONS: No interaction but joint effects on ARM risk were evident for the LOC387715 polymorphisms with current smoking, three inflammatory markers, and PAI-1.

SOURCE OF SUPPORT: American Health Assistance Foundation (Macular Degeneration Research Grant [2003]), Australian National Health & Medial Research Council (IDs 974159, 991407, 211069), and Intramural Research Program, National Eye Institute, National Institutes of Health, U.S. Department of Health and Human Services.

NOTES

What Do Different Visual Function Questionnaires Measure?

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OBJECTIVE: The many visual function questionnaires (VFQs) differ in number of items, item content, and response categories. Despite differences, all VFQs were designed to measure vision-related functional ability in visually impaired people. Our objective was to determine whether four popular VFQs measure the same variable in visually impaired patients.

METHODS: Two of four VFQs (ADVS, NEI-VFQ, VF-14, VAQ), plus either the SF-36 or the SIP, were administered by telephone to 407 consecutive low vision clinic patients. Thus, each instrument was administered to just over 200 patients, and there were over 100 patients for each of the 15 pairings of instruments. Separate Rasch analyses were performed on patient responses to each VFQ and to the physical and mental health domains in the SF-36. The SIP responses were analyzed using Thurstone's equal appearing intervals method.

RESULTS: Person measure estimates from the four VFQs were highly correlated ($0.64 < r < 0.91$). From principal components analysis we concluded that the first principal component accounted for 86% of the variance and the second accounted for 9%. The ADVS, NEI-VFQ, and VF-14 loaded most heavily on the first principal component; the VAQ loaded most heavily on the second. Person measures estimated from the mental health and physical domains of the SF-36 were uncorrelated with each other and with person measures estimated from the VFQs. The same is

true of the corresponding domains in the SIP. Principal components analysis loaded the physical and mental health person measure estimates on the third and fourth principal components, respectively, with the VFQ measures on the first and second.

CONCLUSIONS: The four VFQs measure the same vision-related functional ability variable in low vision patients. There is evidence of a possible second source of variability that contributes to VFQ responses, with the VAQ loading most heavily on the second source. This second source of variability cannot be attributed to physical or mental health factors.

SOURCE OF SUPPORT: National Eye Institute, National Institutes of Health, U.S. Department of Health and Human Services (EY012045).

NOTES

Evaluation of a Minimum Clinically Meaningful Change in NEI-VFQ Scores

Miskala P H *(National Eye Institute, Bethesda)* for the Submacular Surgery Trials Research Group

OBJECTIVE: To evaluate responsiveness of the NEI-VFQ to changes in visual acuity (VA) and to estimate a minimum clinically meaningful change in the NEI-VFQ scores.

METHODS: Data were combined from three clinical trials of submacular surgery for subfoveal choroidal neovascularization. Patients who had NEI-VFQ interviews and VA measurements at baseline and 2 years of follow-up were included in the analysis that consisted of anchor-based and distribution-based methods.

RESULTS: Of 1,015 patients enrolled, 828 patients had NEI-VFQ interviews and VA measurements at baseline and at 2 years later. Median age of patients was 75 years (range 18 to 94); 55% were women and 97% were non-Hispanic white. A 2-line change in VA of the better-seeing eye translated to a 3.4-point change in the overall NEI-VFQ score and from 2.4-point to 7.0-point changes in nine subscale scores. The standardized response mean (SRM) for the overall NEI-VFQ score in patients with a 2-line VA gain was 0.6 and for patients with 2-line VA loss was −0.3. In a subgroup of patients with a 2-line VA loss in the better-seeing eye, patients who had greater than median (62.9) overall NEI-VFQ score at baseline had an SRM of −1.0 for the overall NEI-VFQ score and patients who had a median or lower overall NEI-VFQ scores at baseline had an SRM of 0.2 for the overall NEI-VFQ score. Standard deviation estimates suggested that a 4-point change on the overall NEI-VFQ and

a 5-point change in the subscale scores corresponded to a small clinically meaningful change.

CONCLUSIONS: The NEI-VFQ was responsive to 2-year changes in visual acuity. A 4-point change in the overall NEI-VFQ and a 5-point change in the subscale scores may be considered minimum clinically meaningful changes in the NEI-VFQ. Responsiveness of the NEI-VFQ to within-individual changes was weaker when the NEI-VFQ scores were poor at baseline.

SOURCES OF SUPPORT: National Eye Institute, National Institutes of Health, U.S. Department of Health and Human Services (U10 EY011547, U10 EY011557, U10EY011558).

NOTES

New Advances in Mortality Analysis: Direct and Indirect Effects of Visual Impairment and Ocular Disease on Mortality Estimated in Structural Equation Models

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Lee DJ, Lam BL, Zheng DD, Arheart KL, Caban AJ

OBJECTIVES: The objective is twofold: (1) demonstrate Cox regression modeling capabilities in the context of a structural equation model with latent variables (SEM), and (2) use this method to estimate the effects of ocular disease and visual impairment on mortality, both directly and indirectly through self-rated health and functional disability.

METHODS: A SEM was used to analyze National Health Interview Survey (NHIS) data pooled over 1986-1994, with available mortality linkage through 1997 (n=116,420). The model simultaneously estimates a series of equations including the direct and indirect effects of visual impairment on mortality with visual impairment modeled as a function of ocular disease: glaucoma, cataract, and retinopathy. The model provides tests of mediation allowing for a better assessment of the health mechanisms through which ocular disease and visual impairment affect death. Logistic, Poisson, and hazard ratio parameters are estimated simultaneously in the model. Functional disability is parameterized as a latent variable measured by three indicators of disability. Latent variables remove random measurement error in indicators to provide for less biased path estimates.

RESULTS: Not surprisingly, ocular disease increases the odds of visual impairment. For example, the odds ratios of

some visual impairment relative to no visual impairment are 2.05, 12.28, and 1.16 for glaucoma, cataract and retinopathy, respectively. Severe visual impairment directly increases risk of mortality (hazard ratio: 1.22 [95% CI: 1.13 - 1.32]). Severe visual impairment also operates through self-rated health to affect death, increasing poor health by 89%, which in-turn increases the hazard of death (HR=1.19).

CONCLUSIONS: Cox regression modeling capabilities in SEM have improved dramatically in recent years, allowing investigators to examine both direct and indirect influences of ocular conditions on mortality risk. SEMs also are emerging as a superior method for performing population level analysis on ocular survey data, permitting proper estimation of models with adjustment for complex sample designs.

SOURCE OF SUPPORT: National Eye Institute, National Institutes of Health, U.S. Department of Health and Human Services (R03 EY016481).

NOTES

Comparison of Mortality in Patients Enrolled Versus Eligible Patients Not Enrolled in the Collaborative Ocular Melanoma Study (COMS) Randomized Trial of Pre-Enucleation Radiation of Large Choroidal Melanoma

Gilson MM *(The Johns Hopkins University, Baltimore*), Diener-West M, Hawkins BS for the COMS Group

OBJECTIVE: To compare mortality rates among patients enrolled in the Collaborative Ocular Melanoma Study (COMS) randomized trial of pre-enucleation radiation therapy (PERT) of large choroidal melanoma with mortality rates among eligible patients not enrolled.

METHODS: COMS clinical centers reported to the COMS Coordinating Center all patients with choroidal melanoma examined between November 1986 and December 1994 (whether eligible for the PERT trial or not). In an ancillary study, we searched medical records of participating clinical centers, the Social Security Death Index, and the National Death Index to determine vital status of eligible patients not enrolled. Cox proportional hazards analysis was used to compare survival of enrolled patients versus eligible patients not enrolled.

RESULTS: 129 of 299 eligible patients not enrolled in the COMS PERT trial were reported by clinical centers with IRB approval to participate in this ancillary study. There were no statistically significant differences between the baseline characteristics of the 170 patients not included in this ancillary study and the 129 patients included. 73 of 128 patients with available data were reported as deceased. To

compare the published COMS PERT trial mortality with mortality of eligible patients not enrolled, we analyzed deaths within 10 years of baseline reporting and before July 31, 2000. Previously identified prognostic covariates, i.e., age and longest tumor diameter, were confirmed to predict survival; trial enrollment was not predictive.

CONCLUSIONS: The results of the COMS PERT trial appear to be generalizable to all eligible patients, but may not be generalizable to patients meeting key exclusion criteria.

SOURCE of SUPPORT: National Eye Institute, National Institutes of Health, U.S. Department of Health and Human Services (T32 EY07127 and U10 EY06287).

NOTES

Extension of the Rank Sum Test for Observational Clustered Data: Two-Group Comparisons with Group Membership Defined at the Subunit Level

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OBJECTIVE: The Wilcoxon rank sum test is widely used for two-group comparisons for non-normal data. An assumption of this test is independence of sampling units both between and within groups. In ophthalmology, data often are collected on two eyes of an individual which are highly correlated. In ophthalmological clinical trials, randomization usually is performed at the subject level, but the unit of analysis is the eye. If the eye is used as the unit of analysis, then a modification to the usual Wilcoxon rank sum variance formula must be made to account for the within cluster dependence. In observational studies of clustered data, where the unit of analysis is the subunit, group membership may be defined at the subunit level. For example, binary eye-specific covariates may be present (scored as exposed or unexposed) and one wishes to compare non-normally distributed outcomes between exposed and unexposed eyes using the Wilcoxon rank sum test while accounting for the clustering.

METHODS: We present a corrected variance formula for the Wilcoxon rank sum statistic in the setting of eye (subunit) specific covariates and apply it to compare diabetic retinopathy grade in diabetic patients between eyes with high intraocular pressure (IOP) versus eyes with normal IOP. We also present comparisons between the clustered Wilcoxon test and the signed rank test.

RESULTS: Comparisons of the clustered Wilcoxon test and the signed rank test show dramatic differences in power in favor of the clustered Wilcoxon test because it uses data from all subjects while the signed rank test uses only data from subjects where one eye is exposed and the other eye is unexposed.

CONCLUSIONS: This technique should allow for a more efficient use of the Wilcoxon rank sum test in the setting of ophthalmic data with eye-specific covariates.

SOURCE OF SUPPORT: National Eye Institute, National Institutes of Health, U.S. Department of Health and Human Services (R01 EY12269).

NOTES

Estimating the Individual Rate of Progressive Visual Field Loss Among Those with Open Angle Glaucoma Using Population-Based Prevalence Data

Broman AT ***(The Johns Hopkins University, Baltimore),*** **Katz J, Muñoz B, Bandeen-Roche K, Tielsch J, Friedman DS, West SK, Quigley HA**

OBJECTIVE: To estimate the rate of worsening of visual field damage among open angle glaucoma (OAG) subjects from two cross-sectional studies.

METHODS: OAG subjects from the Baltimore Eye Survey (BES) and the Salisbury Eye Evaluation (SEE) were chosen based on Foster's definition: a vertical cup-to-disc ratio of 0.7 or higher and an abnormal visual field test by standard criteria. Our measure of OAG damage was mean deviation (MD) of the Zeiss-Humphrey automated field test in the worse eye. The average individual rate of damage progression was estimated based on age-specific mean damage from OAG cases in the BES and SEE surveys and average duration of OAG, which was estimated in a life-table approach using OAG incidence estimates from the Melbourne Visual Impairment Project and the Barbados Eye Study. The individual rate of worsening was estimated separately for whites and blacks, with confidence limits estimated by bootstrapping.

RESULTS: There were 135 black and 94 white OAG subjects (age range, 40 to 94 years) from the BES and SEE studies. Average MD in the worse eye was −11.0 dB (SD = 7.5) in whites, and −12.3 dB (SD=8.9) dB in blacks. The cross-sectional rate of change (in dB/year of age) was −0.34

(SE = 0.09) in whites and −0.36 (SE = 0.06) for blacks. We estimated an individual rate of progression of −0.88 dB/year (SE = 0.08) in whites, and −0.90 dB/year (SE=0.07) in blacks.

CONCLUSIONS: Long-term evaluations of the rate of OAG progression are unlikely to be obtained from unselected populations for several reasons, including small numbers of cases. We provide estimates of the rate of individual field loss among blacks and whites. Additional analyses are underway for Hispanic and Chinese persons. Refinement of the estimated rate of progression will include the effect of cataract. A model using maximum likelihood estimation is under development for comparison to the present analysis.

SOURCE OF SUPPORT: National Eye Institute, National Institutes of Health, U.S. Department of Health and Human Services (EY 01765) and unrestricted support from Livingston and Saranne Kosberg.

NOTES

The British Ophthalmological Surveillance Unit for the Study of Rare Eye Disease: Nine Years of Nation-wide Surveillance Across the United Kingdom

Foot BG (*The Royal College of Ophthalmologists, London*), Stanford MR

OBJECTIVES: To describe the methodology and achievements of a nation-wide population-based active surveillance system for case ascertainment of rare eye conditions in the United Kingdom (UK).

METHODS: Individual researchers submit possible studies to the British Ophthalmological Surveillance Unit (BOSU). Major criteria defining suitability of a study are a predicted annual incidence of less than 1/100 000, a clear case definition that can be recognized by ophthalmologists, ethical approval, and high public health or scientific importance or implications for service provision. External validation using capture-recapture analysis is encouraged. Following peer review and approval the study is placed on the BOSU report card which is sent to all ophthalmologists with clinical autonomy in the UK every month. Ophthalmologists return the card to indicate whether a case has or has not been seen. Investigators are notified of all cases and then distribute a clinical questionnaire. Results are fed back through a six-monthly newsletter, conference presentations, and peer-reviewed articles.

RESULTS: The BOSU started surveillance in July 1997. Over 9 years the BOSU has assisted 27 studies which have led to 21 peer-reviewed publications and 42 conference presentations. The system includes 1,089 ophthalmologists.

The mean card return rate has risen from 58% in year 1 to 78% in year 9 with 88% of ophthalmologists participating regularly. External validation indicates that the BOSU identifies between 69% and 100% of all cases of interest. Conditions studied have included conditions of public health interest (e.g. childhood blindness), scientific interest (e.g. sympathetic ophthalmia, and complications of common surgical procedures (e.g. endophthalmitis following cataract surgery).

CONCLUSION: This unique population-based surveillance system has demonstrated an effective and sustainable method for prospective case identification of and subsequent data collection regarding rare ophthalmic conditions. The BOSU receives the continued support of ophthalmologists in the UK. This method has led to meaningful epidemiological studies of conditions that otherwise could be studied only through unrepresentative retrospective case series.

SOURCES OF SUPPORT: Guide Dogs for the Blind Association, British Eye Research Foundation.

NOTES

Apolipoprotein E Gene and Retinal Microvascular Signs in Older People: The Cardiovascular Health Study

Sun C *(University of Melbourne, Australia)*, Tikellis G, Liew G, Klein R, Larsen EK, Wong TY

OBJECTIVE: To examine the association between apolipoprotein E (APOE) gene polymorphisms and retinal microvascular signs in older people.

METHODS: A total of 2,152 persons aged 69 to 96 years from four US communities participating in a population-based, cross-sectional study (Cardiovascular Health Study) had retinal photographs taken of one randomly selected eye. We used standard protocols to grade photographs for the presence of retinal microvascular signs (retinopathy, arterio-venous nicking and focal arteriolar narrowing) and a computer-assisted method to measure retinal vessel diameters. We analyzed DNA extracted from blood samples of participants for common allelic variants of the APOE gene.

RESULTS: After adjusting for age, gender, systolic blood pressure, smoking history, total serum cholesterol and other risk factors, white participants who were carriers of ε2 and ε4 alleles were more likely to have arterio-venous nicking than ε3/ε3 homozygotes, with odds ratio (OR) = 1.70 (95% confidence interval [CI], 1.03-2.83) for ε2 carriers and OR = 1.74 (95% CI, 1.06-2.84) for ε4 carriers. In white participants without hypertension, the associations remained significant only for ε4 carriers (OR = 2.32, 95% CI 1.18-4.57). Among non-hypertensive white participants, carriers of the ε2 allele had significantly narrower retinal arteriolar diameters (adjusted mean arteriolar diameter of

163.5 μm, 95% CI 160.1-167.0) compared to ε3/ε3 homozygotes (167.8 μm, 95% CI 166.0-169.6). There were insufficient numbers of African-Americans for analysis.

CONCLUSIONS: In this older population, white participants who were carriers of the APOE ε2 and ε4 alleles were more likely to have arterio-venous nicking. However, other retinal signs were not related to APOE polymorphism.

SOURCES OF SUPPORT: National Heart, Lung, and Blood Institute (N01-HC-85079 through N01-HC-85086, N01-HC-35129, N01 HC-15103, N01 HC-55222, U01 HL080295, and R21-HL077166) and National Institute of Neurological Disorders and Stroke, National Institutes of Health, U.S. Department of Health and Human Services, and the Sylvia and Charles Viertel Foundation.

NOTES

Re-examining the Relationship of Retinopathy to Fasting Plasma Glucose: The Blue Mountains Eye Study

Liew G (*University of Sydney, Australia*), Wong TY, Mitchell P, Wang JJ

OBJECTIVE: The close relationship between plasma glucose and retinopathy underlies current international definitions for diagnosing diabetes. However, previous studies that examined this relationship had limitations and may have underestimated retinopathy prevalence. We examined the relationship of fasting plasma glucose (FPG) to retinopathy and the ability of currently used FPG cut-offs to discriminate prevalent and incident retinopathy.

METHODS: The population-based Blue Mountains Eye Study obtained 6 high quality retinal photographs in each eye of 3,162 participants living in two postcode areas west of Sydney, Australia. Photographs were graded for retinopathy signs (microaneurysms, hemorrhages, soft or hard exudates) according to the Wisconsin protocol. FPG was measured from fasting venous blood samples taken at the time of photography.

RESULTS: Baseline retinopathy was present in 364 (11.5%) participants, with 54 (31.4%) above and 310 (10.4%) below a FPG cut-off of 7.0 mmol/l (126 mg/dl). The sensitivity of this cut-off for detecting baseline retinopathy was 14.8%, with specificity 95.8% and positive predictive value 31.4%. The area under the receiver operating characteristic (ROC) curve for FPG and retinopathy was 0.56. Similar values were obtained using FPG cut-offs of 6.1 mmol/l (110mg/dl) and 7.8 mmol/l (140mg/dl). The performance of a baseline FPG 7.0 mmol/l (126 mg/dl) cut-off in predicting incident

retinopathy after 5 years improved slightly, with sensitivity 15.0%, specificity 97.4%, positive predictive value 46.2%, and area under the ROC curve 0.60.

CONCLUSION: In the general population, retinopathy is more prevalent than previously reported, even at levels of FPG considered 'normal'. As a result, the ability of FPG to discriminate between persons with and without prevalent and incident retinopathy is poor, suggesting that diabetes definitions based on the relationship between FPG and retinopathy may require re-examination.

SOURCES OF SUPPORT: Australian National Health and Medical Research Council, Canberra, Australia (grants 153948 and 302068)

NOTES

Prevalence of Refractive Errors in a Population of Low-Income Preschoolers

Brody BL *(University of California, San Diego),* Roch-Levecq A-C, Klonoff-Cohen HS, Brown SI

OBJECTIVE: To estimate the prevalence of refractive errors in a population of low-income preschoolers.

METHOD: Between January 2002 and June 2004, 639 children were selected randomly in two waves from a population-based program serving low-income preschoolers 3 to 5 years of age from Head Start and San Diego City preschools. Children were examined by optometrists in the mobile eye clinic of the UCSD Department of Ophthalmology for the presence of refractive errors, defined as myopia 2D or greater, or hyperopia 4D or greater, and/or astigmatism 1.75D or greater, and/or anisometropia 1.25D or greater; amblyopia defined as a 2-line acuity difference between eyes with acuity worse than 20/30 in either eye, and strabismus, defined as eye misalignment. Visual acuity was assessed using the B-VAT PC. Full astigmatic errors were corrected, and hyperopic refractive errors were under-corrected by 1.50 D to 2.50 D, or by 3.00 D if the hyperopic component was +7.00 D or greater. Mean refractive errors were reported in power vector representations of sphero-cylinders. Data from the 510 (79.8%) children who received a full cycloplegic retinoscopy were analyzed.

RESULTS: The sample was 50% female, 73.7% Latino, with a mean age of 4.35 years. Prevalence of simple myopia and myopia with astigmatism was 2.9%, (mean refractive error (OD MRE) = −0.31 −2.04 x 17), simple hyperopia and hyperopia with astigmatism 7.5% (OD MRE = +4.34 −0.44 x 141), astigmatism 5.5% (OD MRE = +2.86 −1.97 x 172), in

at least one eye, and anisometropia 3.1% (OD MRE = +1.48 +0.08 x 150; OS MRE = +1.84 +0.27 x 127). Amblyogenic risk factors were found in 6.5% while strabismus was present in 0.4% of the children. The rate of prescription was 16.5%; 80.4% were emmetropic (OD MRE = +1.50 −0.14 x 15).

CONCLUSION: To our knowledge, this is the first study to report that hyperopia and astigmatism were the most frequent refractive errors in a population of predominantly Latino low-income preschoolers. Other studies are needed to confirm or refute these results.

SOURCE OF SUPPORT: Foster Fellowship in Vision & Development and Save Our Children's Sight Fund.

NOTES

Parental History of Myopia, Sports and Outdoor Activities, and Future Myopia

Jones LA ***(Ohio State University, Columbus),*** **Sinnott L, Mutti DO, Mitchell GL, Moeschberger ML, Zadnik K**

OBJECTIVE: To investigate whether parental history of myopia and/or children's visual activity levels can predict juvenile-onset myopia.

METHODS: Survey-based data from Orinda Longitudinal Study of Myopia (OLSM) subjects from 1989 to 2001 were used to evaluate potential predictors of future myopia. Univariate and multiple variable logistic regression analyses were performed; receiver operator characteristic curves (ROC) were generated.

RESULTS: Of 514 children, 111 (21.6%) became myopic. Differences between future myopes and non-myopes in the third grade were seen for the number of myopic parents ($p < 0.001$) and for the number of sports/outdoor activity hours performed per week (11.65 ± 6.97 hours for non-myopes vs. 7.98 ± 6.54 hours for future myopes, $p < 0.001$). Areas under the ROC curves showed three variables with a predictive value better than chance: the number of myopic parents, the number of sports/outdoor activity hours per week, and the number of reading hours per week. After controlling for sports/outdoor hours per week and parental myopia history, reading hours per week was no longer a statistically significant factor. The area under the curve for the parental myopia history and sports/outdoor activities model was 0.730. A significant interaction in the logistic model showed a differential effect of sports/outdoor activity hours per week based on the child's number of myopic parents.

CONCLUSIONS: The number of hours of reading per week that a child performed was not associated with future myopia after controlling for parental myopia and sports/outdoor activities. Parental history of myopia and sports/outdoor activity hours per week, with an interaction between the two variables, were good predictors of future myopia when evaluated in the third grade.

SOURCES OF SUPPORT: National Eye Institute and Office of Minority Research, National Institutes of Health, U.S. Department of Health and Human Services (U10-EY08893 and R24-EY014792), the Ohio Lions Eye Research Foundation, and the E.F. Wildermuth Foundation.

NOTES

Seven-Year Results from the Correction of Myopia Evaluation Trial (COMET) Cohort

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OBJECTIVES: (1) To evaluate factors associated with different levels of myopia at 7 years in the COMET cohort, and (2) to evaluate whether the 3-year treatment benefit of progressive addition lenses (PALs) in children with reduced accommodative response and near esophoria at baseline was sustained at 7 years.

METHODS: COMET enrolled 469 ethnically diverse children (6-11 years old) with myopia between −1.25 and −4.50D. They were randomized to either PALs or single vision lenses (SVLs) and followed for 5 years in their original lens assignment and 2 years beyond wearing PALs, SVLs, or contact lenses. Refractive error was measured annually by cycloplegic autorefraction. Other measurements included accommodative response and phoria. Data were analyzed, based on the mean of the two eyes, by logistic and linear regression.

RESULTS: 420/469 (90%) of the subjects provided 7-year data. Younger (6-7 years) versus older (11 years) age at baseline was a significant risk factor (OR = 18.9, 95% CI = 6.6 - 54.7) for having myopia < −5.86D (the quartile with the most myopia) after 7 years. Not surprisingly, more baseline myopia (≤ −2.25D) was also a significant risk factor for more myopia at 7 years (OR = 14.1, 95% CI = 7.0 - 28.6). While ethnicity was not associated overall with 7-year myopia, analyses comparing the highest and lowest myopia quartiles

showed that African-Americans had high myopia significantly less often than other ethnic groups ($p < 0.05$). There were no gender or treatment group differences in the amount of myopia at 7 years. At 7 years children with reduced accommodative response (< 2.56D for a 33 cm target) and near esophoria had a statistically significant treatment effect of 0.74D ($p = 0.02$).

CONCLUSIONS: Children with the most myopia after 7 years of follow-up were younger and had the most myopia at baseline. They also more often were white, Asian, or Hispanic rather than African-American. In children with reduced baseline accommodation and near esophoria, the treatment benefit of wearing PALs was sustained over time.

SOURCE OF SUPPORT: National Eye Institute, National Institutes of Health, U.S. Department of Health and Human Services (EY11756, EY11805).

NOTES

Ethnic Disparities in Visual Impairment and Visual Impairment Due to Uncorrected Refractive Error in the U.S.

Vitale S *(National Eye Institute, Bethesda),* Sperduto R, Ellwein L, Ferris FL, Cotch MF

OBJECTIVE: To estimate ethnicity-specific differences in the prevalence of visual impairment (VI) and VI due to uncorrected refractive error in the U.S. using nationally representative survey data.

METHODS: In the 1999-2002 National Health and Nutrition Examination Survey (NHANES), presenting distance visual acuity (VA) (measured with usual corrective lenses, if any) and distance VA after automated refraction were obtained using an autorefractor from 93% of 14,203 participants aged 12 and older. Ethnicity was reported by the participant.

RESULTS: More than 6% of the U.S. population aged 12 and older had VI (presenting VA worse than 20/40 in the better-seeing eye). Of these, over 80% had VI due to uncorrected refractive error (VA that improved to 20/40 or better in the better-seeing eye after automated refraction). Prevalence of VI was higher among the youngest and oldest age groups for all ethnicities. Across all age groups, white participants had less VI than Black, Hispanic, and Asian/Other participants. Prevalence by age and ethnicity showed similar trends for VI and VI due to uncorrected refractive error.

	Age , years			
	12-19	**20-39**	**40-59**	**60+**
Visual impairment:				
Black	12.6	8.9	4.5	10.9
Hispanic	13.1	8.1	7.6	18.7
White	7.8	3.9	3.6	7.3
Asian/Other	11.0	9.0	7.9	20.4
Visual impairment due to uncorrected refractive error :				
Black	11.7	7.8	3.9	7.0
Hispanic	12.5	7.7	6.7	13.3
White	7.2	3.4	3.4	4.1
Asian/Other	10.2	8.3	7.9	12.5

CONCLUSIONS: We found marked ethnic differences in the prevalence of VI and of VI due to uncorrected refractive error across all age groups. National population-based surveys afford a unique opportunity to examine health disparities among ethnic groups.

SOURCES OF SUPPORT: National Center for Health Statistics, Center for Disease Control and Prevention, and National Eye Institute (NHANES Vision Component, and Intramural Research Program grant Z01EY000402), National Institutes of Health, U.S. Department of Health and Human Services.

NOTES

Prevalence of Myopia in an Urban Malay Population: The Singapore Malay Eye Study (SiMES)

Saw S-M ***(National University of Singapore, Singapore)*****, Wong WL, Sandar M, Wong TY**

OBJECTIVE: To estimate the prevalence of myopia in a population-based study of eye diseases in Singaporean Malays.

METHODS: A population-based, prevalence survey of Malays aged 40-79 years in Singapore was conducted in the southwestern part of Singapore. An age-stratified (10-year age groups) random sampling procedure was used to select from a national database 5,600 Malay names. Eligible participants were invited during a home visit or by telephone to travel to a central clinic for a standard comprehensive eye assessment. Refractive error examinations included . subjective refraction by trained ophthalmologists and autorefraction using the Canon RK-F1 table-mounted autorefractor. Myopia was defined as spherical equivalent of −0.5 diopters (D) or less and high myopia as spherical equivalent of at least −5.0 D or less. Prevalence rates were adjusted to the 2000 Singapore Census.

RESULTS: Of the 5,600 names selected, 4,168 participants (74.4%) were determined to be eligible to participate. Of these, 3,280 (78.7%) were examined in the clinic, 41 (1%) were examined in their homes, 789 (18.9%) declined to participate, and 58 (1.4%) could not be contacted. Refractive error data were available for 3,247 adults. The crude prevalence rate of myopia was 25.3% [95% confidence interval (CI), 23.7 - 26.8] and the age-adjusted rate was 26.6% (95% CI, 26.3 - 26.8). The crude prevalence rate of

high myopia was 3.7% (95% CI, 3.6 - 3.8) and the age-adjusted rate was 3.1% (95% CI, 2.5 - 3.7). Prevalence rates of myopia were higher in females (27.6%) compared with males (22.7%) (p=0.001). There was a U-shaped relationship between myopia and age. The rates of myopia were 31.1% for adults aged 40-49 years, 20.2% for 50-59 years, 17.6% for 60-69 years, and 33.8% for 70-80 years.

CONCLUSIONS: The rates of myopia are fairly high in Singapore Malay adults (26.6%), but not as high as previously reported in similarly aged Singapore Chinese (38.7%) in the Tanjong Pagar study.

SOURCE OF SUPPORT: National Medical Research Council, Singapore.

A Methodological Estimation of Quality Adjusted Life Year Losses Associated with Visual Field Decrements

Rein DB ***(RTI International, Atlanta)***

OBJECTIVE: To develop a function to describe quality adjusted life year (QALY) decrements associated with visual field loss for use in cost-effectiveness models**.**

METHODS: We categorized patient visual field defect in decibels (dBs) into five categories: mild and moderate impairment, U.S. blindness, WHO blindness, and worse than WHO blindness. To categorize visual field defects, we applied the rationale of the Snellen visual acuity scale to the ability to perceive luminance measured in apostilbs (abs). On the Snellen scale, those with mild and moderate impairment, U.S. blindness, WHO blindness, and worse than WHO blindness require 2, 3.15, 10, 20, and 40 times as much stimuli as a normally sighted person to perceive the same information. We applied these acuity stimuli multiples to the luminance perception (15 abs) of a person with normal visual field, adjusting to account for the greater abs scale. We converted abs decrements into dBs using a standard conversion formula. We then assigned each visual field category the same the QALY decrement associated with the equivalent visual acuity category. Finally, using regression, we predicted QALY losses as a polynomial function of dB decrements.

RESULTS: We defined mild and moderate impairment, U.S. blindness, WHO blindness, and worse than WHO blindness as mean decrements of 15 to 16; 17 to 21; 22 to 24; 25 to 27; and 28 and greater dBs respectively. Our regression yielded the function, QALYs = −0.0111 x dBs −0.0003 x

dBs2 setting the dBs equal to the mean deviation in the better-seeing eye.

CONCLUSIONS: Our results suggest a convex and downward sloping relationship between dBs of visual field losses and QALY decrements. QALY losses accumulate slowly at first and then increase rapidly as field loss progresses. This observation is consistent with recent empirical findings reporting minimal QALY losses associated with small visual field defects.

SOURCE OF SUPPORT: Center for Disease Control and Prevention: National Vision Program

NOTES

Pilot Study of Provider Attitudes Towards Complementary and Alternative Medicines in Eye Care

Lee P (*Duke University, Durham*), Rafferty W, Lobach D, Hunt M, Macri J

OBJECTIVE: Other than a 5% rate of usage of complementary and alternative medicine (CAM) in glaucoma care reported by Rhee et al, little information exists on the use of CAM in eye care, although up to 42% of the United States (USA) adult population uses at least one CAM on an annual basis. We performed an initial pilot study on the attitudes and perspectives of eye care providers about patient use of CAM for eye care.

METHODS: Information was elicited from community-based providers in the southeastern USA via a self-administered survey questionnaire regarding attitudes towards CAM therapies and patient use of CAM modalities.

RESULTS: Analysis of the initial 50 surveys revealed that providers believed that no alternative therapies were harmful and that several were likely to be beneficial, specifically religious beliefs and use of prayer as well as vitamins and nutritional supplements. There was high concordance between the provider's personal beliefs of the benefit or harm of a CAM and their discouragement or support of a patient's use of the same CAM.

CONCLUSIONS: While most CAM approaches were rated neutral by the eye care providers, belief in the benefit of specific CAM modalities in one region of the USA suggests that additional research into the use of CAM in eye care, including both potential risks and benefits, is warranted.

SOURCE OF SUPPORT: Research to Prevent Blindness; Carr Family.

NOTES

Relative Economic Value of Alternative Methods of Screening for Visual Impairment in Preschoolers

Frick KD *(The Johns Hopkins University, Baltimore)*, Akpala CU, and the Vision in Preschoolers Study Research Group

OBJECTIVE: To determine whether the most economically desirable method of screening preschool children for visual impairment depends on the number screened and the economic value of detection and correction.

METHODS: The economic value of screening was simulated using data from the Vision in Preschoolers (VIP) efficacy study, the literature, and publicly available sources. VIP compared screening by nurses and lay persons using Stereo Smile, Lea visual acuity testing, Retinomax autorefractor, and the Sure Sight vision screener. VIP data included the distribution of times for each type of screener to use each device (<1-17 minutes), each screener-device combination's sensitivity (range 0.45-0.68) and the standard errors, and specificity. Repeated simulations were conducted by obtaining 50,000 random draws from the distributions of times and sensitivities. The cost and value of parents' time required for post-screening eye examinations entered the model. Screening device costs were converted to annual figures using total and maintenance costs and expected lifetime. The net economic value of identifying and correcting visual impairment in preschoolers is unknown and was varied from $0-$10,000. The number of children to be screened was varied from 100-1000 to explore the effect of screening small versus larger populations.

RESULTS: For assumed lifetime economic gains less than $200 resulting from identification of preschool visual impairment, no screener-device combination provides positive economic benefit. For assumed lifetime economic gains of at least $1000, the nurse-Retinomax combination yielded the greatest economic benefit in over 70% of the simulations of screening 1000 children. When fewer children are to be screened, the Sure Sight vision screener used by either screener type may be the most economically favorable.

CONCLUSIONS: The nurse-Retinomax combination was the most economically desirable combination for screening 1000 children. Further research on effectiveness and lifetime net economic value of identifying and correcting visual impairment in preschoolers is necessary to clarify the most economically desirable way to screen smaller populations.

SOURCE OF SUPPORT: . National Eye Institute, National Institutes of Health, U.S. Department of Health and Human Services (U10EY12534; U10EY12545; U10EY12547; U10EY12550; U10EY12644; U10EY12647; and U10EY12648).

NOTES

Cost Effectiveness of Treatments for Age-Related Macular Degeneration

Gower EW *(The Johns Hopkins University, Baltimore)*, Cassard SD, Bass EB, Schein OD, Bressler NM

**** Chosen Best Symposium Paper by a Young or New Investigator ****

OBJECTIVE: To estimate the cost-effectiveness of pegaptanib sodium injections or ranibizumab injections compared to treatment with verteporfin photodynamic therapy (PDT). Age-related macular degeneration (AMD) is the leading cause of vision loss among the elderly in the western world. In the past five years, three treatments have become available to treat choroidal neovascularization (CNV): Verteporfin (PDT), pegaptanib sodium injections, and ranibizumab. Each treatment typically requires repeated dosing to achieve an effect; long-term benefits of treatment have not yet been examined because of the short time during which these treatments have been available. The therapies are costly, since each individual procedure entails significant expense, the treatments must be repeated for optimal benefit, and the population that can potentially benefit from treatment is large.

METHODS: We conducted a cost-utility analysis from the third-party payer perspective to estimate the cost-utility of each of these therapies using a Markov chain model. Data sources included: treatment efficacy, complications and disutility associated with complications, utility valuation, and anticipated costs from published clinical trial results, Medicare reimbursement schedules, and expert opinion. TreeAge software was used to determine the difference in cost per QALY for each of the three treatments. This decision model was structured to determine whether

pegaptanib sodium or ranibizumab should be prescribed instead of PDT for patients with predominantly classic CNV.

RESULTS: Ranibizumab was the most expensive treatment, but had the highest utility, while PDT was the least costly and had the second highest utility. Pegaptanib sodium was roughly twice as costly as PDT to achieve nearly the same effect. In this model, PDT dominated pegaptanib due to lower costs and minimally higher effectiveness. No dominance was seen between ranibizumab and PDT because of the increased utility and cost of ranibizumab.

CONCLUSIONS: Long-term relative costs and effectiveness of these treatments should be monitored as use of these therapies becomes widespread and new therapies become available for neovascular AMD.

SOURCE OF SUPPORT: Novartis Ophthalmics.

NOTES

Night Vision and Risk of Vision Loss, Choroidal Neovascularization, and Geographic Atrophy in the Complications of Age-related Macular Degeneration Prevention Trial (CAPT)

Ying G-S *(University of Pennsylvania, Philadelphia)*, Liu C, Maguire MG, and the CAPT Research Group

OBJECTIVE: To assess the association of baseline night vision with subsequent 3-lines loss in visual acuity (VA), choroidal neovascularization (CNV) and geographic atrophy (GA) in CAPT participants.

METHODS: 1,052 participants with ≥10 large drusen (≥125μm) and VA ≥ 20/40 in each eye participated with one eye randomly assigned to laser treatment and the contralateral eye to observation. At baseline, each participant self-administered a 10-item questionnaire on night vision (NVQ-10). The NVQ score range is 100 (no night vision symptoms) to 0 (worst rating for all symptoms). VA testing (ETDRS Charts 1, 2) was performed by certified examiners at baseline, 6 months and annually. Trained readers identified CNV as leakage on fluorescein angiography and GA as ≥ 1 DA combined area on color photographs. Evaluation of the baseline NVQ-10 score as a risk factor for vision loss, CNV, and GA was based on repeated-measures logistic regression and survival analysis of data from both treated and observed eyes combined, with adjustment of treatment effect; adjustments for significant participant and ocular risk factors were also were made.

RESULTS: At baseline, the mean (SD) NVQ-10 score was 70 (20), and the median was 73.0 (range: 3 - 100). Compared

to participants with higher NVQ-10 score (4th quartile), participants with lower scores (1st, 2nd, 3rd quartiles) had increased risk of 3-lines losses in VA [odds ratio and 95% C.I.: 2.39 (1.69 - 3.40), 2.27 (1.39 - 3.24), 1.95 (1.36 - 2.79) respectively]; increased risk of incident GA [relative risk (RR): 3.39 (1.81 - 6.35), 2.50 (1.31 - 4.76) and 1.46 (0.72 - 2.98)], and increased risk of CNV [RR: 1.59 (1.05 - 2.41), 1.79 (1.18 - 2.71), 1.70 (1.13 - 2.56)]. Adjustment for participant and ocular characteristics had little impact.

CONCLUSIONS: CAPT participants who reported more night vision symptoms at baseline had an increased risk of 3-lines loss in VA and incident CNV and GA. These associations are independent of established risk factors.

SOURCES OF SUPPORT: National Eye Institute, National Institutes of Health, U.S. Department of Health and Human Services (EY12279 and EY12211).

NOTES

Incidence of and Risk Factors for Age-Related Macular Degeneration in Older Women: The Study of Osteoporotic Fractures

Coleman AL *(University of California at Los Angeles, Los Angeles)*, Seitzman RL, Yu F, Cauley JA, Ensrud KE, Stone KL, Cummings SR, Hochberg MC, Pedula K, Thomas G, Mangione CM, and the Study of Osteoporotic Fractures Research Group

OBJECTIVES: To estimate the incidence of age-related macular degeneration (AMD) in a population of older Caucasian and African-American women and to examine the associations of alcohol use, smoking history, and diabetes with incident AMD.

METHODS: Subjects were women who attended the Study of Osteoporotic Fractures year-10 and year-15 follow-up clinic visits and had fundus photographs taken in the same eye at both visits (n=2,017; mean age at year-10 visit=78.2 years; 256 African-American and 1,761 Caucasian women). Forty-five degree stereoscopic fundus photographs were graded for AMD using a modification of the Wisconsin Age-Related Maculopathy Grading System by two masked graders. Disagreements between the graders were adjudicated by a retinal specialist. Smoking history, alcohol consumption, and diabetes status were ascertained with questionnaires. Logistic regression was used to test whether these potential risk factors were associated with incident early or late AMD.

RESULTS: The overall 5-year AMD incidence was 18.6% for early and 5.5% for late. Both early and late AMD incidence were greater in Caucasian than African-American women.

Early AMD incidence ranged in Caucasian women from 18.2% in those ≤ 79 years to 24.3% in those 80-84 years but was observed at the lower rate of 11.8% in those ≥85 years. In contrast, early AMD incidence in African-American women ranged from 12.4% in those ≤79 years to 6.3% in those 80-84 years. Only 2 African-American women were ≥85 years old. Late AMD incidence increased in Caucasian women with age, from 4.1% in those ≤79 years to 14.7% in those ≥85 years. There were only 2 late AMD cases in African-American women, precluding reliable estimation. After adjustment for confounders, alcohol consumption was significantly associated with an elevated risk of early AMD (OR = 1.43; 95% CI: 1.04 - 1.96).

CONCLUSIONS: These findings are consistent with a lower risk of AMD in African-Americans compared to Caucasians. Lower incidence of early AMD in the oldest old may indicate a threshold effect for the competing risk of death. The role of alcohol consumption as a risk factor is more evident for early than for late AMD.

SOURCE OF SUPPORT: National Institutes of Health, U.S. Department of Health and Human Services (EY013626-3, AG05407, AR35582, AG05394, AR35584, AR35583, AG08415) and Research to Prevent Blindness.

NOTES

Statin Use and the Incidence of Choroidal Neovascularization in the Complications of Age-related Macular Degeneration Prevention Trial (CAPT)

Liu C *(University of Pennsylvania, Philadelphia)*, Ying G-S, Maguire MG, McCannel C, and the CAPT Research Group

OBJECTIVE: To evaluate the impact of statin use on the incidence of choroidal neovascularization (CNV) among CAPT patients with early age-related macular degeneration (AMD).

METHODS: 1,052 participants with 10 or more large (>125 μm) drusen and visual acuity ≥ 20/40 in each eye enrolled in CAPT. Participants who had their final CAPT clinic visit after May 2005 were interviewed about their history of use of cholesterol-lowering drugs, including statins. Trained readers identified CNV based on the review of fluorescein angiograms taken at annual follow-up visits and when patients reported symptoms. Person-specific incidence rates of CNV associated with statin use were calculated using person-years and survival analysis techniques with covariate adjustment.

RESULTS: Among 744 patients who provided a medication history, 86 started statins before CAPT enrollment, 28 started at in the same year as CAPT enrollment, 182 started during CAPT participation, and 448 never had used statins. By person-years analysis, the annual incidence rate of CNV was 5.63% in the statin exposure group and 4.47% in the non-statin exposure group, relative risk (RR) and 95% C.I. are 1.26 (0.88-1.77). When the incidence rate of CNV

among those who started statins before CAPT (4.31%) was compared to that of never users (4.25%), the RR was 1.01. By survival analysis of time to CNV, the RR for those who started statins before CAPT as compared to non-users was 1.02 (0.62-1.68) and 1.03 (0.62-1.70), respectively, without and with adjustment by age, cigarette smoking, hypertension and baseline focal hyperpigmentation status.

CONCLUSIONS: Despite strong protective effects reported from some previous studies, there was no evidence of a strong protective effect of statin use on incidence of CNV among CAPT patients.

SOURCE OF SUPPORT: National Eye Institute, National Institutes of Health, U.S. Department of Health and Human Services (EY 12279 and EY 12211).

NOTES

The Relationship of Omega-3 Long-chain Polyunsaturated Fatty Acid (LCPUFA) Intake and Regular Aspirin Use with Prevalent Neovascular Age-Related Macular Degeneration

SanGiovanni JP *(National Eye Institute, Bethesda)*, Chew EY, Reed GF, Agron E, Sperduto RD, Clemons TE, Ferris FL, for the Age-Related Eye Disease Study (AREDS) Research Group

OBJECTIVE: To investigate the relationship of omega-3 LCPUFA intake and regular aspirin (ASA) use with prevalent neovascular (NV) age-related macular degeneration (AMD) in the Age-Related Eye Disease Study. LCPUFAs are capable of reacting through ASA-driven pathways to generate a family of bioactive molecules with vaso- and immunoregulatory properties.

METHODS: In this case-control study of 657 people with NV AMD and 1,112 people without AMD we administered a validated food frequency questionnaire and a drug use questionnaire to obtain estimates of habitual LCPUFA intake and regular ASA use. We applied multivariable logistic regression with nutrient- and non-nutrient-based covariates to analyze these data.

RESULTS: Participants who reported the highest omega-3 LCPUFA intake and the longest duration of ASA use were also the least likely to have NV AMD. The likelihood of NV AMD associated with highest vs. lowest reported docosahexaenoic acid (DHA) intake was reduced among subjects those who reported never regularly using ASA (OR = 0.6; 95%CI = 0.3 - 0.9). The likelihood was further

reduced among those who regularly had used ASA for at least 3 months (OR = 0.4; 95%CI = 0.2 - 0.8) or at least 5 years (OR=0.2; 95%CI = 0.1 - 0.7). Eicosapentaenoic acid (EPA) intake was protective against NV AMD only in regular ASA users. For participants who reported never regularly using ASA, the OR was 1.0 (95%CI = 0.6-1.5). Values were 0.4 (95%CI = 0.2 - 0.8) and 0.2 (95%CI = 0.1 - 0.8) for subjects who reported regular use of ASA for at least 3 months and at least 5 years, respectively.

CONCLUSIONS: The relationship of omega-3 LCPUFA intake with NV AMD may be modified by regular ASA use. While the constraints of our experimental design do not allow us conclusively to rule out the possibility that our results may be explained by unmeasured covariates, these novel findings provide a reasonable basis for investigating mechanisms driving LCPUFA-ASA-NV AMD relationships.

SOURCE OF SUPPORT: Intramural Program, National Eye Institute, National Institutes of Health, U.S. Department of Health and Human Services**.**

NOTES

The Association of Dietary Lutein/ Zeaxanthin and Omega-3 Long-Chain Polyunsaturated Fatty Acids and Advanced Age-Related Macular Degeneration in the Age-Related Eye Disease Study (AREDS)

Chew EY ***(National Eye Institute, Bethesda),***
SanGiovanni JP, Clemons T, Ferris FL, Milton RC, for the AREDS Research Group

OBJECTIVE: To evaluate the relationship between dietary intake of carotenoids and omega-3 long-chain polyunsaturated fatty acids (LCPUFAs) and the prevalence of age-related macular degeneration (AMD) in the Age-Related Eye Disease Study (AREDS).

METHODS: In this case-control analysis of 4,519 AREDS participants, AMD severity at enrollment was assessed from stereo color fundus photographs. Subjects completed a semi-quantitative food frequency questionnaire at enrollment. Nutrient intake estimates were energy-adjusted with the nutrient density model. We used multiple logistic regression methods to evaluate the relationship of major dietary carotenoids with AMD status (no AMD, intermediate drusen, large drusen, geographic atrophy [GA], or neovascular [NV] AMD) at enrollment.

RESULTS: Lutein/zeaxanthin was the only major dietary carotenoid variable that showed a protective association with AMD at highest intake levels and that persisted in multivariable models. Compared with subjects without AMD, and after statistical adjustment for nutrient- and nonnutrient-based covariates, the likelihood of advanced AMD (either NV AMD or GA) was statistically significantly

decreased for the highest vs. lowest quintiles of lutein/zeaxanthin intake (OR = 0.7 for NV AMD; 95% CI, 0.5 - 0.9 and OR = 0.5 for GA; 95% CI, 0.2 - 0.9). The risk of intermediate AMD (large or extensive intermediate drusen) also was statistically significantly decreased for the highest vs. lowest quintiles of lutein/zeaxanthin intake (OR=0.73; 95%CI, 0.56–0.96). The risk for neovascular AMD was significantly decreased for the highest vs. lowest quintiles of total omega-3 LCPUFA intake (OR = 0.6; 95% CI, 0.4 – 0.9), after statistical adjustment for all nutrient- and nonnutrient-based covariates. No relationships were found for the early AMD groups.

CONCLUSION: In AREDS participants, a higher intake of lutein/zeaxanthin or omega-3 long chain polyunsaturated fatty acids was associated with a decreased likelihood of having advanced AMD. These observational findings currently are being tested in a prospective, randomized controlled clinical trial, the Age-Related Eye Disease Study 2.

SOURCE OF SUPPORT: Intramural Program, National Eye Institute, National Institutes of Health, U.S. Department of Health and Human Services.

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C H R O N O L O G Y

U.S. Symposia on Ocular Epidemiology

June 10-11, 1982 — Bethesda, Maryland
Symposium on the Epidemiology of Eye Diseases — and Visual Disorders

June 5-7, 1985 — Bethesda, Maryland
Second NEI Symposium on Eye Disease Epidemiology

March 25-27, 1991 — Bethesda, Maryland
Third National Eye Institute Symposium on Eye Disease Epidemiology

January 29-31, 2007 — Sarasota, Florida
Fourth U.S. Symposium on Ocular Epidemiology

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