

# Refraction and Change in Refraction Over a 20-Year Period in the Beaver Dam Eye Study

Samantha Bomotti,<sup>1</sup> Bryan Lau,<sup>1</sup> Barbara E. K. Klein,<sup>2</sup> Kristine E. Lee,<sup>2</sup> Ronald Klein,<sup>2</sup> Priya Duggal,<sup>1</sup> and Alison P. Klein<sup>1,3,4</sup>

<sup>1</sup>Department of Epidemiology, Johns Hopkins Bloomberg School of Public Health, Johns Hopkins University, Baltimore, Maryland, United States

<sup>2</sup>Department of Ophthalmology and Visual Sciences, University of Wisconsin School of Medicine and Public Health, University of Wisconsin-Madison, Madison, Wisconsin, United States

<sup>3</sup>Department of Oncology, Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins, Johns Hopkins University, Baltimore, Maryland, United States

<sup>4</sup>Department of Pathology, Johns Hopkins School of Medicine, Johns Hopkins University, Baltimore, Maryland, United States

Correspondence: Alison P. Klein, Department of Oncology, Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins, 1550 Orleans Street CRBII, Room 354, Baltimore, MD 21205, USA; aklein1@jhmi.edu.

PD and APK contributed equally to the work presented here and should therefore be regarded as equivalent authors.

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**PURPOSE.** Hyperopic shifts in refraction have been consistently reported in adults over 40, followed by myopic shifts after age 70. Although potential factors underlying these changes in refraction in older adults have been investigated previously, the studies were restricted by the limited longitudinal data available. The authors of this study sought to better characterize the long-term trajectory of refraction in older adults using 20 years of prospective data.

**METHODS.** The impact of cohort effects on refraction over 20 years was examined. Generalized estimating equations were used to evaluate the etiologic factors underlying refraction and changes in refraction measured over a 20-year period (1988–2010) among adults over age 40 from the Beaver Dam Eye Study.

**RESULTS.** Only individuals with nuclear cataract experienced a myopic shift in refraction, showing a 0.25 diopter (D) decrease (95% confidence interval [CI]: –0.44 D to –0.07 D) over a five-year period. Individuals with mild and moderate nuclear sclerosis showed varying degrees of hyperopic shifts over five years (0.22 D: 95% CI: 0.20 D–0.25 D; 0.23 D: 95% CI: 0.20 D–0.27 D, respectively).

**CONCLUSIONS.** Nuclear cataract is the primary contributor to the myopic shift among older individuals. Birth cohort effects on baseline refraction but not change in refraction were observed.

Keywords: refraction, refractive error, nuclear cataract

Refractive errors, namely myopia and hyperopia, are the main cause of visual impairment in the United States and the world.<sup>1–3</sup> An estimated 153 million individuals worldwide are visually impaired from uncorrected refractive errors, and nearly two-thirds of these individuals are over the age of 50.<sup>2</sup> In addition, over 25% of those 40 years and older in Western European countries and the United States have refractive errors resulting in impaired vision.<sup>4</sup> As the population ages,<sup>5</sup> accurate data is needed on the natural history of refraction after age 40 to anticipate their future healthcare needs.

Population-based studies investigating changes in refraction with age among older adults have consistently reported individuals becoming hyperopic with age before 70 and then more myopic after the age of 70. The observed myopic shift among older individuals has been attributed to the influence of nuclear sclerosis severity (nuclear cataract).<sup>6–12</sup> Gender, diabetes, and education have also been associated with refraction and refractive change; however, the relationship of these factors in the presence of birth-cohort effects cannot be precisely determined.<sup>6–10,13–20</sup>

Due to the limited amount of longitudinal data available, previous studies have only examined refraction over periods of 5 or 10 years. These studies used baseline values of relevant

factors only to examine the associations.<sup>6–10,18</sup> To better characterize the trajectory of refraction over longer periods in older adults, this study evaluated the influence of etiologic factors on refraction and changes in refraction in individuals over age 40 using time-updated measures collected over a period of 20 years from the Beaver Dam Eye Study (BDES).

## METHODS

### Beaver Dam Eye Study

Recruitment and study design procedures for the BDES have been described in detail previously.<sup>18,21–24</sup> Briefly, a private census was conducted in the city and township of Beaver Dam, Wisconsin, beginning in 1987. The census identified 5924 residents between the ages of 43 and 84 from 3715 households. A total of 602 pedigrees were reconstructed from 2783 eligible participants who had confirmed familial relationships. Of the 5924 eligible residents, 83% ( $n = 4972$ ) were recruited for the baseline examination. Ninety-nine percent of the population was of European ancestry by self-report, with very few individuals reporting non-European ancestry.



The baseline ocular examination included a standardized evaluation of noncycloplegic refraction using the Humphrey 530 refractor (Humphrey, Humphrey, Inc., San Leandro, CA, USA).<sup>21</sup> The standard formula for refraction (sphere + 0.5 × cylinder) was used to calculate the mean spherical equivalent in diopters (D) for each eye. Grades of the severity of nuclear lens opacity (nuclear sclerosis) were assigned by trained photographers using a 5-point scale based on slit-lamp lens photographs.<sup>25,26</sup> Age, gender, years of education, and diabetes status were collected from a personal history questionnaire conducted at the baseline examination. An individual was considered to have diabetes if there was a self-report of diabetes in conjunction with treatment (insulin or diet), or elevated glucose, or glycosylated hemoglobin levels.

Follow-up examinations were conducted every five years. A total of 3721 (5 years), 2962 (10 years), 2375 (15 years), and 1913 (20 years) individuals participated in the follow-up examinations, respectively. A majority (68.9%) of losses to follow-up were due to death. Measurements made during the baseline examination were repeated using similar procedures for all follow-up examinations.

The Institutional Review Board at the University of Wisconsin approved the study. Written informed consent was obtained from all subjects prior to enrollment. The study was performed in accordance with the tenets of the Declaration of Helsinki.

### Trait Definitions

Refraction was measured as a quantitative trait of spherical equivalent at each visit and was the primary outcome. Shifts toward myopia (nearsightedness) were defined as changes in spherical equivalent over time resulting in a negative change, while shifts toward hyperopia (farsightedness) were defined as changes in spherical equivalent resulting in a positive change.<sup>7,27</sup> Nuclear sclerosis grade was categorized as: mild (grade of 1 or 2), moderate (grade 3), or severe (grade 4 or 5). Severe nuclear sclerosis (grade 4 or 5) indicates nuclear cataract.

### Exclusion Criteria

The few individuals of non-European ancestry ( $n = 31$ ), individuals with differences in baseline refraction between the right and left eyes  $> \pm 4$  D ( $n = 23$ ), and individuals without baseline examination ( $n = 45$ ) measures were excluded. In addition, eyes that had undergone refractive surgery, eyes with no lens, eyes with an intraocular lens, or eyes with best corrected visual acuity of 20/200 or worse at the time of the baseline examination were excluded from the study ( $n = 319$ ). Eyes developing one of these conditions at subsequent visits were censored upon development of the specific condition. If a participant failed to attend a visit but returned for a subsequent visit, only the absentee visit was removed (removal of these individuals with visit gaps in a sensitivity analysis showed negligible changes in the results, indicating inclusion of these individuals in the final model did not affect inferences made). Individuals with missing data were also excluded ( $n = 161$ ), leaving 4393 individuals available for study. The full BDES cohort includes all individuals who participated in the BDES at baseline ( $n = 4972$ ).

### Statistical Analysis

Longitudinal analysis was modeled using generalized estimating equations with robust variance estimation in Stata Version 13.<sup>28-30</sup> An independent working correlation structure was employed.<sup>31</sup> Refraction was used as a time-varying outcome, and

nuclear sclerosis severity and diabetes were included as time-varying factors. Both time-varying factors were lagged by one visit, and values for the refraction outcome began at visit 2 to establish temporality. For example, nuclear sclerosis grade at visit 1 would predict refraction at visit 2. Age was partitioned into baseline age and change in age from baseline to distinguish baseline cohort effects from longitudinal effects of aging. Gender, education, baseline age, and baseline refraction were carried forward from baseline. Baseline age, baseline education level, and baseline refraction were centered at their mean values. Interactions among factors were considered. Beta coefficients for each factor in the model were reported and used to estimate the change in refraction for each increase in level of the relevant factor. These beta coefficients were also used to estimate the five-year changes in refraction within each category of nuclear sclerosis severity. The left and right eyes behaved similarly, so only the results of the right eye are presented. Birth cohorts (Figs. 1, 2) were defined among all 4393 individuals by year of birth and grouped into four-year intervals to evenly distribute samples across groups. Birth cohorts with less than 200 observations were not included in the figures.

### Inverse Probability Weighting

Inverse probability weighting was employed among the 4393 individuals with complete data after exclusions to standardize the estimation of change in refraction from the subset of individuals not lost to follow-up over the course of the study to the original BDES cohort recruited at baseline.<sup>32-34</sup> Three inverse probability weights were calculated to account for the three loss to follow-up reasons: (1) death, (2) refusal to participate or selective participation in the interview component of the visit only, and (3) censoring following insertion of an intraocular lens or removal of lens, refractive surgery, or best corrected visual acuity of 20/200 or worse. These weights were combined and incorporated into the longitudinal analysis.

## RESULTS

### Study Participants

Table 1 shows the distributions of the individuals available for study ( $n = 4393$ ), the subset of individuals included in the longitudinal analysis after excluding those who did not return after visit 1 ( $n = 3163$ ), and the full BDES cohort ( $n = 4972$ ). The full BDES cohort appeared slightly older and more hyperopic, with more individuals having diabetes and nuclear cataract compared to the 3163 individuals included in the analysis. There were negligible differences between individuals in the full BDES cohort and the 4393 individuals available for study (Table 1).

Just over 10 percent (10.9%) of the individuals available for study ( $n = 4393$ ) were lost to follow-up due to death in the first five years of the BDES. A total of 4.7% of the remaining cohort were lost in the last five years of the study. Of the 4393 individuals, 7.6% refused to continue to participate or participated only in the interview component of the examination after visit 1, while 2.8% of remaining individuals dropped out in the last five years of the study. Finally, 6.8% of the 4393 individuals were censored due to insertion of an intraocular lens or removal of lens, refractive surgery, or best corrected visual acuity of 20/200 or worse in the first five years of the BDES, while 5.1% of remaining individuals were censored in the last five years.

### Age and Birth Cohort

Figure 1A shows the changes in refraction by age and birth cohort among all participants. Each birth cohort followed

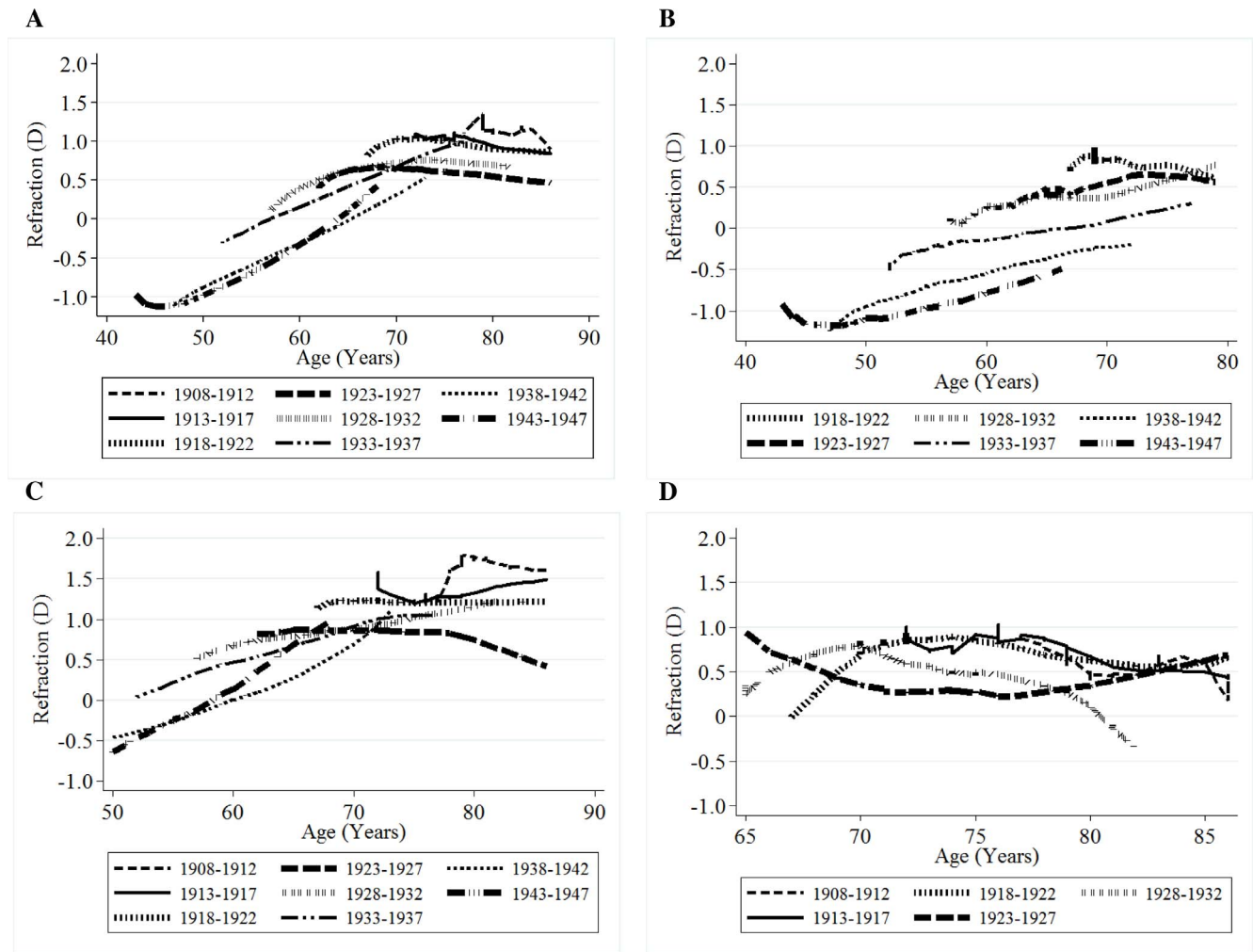


FIGURE 1. Lowess curves of refraction in diopters (D) by age and year of birth for 4393 participants of the Beaver Dam Eye Study (Beaver Dam, Wisconsin, 1988–2010) among: (A) all participants, (B) among those with mild (grades 1 or 2) nuclear sclerosis, (C) among those with moderate (grade 3) nuclear sclerosis, or (D) among those with severe (grades 4 or 5) nuclear sclerosis. Birth cohorts containing fewer than 200 individuals were not included.

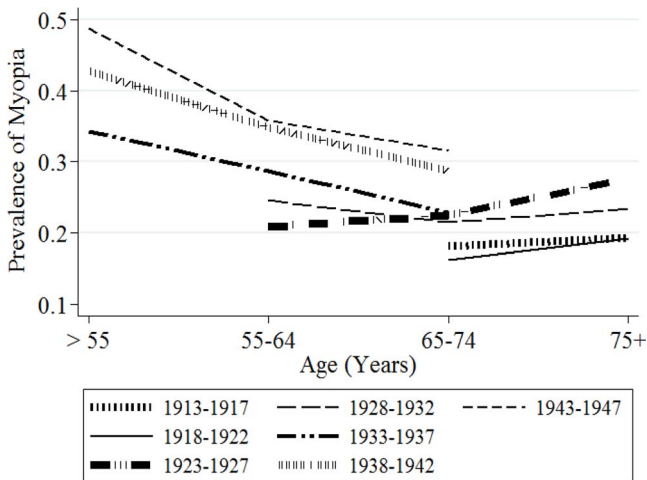


FIGURE 2. Lines connecting prevalence estimates of myopia at different ages, by year of birth for 4393 participants of the Beaver Dam Eye Study (Beaver Dam, Wisconsin, 1988–2010). Birth cohorts containing fewer than 200 individuals were not included.

similar patterns of changing refraction with age, as evidenced by the consistent slopes representing these changes in refraction. The trajectories of refraction with age, regardless of birth cohort, showed a hyperopic shift among those under the age 70 followed by a transition to a myopic shift among those older than 70. However, values of refraction at a given age did differ across birth cohorts, with individuals born more recently being more myopic compared with individuals born earlier. After about age 70, refraction no longer appeared to differ significantly across cohorts.

Figure 2 shows the prevalence of myopia by age and birth cohort among all BDES participants. The prevalence of myopia decreases with age until around age 70, then increases slightly thereafter. Individuals born more recently have a higher prevalence of myopia overall compared to those born in earlier years, regardless of age. This pattern becomes less discernable in older ages.

### Nuclear Sclerosis

The relationship of refraction patterns with age varied by nuclear sclerosis severity in the BDES (Figs. 1B–1D). Individuals with mild nuclear sclerosis showed positive slopes, indicating hyperopic changes in refraction with age (Fig. 1B).

**TABLE 1.** Characteristics of Participants of the Beaver Dam Eye Study at Baseline, Beaver Dam, Wisconsin, 1988–1990

Characteristic	BDES Participants Available for Study (N = 4393)*	BDES Participants Included in Analysis (N = 3163)†	Total BDES Participants (N = 4972)‡
Age (years), mean (SD)	61.2 (10.8)	59.0 (9.9)	62.0 (11.2)
Male gender, n (%)	1945 (44.3)	1411 (44.6)	2188 (44.0)
Education (years), mean (SD)	12.0 (2.8)	12.3 (2.7)	12.0 (2.9)
Type II diabetes, n (%)	358 (8.2)	206 (6.5)	441 (9.0)
Nuclear sclerosis grade, n (%)			
1 or 2	2503 (57.0)	2028 (64.1)	2577 (56.8)
3	1338 (30.5)	909 (28.7)	1369 (30.2)
4 or 5	552 (12.6)	226 (7.2)	594 (13.1)
Refraction (D), mean (SD)	0.24 (2.3)	0.1 (2.3)	0.25 (2.3)

BDES, Beaver Dam Eye Study; D, diopters; SD, standard deviation.

\* All individuals available for study (including individuals who did not return after visit 1).

† Individuals included in longitudinal model, excluding those who did not return after visit 1.

‡ The total number of individuals in the BDES.

Individuals with moderate nuclear sclerosis followed a similar pattern, with slopes leveling off after age 70 (Fig. 1C). Only those with nuclear cataract (severe nuclear sclerosis) showed predominantly negative slopes, indicating myopic shifts in refraction with age (Fig. 1D). As participants aged, nuclear sclerosis severity increased.

The longitudinal models suggest the trajectory of refraction with age differs depending on nuclear sclerosis severity (Table 2). An annual 0.05 D (95% CI: -0.09 D to -0.01 D) decrease (myopic shift) in refraction was observed among individuals with nuclear cataract after adjustment for baseline age, baseline refraction, gender, education, and diabetes status. Among individuals with mild (0.05 D, 95% CI: 0.04 D–0.05 D) or moderate (0.05 D, 95% CI: 0.04 D–0.05 D) nuclear sclerosis, a positive increase (hyperopic shift) in refraction each year were observed after inclusion of the same factors in the model (Table 2). Those with mild and moderate nuclear sclerosis experienced a 0.22 D (95% CI: 0.20 D–0.25 D) and 0.23 D (95%

CI: 0.20 D–0.27 D) increase in refraction, respectively, over a five-year period while those with nuclear cataract experienced a 0.25 D (95% CI: -0.44 D to -0.07 D) decrease in refraction over the same time period (Table 3).

**Additional Risk Factors Associated With Refraction Across Follow-up**

After accounting for baseline refraction, gender and diabetes status were significantly associated with refraction over the course of follow-up. Males had a 0.14 D (95% CI: -0.20 D to -0.08 D) lower refraction compared to females, whereas persons with diabetes had a 0.26 D (95% CI: 0.14 D–0.37 D) higher refraction compared to persons without diabetes, adjusted for other factors. A previous association between education level and baseline refraction has been described in this cohort.<sup>18</sup> In the current analysis, which controlled for baseline refraction, there was no additional association between education and refraction over the course of follow-up.

**TABLE 2.** Estimated Associations of Various Factors With Refraction During Follow-up Among Participants of the Beaver Dam Eye Study, Beaver Dam, Wisconsin, 1988–2010

Factor*	N†	Effect Size‡	95% CI
Baseline age (years)	7667	-0.02	-0.02, -0.01
Mild nuclear sclerosis	2462		
Moderate vs. mild nuclear sclerosis	3807	-0.07	-0.14, -0.02
Severe vs. mild nuclear sclerosis	1398	-0.72	-0.92, -0.53
Change in age from baseline (years)			
Mild nuclear sclerosis	2462	0.05	0.04, 0.05
Moderate nuclear sclerosis	3807	0.05	0.04, 0.05
Severe nuclear sclerosis	1398	-0.05	-0.09, -0.01
Gender			
Female	4210		
Male	3457	-0.14	-0.20, -0.08
Diabetes status			
No	6784		
Yes	883	0.26	0.14, 0.37
Baseline refraction (D)	7667	1.01	1.00, 1.03

CI, confidence interval; D, diopters.

\* Model contain gender, education, and diabetes status. Change in age, nuclear sclerosis, and diabetes status are lagged by one visit.

† Person-visits remaining after exclusions, by category.

‡ Effect size estimate represents the mean change in refraction (D) with each one-unit increase in each factor.

**TABLE 3.** Mean Changes in Refraction by Age and Nuclear Sclerosis Grade Across Visits Among Participants of the Beaver Dam Eye Study, Beaver Dam, Wisconsin, 1988–2010

Factor*	N†	Mean 1-Year Change‡	95% CI	Mean 5-Year Change‡ (D)	95% CI
Nuclear sclerosis grade					
1 or 2	2462	0.05	0.04, 0.05	0.22	0.20, 0.25
3	3807	0.05	0.04, 0.05	0.23	0.20, 0.27
4 or 5	1398	-0.05	-0.09, -0.01	-0.25	-0.44, -0.07

CI, confidence interval; D, diopters.

\* Model includes baseline age (centered), change in age from baseline, nuclear sclerosis, an interaction between change in age and nuclear sclerosis, gender, education level (centered), diabetes status, and baseline refraction (centered). Change in age, nuclear sclerosis, and diabetes status are lagged by one visit.

† Person-visits included in the model, by nuclear sclerosis category.

‡ The mean one-year estimate represents the mean change in refraction with each one-year increase in age from baseline, which varies by nuclear sclerosis severity, adjusted for all other factors in the model. The adjusted mean 5- and 10-year changes in refraction were estimated by multiplying the beta coefficient for change in age from baseline by 5 or 10 years, separately by each category of nuclear sclerosis severity.



## DISCUSSION

This study confirms a hyperopic shift among individuals aged 40 to 70 (and corresponding decrease in myopia prevalence), followed by a clear myopic shift (and increase in myopia prevalence) after age 70.<sup>6-10</sup> These ocular shifts were observed independent of birth cohort, indicating that the changes in refraction over time in older individuals were primarily the development of age-related cataract. Birth year did not alter their trajectory of refraction in adulthood. However, baseline levels of refraction were affected by birth cohort; prior to the age of 70, individuals born more recently were more myopic. These cohort effects largely disappeared after age 70, and follow-up time was limited in the older cohorts. As such, in our longitudinal models, age was partitioned into baseline age and change in age to reflect these cohort and longitudinal effects.

The higher prevalence of myopia in more recent birth cohorts is demonstrated in Figure 1. This figure, along with Figure 2, demonstrate the need to account for both age effects and birth cohort effects when studying refraction and refractive errors. Our findings are consistent with a previous study reporting an increase in prevalence of myopia in US adults between 1971-1972 and 1999-2004.<sup>35</sup>

Previous analysis of the baseline data in the BDES cohort demonstrated that educational level at baseline was also higher among younger individuals.<sup>18</sup> The current analysis shows that after baseline refraction is accounted for, education does not influence longitudinal patterns in refraction. These findings—along with a recent UK study that demonstrates myopic shifts with each additional year of schooling<sup>36</sup>—suggest that the impact of education is on baseline levels of refraction but does not influence changes in refraction in later adulthood. Given the age of this cohort, educational attainment was stable during follow-up and, as such, this finding is not surprising.

This work supports previous studies demonstrating nuclear sclerosis severity, which worsens with age,<sup>37-44</sup> largely influencing the myopic shifts among older individuals.<sup>11,12</sup> Several cross-sectional studies established a significant association between nuclear lens opacity and prevalence of myopia.<sup>45-48</sup> Previously studies in the BDES cohort demonstrate a strong relationship between nuclear sclerosis severity and myopic changes in refraction in the BDES over both 5-year<sup>6</sup> and 10-year periods.<sup>7</sup> The Blue Mountains Eye Study confirmed this finding<sup>9,10</sup> and concluded that nuclear cataract was the principal cause of the myopic shift in refraction among older people.<sup>12</sup> While cohort effects on refraction are important to consider, they do not explain myopic shifts in older adults. However, these studies had a limited ability to examine cohort effects due to their cross-sectional or more limited follow-up. In this 20-year study, only those with nuclear cataract showed a myopic shift independent of birth cohort, while those without nuclear cataract showed a hyperopic shift. Over 10 years, this study indicated that those without nuclear cataract experienced approximately a 0.5 D hyperopic shift in refraction, while those with nuclear cataract experienced a 0.5 D myopic shift in refraction. Even though this change assumes nothing, other than age, is changing in these individuals, it indicates an etiologic effect of nuclear cataract on refractive shifts. This information allows clinicians to predict future changes in refraction in their patients and plan for future eye care needs.

The patterns observed in this and prior BDES studies are largely consistent with two other recent longitudinal studies conducted in Iran<sup>49</sup> and China.<sup>50</sup> Both studies observed a hyperopic shift in middle-aged individuals and a myopic shift in older individuals, which was associated with nuclear cata-

ract.<sup>49,50</sup> This consistency implies the longitudinal patterns described in the BDES are similar to those patterns observed in other human populations outside the United States, including Middle Eastern and East Asian populations.

Of the factors associated with refraction, diabetes was the most modifiable factor in this study. Those with diabetes showed a higher refraction compared to those without diabetes, indicating that having diabetes is a risk factor for refractive errors. Being male was associated with a lower refraction during follow-up compared with women in this study. However, the associations between nuclear sclerosis, change in age, and refraction were unchanged, indicating the inclusion of diabetes and gender in the final model did not affect the reported findings.

There are several strengths to this study. The original cohort recruited for the baseline examination constituted 83% of all individuals in Beaver Dam in 1987 who were between the ages of 43 and 86 years, making the study sample representative of older adults in Beaver Dam at the time. This makes the current study results generalizable to other older European-American populations. In this study, there were 20 years of follow-up measurements, which allowed accurate capture the trajectories of refraction across multiple time points. To our knowledge, this is the longest amount of time covered for any population-based study investigating changes in refraction.<sup>7,10</sup>

The etiology of refraction and refractive shifts in older individuals is important to characterize and understand when anticipating future public health needs. Information on how refraction changes in older persons can be useful for refractive surgeons trying to predict changes in refraction that are likely to occur in their patients. This study further demonstrates that refraction is not stable in adulthood (as previously thought) and that nuclear cataract predicts these changes. Given that nuclear cataract is the most common type of age-related cataract and the leading cause of blindness worldwide,<sup>1,42,51</sup> close monitoring of individuals with cataracts is of particular importance for changes in refraction and proper intervention.

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