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ORIGINAL ARTICLE



Myopia progression patterns among paediatric patients in a clinical setting

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Abstract

Purpose: This retrospective analysis of electronic medical record (EMR) data investigated the natural history of myopic progression in children from optometric practices in Ireland.

Methods: The analysis was of myopic patients aged 7–17 with multiple visits and not prescribed myopia control treatment. Sex- and age-specific population centiles for annual myopic progression were derived by fitting a weighted cubic spline to empirical quantiles. These were compared to progression rates derived from control group data obtained from 17 randomised clinical trials (RCTs) for myopia. Linear mixed models (LMMs) were used to allow comparison of myopia progression rates against outputs from a predictive online calculator. Survival analysis was performed to determine the intervals at which a significant level of myopic progression was predicted to occur.

Results: Myopia progression was highest in children aged 7 years (median: -0.67 D/year) and progressively slowed with increasing age (median: -0.18 D/ year at age 17). Female sex (p < 0.001), a more myopic SER at baseline (p < 0.001) and younger age (p < 0.001) were all found to be predictive of faster myopic progression. Every RCT exhibited a mean progression higher than the median centile observed in the EMR data, while clinic-based studies more closely matched the median progression rates. The LMM predicted faster myopia progression for patients with higher baseline myopia levels, in keeping with previous studies, which was in contrast to an online calculator that predicted slower myopia progression for patients with higher baseline myopia. Survival analysis indicated that at a recall period of 12 months, myopia will have progressed in between 10% and 70% of children, depending upon age.

Conclusions: This study produced progression centiles of untreated myopic children, helping to define the natural history of untreated myopia. This will enable clinicians to better predict both refractive outcomes without treatment and monitor treatment efficacy, particularly in the absence of axial length data.

KEYWORDS

centile, epidemiology, myopia, myopia progression

INTRODUCTION

The prevalence of myopia is increasing globally and has become the 'new normal' among young people in parts of Asia, affecting in excess of 90% of individuals in certain urban populations, including up to 20% with high myopia.^{1–6} Myopia prevalence has almost doubled over a 30year period in teenagers and adults in the United States,⁷

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and reached more than 50% of young adults in parts of Europe.⁸ Importantly, the average degree of myopia in the population is also on the rise.⁷ Myopia onset appears to be occurring earlier,⁹ and a younger age of onset is associated with faster myopia progression and a greater severity in adulthood.¹⁰ The rate of myopia progression is an important clinical parameter as it directly links to final myopic refractive error and the risk of vision loss. For example, each additional one dioptre of myopia is estimated to increase the risk of developing myopic macular degeneration (MMD) by as much as 67%.¹¹ It is estimated that the number of people with vision impairment or blindness due to MMD is set to increase almost sixfold to reach 37.2 million vision impaired and a further 18.5 million blind by 2050, if left unchecked.¹²

Effective treatments are now available and have been shown to limit myopia progression rates and delay or prevent myopia onset in clinical trials.^{13,14} Despite the increasing emphasis on myopia control, there is only limited data available regarding the natural history of myopia progression in representative populations not undergoing active myopia management.^{15–18} Defining the range of myopia progression rates expected at different ages would allow clinicians to identify those who would benefit most from treatment and to potentially assess myopia treatment efficacy outside the setting of a clinical trial.

Control group data from randomised controlled trials (RCTs) have been proposed as a basis for predicting myopic progression, yet clinical trial cohorts are not recruited in a population-representative manner and, thus, may not reflect 'real-world' myopia progression due to recruitment biases. In the absence of cohort studies, the most ecologically valid data source for predicting myopic progression in the 'real world' are patients from clinical practice, examined according to practice norms. Electronic medical records (EMRs) represent a potentially valuable big data resource with the capacity to answer epidemiological and clinical research guestions. The potential of big data analytics to monitor population trends in refractive error has received relatively little attention but has recently been applied for ophthalmic purposes.¹⁹ EMRs, for example, have been used to assess temporal trends in refractive error,²⁰ to evaluate the prevalence of macular complications among patients with myopia,²¹ to explore the epidemiology of cataract,²² low vision,²³ dry eye disease²⁴ and the association between refractive error and glaucoma²⁵ among others. Most notably, machine learning methods have recently been applied to real-world clinical refraction EMR data to develop an algorithm to predict the future development of high myopia.²⁶

This study was designed to explore the natural history of myopic progression using EMR data from community optometric practices in Ireland, create myopia progression centiles and compare these findings with those from clinical trial control groups.

Key points

- In this clinic-based population, faster myopia progression was observed among younger children, females and those with a higher presenting level of myopia.
- Myopia progression progressively slowed with increasing age; however, 35% of those aged 16 were still progressing 0.25 dioptres or more per year.
- Predictive tools that rely on clinical trial data appear biased towards faster myopia progression, are inconsistent with real-world observations and should be used with caution when predicting future progression or assessing treatment efficacy.

METHODS

Optometry practice owners in the Republic of Ireland using the Acuitas practice management system (Ocuco Ltd. ocuco.com/) were invited to provide anonymised EMR data from their clinical practice records. The study was approved by the Research Ethics and Integrity Committee at Technology University Dublin. The anonymised data were extracted remotely by the EMR provider following the provision of explicit consent from the data (practice) owners. The data extracted comprised all practice records since first use up to the date of extraction for each practice (all data extracted during January 2022). At the time of extraction, all personally identifying information was removed, and a new unique identifying number was randomly assigned to each patient attending a given practice within the EMR data, allowing the anonymisation of patients while allowing individual patient data to be tracked across multiple visits to that practice. The data available for each patient included demographic, refractive, visual acuity, binocular vision, contact lens, ocular health and clinical management data.

Refractive error change was determined among patients with multiple eye examination visits during the period from 1 January 2010 to 31 December 2019. This date range was chosen to avoid any potential effects of COVID-19 social restrictions. Sphero-cylindrical data from recorded spectacle prescriptions were used to compute spherical equivalent refraction (SER). Myopia was defined according to the International Myopia Institute standards,²⁷ with myopia defined as a SER of \leq -0.50D in the right eye. Only myopic patients, aged 7–17 years inclusive, who attended more than one eye examination with an interval of at least 11 months between visits and were not undergoing myopia control treatment were included in the analysis. Right eye myopia progression THE COLLEGE OF OPTOMETRISTS

rates were annualised by dividing the difference in myopia between subsequent visits by the time in years elapsed between those visits.

Sex- and age-specific population centiles for annual myopic progression were derived by fitting weighted cubic splines to age- and sex-specific empirical guantiles of myopia progression. These were compared to myopia progression rates derived from control (non-treated) group progression data obtained from 17 Western RCTs for myopia published from 1989 to 2020.28-44 A comparison was also made to two European clinic-based studies reporting myopic progression rates.^{45,46} Myopia progression was assessed using linear mixed models (LMMs) with SER progression as the outcome, age, sex and SER as fixed effect covariates and random intercept terms for the subject. LMMs were used to allow comparison of the modelpredicted progression rates against digitised progression data outputs from the Brien Holden Vision Institute (BHVI) online myopia progression calculator (https://bhvi.org/ myopia-calculator-resources/) for 10-, 12- and 14-year-old Caucasian children with presenting myopia levels of -1.00, -2.00 and -3.00 DS.

A Kaplan–Meier survival analysis was performed to determine the intervals at which a myopic progression is predicted to occur at various ages for four thresholds of myopic progression: >-0.25, >-0.50, >-0.75 and >-1.00 D/year. Data were analysed using the R programming language (R Core Team 2020, R-project.org/).

RESULTS

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Electronic medical record data were extracted from 40 optometry practices across Ireland and included data from 1,066,366 practice visits by 402,294 unique patients, representing approximately 5% of the Irish population.⁴⁷ Of these unique patients, 4180 individuals (female n = 2410, 58%) were myopic at their first visit, were aged between

TABLE 1 Baseline characteristics of the study population.

7 and 17 years, were not undergoing myopia control treatment and had a minimum of two visits at least 11 months apart at which a spectacle prescription was recorded. A detailed description of the study population, including the median time from the first to last visit, number of visits and initial refractive state, is given in Table 1. The number of patients in each age group at their initial visit is shown in Figure 1.

Progression by age

Myopia continued to progress in the majority of patients across the entire patient age range, with 53.0% of children exhibiting myopic progression of at least -0.25 D/year. The annualised rate of myopia progression was highest in younger children aged 7 years, with a median progression of -0.67 (IQR: -1.32 to -0.25) D/year, which progressively slowed to a median progression of -0.18 (IQR: -0.35 to 0.00) D/year by age 17 (Table 2 and Figure 2). Although progression rates reduced with age, among 17-18 years old, a small but significant proportion (approximately 1 in 3) were still progressing at the last follow-up. Another important finding is that, even among the youngest group, not all myopes showed progression. Approximately 1 in 6 of the 7- to 8-year-old group did not show progression, in keeping with reported non-progression rates in clinical trials.44

Quantile regression revealed that both age and sex were predictive of myopic progression. Younger age (Figures 3 and 4) and female sex had the effect of increasing the annualised rate of myopic progression. With increasing age, median annual progression slowed by 0.040 D/year (95% Cl: 0.036, 0.043, p < 0.001), and females had a median progression rate of 0.055 D/year faster than males (95% Cl: 0.041, 0.069, p < 0.001). This relationship varied with the progression rate. Median progression for all ages was -0.38 D/year for females and -0.33 D/year for males. At the

	Number of pati	ents		Numberof	
Age (years) at initial visit	Female	Male	visit 1 and final visit ^a	visits ^a	SER at visit 1 ^a (D)
7	115	65	3.49 (2.13–5.24)	4 (2–5)	-1.25 (-1.75 to -0.88)
8	152	127	3.28 (1.95–4.87)	3 (2–5)	-1.25 (-1.75 to -0.88)
9	222	176	3.06 (1.66–4.98)	3 (2–5)	-1.25 (-1.75 to -0.88)
10	253	190	2.97 (1.87–4.64)	3 (2–4)	-1.25 (-1.88 to -1.00)
11	321	181	3.13 (1.99–4.81)	3 (2–4)	-1.38 (-2.00 to -1.00)
12	359	240	3.18 (2.05–4.43)	3 (2–4)	-1.25 (-2.00 to -0.88)
13	313	260	2.92 (1.99–3.73)	3 (2–3)	-1.25 (-2.00 to -0.88)
14	296	195	2.26 (1.72–2.87)	2 (2–3)	-1.31 (-2.00 to -0.88)
15	209	131	1.79 (1.41–2.13)	2 (2–2)	-1.25 (-2.00 to -0.88)
16	83	59	1.15 (1.02–1.36)	2 (2–2)	-1.25 (-2.00 to -0.88)

Abbreviations: D, dioptres; SER, spherical equivalent refraction. ^aData are median (interquartile range).



FIGURE 1 Age and sex distribution of the study population at baseline. The number of patients reduces at older ages as visits from patients aged 18 and over were excluded, meaning those at older ages at baseline had less time to return for a subsequent visit.

90th centile, progression for all ages was -0.93 D/year for females and -0.82 D/year for males.

Comparison of clinical practice and randomised clinical trial progression

Myopia progression for the RCTs was faster than the median progression observed in the Irish clinical practice data (Figure 5; median SER progression = -0.50 D/year equivalent to the 74th centile). All of the RCTs exhibited mean progression rates higher than the median (50th) centile observed in the EMR data, and one-third exhibited mean progression rates at or above the 75th centile observed in the EMR data (Figure 4). In contrast, clinic-based studies demonstrated mean progression rates at or close to the 50th centile line across multiple ages.

To compare the EMR-derived predicted progression rates against the BHVI online myopia progression calculator, which reported mean progression rates, we used LMMs to fit the EMR data and generate mean predicted myopia progressions. Female sex (estimate: -0.05 D/year, p < 0.001),

a more myopic SER at baseline (estimate: -0.09 D/year for SER and 0.07 D/year for exp[SER], p < 0.001) and younger age (estimate: -0.56 D/year for log[age], p < 0.001) were all found to be predictive of faster myopic progression in the EMR data. When the outputs of this model were compared with the online myopia progression calculator, many of the online calculators' predictions sat within the 95% confidence intervals; however, the direction of the baseline SER effect was reversed between the two models, with the online calculator predicting slower myopia progression with a more myopic baseline SER, while the current model predicted faster myopia progression for higher baseline levels of myopia (Table 3). Additionally, the difference observed in myopic progression between the models was largest for higher baseline myopia levels.

Myopia progression survival analysis

Kaplan–Meier survival analysis found an increasing probability of myopic progression (<-0.25 D) over a longer follow-up period (Figure 6). It was also observed that the

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youngest patients were more likely to experience myopic progression (<-0.25 D) over the shortest period (Figure 6). This analysis also determined the proportion of progressing myopes that exhibited a defined amount of refractive progression at various eye examination intervals. The

TABLE 2	Myopic progression observed for female and male
patients atte	nding for a follow-up visit at each age.

Age (years)	Female myopic progression (D/year) ^a	Male myopic progression (D/year) ^a
7	-0.61 (-1.25 to -0.25)	-0.73 (-1.38 to -0.25)
8	-0.63 (-1.14 to -0.21)	-0.48 (-1.03 to -0.20)
9	-0.51 (-0.93 to -0.19)	-0.48 (-0.79 to -0.08)
10	-0.51 (-0.85 to -0.23)	-0.39 (-0.74 to -0.09)
11	-0.48 (-0.77 to -0.23)	-0.33 (-0.63 to -0.13)
12	-0.43 (-0.75 to -0.19)	-0.33 (-0.64 to -0.13)
13	-0.36 (-0.60 to -0.13)	-0.28 (-0.54 to -0.10)
14	-0.31 (-0.54 to -0.12)	-0.25 (-0.48 to -0.07)
15	-0.25 (-0.50 to -0.08)	-0.24 (-0.41 to 0.00)
16	-0.21 (-0.41 to 0.00)	-0.17 (-0.32 to 0.00)
17	-0.19 (-0.40 to -0.04)	-0.14 (-0.30 to 0.00)

Abbreviation: D/year, dioptres per year.

^aData are median (interquartile range).

proportion of patients who progressed to at least -0.25 D varied for different recall durations (Table 4). Approximately 94% of 7 years old, for example, experienced progression of at least -0.25 D within 18 months, compared with 62% of 12 years old and 29% of 17 years old.

DISCUSSION

A number of important observations can be drawn from this analysis of clinical practice data, which represents the largest single study of myopia progression in Irish children and adolescents to date. The rate of myopia progression was clearly influenced by age, sex and the present level of myopia. These findings agree with published data, in which age at baseline has been consistently reported as the most significant factor associated with myopic progression, irrespective of sex or race.^{16,48–50} The strong influence of age was evidenced both in the raw data analysis, which showed that younger children exhibited faster progression, and in the centile analysis, which revealed that the peak rate of progression occurred at age 7-8 and was lower at older ages. Myopia progression was also influenced by sex, with females exhibiting faster myopia progression. This is likely due to the age of the participants in this study, as sex



FIGURE 2 Annualised change of myopia for female and male patients, demonstrating faster progression in female patients across almost all ages and reducing progression with increasing age.



FIGURE 3 Centile analysis of annual change in refraction showing the annualised rate of change is age dependent, being faster at younger ages.

differences in myopia progression appear to be present at younger ages but are not present at older ages. It has previously been reported that myopia prevalence is higher at younger ages in females,⁵¹ indicating myopia progression is faster at younger ages in females. By adulthood, these differences were not apparent,⁵² implying that male myopes may catch up over time. The presenting level of myopia was also found to influence myopia progression, with greater progression observed in those with higher baseline myopia. This finding has been observed before but is not reported consistently in the literature. Baseline myopia has been observed to be a significant predictor of myopia progression in several control studies in various populations^{53–55} and some cohort studies.^{56,57} However, this relationship has not been observed in other control^{32,58} and cohort investigations.⁵⁹

The observed age-matched rate of progression was substantially lower in the EMR data relative to that found in Western clinical trials. It should be noted that two of the comparison RCTs^{33,36} required a minimum level of myopia progression, which may partially explain the high level of control group myopia progression in these studies; however, a re-analysis excluding these investigations made minimal difference to the overall control group median myopic progression (-0.50 vs. -0.49 D/year) and was still much worse than that observed in the EMR data (-0.35 D/year). The observation that real-world progression is

markedly slower on average in the EMR (-0.37 D per year in 6-16 years old) compared with previously reported pooled clinical trial data (-0.55 D per year in 6-16 years old)⁴⁸ is important and potentially relevant to the management of myopia in everyday practice. Data from myopia intervention trial control groups have been proposed as a source of reference growth data and have been deployed in several languages as freely accessible predictive online calculators for use in clinical practice (e.g., https://bhvi.org/ myopia-calculator-resources/). Clinical trial participants are not typically recruited in a population-representative manner, and myopia-control clinical trial participants are potentially biased and may not represent myopia progression patterns likely to be encountered in everyday practice. The finding that the BHVI calculator appears to underestimate myopia progression for those with higher levels of baseline myopia (Table 3) has previously been observed in other populations. Yang et al.⁶⁰ reported similar findings in a Chinese population, with the BHVI calculator tending to overestimate progression at lower SER and underestimate progression at higher SER, a finding that was inconsistent with the pattern observed in the clinical data. Collectively, the issues of restrictive inclusion criteria, small numbers of participants and biased 'self-selection' appear to limit the applicability of trial data to clinical practice.

There is increasing recognition that in Western countries, myopic progression extends beyond 16 years of

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FIGURE 4 Centile analysis of annual change in spherical equivalent refraction for female and male patients from age 7 to 17 years old.

age.⁶¹ This present study confirmed that finding, with 35% and 13% of 16–17 years old showing annualised progression of at least -0.25 and -0.50 D, respectively. Continued progression in this older age group has also been observed in other investigations. The COMET study, for example, reported a high prevalence of progressive myopia among older individuals, with 23% of 18 years old exhibiting myopia progression of at least -0.50 D/year.⁵⁰ The DREAM study observed that among participants 16-18 years of age, those above the 75th centile for myopia progression advanced at least -0.25 D/year.45 The collective findings from both the current and previous studies suggest that clinicians need to consider the implications of longer-term myopia progression in their clinical decision-making process regarding the need for and potential benefit of myopia management in individual patients. As noted above, a substantial number of participants of all ages with myopia did not progress at all. This non-progressor proportion increased from approximately 15% among 7-8 years old to 39% among 15–17 years old. Due to the costs and increased chair-time associated with myopia control treatments, identifying children who are unlikely to progress and thus do not need myopia control treatment is an important part of clinical myopia management. Our survival analysis indicates that a conservative approach with relatively short recall periods is required to detect all significant myopia

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progression in a timely manner. The proportion of children that experienced myopic progression increased as a function of the recall interval, but even at a 12-month interval, 25%-62% of children aged <12 years had myopia progression of <-0.50 D/year, compared to 14% of adolescents aged >13 years. Past myopic progression alone has not been found to correlate well with predicted future progression,⁶² so clinicians should consider the individual child and their specific risk factors in totality when determining the appropriate recall period. For those children prescribed a myopia control treatment, it may be expected that myopic progression will reduce; however, 6 monthly recalls may still be warranted to ensure continued progression is not taking place due to treatment non-compliance or ineffective treatments.

The ability to estimate reliably the expected refractive error progression of a presenting myopic or pre-myopic patient is valuable for clinical practitioners. The development of predictive analytic tools such as centile charts of refraction and axial eye growth could guide clinical decision-making, provide reference data to assess myopia control treatment efficacy and facilitate enhanced communication with patients. A number of cross-sectional data sources have been used to develop population centile curves of refraction and axial length, ^{63–65} and the practical application of such charts for monitoring eye growth and



FIGURE 5 European electronic medical record-derived myopic progression centiles versus 17 Western randomised clinical trial^{28–44} control group progression data and two Western clinic-based studies^{45,46} (Polling; blue solid line and Tricard; purple solid line). Black lines are data from the current study. All comparison studies reported mean progression rates, apart from Polling et al.⁴⁵ which reported median progression rates.

TABLE 3	Linear mixed models derived myopic progression for ages 10, 12 and 14 years and spherical equivalent refraction (SER) values of -1.00,
-2.00 and -3	3.00 compared with a predictive online myopia progression calculator.

Age (years)	Spherical Equivalent Refraction (D)	Predicted myopic progression (95% Cl) [D/year]	BHVI predicted progression (D/year)
10	-1.00	-0.27 (-0.51, -0.04)	-0.38
	-2.00	-0.48 (-0.66, -0.28)	-0.34
	-3.00	-0.59 (-0.78, -0.40)	-0.31
12	-1.00	-0.17 (-0.41, -0.07)	-0.30
	-2.00	-0.38 (-0.59, -0.17)	-0.27
	-3.00	-0.49 (-0.68, -0.29)	-0.24
14	-1.00	-0.09 (-0.33, +0.16)	-0.26
	-2.00	-0.29 (-0.51, -0.07)	-0.22
	-3.00	-0.40 (-0.60, -0.20)	-0.20

Abbreviations: BHVI, Brien Holden Vision Institute; D, Dioptres; D/year, dioptres per year.

refractive development in children with progressive myopia has been recently described.⁶⁶ Clinically relevant analyses of the rate of refractive change require more detailed longitudinal data sets for comparison. The current study is important, therefore, in the exploitation of an extensive database of longitudinal EMR refraction data to produce population progression centiles that chart the rate of change in refraction among untreated children. Given that the real-world applicability of EMR-sourced refraction data has also been demonstrated for the prediction of high myopia,²⁶ it would seem that, despite its limitations, EMR data can be exploited in ways that inform health policy and practice and can facilitate the evolution of the clinical management of myopia.

While myopia is almost exclusively managed by community optometrists in Ireland and spectacle coverage

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FIGURE 6 Kaplan-Meier survival curves demonstrating the probability of a myopic child not having myopic progression ranging from \geq -0.25 D/year to \geq -1.00 D/year over time for ages 7-17 years.

among myopic children is likely to be high due to reports of very high correction in children with refractive error,⁶⁷ it is possible that children with syndromic myopia or who experience barriers to accessing health care may be managed within secondary or tertiary care settings and are underrepresented in the current data set. A further limitation is that all the EMR data described derives from one country, which may potentially have lower myopia progression rates than those found in other Western countries. The Northern Ireland Childhood Errors of Refraction (NICER) longitudinal study did observe lower myopic progression in a Northern Irish setting. However, the number of myopic children with longitudinal data in that study was very small, thereby limiting the ability to draw conclusions about myopia progression in Ireland.¹⁵ The Myopia Outcome Study of Atropine in Children (MOSAIC)⁴³ and Childhood Atropine for Myopia Progression (CHAMP)⁴⁴ low-dose atropine trials did include Irish children, with the control groups in both studies demonstrating mean progression above the EMR-derived median centile. EMR data is open to criticism in relation to its lack of standardisation, its heterogeneity and the use of non-cycloplegic refraction among other limitations. However, such data are likely representative of myopia

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progression patterns observed in routine clinical practice and is, therefore, ecologically valid. The power of big data and machine learning tools is such that optometric EMR data may provide a valuable representation of myopia progression within a population, particularly in the absence of longitudinal population studies.

CONCLUSION

We used a large EMR data set to identify the age- and sexspecific range of myopia progression within an untreated population of Irish myopic children. This study produced progression centiles of untreated Irish myopic children, helping to define the natural history of untreated myopia. Younger age was the strongest factor associated with faster myopia progression, but females and children with higher myopia were also at higher risk of faster progression. Clinical trial control group data were not usefully representative of myopia progression in this clinical population, highlighting the need for real-world data when establishing population references. These references will enable clinicians to better predict refractive outcomes

	6 months				12 months				18 months				24 months			
Initial age (years)	<-0.25D/ year	<-0.50 D/ year	<-0.75 D/ year	<-1.00 D/ year	<-0.25D/ year	<-0.50 D/ year	<-0.75 D/ year	<-1.00 D/ year	<-0.25D/ year	<-0.50 D/ year	<-0.75 D/ year	<-1.00 D/ year	<-0.25 D/ year	<-0.50D/ year	<-0.75 D/ year	<-1.00D/ year
7	17	14	14	13	70	62	52	43	94	87	78	71	e	е	e	в
8	12	12	10	6	49	43	35	30	80	71	56	43	88	79	57	47
6	6	9	4	4	41	33	25	20	74	63	47	33	87	74	52	38
10	4	4	c	c	32	26	18	12	70	57	39	24	83	68	44	26
11	6	5	4	m	32	25	17	10	65	49	31	16	79	60	38	17
12	5	4	c	2	29	22	14	6	62	46	29	15	76	55	34	17
13	4	ε	m	2	24	16	10	7	53	35	20	10	70	44	24	12
14	c	n	2	2	21	14	8	5	49	32	14	7	64	39	18	8
15	2	2	1	1	17	10	6	4	40	23	12	9	55	31	14	a
16	2	2	2	-	10	7	4	e	27	15	7	4	42	21	10	4
17	ŝ	2	2	2	14	6	5	S	29	17	6	4	40	20	6	5
Abbreviation:	D/year, diopt	res per year.														

without treatment and to monitor treatment efficacy, particularly in the absence of axial length data.

AUTHOR CONTRIBUTIONS

Michael Moore: Conceptualization (equal); data curation (equal); formal analysis (equal); investigation (equal); methodology (equal); visualization (lead); writing – original draft (lead). **Gareth Lingham:** Conceptualization (equal); data curation (equal); formal analysis (equal); investigation (equal); methodology (equal); visualization (supporting); writing – review and editing (equal). **Daniel I. Flitcroft:** Conceptualization (equal); formal analysis (supporting); investigation (supporting); methodology (supporting); project administration (equal); visualization (supporting); writing – review and editing (equal). **James Loughman:** Conceptualization (supporting); methodology (supporting); investigation (supporting); methodology (supporting); writing – review and editing (equal). **James Loughman:** Conceptualization (lead); visualization (supporting); writing – review and editing (equal).

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'No data available.

CONFLICT OF INTEREST STATEMENT

MM has a consultancy relationship with Alcon Eye Care. GL is employed by Ocumetra in the field of myopia management. DIF has received research grant funding support from the Health Research Board (Ireland), Vyluma, Dopavision, Ocumension and CooperVision; has consultancy or other relationships with Dopavision, Essilor, Johnson & Johnson, Thea Pharmaceuticals and Vivior; has received equipment on loan from Topcon, Ocumension and CooperVision; has two patents pending (one in myopia management data analytics and one in biomonitoring for low-dose atropine treatment in myopia); and is Founding Director of Ocumetra, all in the field of myopia management. JL has received research grant funding support from the Health Research Board (Ireland), Vyluma, Topcon, Dopavision, Ocumension and CooperVision; has consultancy relationships with Dopavision, Ocuco, Topcon and Ebiga Vision; has received honoraria from Thea Pharmaceuticals and Ocuco for lectures; has received equipment on loan from Topcon, Ocumension and CooperVision; has two patents pending (one in myopia management data analytics and one in biomonitoring for low-dose atropine treatment in myopia); and is Founding Director of Ocumetra, all in the field of myopia management.

DATA AVAILABILITY STATEMENT

The data from this study are available on request. The TU Dublin Research and Ethics Committee has placed restrictions on disseminating this data. Data access requests can be sent to researchethics@tudublin.ie, quoting ethics approval REC-18-124.

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THE COLLEGE OF

PATIENT CONSENT

Patient-level consent was not required due to the nature of the anonymisation of the data.

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REFERENCES

- 1. Foster PJ, Jiang Y. Epidemiology of myopia. Eye. 2014;28:202-8.
- Holden B, Sankaridurg P, Smith E, Aller T, Jong M, He M. Myopia, an underrated global challenge to vision: where the current data takes us on myopia control. *Eye.* 2014;28:142–6.
- Holden BA, Fricke TR, Wilson DA, Jong M, Naidoo KS, Sankaridurg P, et al. Global prevalence of myopia and high myopia and temporal trends from 2000 through 2050. *Ophthalmology*. 2016;123:1036–42.
- Pan CW, Dirani M, Cheng CY, Wong TY, Saw SM. The age-specific prevalence of myopia in Asia: a meta-analysis. *Optom Vis Sci.* 2015;92:258–66.
- Pan CW, Ramamurthy D, Saw SM. Worldwide prevalence and risk factors for myopia: prevalence and risk factors for myopia. *Ophthalmic Physiol Opt*. 2012;32:3–16.
- Ding BY, Shih YF, Lin LLK, Hsiao CK, Wang IJ. Myopia among schoolchildren in East Asia and Singapore. Surv Ophthalmol. 2017;62:677–97.
- 7. Vitale S. Increased prevalence of myopia in the United States between 1971–1972 and 1999–2004. *Arch Ophthalmol*. 2009;127:1632–9.
- Wolfram C, Höhn R, Kottler U, Wild P, Blettner M, Bühren J, et al. Prevalence of refractive errors in the European adult population: the Gutenberg Health Study (GHS). *BrJ Ophthalmol*. 2014;98:857–61.
- 9. Tsai TH, Liu YL, Ma IH, Su CC, Lin CW, Lin LLK, et al. Evolution of the prevalence of myopia among Taiwanese schoolchildren. *Ophthalmology*. 2021;128:290–301.
- 10. Sankaridurg PR, Holden BA. Practical applications to modify and control the development of ametropia. *Eye*. 2014;28:134–41.
- 11. Bullimore MA, Brennan NA. Myopia control: why each diopter matters. *Optom Vis Sci.* 2019;96:463–5.
- 12. Fricke TR, Jong M, Naidoo KS, Sankaridurg P, Naduvilath TJ, Ho SM, et al. Global prevalence of visual impairment associated with myopic macular degeneration and temporal trends from 2000 through 2050: systematic review, meta-analysis and modelling. *Br J Ophthalmol.* 2018;102:855–62.
- Sankaridurg P, Berntsen DA, Bullimore MA, Cho P, Flitcroft I, Gawne TJ, et al. IMI 2023 digest. *Invest Ophthalmol Vis Sci.* 2023;64:ARVO E-Abstract 7.
- 14. Yam JC, Zhang XJ, Zhang Y, Yip BHK, Tang F, Wong ES, et al. Effect of low-concentration atropine eyedrops vs placebo on myopia incidence in children: the LAMP2 randomized clinical trial. *JAMA*. 2023;329:472–81.
- McCullough SJ, O'Donoghue L, Saunders KJ. Six year refractive change among white children and young adults: evidence for significant increase in myopia among white UK children. *PLoS One*. 2016;11:e0146332. https://doi.org/10.1371/journal.pone.0146332
- French AN, Morgan IG, Burlutsky G, Mitchell P, Rose KA. Prevalence and 5- to 6-year incidence and progression of myopia and hyperopia in Australian schoolchildren. *Ophthalmology*. 2013;120:1482–91.
- 17. Mutti DO, Hayes JR, Mitchell GL, Jones LA, Moeschberger ML, Cotter SA, et al. Refractive error, axial length, and relative peripheral refractive error before and after the onset of myopia. *Invest Ophthalmol Vis Sci.* 2007;48:2510–9.
- 18. Tideman JWL, Polling JR, Jaddoe VWV, Vingerling JR, Klaver CCW. Environmental risk factors can reduce axial length elongation and

myopia incidence in 6- to 9-year-old children. Ophthalmology. 2019;126:127–36.

- Moore M, Loughman J, Butler JS, Ohlendorf A, Wahl S, Flitcroft DI. Application of big-data for epidemiological studies of refractive error. *PLoS One*. 2021;16:e0250468. https://doi.org/10.1371/journal. pone.0250468
- 20. Yang L, Vass C, Smith L, Juan A, Waldhör T. Thirty-five-year trend in the prevalence of refractive error in Austrian conscripts based on 1.5 million participants. *Br J Ophthalmol*. 2020;104:1338–44.
- Leveziel N, Marillet S, Dufour Q, Lichtwitz O, Bentaleb Y, Pelen F, et al. Prevalence of macular complications related to myopia—results of a multicenter evaluation of myopic patients in eye clinics in France. *Acta Ophthalmol*. 2020;98:e245–51.
- Waudby CJ, Berg RL, Linneman JG, Rasmussen LV, Peissig PL, Chen L, et al. Cataract research using electronic health records. *BMC Ophthalmol*. 2011;11:32. https://doi.org/10.1186/1471-2415-11-32
- Swenor BK, Guo X, Boland MV, Goldstein JE. Leveraging electronic health records to identify and characterize patients with low vision. *Ophthalmic Epidemiol*. 2019;26:132–9.
- Donthineni PR, Kammari P, Shanbhag SS, Singh V, Das AV, Basu S. Incidence, demographics, types and risk factors of dry eye disease in India: electronic medical records driven big data analytics report I. Ocul Surf. 2019;17:250–6.
- Shen L, Melles RB, Metlapally R, Barcellos L, Schaefer C, Risch N, et al. The association of refractive error with glaucoma in a multiethnic population. *Ophthalmology*. 2016;123:92–101.
- Lin H, Long E, Ding X, Diao H, Chen Z, Liu R, et al. Prediction of myopia development among Chinese school-aged children using refraction data from electronic medical records: a retrospective, multicentre machine learning study. *PLoS Med.* 2018;15:e1002674. https://doi.org/10.1371/journal.pmed.1002674
- Flitcroft DI, He M, Jonas JB, Jong M, Naidoo K, Ohno-Matsui K, et al. IMI—defining and classifying myopia: a proposed set of standards for clinical and epidemiologic studies. *Invest Opthalmol Vis Sci.* 2019;60:M20–30.
- 28. Walline JJ. A randomized trial of the effects of rigid contact lenses on myopia progression. *Arch Ophthalmol*. 2004;122:1760–6.
- Walline JJ, Jones LA, Sinnott L, Manny RE, Gaume A, Rah MJ, et al. A randomized trial of the effect of soft contact lenses on myopia progression in children. *Invest Opthalmol Vis Sci.* 2008;49:ARVO E-Abstract 4702.
- Siatkowski RM, Cotter SA, Crockett RS, Miller JM, Novack GD, Zadnik K. Two-year multicenter, randomized, double-masked, placebocontrolled, parallel safety and efficacy study of 2% pirenzepine ophthalmic gel in children with myopia. J AAPOS. 2008;12:332–9.
- Fulk GW, Cyert LA, Parker DE. A randomized trial of the effect of single-vision vs. bifocal lenses on myopia progression in children with esophoria. *Optom Vis Sci.* 2000;77:395–401.
- Chamberlain P, Peixoto-de-Matos SC, Logan NS, Ngo C, Jones D, Young G. A 3-year randomized clinical trial of MiSight lenses for myopia control. *Optom Vis Sci.* 2019;96:556–67.
- Aller TA, Liu M, Wildsoet CF. Myopia control with bifocal contact lenses: a randomized clinical trial. Optom Vis Sci. 2016;93:344–52.
- Adler D, Millodot M. The possible effect of undercorrection on myopic progression in children. *Clin Exp Optom*. 2006;89:315–21.
- 35. Walline JJ, Greiner KL, McVey ME, Jones-Jordan LA. Multifocal contact lens myopia control. *Optom Vis Sci*. 2013;90:1207–14.
- Anstice NS, Phillips JR. Effect of dual-focus soft contact lens wear on axial myopia progression in children. *Ophthalmology*. 2011;118:1152–61.
- Walline JJ, Walker MK, Mutti DO, Jones-Jordan LA, Sinnott LT, Giannoni AG, et al. Effect of high add power, medium add power, or single-vision contact lenses on myopia progression in children: the BLINK randomized clinical trial. JAMA. 2020;324:571–80.
- Berntsen DA, Sinnott LT, Mutti DO, Zadnik K. A randomized trial using progressive addition lenses to evaluate theories of myopia progression in children with a high lag of accommodation. *Invest Ophthalmol Vis Sci.* 2012;53:640–9.

- Gwiazda J, Hyman L, Hussein M, Everett D, Norton TT, Kurtz D, et al. A randomized clinical trial of progressive addition lenses versus single vision lenses on the progression of myopia in children. *Invest Ophthalmol Vis Sci.* 2003;44:1492–500.
- Parssinen O, Hemminki E, Klemetti A. Effect of spectacle use and accommodation on myopic progression: final results of a three-year randomised clinical trial among schoolchildren. *Br J Ophthalmol.* 1989;73:547–51.
- Ruiz-Pomeda A, Pérez-Sánchez B, Valls I, Prieto-Garrido FL, Gutiérrez-Ortega R, Villa-Collar C, et al. A 2-year randomized clinical trial. *Graefes Arch Clin Exp Ophthalmol.* 2018;256:1011–21.
- Garcia-del valle AM, Blázquez V, Gros-Otero J, Infante M, Culebras A, Verdejo A, et al. Efficacy and safety of a soft contact lens to control myopia progression. *Clin Exp Optom.* 2021;104:14–21.
- Loughman J, Kobia-Acquah E, Lingham G, Butler J, Loskutova E, Mackey DA, et al. Myopia outcome study of atropine in children: two-year result of daily 0.01% atropine in a European population. *Acta Ophthalmol.* 2023. https://doi.org/10.1111/aos.15761
- 44. Zadnik K, Schulman E, Flitcroft I, Fogt JS, Blumenfeld LC, Fong TM, et al. Efficacy and safety of 0.01% and 0.02% atropine for the treatment of pediatric myopia progression over 3 years: a randomized clinical trial. JAMA Ophthalmol. 2023;141:990–9.
- 45. Polling JR, Klaver C, Tideman JW. Myopia progression from wearing first glasses to adult age: the DREAM Study. *Br J Ophthalmol.* 2022;106:820–4.
- Tricard D, Marillet S, Ingrand P, Bullimore MA, Bourne RRA, Leveziel N. Progression of myopia in children and teenagers: a nationwide longitudinal study. *Br J Ophthalmol*. 2021;106:1104–9.
- 47. Longwill S, Moore M, Flitcroft DI, Loughman J. Using electronic medical record data to establish and monitor the distribution of refractive errors. *J Optom*. 2022;15:S32–42.
- Donovan L, Sankaridurg P, Ho A, Naduvilath T, Smith EL, Holden BA. Myopia progression rates in urban children wearing single-vision spectacles. *Optom Vis Sci.* 2012;89:27–32.
- 49. Pärssinen O, Da SZ, Tan CS, Lanca C, Kauppinen M, Saw SM. Comparison of myopic progression in Finnish and Singaporean children. *Acta Ophthalmol*. 2020;99:171–80.
- 50. Hyman L. Myopia stabilization and associated factors among participants in the correction of myopia evaluation trial (COMET). *Invest Ophthalmol Vis Sci.* 2013;54:7871–83.
- Rudnicka AR, Kapetanakis VV, Wathern AK, Logan NS, Gilmartin B, Whincup PH, et al. Global variations and time trends in the prevalence of childhood myopia, a systematic review and quantitative meta-analysis: implications for aetiology and early prevention. Br J Ophthalmol. 2016;100:882–90.
- Williams KM, Verhoeven VJM, Cumberland P, Bertelsen G, Wolfram C, Buitendijk GHS, et al. Prevalence of refractive error in Europe: the European Eye Epidemiology (E3) Consortium. *Eur J Epidemiol.* 2015;30:305–15.
- 53. Pärssinen O, Lyyra AL. Myopia and myopic progression among schoolchildren: a three-year follow-up study. *Invest Ophthalmol Vis Sci.* 1993;34:2794–802.
- 54. Wu PC, Yang YH, Fang PC. The long-term results of using lowconcentration atropine eye drops for controlling myopia progression in schoolchildren. *J Ocul Pharmacol Ther.* 2011;27:461–6.

- Loh KL, Lu Q, Tan D, Chia A. Risk factors for progressive myopia in the atropine therapy for myopia study. Am J Ophthalmol. 2015;159:945–9.
- Verkicharla PK, Kammari P, Das AV. Myopia progression varies with age and severity of myopia. *PLoS One*. 2020;15:e0241759. https://doi. org/10.1371/journal.pone.0241759
- 57. Saw SM, Nieto FJ, Katz J, Schein OD, Levy B, Chew SJ. Factors related to the progression of myopia in Singaporean children. *Optom Vis Sci.* 2000;77:549–54.
- Lam CSY, Tang WC, Tse DY, Lee RPK, Chun RKM, Hasegawa K, et al. Defocus Incorporated Multiple Segments (DIMS) spectacle lenses slow myopia progression: a 2-year randomised clinical trial. Br J Ophthalmol. 2020;104:363–8.
- Jones LA, Sinnott LT, Mutti DO, Mitchell GL, Moeschberger ML, Zadnik K. Parental history of myopia, sports and outdoor activities, and future myopia. *Invest Opthalmol Vis Sci.* 2007;48:3524–32.
- Yang Y, Cheung SW, Cho P, Vincent SJ. Comparison between estimated and measured myopia progression in Hong Kong children without myopia control intervention. *Ophthalmic Physiol Opt.* 2021;41:1363–70.
- 61. Bullimore MA, Lee SSY, Schmid KL, Rozema JJ, Leveziel N, Mallen EAH, et al. IMI—onset and progression of myopia in young adults. *Invest Ophthalmol Vis Sci.* 2023;64:ARVO E-Abstract 2.
- Mutti DO, Sinnott LT, Brennan NA, Cheng X, Zadnik K. The limited value of prior change in predicting future progression of juvenileonset myopia. *Optom Vis Sci.* 2022;99:424–33.
- Tideman JWL, Polling JR, Vingerling JR, Jaddoe VWV, Williams C, Guggenheim JA, et al. Axial length growth and the risk of developing myopia in European children. *Acta Ophthalmol.* 2018;96:301–9.
- 64. Sanz Diez P, Yang LH, Lu MX, Wahl S, Ohlendorf A. Growth curves of myopia-related parameters to clinically monitor the refractive development in Chinese schoolchildren. *Graefes Arch Clin Exp Ophthalmol.* 2019;257:1045–53.
- Chen Y, Zhang J, Morgan IG, He M. Identifying children at risk of high myopia using population centile curves of refraction. *PLoS One*. 2016;11:e0167642. https://doi.org/10.1371/journal.pone.0167642
- Klaver C, Polling JR, Erasmus Myopia Research Group. Myopia management in The Netherlands. Ophthalmic Physiol Opt. 2020;40:230–40.
- Harrington SC, Stack J, Saunders K, O'Dwyer V. Refractive error and visual impairment in Ireland schoolchildren. *Br J Ophthalmol.* 2019;103:1112–8.

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