1.1

Epidemiology of Myopia and Myopic Shift in Refraction

Barbara E.K. Klein*

There have been many recent publications concerning myopia. Some are population-based while others reflect specific exposure groups. This chapter includes the findings from many of these publications and describes some of the risk factors/risk indicators for myopia, including personal exposures, family similarities and possible genetic correlates of his or her refractive state.

Introduction

Myopia has become a focus of ocular epidemiologic research worldwide for many reasons. There are no current national prevalence estimates of myopia in U.S. children, but the Eye Disease Prevalence Research Group estimated that there were 30,358 cases of myopia of $-1.0$ D or less (more minus) in U.S. adults 40-years of age or older, of whom 5308 had a refractive error of $-5.0$ D or less.¹ It has been estimated that the costs of correcting myopic refractive errors, either by spectacles or contact lenses, was about 2 billion dollars per year in the U.S. in 1983–87,² and about 4.6 billion dollars more recently; according to the authors, this is a conservative estimate.³ Current cost estimates would need to include more modern methods of refractive surgery primarily involving the cornea and lensectomy with or without lens implant. These costs are a significant burden for individuals and health systems that are privately or publicly funded. More importantly, myopia, especially higher degrees of myopia, has occupational, medical and quality of life consequences for individuals.

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Myopia has been considered to be a problem with origins in childhood. The estimated prevalence in 6-year-olds is 2% and in 15-year-olds, 15%. However, adult onset myopia is not an infrequent occurrence. Furthermore, myopic shifts in refraction can occur across the lifespan, although more common in the first two decades than in older persons, and affects those with hypermetropic refractive errors and emmetropes as well as myopes. Thus, this chapter will describe the distribution of myopia and myopic shifts in refraction as reflected in a (non-scientific) sample of studies worldwide in children and adults.

In addition, risk factors that have been evaluated for myopia will be briefly described. The list of risk factors includes a brief description of familiality or family aggregation and in some cases, actual genetic loci. The reader should be aware that a comprehensive review paper of epidemiology of myopia was published in 1996. In addition, a description of the literature on refraction in general was published in 2008. The material in this chapter overlaps in part the information in these two sources.

**Methodologic Issues**

Studies reported upon in this chapter are of several types, including traditional population-based surveys, studies of special exposure groups such as students, occupationally exposed workers, social or ethnic groups, and rural or urban groups. Some studies were performed on convenience samples, although these were largely avoided. In addition, some studies are cross-sectional, while others incorporate longitudinal follow-up. Some case-control studies have been included as well. Risk factors or risk indicators of myopia are briefly discussed. In addition, no survey of risk factors associated with virtually any condition is complete without at least a brief review of genetic correlates of the condition. To that end, this chapter includes some investigations that have approached the study of myopia using the tools of statistical genetics, with data sources from population-based, family, and twin studies, and combinations of these designs. The field of genetics is progressing rapidly and will be further advanced by the time of the publication of this tome. Nevertheless, although the content will be somewhat dated, the approach to investigating these important determinants will still be relevant.

Measurement techniques of refraction varied between studies. In most studies in children and in some studies in adults, cycloplegic agents were
instilled prior to refraction and, among these, different pharmacologic agents were used, likely resulting in some variation in the actual amount of cycloplegia attained. In other studies, no cycloplegic agents were used. The data may have been reported only as continuous data with mean refraction given, while in other cases, the authors reported the data in categories. When the latter was so, the category limits for myopia (and for hyperopia and emmetropia as well) may have differed between studies. Objective refraction was performed in some studies and subjective refraction or refinement in others. In addition, the testing for refraction was based on best corrected distance acuity. This may differ with regard to the use of charts or projection and distances. These details may not have been reported in the publications reviewed. Automated refractors may have been used and these devices differ in design, and consequently could yield systematic differences between results. Lastly, many studies reported the spherical equivalent, while others only gave spherical refraction. All these factors are likely to have led to variation in the reported measure of the refraction, resulting in different estimates of the proportion of persons classified as myopic (and emmetropic and hyperopic). In some cases, the “errors” so induced may not have been unbiased. In addition, there were, no doubt, actual errors and statistical variation around the measurements that were, in general, not reported at all. Despite these concerns, some common findings emerged and some directions for further research have been provided as well. Because the thrust of this volume is on myopia, a refractive state, ocular biometry will not be discussed, although myopia results anatomically and physiologically from the biometry.

**Review of Studies (Table 1)**

For the sake of space and because of the possibility that there have been temporal changes in the distribution of refraction, only the more recent publications have been reviewed for the purpose of this chapter. Epidemiologic studies of refraction have burgeoned and now there are data from studies across the age span and in many different ethnic and cultural groups. For the sake of brevity, a limited amount of descriptive material from each study has been included; however, interested readers could refer to the reference citations. Still, this review is not exhaustive but is merely a (non-systematic) sample of studies of myopia.
Table 1. Overview of Studies

<table>
<thead>
<tr>
<th>Location/Study</th>
<th>Population-based</th>
<th>N*</th>
<th>Age (Years)</th>
<th>Cycloplegic</th>
<th>Definition of Myopia (SE)</th>
<th>Prevalence (%)</th>
<th>Eye</th>
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<td>1724</td>
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<td>663</td>
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*(Continued)*
### Table 1. Epidemiology of Myopia (Continued)

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<tr>
<th>Location/Study</th>
<th>Population-based</th>
<th>Age (Years)</th>
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<th>Definition of Myopia (SE)</th>
<th>Prevalence (%)</th>
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<td>1518</td>
<td>43.2 ± 9.8</td>
<td>≤−0.5</td>
<td>29.2</td>
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**Abbreviations:** SE = spherical equivalent; CLEERE = Collaborative Longitudinal Evaluation of Ethnicity and Refractive Error; LALES = Los Angeles Latino Epidemiologic Study; BDES = Beaver Dam Eye Study; VIP = Visual Impairment Project.

* = with refraction data.
The Sydney Myopia Study evaluated refraction in a sample of 6- to 7-year-old school children. The mean spherical equivalent refraction in these children was +1.26 D in the right eyes. The boys were slightly more likely to be myopic than the girls, and white children were slightly less likely to be myopic than non-whites. In the 12-year-old children in that study, spherical equivalent was less positive than in the younger children. Investigators from six sites in the U.S. pooled their data on refractive errors and ocular biometry in school children ages 6 to 14+ years. The students were from different ethnic backgrounds. They found no difference in average spherical equivalent between girls and boys; there was a shift towards myopia with increasing age in both.

There were 663 subjects who were 15-years of age or younger in the Andhra Pradesh Eye Disease Study (Table 1). Myopia was less common in those 15-years of age and younger (about 4%) than in older persons (19%). The first reported myopes were about 5-years-old.

The prevalence of myopia in Chinese school children 7–9-years of age in Singapore was 29%, with successively higher prevalences with increasing age. The age when the tendency for increasing myopia levels off is uncertain. Studies of university students suggest that this may continue into the third decade, although there may be the confounding effect of near work activities in these subjects.

The Beaver Dam Eye Study reported that 28.1% of women and 24.0% of men 43–86-years of age were myopic. A difference between men and women was true throughout the age range. Overall, the prevalence was 26.2%. Wu reported that the prevalence of myopia decreased with age until 60 years but increased thereafter in a population of Afro-Caribbeans. The Visual Impairment Project conducted in Victoria, Australia, included urban and rural persons. Prevalence decreased with increasing age; the overall prevalence was 17%. Overall, sex was not associated with myopia, but after age correction, women were slightly more likely to have a hyperopic refractive error. The Blue Mountains Eye Study is a population-based study of 3654 persons, 49–97-years of age. The Baltimore Eye Survey reported on refraction in 2200 African Americans and 2659 white Americans in Baltimore. Overall, 25% of the population was myopic and whites had higher myopia on average than blacks. Myopia declined with increasing age. The Los Angeles Latino Eye Study found that in 5588 adults 40-years of age or older, the mean spherical equivalent was 0.02 D (+/−1.66) in men and 0.18 D (+/−) in women, and that on average there was 0.04 D...
increase in spherical error per year for those 40- to 79-years of age, and −0.07 D per year for those 80-years of age and older.

Many of the studies on prevalences or case-control studies with past ocular history available reported on myopic shifts in refraction, i.e. a change in the sphere or spherical equivalent of the refractive correction in a negative direction even within the hyperopic range. In general, in children there is a shift towards more myopic refraction with increasing age. Thorn and colleagues have modeled myopia progression in children using double exponential growth function (Gompertz function).21,22 These investigators estimated that refraction stabilizes in 80% of children by about 19-years of age. This tendency extends past ages that are usually considered to be childhood.

In a group of 432 patients being followed up regularly at a clinic, longitudinal measures of refraction were reviewed over about a 10-year course.23 Myopic shifts in refraction occurred in some persons through the seventh decade of life. The mean amount of shift decreased with increasing decade of life, from an average of −0.6 D in the third decade to −0.4 D in the fourth decade and −0.3 D in the fifth decade.

**Cohort Effects on Myopia**

Mutti and Zadnick reported on an apparent birth cohort effect on myopia in three population-based and one family-oriented study of refraction.24 They found that the prevalence of myopia standardized to 44.5- to 49.5-years of age increased in cohorts from about 1900 to about 1940. The most impressive increase in prevalence occurred in those born between 1920 and 1935. Wensor observed, aside from a higher prevalence of myopia in those of younger age in the Visual Impairment Project, that those in younger age groups were more likely to have reported wearing a spectacle correction for distance between 10- and 19-years of age.17 In addition, those who were 40–49-years of age reported wearing a myopic correction at age 40 more often as compared with those who were 70-years of age or older at the time of the survey. Bengtsson and Grodum reported decreased spherical equivalent power in 65- to 74-year-olds in persons with more recent birth year.25 Lee and colleagues found a birth cohort effect in adults participating in the Beaver Dam Eye Study.26 They found that for persons of the same age, those born more recently were more likely to be myopic than those born in earlier years.
In summary, in adults of largely European background there appears to be a cohort effect on myopia.

**Risk Factors for Myopia**

Risk factors for myopia or myopic shifts in adults are given in Table 2. A description of these and other risk factors in children and in adults is given below.

**Near work**

Much of the information on the association of near work with myopia in children is inferred from estimated intensity of school work or reading. A study in Hong Kong examined fishing families and found an association between education and myopia. Hepsen and colleagues reported on greater frequency of progression of myopia in children from private schools as compared with apprentices in a skilled labor group. Saw and colleagues reported a significant association between the degree of myopia and the

<table>
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<tr>
<th>Location/Study</th>
<th>Age</th>
<th>Gender</th>
<th>SES/Income</th>
<th>Near Work/Education</th>
<th>Nuclear Cataract</th>
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Abbreviations: SES = socioeconomic status; BDES = Beaver Dam Eye Study; VIP = Visual Impairment Project; LALES = Los Angeles Latino Epidemiologic Study; Inf. = inferred.

* Direction not given as associations may vary by strength and direction between categories of some characteristic.

** Near work was associated but not education.
+ Association found.
0 Association evaluated but not found.
number of books read per week in a group of Singaporean school children. Recently, Rose and colleagues reported a marked difference in the prevalence of myopia between Australian and Chinese Singaporean 6- to 7-year-old school children. The prevalence in Australians was 3.3% and in Singaporeans, 29.1%, despite the fact that the Australians read more books per week and did more hours of homework per week. The possibility that recent increases in years of preschool instruction for Singaporean children may be related to the higher prevalence in these children.

Khader and colleagues found that myopic children were likely to spend more time reading and writing and using the computer than their non-myopic school mates, but the analyses were not adjusted for age, which is likely to be an important confounder in these analyses. Rah and colleagues in a study of myopia in parents and children have found that there is an association between near work and myopia, but speculated that the actual strength of the association was probably imprecise because of the inaccuracy of measures of near work. They suggest that better methods of reporting near work activities are needed for future myopia research in children.

A relationship between near work activity and myopic change in refractive error has been found in adults. Microscopists have been shown to have higher prevalence of myopia than the general population and higher prevalence of adult progression of myopia, but a comparison group was lacking in this report. Studies of other specific exposure groups, e.g. medical students, suggest that these persons have greater prevalence of myopia than other similarly aged groups. Wu et al. reported that adults who reported near work activities were more likely to be myopic as compared with others in the population. Few studies in adults have had careful, precise measures of near work and therefore it is yet to be established whether near work activity is the important exposure and not just a confounder of other important possible causes.

Education/Income

Education and income are considered together because it is usually not possible to separate the effects of these two exposures. The association of more myopic refractive error with level of educational achievement (and usually with income as well) in children and adults has been found in most
It is thought that this reflects near work activities, although there is a dearth of studies that assess the relationship quantitatively and by specific activity as noted above. The education/refraction association relation may reflect common genetic determinants of intelligence (or educational achievement) and refraction. It is noteworthy that education was not associated with change in refraction in two large epidemiologic studies of adults.

**Outdoor activity**

Ip et al. reported a small effect of hours spent outdoors on refraction (more hyperopic) in children in the Sydney Myopia Study. This finding was extended by Rose and colleagues, who reported on refraction in a sample of 6- and 12-year-old school children in Sydney, Australia. They found an inverse association of total time outdoors with refraction after adjusting for near work, parental myopia, and ethnicity. Hours spent playing sports was inversely associated with myopia in a study of 1777 students aged 12- to 17-years old in Amman, Jordan, but these data were not adjusted for age.

Jones and colleagues reported that lower amounts of sports and outdoor activities increased the odds of children, with two myopic parents, becoming myopic. The chances of children with no myopic parents becoming myopic was the lowest in the children with the greatest amount of sports and outdoor activities. Higher levels of total time spent outdoors, rather than sports per se, were associated with less myopia after adjustment is made for near work, parental myopia, and ethnicity. Rose and colleagues reported that Australian 6- to 7-year-olds spent more hours in outdoor activities than Singaporean children of the same age, the latter having a higher prevalence of myopia. Jacobsen and colleagues reported an apparent protective effect of physical activity for development of myopia over a two-year interval in a group of medical students in Copenhagen.

There is no data to suggest that physical activity or sports has any effect on refraction or change in refraction in adults.

**Age**

In childhood, increasing age is associated with increasing prevalence of myopia. In adults, increasing age is associated with a hyperopic shift unless cataract is present when there may then be increasing myopia.
Race/Ethnicity

The comparisons that have been described are based on published data from many different studies and so comparison between the groups described is usually not based on uniform criteria for inclusion, nor are the methods of refraction identical. Nevertheless, the generalizations about the differences between the racial/ethnic groups are correct. Adult Chinese in Singapore have a higher prevalence of myopia than similarly aged European-derived populations; Mongolians have a lower prevalence of myopia than the Chinese in Singapore and Taiwan and similar prevalences to populations of largely European background; Eskimos have a lower prevalence of myopia than Whites, Blacks and Chinese; and Barbadians have higher prevalences of hyperopia and myopia than European-derived populations. For the last study, the authors suggest that this may be due to higher prevalences of cataract, glaucoma and other ocular conditions in Barbadians.

Nuclear cataract

Nuclear cataract has been found to be associated with myopia in many studies (Table 2). This is thought to reflect the increased power of the more sclerotic lens and not a reflection of increased axial length.

Family aggregation/Genetics

This section will briefly address the genetic epidemiologic evidence to support the notion that myopia has both environmental and genetic determinants. Study designs include population-based and traditional pedigree studies. The primary question involves determining how much of the clustering of myopia in the families reflects common exposures and how much is due to hereditary factors. The section starts with studies based on phenotype and then a few studies that examine genes or genetic markers are briefly described.

Siblings

The presence of myopia in a sibling was associated with increased odds of myopia in school children in Amman, Jordan. In the Framingham Offspring Eye Study, the odds of the subjects having myopia was significantly
increased when a sibling was myopic (OR varied from 2.50 to 5.13, depending upon the age difference of the siblings).51

In the adult population participating in the Beaver Dam Eye Study, Lee and colleagues reported a sibling correlation of a refractive error of 0.37 (1418 sibling pairs).46 There was no correlation of refraction between spouse pairs. The odds ratios for myopia were similar to those for sister-sister, sister-brother and brother-brother pairs, being 4.64, 4.53, and 3.36, respectively. These data in adults suggest strong familial effects on refraction, and, although the relative importance of environment and genetics were not partitioned, the findings are compatible with the existence of important genetic determinants of refraction across its range.

In data from the Salisbury Eye Evaluation Study that included 274 older adult sibships, Wojciechowski and colleagues found an OR of 2.65 (95% CI: 1.67-4.19) for myopia threshold of −0.050; neither gender nor race (black or white) had a significant effect on this relationship.48 Eskimo families showed correlations between sibs but not between parents and children, suggesting environmental effects; there was virtually no myopia in grandparents or parents but 58% of children were myopic.52

**Parent-child**

In a case-control study of myopia in 1853 school children in Oman, the presence of myopia in parents was associated with myopia in the children.53 In the study in Jordanian school children, the odds of a child being myopic increased with the number of myopic parents.39

Saw and her colleagues found that the progression of myopia in children was greater for those children whose parents were myopic.54 This finding was also reported by Lam and colleagues who examined the effects of parental myopia on myopia (n = 7560) and myopic shift (n = 2628) over one year in their children.55 Children with a greater number of myopic parents were more myopic and had a greater average myopic shift. Analyses were adjusted for age, gender, parental education and near work performed by the child.

**Other family members**

Klein and colleagues evaluated the possibility of a familial effect on refraction for several different sorts of family relationships (sibs, parents and children, avunculars and cousins).56 She found stronger correlations
between sibling and cousin pairs than between parents and children and avuncular pairs. Segregation analysis did not support the involvement of a single major locus across the range of refractive error but models allowing for polygenic effects provided a better fit. This suggests that several genes of modest effect may influence refraction, possibly in conjunction with environmental factors.

**Genetics**

High myopia, sometimes associated with other anomalies, has been associated with several genes.\(^{57-60}\) Some of the regions associated with high myopia have been mapped to chromosomes 18p11.3 (MYP2),\(^{61}\) 12q21 to 23 (MYP3),\(^{62}\) 17q21 to 22 (MYP5)\(^{63}\) and to other sites.\(^{57,59,62-68}\) Moderate myopia has been mapped to 22q13\(^{69}\) and 8p23.\(^{70,71}\)

Simpson and colleagues examined the association of PAX 6 and SOX2 with refraction in a British cohort.\(^{72}\) They found no relationship of these genes to myopia or other spherical refractions, although Hewitt and colleagues\(^{60}\) and Tsai and colleagues\(^{73}\) did find associations with severe myopia. Hammond and his colleagues reported a susceptibility locus for myopia in the PAX6 gene region in their study of twins.\(^{70}\) In contrast, Schache and colleagues did not report linkage to this site in their study of 233 adult dizygotic Australian twin pairs.\(^{64}\) It is possible that the twins in this study are in some way selectively different from the twins in Hammond’s study. Such lack of consistency is not uncommon in genetic studies of complex traits. Klein and colleagues found evidence of linkage of refraction to regions on 22q, previously linked to myopia, and also to novel regions on 1q and 7p.\(^{74}\) These authors interpret their data to confirm the notion that refraction is a complex trait likely influenced by several genetic (and environmental/behavioral) exposures.

This brief review of genetic studies of myopia is not meant to be comprehensive nor orderly, but to illustrate the importance of having large enough samples of cases to meaningfully address the potential importance of genes of modest effects that are likely to interact with other genetic and environmental factors to influence the phenotype. Furthermore, epidemiologic studies are essential to address these relationships in general populations as opposed to ascertained groups and twins. These goals are unlikely to be achieved by any one group of investigators; they require judicious and thoughtful harmonizing of phenotype definitions, appropriate stratification, uniform genotyping, and a consistent
approach to data analysis. Replication of findings in other groups is essential to validate findings.

Comments

I have summarized some of the information about the epidemiology of myopia that has appeared in the recent literature. In addition, I have reviewed some of the risk factor data. To “prove” some etiologic and therapeutic hypotheses, randomized controlled clinical trials often provide the best evidence of causal relationships. However, for most questions relating to causes and treatments for myopia, clinical trials cannot be performed. For example, it is unethical and not feasible to randomly assign near work for a period of time in order to determine causal effects of this risk factor. Treatment with drugs to modify accommodative mechanisms has proven to be of limited effect and may not be long-lasting. Treatment with optical approaches has also been of limited success.75 Thus, we must rely largely on well planned and executed epidemiologic (and genetic) studies to enlighten us about the development and course of myopia and other refractive errors, and to search for preventive measures that might alter the refractive status of persons “at risk.”

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References


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