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Association of Axial Length With Risk of Uncorrectable Visual Impairment for Europeans With Myopia

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IMPORTANCE Myopia (ie, nearsightedness) is becoming the most common eye disorder to cause blindness in younger persons in many parts of the world. Visual impairment due to myopia is associated with structural changes of the retina and the globe because of elongation of the eye axis. How axial length—a sum of the anterior chamber depth, lens thickness, and vitreous chamber depth—and myopia relate to the development of visual impairment over time is unknown.

OBJECTIVES To evaluate the association between axial length, spherical equivalent, and the risk of visual impairment and to make projections of visual impairment for regions with high prevalence rates.

DESIGN, SETTING, AND PARTICIPANTS This cross-sectional study uses population-based data from the Rotterdam Study I (1990 to 1993), II (2000 to 2002), and III (2006 to 2008) and the Erasmus Rucphen Family Study (2002 to 2005) as well as case-control data from the Myopia Study (2010 to 2012) from the Netherlands. In total, 15 404 individuals with data on spherical equivalent and 9074 individuals with data on axial length were included in the study; right eyes were used for analyses. Data were analyzed from September 2014 to May 2016.

MAIN OUTCOMES AND MEASURES Visual impairment and blindness (defined according to the World Health Organization criteria as a visual acuity less than 0.3) and predicted rates of visual impairment specifically for persons with myopia.

RESULTS Of the 15 693 individuals included in this study, the mean (SD) age was 61.3 (11.4) years, and 8961 (57.1%) were female. Axial length ranged from 15.3 to 37.8 mm; 819 individuals had an axial length of 26 mm or greater. Spherical equivalent ranged from −25 to +14 diopters; 796 persons had high myopia (ie, a spherical equivalent of −6 diopters or less). The prevalence of visual impairment varied from 1.0% to 4.1% in the population-based studies, was 5.4% in the Myopia Study, and was 0.3% in controls. The prevalence of visual impairment rose with increasing axial length and spherical equivalent, with a cumulative incidence (SE) of visual impairment of 3.8% (1.3) for participants aged 75 years with an axial length of 24 to less than 26 mm and greater than 90% (8.1) with an axial length of 30 mm or greater. The cumulative risk (SE) of visual impairment was 5.7% (1.3) for participants aged 60 years and 39% (4.9) for those aged 75 years with a spherical equivalent of −6 diopters or less. Projections of these data suggest that visual impairment will increase 7- to 13-fold by 2055 in high-risk areas.

CONCLUSIONS AND RELEVANCE This study demonstrated that visual impairment is associated with axial length and spherical equivalent and may be unavoidable at the most extreme values in this population. Developing strategies to prevent the development of myopia and its complications could help to avoid an increase of visual impairment in the working-age population.

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Myopia (ie, nearsightedness) is a common refractive error and is generally considered a nonthreatening condition that can be corrected with eyewear, contact lenses, or refractive surgical procedures. Nonetheless, the incidence of myopia has increased rapidly during the past 30 years, predominantly in East Asia.[1-4] The trait results from excessive growth of the eyes' axial length, which is a sum of the anterior chamber depth, lens thickness, and vitreous chamber depth.[5-7] High myopia is defined as a spherical equivalent of −6 diopters (D) or less with an axial length generally exceeding 26 mm.[8] The frequency of high myopia in the general population is estimated to be 3% to 20%.[3,9-11]

High myopia is currently one of the leading causes of legal blindness in developed countries because of complications occurring in adulthood, such as myopic macular degeneration, early cataract, retinal detachment, and/or glaucoma.[11] The rapid increase in prevalence combined with the sight-threatening complications represents a significant public health burden.[12,13] Studies addressing the association between myopia and ocular pathology found that few eyes with mild to moderate myopia develop ocular pathology in contrast to many eyes with high myopia.[14-18] From this, it seems a logical assumption that a longer axial length is associated with higher risks of visual impairment.[16,19,20] Nevertheless, to our knowledge, precise risk estimates of the association between axial length and lifetime visual function are currently lacking.

In this study, we investigated the association between axial length, spherical equivalent, and visual impairment as a function of age. We combined epidemiologic studies from the same research center to maximize the number of persons with very long axial lengths and high spherical equivalents and to achieve sufficient statistical power for lifetime analyses. Next, we extrapolated our risk estimates to make a prediction of the rise in visual impairment in regions that have recently experienced a high increase in myopia prevalence. The goal of our study was to provide insights into the potential visual morbidity of the myopic shift that is occurring all over the world.

Key Points

Question What is the association between axial length, refractive error, and risk of visual impairment?

Findings In this cross-sectional study of data from several population-based studies and a case-control study in the Netherlands, axial lengths of 26 mm and greater and refractive errors of −6 diopters and less were significantly associated with an increased lifetime risk of visual impairment.

Meaning Extrapolating these results to regions that have recently experienced a strong rise in myopia indicates that myopia will become the most important cause of blindness.

Methods

Study Population

This study included cross-sectional data from 15 693 persons of European descent 25 years or older from the population-based cohort studies Rotterdam Study I, II, and III, and the genetic-isolated study Erasmus Rucphen Family Study as well as the case-control Myopia Study (MYST), all of which were conducted in or near Rotterdam, the Netherlands. All participants with available data on best-corrected visual acuity and axial length or spherical equivalent were included. The rationale and study design of the studies have been described previously.[21,22] A short description of each study can be found in the eMethods in the Supplement. Measurements in all studies were collected after receiving approval from the Medical Ethics Committee of the Erasmus University Medical Center, and all participants provided written informed consent in accordance with the Declaration of Helsinki.

Ophthalmic Examination

Participants in the Rotterdam Study I, II, and III, Erasmus Rucphen Family Study, and MYST received an extensive ophthalmological examination as described previously.[21] This examination included a noncycloplegic measurement of refractive error for both eyes using the Topcon RM-A2000 Auto-Refractor (Topcon Optical Company). After additional subjective refraction, best-corrected visual acuity was measured using the Lighthouse Distance Visual Acuity Test, a modified version of the Early Treatment Diabetic Retinopathy Study chart.[23] Axial length was measured using the Lenstar LS900 (Laméris Ootech) for participants in the Rotterdam Study I and II or the A-scan function of the PacScan 300 AP (Sonomed Escalon) for participants in the Erasmus Rucphen Family Study and the Rotterdam Study III. Measurements of axial length were introduced in a later phase of the Rotterdam Study I, II, and III; therefore, measurements of axial length were available in 5686 study participants of these studies. Participants from MYST with an axial length greater than 30 mm underwent an A-scan.

Statistical Analysis

All subsequent analyses were performed on right eyes; left eyes were used if measurements on right eyes were not available. The spherical equivalent was calculated using the standard formula, ie, adding the size of the sphere with half the size of the cylinder. In the analyses regarding spherical equivalent, persons with a history of cataract or refractive surgical procedures were excluded unless data on the spherical equivalent prior to the procedure were available. Visual impairment was defined as a best-corrected visual acuity of less than 0.3 to 0.05 or greater and blindness was defined as a best-corrected visual acuity less than 0.05, according to the World Health Organization criteria.[24]

We investigated the association of axial length and spherical equivalent with risk of visual impairment as well as axial length or spherical equivalent and birth year with risk of visual impairment using ordinary least squares linear regression models, with restricted cubic splines with 3 knots (10th, 50th, and 90th percentiles) for axial length and birth year and 5 knots (5th, 27.5th, 50th, 72.5th, and 95th percentiles) for spherical equivalent and birth year. In the analyses of axial length and spherical equivalent with birth year, participants from MYST were excluded because of the study design. Prevalence estimates were calculated in percentages as the num-

ber of visually impaired divided by the number in the total group multiplied by 100.

Logistic regression was used to calculate odds ratios (ORs) for visual impairment by axial length or spherical equivalent categories. We categorized axial length as less than 24 mm, 24 to less than 26 mm, 26 to less than 28 mm, 28 to less than 30 mm, and 30 mm or greater and spherical equivalent as greater than −0.5 D, −0.5 to greater than −3 D, −3 to greater than −6 D, −6 to greater than −10 D, −10 to greater than −15 D, and −15 D or less. High myopia was defined as a spherical equivalent of −6 D or less. Quadratic terms were used to test for nonlinearity of visual impairment risk. Participants were categorized as younger than 60 years or 60 years or older for analyses, which were adjusted for sex, age, and cohort. Analyses on axial length were additionally adjusted for height.[25] Cumulative risk of visual impairment (ie, a visual acuity less than 0.3) was estimated by axial length and spherical equivalent categories using Kaplan-Meier product limit analysis. All participants 75 years and older were censored at 75 years to ensure unbiased estimates.

Projections of Future Visual Impairment

To demonstrate the potential burden of visual impairment with the increasing prevalence of myopia, we extrapolated the risk estimates from the current study to published reports on populations with high myopia.[26] We considered 5 studies from Singapore,[27-31] 4 studies from the Republic of Korea,[32-35] and 1 European consortium study[4]; all studies were population-based, used autorefraction or subjective refraction, and reported age-specific myopia prevalence. Prevalence by birth decade was calculated by extracting the age of participants from start year of the study. Weighted prevalence was calculated by birth decade for each region. The projected increase in prevalence of visual impairment was calculated using the reported myopia prevalence and this study's cumulative risk of visual impairment. Ordinary least squares linear regression models were performed in R. Other statistical analyses were performed using SPSS version 21.0 (IBM). Statistical significance was set at $P < .05$.

Results

General Characteristics

The selection of participants eligible for the current analysis is shown in eFigure 1 in the Supplement; the distribution of general characteristics is summarized in **Table 1**. Data on axial length were available for 9074 participants, and data on spherical equivalent were available for 15 404 participants. The studies included 819 persons with an axial length of 26 mm or greater, and 796 persons had high myopia (ie, a spherical equivalent of −6 D or less). The weighted mean (SD) axial length was 23.51 mm (1.23) in the population studies, 27.47 mm (1.82) in MYST participants, and 23.53 mm (0.83) in controls. The population-based studies showed a slight sex difference; males had a longer mean axial length than females (23.73 mm vs 23.16 mm; $P < .001$) and were more likely to have an axial length of 26 mm or greater (4.9% vs 2.3%; $P < .001$). Visual impairment ranged from 1.0% to 4.1% in the population-based studies, was 5.4% in MYST participants, and was 0.3% in controls. Visual impairment was not associated with sex in any study (1.3% of males vs 1.2% of females; $P = .69$). The association between axial length and spherical equivalent (adjusted for age, sex, and height) is shown in eFigure 2 in the Supplement ($R^2 = 0.71$).

Cohort Effect

Because the cohorts had different starting points in time, we considered a potential cohort effect. We observed a linear increase in axial length with birth year (**Figure 1**A) and estimated an axial length increase of 0.008 mm/y (SE, 0.003; $P = .007$), adjusted for height, sex, and cohort. Similarly, we found a shift from hyperopia to myopia with more recent birth years, in particular from 1920 onwards (Figure 1B) and a higher overall myopia prevalence in the younger cohorts (Table 1).

Visual Impairment in MYST vs Population-Based Cohorts

To investigate potential selection bias for visual impairment in MYST, we compared the proportion of eyes with visual impairment as a function of axial length between studies. We observed similar frequencies of visual impairment in 2 axial length strata in the population-based studies and MYST (<26 mm, 0.8% vs 1.2%; $P = .66$; ≥26 mm, 7.1% vs 4.0%; $P = .09$). Because the population-based studies included more participants 60 years and older, the proportion of persons with visual impairment was higher in all refractive error strata. However, after adjusting for age, there was no difference in the prevalence of visual impairment between the population-based studies and MYST (high myopia: OR, 1.51; 95% CI, 0.37-6.2; $P = .56$; nonhigh myopia: OR, 0.66; 95% CI, 0.35-1.23; $P = .19$), indicating that the selection of particularly visually impaired persons in MYST was unlikely and that combining study data is valid. Refractive and cataract surgical procedures were performed more often in participants with higher axial lengths (population-based studies, 23.92 vs 23.50 mm; $P = .007$; MYST, 27.94 vs 25.81 mm; $P < .001$) and participants with visual impairment (population-based studies, 11% [75 of 686] vs 3% [387 of 14 514]; $P < .001$; MYST, 10% [13 of 128] vs 3% [30 of 893]; $P < .001$).

In participants with an axial length of 26 mm or greater, the frequency of visual impairment was 6.1%, which increased exponentially with age ($P < .001$). The groups were stratified by age as younger than 60 years or 60 years or older. In the younger age group, the prevalence of visual impairment in eyes with axial lengths of 26 mm or greater and less than 26 mm was 4.1% vs 0.9%, respectively. In the older age group, the prevalence of visual impairment was 13.0% vs 1.6%, respectively. With respect to refractive error, the prevalence of visual impairment in these axial lengths was 5.3% in persons with myopia vs 3.7% in persons without myopia in the older group and 1.5% vs 0.9% in the younger group.

Risk of Visual Impairment as a Function of Axial Length and Spherical Equivalent

Subsequently, we combined data from all cohorts, maximizing statistical power. First, we performed a logistic regression analysis to estimate the OR of visual impairment with in-

Table 1. General Characteristics of the Study Participants by Axial Length and Spherical Equivalent

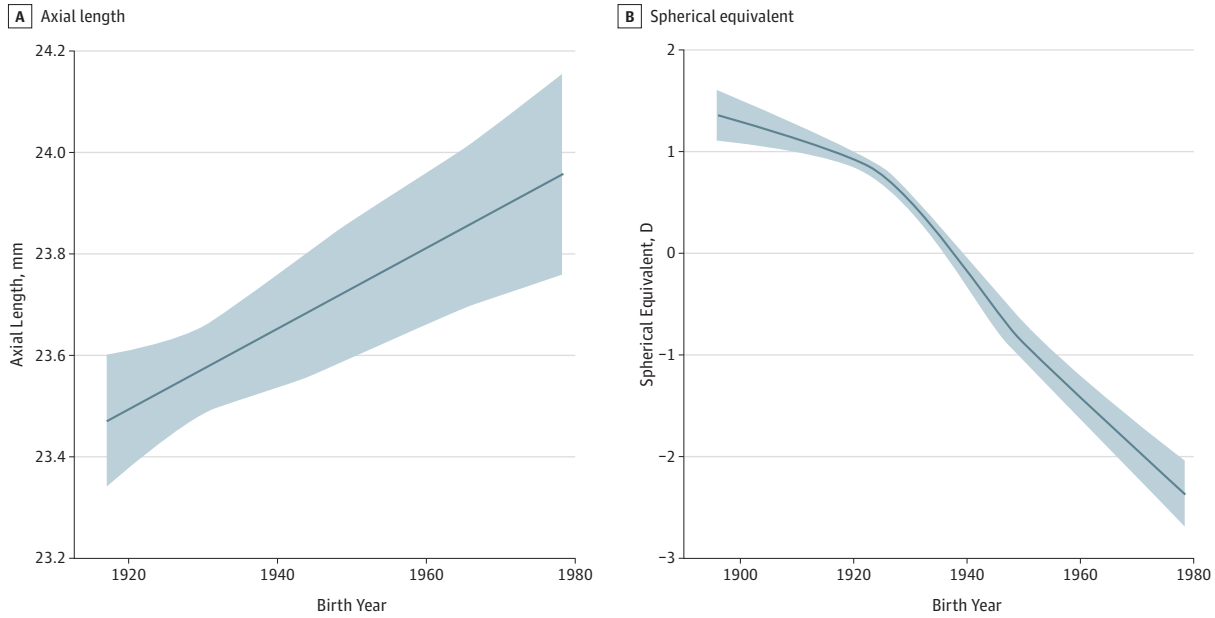
Characteristic	No. (%)					
					MYST	
	RS-I	RS-II	RS-III	ERF	Participants	Controls
Axial length, No.	1005	1524	3157	2353	672	363
Male	443 (44.1)	697 (45.7)	1376 (43.6)	1058 (45.0)	249 (37.1)	174 (47.9)
Age, y						
Mean (SD)	62 (5)	62 (5)	57 (7)	50 (13)	47 (13)	50 (13)
Range	55 to 80	55 to 88	46 to 89	25 to 87	25 to 80	25 to 89
<60	443 (44.1)	659 (43.2)	2237 (70.9)	1785 (75.9)	555 (82.6)	284 (78.2)
≥60	562 (55.9)	865 (56.8)	920 (29.1)	568 (24.1)	117 (17.4)	79 (21.8)
Axial length, mm						
Mean (SD)	23.5 (1.3)	23.6 (1.2)	23.7 (1.3)	23.3 (1.1)	27.5 (1.8)	23.5 (0.8)
<24	706 (70.2)	1076 (70.6)	2031 (64.3)	1871 (79.5)	2 (0.3)	259 (71.3)
24 to <26	269 (26.8)	396 (26.0)	976 (30.9)	441 (18.7)	126 (18.8)	102 (28.1)
26 to <28	26 (2.6)	46 (3.0)	134 (4.2)	39 (1.7)	340 (50.6)	2 (0.6)
28 to <30	1 (0.1)	3 (0.2)	15 (0.5)	2 (0.1)	132 (19.6)	0
≥30	3 (0.3)	3 (0.2)	1 (0.0)	0	72 (10.7)	0
Visual acuity						
>0.5	980 (97.5)	1467 (96.3)	3030 (96.0)	2270 (96.5)	582 (86.6)	360 (99.1)
>0.3 to 0.5	19 (1.9)	27 (1.8)	94 (3.0)	51 (2.2)	48 (7.2)	2 (0.6)
>0.05 to 0.3	6 (0.6)	16 (1.0)	23 (0.7)	24 (1.0)	23 (3.4)	0
≤0.05	0	14 (0.9)	10 (0.3)	8 (0.3)	19 (2.8)	1 (0.3)
Spherical equivalent, No.	6382	2465	3405	2261	538	353
Male	2605 (40.8)	1127 (45.7)	1487 (43.7)	1017 (45.0)	198 (36.8)	170 (48.2)
Age, y						
Mean (SD)	70 (9)	64 (7)	57 (6)	50 (13)	46 (13)	49 (13)
Range	55 to 106	55 to 95	46 to 87	25 to 80	25 to 80	25 to 79
<60	1155 (18.1)	878 (35.6)	2472 (72.6)	1738 (76.7)	455 (84.6)	279 (79.0)
≥60	5227 (81.9)	1587 (64.4)	933 (27.4)	523 (23.3)	83 (15.4)	74 (21.0)
Spherical equivalent, D						
Mean (SD)	0.87 (2.5)	0.49 (2.5)	−0.30 (2.6)	0.12 (2.1)	−10.0 (3.6)	0.03 (1.0)
>−0.5	5158 (80.8)	1863 (75.6)	2131 (62.6)	1636 (72.4)	0	261 (74.0)
−0.5 to >−3	769 (12.1)	379 (15.4)	774 (22.7)	479 (21.2)	0	88 (24.9)
−3 to >−6	346 (5.4)	179 (7.3)	390 (11.5)	112 (5.0)	39 (7.2)	4 (1.1)
−6 to >−10	81 (1.3)	34 (1.3)	100 (2.9)	30 (1.3)	263 (48.9)	0
−10 to >−15	19 (0.3)	7 (0.3)	8 (0.2)	3 (0.1)	187 (34.8)	0
≤−15	9 (0.1)	3 (0.1)	2 (0.1)	1 (0.0)	49 (9.1)	0
Visual acuity						
>0.5	5562 (87.2)	2323 (94.2)	3270 (96.0)	2185 (96.6)	474 (88.1)	350 (99.1)
>0.3 to 0.5	557 (8.7)	82 (3.3)	102 (3.0)	45 (2.0)	35 (6.5)	2 (0.6)
>0.05 to 0.3	186 (2.9)	36 (1.5)	23 (0.7)	23 (1.0)	15 (2.8)	0
≤0.05	77 (1.2)	24 (1.0)	10 (0.3)	8 (0.4)	14 (2.6)	1 (0.3)

Abbreviations: D, diopter; ERF, Erasmus Rucphen Family Study; MYST, Myopia Study; RS, Rotterdam Study.

creased axial length and spherical equivalent in the 2 age strata. In the younger age group, eyes with an axial length of 28 mm or greater had 11- to 24-times higher risk for visual impairment than eyes with axial lengths less than 24 mm. In the older age group, axial lengths of 26 mm or greater had higher risk across all categories (ORs, 3 to 94) than eyes with axial lengths less than 24 mm (**Table 2**). For those with data on spherical equivalent, trends were similar, with the highest risks for persons with high myopia (Table 2). When axial length and spherical equivalent were both added to the model, axial length still had a significant association with visual impairment (OR, 1.46; 95% CI, 1.09-1.97) whereas spherical equivalent did not (OR, 0.98; 95% CI, 0.86-1.10).

Next, we examined the cumulative risk of visual impairment in relation to axial length and spherical equivalent (**Figure 2**). For participants 75 years or older, the cumulative risk (SE) of visual impairment was 6.9% (1.3) for eyes with axial lengths less than 24 mm, 3.8% (1.3) for axial lengths of 24 to less than 26 mm, 25.4% (10.3) for axial lengths of 26 to less than 28 mm, 26.6% (8.1) for axial lengths of 28 to less than 30 mm,

Figure 1. Association Between Birth Year and Axial Length and Spherical Equivalent



The line indicates the predicted mean value for the year, and the gray area indicates the 95% CI. Only data from the Rotterdam Study I, II, and III and the Erasmus Rucphen Family Study were used.

and 90.6% (8.1) for axial lengths of 30 mm or greater. The cumulative risk of visual impairment for eyes with an axial length of 26 to less than 28 mm increased gradually for participants 60 years and older, whereas eyes with an axial length of 28 mm or greater were increasingly visually impaired for participants approximately 45 years and older. Spherical equivalent showed similar trends, although cumulative risks were slightly lower than for axial length. By age 75 years, the cumulative risk (SE) of visual impairment was 2.9% (0.3) for a spherical equivalent greater than −0.5 D, 3.0% (0.8) for −0.5 to greater than −3 D, 5.5% (1.5) for −3 to greater than −6 D, 20.0% (5.9) for −6 to greater than −10 D, 19.9% (6.8) for −10 to greater than −15 D, and 80.3% (11.0) for −15 D or less.

Taken together, all participants who had a spherical equivalent of −6 D or less had a cumulative risk (SE) of visual impairment of 5.7% (1.3) at 60 years and of 39% (4.9) at 75 years. For those with a spherical equivalent of −0.5 or less to greater than −6 D, these risks were 0.8% (0.2) and 3.8% (0.7). These estimates were used for comparison with other areas in the world.

Projection of Visual Impairment to Regions With Increasing Prevalence of Myopia

Reported prevalence estimates of myopia in Singapore, the Republic of Korea, and Western Europe were used to estimate increases in prevalence of visual impairment as a function of birth year. Prevalence rates of visual impairment will rise in all areas, most prominently for adults 75 years and older (**Table 3**). By 2055, visual impairment will have increased 2- to 3-fold in Europe, 3- to 5-fold in Singapore, and even 3- to 6-fold in the Republic of Korea. In the latter country, more than 10% (95% CI, 8-13) of the population aged 75 years will have visual impairment due to myopia.

Table 2. Risk of Visual Impairment by Axial Length and Spherical Equivalent Category by Age

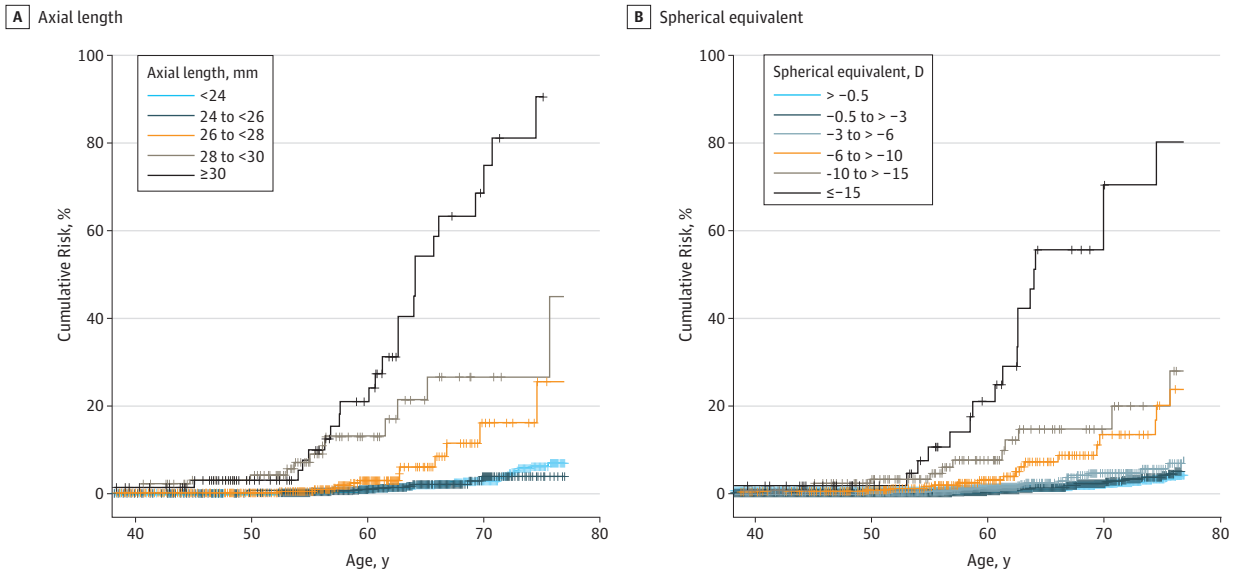
	OR (95% CI)	
Category	<60 y	≥60 y
Axial length, mm		
<24	1 [Reference]	1 [Reference]
24 to <26	0.95 (0.51 to 1.80)	0.65 (0.29 to 1.48)
26 to <28	2.01 (0.88 to 4.62)	3.07 (1.26 to 7.49)
28 to <30	11.01 (5.23 to 23.20)	9.69 (3.06 to 30.71)
≥30	24.69 (11.02 to 55.31)	93.62 (38.35 to 228.55)
Spherical equivalent, D		
>−0.5	1 [Reference]	1 [Reference]
−0.5 to >−3	0.69 (0.34 to 1.43)	0.92 (0.62 to 1.35)
−3 to >−6	1.42 (0.66 to 3.05)	1.71 (1.07 to 2.74)
−6 to >−10	2.95 (1.35 to 6.42)	5.54 (3.12 to 9.85)
−10 to >−15	6.79 (2.87 to 16.06)	7.77 (3.36 to 17.99)
≤−15	27.85 (11.34 to 68.37)	87.63 (34.50 to 222.58)

Abbreviations: D, diopter; OR, odds ratio.

Discussion

In this study, which included several cohorts sequentially executed at the same research center that covered a large range of axial lengths and spherical equivalents, we found increasing prevalence rates of myopia by birth year. Axial length was significantly associated with spherical equivalent, and both were associated with visual impairment. Of all

Figure 2. Cumulative Risk of Visual Impairment



No. at risk

<24 mm	5473	4668	2215	431
24 to <26 mm	2092	1773	712	102
26 to <28 mm	449	347	133	16
28 to <30 mm	123	85	25	5
≥30 mm	71	50	24	4

No. at risk

> −0.5 D	10662	9895	6736	2833
−0.5 to > −3 D	2290	1999	1019	372
−3 to > −6 D	1046	919	465	150
−6 to > −10 D	403	315	135	34
−10 to > −15 D	147	103	47	15
≤−15 D	55	36	20	5

Kaplan-Meier curve of the cumulative risk of visual impairment with increasing age per category of axial length and spherical equivalent.

Table 3. Prevalence of Myopia by Birth Decade and Related Increase in Prevalence of Visual Impairment by Age

Region	Birth Decade	Myopia Prevalence, No. (%)		Surplus of VI, % (95% CI)[a]	
		Myopia	High Myopia	60 y[b]	75 y[c]
Europe, No.					
683	1920-1929	122 (17.9)	9 (1.4)	0.21 (0.11-0.31)	1.17 (0.81-1.54)
6280	1930-1939	1036 (16.5)	94 (1.5)	0.21 (0.11-0.30)	1.16 (0.81-1.51)
17 119	1940-1949	2568 (15.0)	205 (1.2)	0.18 (0.09-0.26)	1.00 (0.69-1.31)
18 888	1950-1959	4552 (24.1)	416 (2.2)	0.30 (0.16-0.44)	1.70 (1.18-2.21)
9792	1960-1969	3437 (35.1)	274 (2.8)	0.42 (0.22-0.61)	2.31 (1.60-3.03)
7906	1970-1979	3178 (40.2)	269 (3.4)	0.49 (0.26-0.72)	2.73 (1.90-3.57)
808	>1980	342 (42.3)	33 (4.1)	0.54 (0.28-0.79)	3.04 (2.13-3.96)
Singapore, No.					
141	<1920	46 (32.6)	4 (3.1)	0.41 (0.22-0.61)	2.33 (1.63-3.04)
1395	1920-1929	324 (23.2)	39 (2.8)	0.32 (0.17-0.48)	1.88 (1.33-2.43)
3236	1930-1939	880 (27.2)	126 (3.9)	0.41 (0.22-0.60)	2.40 (1.71-3.10)
3389	1940-1949	847 (25.0)	142 (4.2)	0.40 (0.22-0.59)	2.41 (1.73-2.10)
4094	1950-1959	1388 (33.9)	270 (6.6)	0.59 (0.32-0.87)	3.61 (2.60-4.62)
2437	1960-1969	1155 (47.4)	280 (11.5)	0.94 (0.51-1.38)	5.85 (4.25-7.45)
15 086	>1970	11963 (79.3)	1976 (13.1)	1.28 (0.68-1.87)	7.62 (5.46-9.80)
Republic of Korea, No.					
63	1920-1929	22 (34.9)	0	0.28 (0.14-0.42)	1.33 (0.85-1.81)
2768	1930-1939	498 (18.0)	28 (1.0)	0.19 (0.10-0.29)	1.04 (0.71-1.37)
3809	1940-1949	602 (15.8)	46 (1.2)	0.19 (0.10-0.27)	1.03 (0.71-1.35)
4344	1950-1959	1381 (31.8)	65 (1.5)	0.33 (0.17-0.49)	1.74 (1.18-2.31)
4516	1960-1969	2692 (59.6)	181 (4.0)	0.67 (0.35-0.99)	3.68 (2.53-4.83)
4381	1970-1979	3189 (72.8)	250 (5.7)	0.86 (0.45-1.27)	4.77 (3.30-6.25)
28 642	>1980	26866 (93.8)	1078 (19.4)	1.70 (0.92-2.49)	10.39 (7.51-13.29)

Abbreviation: VI, visual impairment (ie, a visual acuity <0.3).

[a] 95% CIs were calculated using ±1.96 × SE of the cumulative risk. Proportions are cumulative risks derived from the Rotterdam Studies, Erasmus Rucphen Family Study, and Myopia Study.

[b] Visual impairment at age 60 years was calculated using the formula (% myopia − % high myopia) × 0.008 + % high myopia × 0.057.

[c] Visual impairment at age 75 years was calculated using the formula (% myopia − % high myopia) × 0.038 + % high myopia × 0.39.

persons with high myopia, 39% developed visual impairment by age 75 years. In particular, those at the more extreme ends of the axial length spectrum were at great risk of visual impairment; risk increased from 3.8% in eyes with an axial length less than 26 mm to 25% in eyes with an axial length of 26 mm or greater and more than 90% in eyes with an axial length of 30 mm or greater. Projections of these risks to areas with a high incidence of myopia indicate that visual impairment will rise considerably as the population ages, and 1 in 10 persons will develop visual impairment in the most endemic regions.

Interpretation of Results

These results suggest that more persons will become visually impaired in the following decades. The current prevalence of myopia as well as the expected increase in prevalence are comparable between Europe and the United States,[3] and we expect a similar rise of visual impairment.[36] The current myopia epidemic in Korea, Taiwan, and Singapore will cause an exponential rise in visual impairment to a frequency of 5% to 10% in those 75 years or older after 2040. Our estimates imply that the current lack of intervention will continue. As health and ophthalmic care improve and future preventive and therapeutic means to interfere with the development of myopia advance, these estimates will be overstated.

The relatively young age at onset of visual impairment for persons with myopia contributes to its increased morbidity. The effect of myopia on personal lives and public health can be more devastating than of eye diseases with an older age at onset, like age-related macular degeneration or open-angle glaucoma.[37] An early age-related penetrance of myopic complications was also noted in other studies.[38-42] The increasing prevalence and relatively early onset of visual impairment necessitate the implementation of effective preventive and therapeutic measures. Currently, there is little one can do to counteract morbidity from myopia. Studies have shown that a 40-minute per day increase in outdoor time in schoolchildren will reduce myopia incidence by 10%.[43] Pharmacologically, atropine was shown to be the most effective treatment to reduce myopia progression but has serious adverse effects and shows a rebound effect when medication is stopped.[44,45] Medical treatments of myopia-related complications are increasing but still do not always improve visual outcome.[46] Anti-vascular endothelial growth factor therapy is available for subretinal neovascularization, surgical procedures for detachments and epiretinal membranes, and laser for retinal holes with traction. However, no treatment options are available for the most frequently occurring complication, myopic staphyloma with subsequent retinal atrophy or macular schisis.[17] It is likely that public and scientific awareness of myopia and myopic complications will increase as the current population of persons with high myopia ages and becomes more at risk of visual impairment.

Strength and Limitations

A strength of this study is the use of a large study sample of all Rotterdam cohorts to maximize statistical power and the numbers of persons at the extreme ends of the phenotype. The Rotterdam Study is a well-known population-based study cohort that has used the same methods of assessment of refractive error and visual impairment for more than 25 years. To our knowledge, MYST is the only high myopia case-control study in Europe to date. All studies used identical study protocols and were carried out at the same research center by the same examiners. This increased homogeneity across studies, validating a pooled analysis of outcomes.

Our study had limitations. A potential source of limitation is selective nonparticipation of disabled persons in the population-based studies, as well as selective participation of visually disabled persons in MYST. These biases did not appear to play an important role, as visual impairment per se was not differentially distributed in any of the studies. To project our findings to high-risk regions, we extrapolated data from local prevalence studies. These studies used different methods for biometry and refractive error, but given the small differences of outcome parameters between machines, we do not think this distorted our prediction estimates.[47,48] The cumulative risk in the extremely high myopia group (ie, with a spherical equivalent of -15 D or less) may have been overestimated as a result of the relatively low number at the higher ages. Nevertheless, the strong rise of visual impairment at a relatively early age underscored the lifetime visual morbidity in this category. Another limitation may be the projection of data from a European study population to Asian ethnicities, although there is no evidence that ocular morbidity resulting from myopia varies among ethnicities.

Conclusions

We examined the risk of visual impairment by axial length and spherical equivalent using a very large data set of Europeans. The risk of visual impairment was associated with axial length and spherical equivalent and reached the highest values for persons with high myopia, in particular for eyes with an axial length of 30 mm or greater. Our projections show that, given increasing axial lengths, myopia will bring major threats to the visual health of the public in many societies. Given the global increase of myopia and rise in high myopia, strategies to prevent and overcome visually impairing complications must be developed. This requires increased awareness among policy makers and medical experts regarding myopia-related risks.

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Invited Commentary

Myopia—The Silent Epidemic That Should Not Be Ignored

Jacqueline Chua, PhD; Tien Yin Wong, MBBS, PhD, FRCS(Ed)

It is a commonly held view that ophthalmologists do not care much about myopia, despite the fact that myopia is the most common eye condition worldwide, affecting about 1.5 billion people.[1] Why is this so? First, both the general public and eye care professionals do not perceive myopia as a serious sight-threatening problem.[2] Myopia is regarded as a minor inconvenience; the condition is not considered a disease and can be managed simply with spectacles, contact lenses, or a refractive surgical procedure. Myopia is thus mostly under the clinical care of optometrists and not specialist ophthalmic surgeons. Second, serious blinding ocular complications are thought to affect only a small number of individuals with high myopia (traditionally defined as a spherical equivalent of −6.00 or −8.00 diopters [D] or worse) and are thought to be uncommon for the larger population with simple myopia (traditionally defined as spherical equivalent of −0.50 to −6.00 D).[3] Pathological myopia characterized by early excessive and progressive elongation of the eye with retinal and optic nerve degeneration was reported to be rare.[4] Third, at least in Western societies, myopia is not generally regarded as a major public health issue, and thus, the need for increased government funding for research is clear. As a result, our understanding of the epidemiology, public health effect, risk factors, pathogenesis, and treatment options may not have progressed as much for myopia as for other eye conditions, such as age-related macular degeneration or glaucoma, which are actually less common than myopia in terms of the number of people affected.

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The position that myopia is not important and does not lead to vision impairment is challenged by Tideman et al[5] in this issue of *JAMA Ophthalmology*. The authors examined the lifetime risk of developing visual impairment from myopia, specifically the association between axial length and refractive error with cumulative lifetime risk of visual impairment. Using data from 5 studies with 15 406 participants in the Netherlands, the authors estimated that individuals aged 75 years with myopia and high myopia would have 4% and 39% cumulative risks of visual impairment, respectively.[5] As the normal life expectancy in economically developed countries is now much greater than 75 years, the cumulative risk to 75 years is actually a conservative approximation of the lifetime risk of developing visual impairment. Even then, this article suggests that patients with high myopia have about a 1 in 2.6 chance of developing visual impairment in their lifetimes. While the cause of the visual impairment may be associated with myopic macular degeneration, it may also be associated with other conditions, such as glaucoma and cataract. Unfortunately, the authors did not provide this information, and the specific cause of the myopia-related visual impairment was not presented.

To our knowledge, the current study is the first to estimate the lifetime risk of developing visual impairment in persons with myopia. We hope that this knowledge will change the current perception of the clinical and public health impli-