Myopia in school-aged children with preterm birth: the roles of time spent outdoors and serum vitamin D

Hung-Da Chou ,[1,2] Tsung-Chieh Yao,[2,3] Yu-Shu Huang,[2,4] Chung-Ying Huang,[1,2] Men-Ling Yang,[1,2] Ming-Hui Sun,[1,2] Hung-Chi Chen,[1,2] Chun-Hsiu Liu ,[1,2] Shih-Ming Chu,[2,3] Jen-Fu Hsu,[2,3] Kuan-Jen Chen,[1,2] Yih-Shiou Hwang,[1,2] Chi-Chun Lai,[1,2] Wei-Chi Wu [1,2]

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[1]Department of Ophthalmology, Chang Gung Memorial Hospital, Linkou Medical Center, Taoyuan, Taiwan
[2]College of Medicine, Chang Gung University, Taoyuan, Taiwan
[3]Department of Pediatrics, Chang Gung Memorial Hospital, Linkou Medical Center, Taoyuan, Taiwan
[4]Department of Child Psychiatry and Sleep Center, Chang Gung Memorial Hospital, Linkou Medical Center, Taoyuan, Taiwan

Correspondence to
Professor Wei-Chi Wu, Department of Ophthalmology, Chang Gung Memorial Hospital, Linkou, No. 5 Fu-Hsing Street, Kwei-Shan 333, Taoyuan, Taiwan; weichi666@gmail.com

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ABSTRACT

Aims To analyse the factors associated with myopia in school-aged children with preterm birth and with or without retinopathy of prematurity (ROP).

Methods Children born prematurely between January 2010 and December 2011 were enrolled in this cross-sectional study when they reached school age between April 2017 and June 2018 in a referral centre. The main parameters were cycloplegic refraction, time spent outdoors and serum 25-hydroxyvitamin D (25(OH)D) concentration.

Results A total of 99 eyes from 99 children with a mean age of 6.8 years underwent analysis. The average time spent outdoors was significantly higher in the non-myopic group (0.9 ± 0.5 hours/day) than in the myopic group (0.7 ± 0.3 hours/day) ($p = 0.032$). After adjustment for age, sex, number of myopic parents, ROP severity, near-work time and serum 25(OH)D concentration, more time spent outdoors was correlated with a lower odds of myopia (OR, 0.13 per additional hour per day; 95% CI, 0.02–0.98; $p = 0.048$). Mean serum 25(OH)D concentrations were similar between the myopic and non-myopic groups (49.7 ± 13.6 and 48.8 ± 14.0 nmol/mL; $p = 0.806$) and were not correlated with spherical equivalence power ($r = -0.09$; $p = 0.418$). Vitamin D insufficiency was present in 57% of the participants.

Conclusions Among preterm children with or without ROP, more time spent outdoors was associated with lower odds of myopia. The serum 25(OH)D concentration was not associated with myopia, but a high proportion of the participants had insufficient levels.

INTRODUCTION

Myopia can lead to various complications and it is among the most common reasons for acquired blindness in developed East Asian countries.[1] It is a multifactorial disease that is substantially affected by an individual's social environment.[2] Genetic factors and parental myopia status have also been linked to the refractive error of their children.[3]

In recent years, increased time spent outdoors has been consistently reported to have a protective effect against incident myopia.[4–6] On the other hand, time spent performing near-work activities has also been proposed to be associated with myopia, as has the combination of the two, with near-work time neutralising the effect of time spent outdoors.[7 8]

Two major hypotheses have been proposed to explain the link between outdoor time and myopia. The first hypothesis is focused on dopamine that is released in the retina in response to exposure to bright light.[9] The second one is focused on vitamin D that is synthesised in the skin during sun exposure. As a main biomarker of vitamin D status, lower serum 25-hydroxyvitamin D (25(OH)D) levels are related to a higher prevalence of myopia.[10 11]

However, the above investigations in factors related to myopia have focused on the general population and not on preterm infants. Children with premature birth, especially those with lower birth weights, have a higher risk of developing myopia and retinopathy of prematurity (ROP).[12 13] ROP itself is an important risk factor associated with myopia, and increased severity of ROP is associated with an increased incidence and degree of myopia.[13 14] In addition, studies have demonstrated that infants born at a lower gestational age have a greater risk of vitamin D deficiency compared with more mature infants.[15] However, whether these individuals will have vitamin D deficiency later in life and whether this condition is associated with myopia remain unreported.

Another difference between preterm and full-term eyes was demonstrated in the previous studies that showed that in the preterm children changes in the anterior segment play more role in the development of myopia.[16] However, to more accurately evaluate the structural changes that occur in preterm myopic children, direct comparisons between preterm myopic and non-myopic eyes should be performed. The purpose of this study is to explore the factors associated with myopia in the preterm population and to analyse the structural differences between preterm myopic and non-myopic eyes.

METHODS

Study design and participants

This prospective, cross-sectional study was conducted in Chang Gung Memorial Hospital, Linkou, Taiwan. Written informed consent was obtained from parents for the enrolment of their child in the study.

Children born prematurely between January 2010 and December 2011 were invited to participate in the study when they reached school age between April 2017 and June 2018. Prematurity was defined as birth at less than 37 weeks' gestation.

Children who had aggressive posterior ROP, received vitrectomy for severe ROP, or had other non-ROP-related ocular diseases or conditions that precluded a thorough ocular examination were excluded.

Demographic features, ROP conditions and treatments were gathered from medical records. The indication for ROP treatment was type 1 ROP, as defined by the Early Treatment for Retinopathy of Prematurity Study.[17] Treatment methods included primary intravitreal injection with 0.625 mg of bevacizumab (Avastin; Genentech, San Francisco, California) via the pars plicata or near-confluent 810 nm diode laser photocoagulation performed on the entire area of the avascular retina. Both methods were thoroughly explained to the parents who selected the method to be used. If there was a recurrence of ROP or a lack of treatment response following intravitreal injection of bevacizumab (IVB), the patient was offered additional laser treatment to stop the progression (and vice versa).

Ocular examinations

Myopia was defined as ≤−0.5 dioptres (D) of spherical equivalence (SE) on cycloplegic autorefraction. Before examination, 1 drop of 0.5% proparacaine hydrochloride (Alcaine; Alcon, Puurs, Belgium) was followed by 1 drop of 1% tropicamide (Mydriacyl; Alcon) instilled every 10 min for three times. At more than 30 min after the first drop instillation, the measurements were obtained.[18] Uncorrected distance visual acuity (UCVA) and best-corrected visual acuity (BCVA) were evaluated with a Landolt C-chart at 6 m, and the result was converted into the logarithm of the minimum angle of resolution for statistical analysis. Amblyopia was defined as a BCVA worse than 20/25 in at least one eye after the exclusion of other explanations, such as media opacity or inattention during examination. Strabismus, including phorias and tropias, was evaluated in the clinic using the cover test. Cycloplegic autorefractions and keratometry were measured by an automatic kerato-refractometer (KR-8100; Topcon, Tokyo, Japan). Ocular biometry was measured with an optical coherence biometer (IOL Master; Carl Zeiss, Jena, Germany). For each participant, only the eye with the lower SE was chosen for analysis.

Serum 25(OH)D concentration

Non-fasting blood samples were collected and centrifuged, and serum sample aliquots were stored frozen at −80°C until analysis by an automated electrochemiluminescence-based assay (Elecsys Vitamin D Total Assay, Roche Diagnostics, Mannheim, Germany) in the central laboratory of our institution. The laboratory undergoes annual proficiency testing by the College of American Pathologists and passed the 2016–2018 tests. The participants were categorised as optimal (51–249 nmol/L), insufficient (30–50 nmol/L) or deficient (<30 nmol/L) according to a published global consensus[19] and into tertiles.

Time spent outdoors, near-work time, and television time

The parents completed a questionnaire and provided information, including parental myopia status and educational levels. Educational levels were converted into years of education for calculation. The time that the children spent outdoors was determined by the following question: 'In a typical week during the past 6 months, what was the average amount of time your child spent outdoors per day? (<30 min; 0.5–1, 1–2, 2–4 or >4 hours)'. The above checkboxes were converted to 30 min, 45 min, 1.5 hours, 3 hours and 4 hours, respectively, for statistical analysis. The parents were also asked to estimate the average time per day that their child spent on near-work activities and watching television.

Statistical analysis

Variables were compared between myopic and non-myopic children using either a t-test for continuous variables or Fisher's exact test for categorical variables. The relationships between continuous variables were assessed by Pearson's correlation. A multivariable logistic regression model was used to assess the factors associated with the risk of myopia. Established risk factors of myopia in children[3] and variables of primary interest, including time spent outdoors, serum 25(OH)D concentration and ROP severity, were introduced into the model with adjustment for age and gender. Possible risk factors of myopia (gestational age, birth weight and ROP treatment) were not included in the primary model because these variables are highly correlated with ROP severity and not suitable to analyse simultaneously.[20] Thus, we constructed alternative models in which ROP severity was replaced by the above variables. All statistical analyses were performed using a commercial software (SPSS V.25; IBM). A two-sided p value <0.05 was considered statistically significant, and no adjustment for multiplicity was conducted in this study.

RESULTS

One hundred and three preterm children were initially recruited during the study period. Four children received vitrectomy and were excluded, and the remaining 99 children with a mean age of 6.8 years were included in the final analysis. According to the presence of myopia, the participants were divided into a myopic group (n = 23) and a non-myopic group (n = 76) (table 1). Sex and the mean age, body mass index, number of myopic parents, parental years of education, gestational age and birth weight were not significantly different between the two groups. The prevalence of ROP was higher in the myopic group than in the non-myopic group (60.9% vs 40.8%), but this relationship was not significant (p = 0.055). The distribution of ROP severity between the two groups did not differ significantly. Among the participants with ROP requiring treatment, the results showed that 75% of myopic children were treated with laser or laser + IVB, whereas 65.4% of the non-myopic children were treated with IVB only (p = 0.035).

Ocular functional and structural characteristics

Both UCVA and BCVA were significantly worse in the myopic group, and more children in this group had amblyopia (31.8%, compared with 11.9% in the non-myopic group; p = 0.047) (table 2). Regarding the refraction results, both the mean spherical and cylindrical refractive powers were of a higher magnitude in the myopic group (both p <0.001). The mean keratometrical cylinder power was also significantly higher in the myopic group (p = 0.013).

Regarding other structural dimensions, the mean corneal size and the anterior chamber depth (ACD) were similar between the two groups. However, when comparing the myopic and non-myopic groups, the mean axial length (AL) was longer in the former (23.0 ± 1.0 mm vs 22.2 ± 0.9 mm; p <0.001), indicating that the elongation of the globe played a role in the development of myopia in preterm children (online supplementary figure 1).

Correlation of myopia and serum 25(OH)D concentrations

We analysed the correlations between serum 25(OH)D concentrations, myopia severity and risk and the average time spent outdoors. Univariate analysis showed that serum 25(OH)

Table 1 Clinical features of preterm children according to the presence of myopia

Variables	Myopic group (n=23)	Non-myopic group (n=76)	*P* value*
Age, mean (SD), year	6.9 (0.6)	6.8 (0.7)	0.284
Male, No. (%)	12 (52)	41 (53)	1.000
Body mass index† (n=91), mean (SD)	14.9 (1.1)	15.3 (2.1)	0.421
Gestational age, mean (SD), week	29.1 (4.3)	30.9 (4.4)	0.104
Birth weight, mean (SD), g	1270 (647)	1545 (759)	0.118
ROP severity, No. (%)			
Preterm without ROP	9 (39)	45 (59)	0.196
Mild/type 2 ROP	2 (9)	5 (7)	
Type 1 ROP	12 (52)	26 (34)	
ROP with treatment, No./total (%)	12/23 (52)	26/76 (34)	1.000
ROP treatment method, No. (%)			
IVB only	3 (25)	17 (65)	0.035
Laser only/laser + IVB	9 (75)	9 (35)	
No. of myopic parents (n=94), No./total (%)			
0	2/21 (10)	9/73 (12)	0.935
1	5/21 (24)	20/73 (27)	
2	14/21 (67)	44/73 (60)	
Parental years of education (n=94), mean (SD)	16.0 (1.9)	15.8 (2.1)	0.647
Time spent outdoors (n=92), mean (SD), hour/day	0.7 (0.3)	0.9 (0.5)	0.032
Time spent on near-work activities (n=93), mean (SD), hour/day	2.7 (2.3)	2.5 (1.8)	0.708
Television time (n=76), mean (SD), hour/day	0.4 (0.4)	0.5 (0.5)	0.468

*Compared by t-test or Fisher's exact test.
†Calculated as weight in kilograms divided by height in metres squared.
IVB, intravitreal injection; ROP, retinopathy of prematurity.

D concentrations were similar between the myopic (49.7 ± 13.6 nmol/L) and non-myopic (48.8 ± 14 nmol/L) groups (p = 0.806) (table 3) and were not correlated with SE in the whole group (r = −0.09; p = 0.418) or in the myopic subgroup (r = −0.19; p = 0.435), or with the average time spent outdoors in the whole group (p trend = 0.473) or in the myopic subgroup (p trend = 0.836) (online supplementary figure 2). A multivariable linear regression model also showed that none of the above factors were associated with the serum 25(OH)D concentration (online supplementary table 1). An interesting finding was that the prevalence of vitamin D insufficiency was as high as 56.8% in these premature children, with an insufficient mean concentration at 48.8 ± 13.8 nmol/L.

Correlation of myopia with time spent outdoors and on near-work activities

The average time the children spent outdoors was significantly higher in the non-myopic group (0.9 ± 0.5 hours/day) than in the myopic group (0.7 ± 0.3 hours/day) (p = 0.032) (table 1). After adjustment, the multivariable logistic regression analysis revealed that more time spent outdoors was associated with lower odds of myopia (OR, 0.13; 95% CI, 0.02–0.98; p = 0.048) (table 4). The effect of time spent outdoors was still observed in the alternative models (online supplementary table 2).

The average time spent on near-work activities was not different between the myopic and non-myopic groups (table 1). The time spent watching television, which was categorised as a mid-distance viewing activity, was also similar between the two groups.

Correlation between myopia and ROP

Although there were no differences in the distributions of ROP severity and other ROP features, including stage, zone and plus disease, between the myopic and non-myopic groups in the univariate analysis, type 1 ROP was associated with increased odds of myopia (OR, 3.82; 95% CI, 1.14–12.81; p = 0.03) (table 4).

DISCUSSION

In this study, we focused on school-aged preterm children and found that spending more time outdoors was associated with a lower prevalence of myopia in both univariate and multivariate analyses. Conversely, type 1 ROP was related to a higher risk of myopia. The myopic preterm children had significantly longer ALs than those found in the non-myopic preterm children. The serum 25(OH)D level, which is a biomarker of vitamin D status, was not related to myopia but was insufficient in over half of the study population.

The onset and progression of myopia occurs primarily during the preschool or school years. After reaching emmetropia, if the AL continues to increase without coordinated changes in the other ocular components, the eye will shift away from emmetropia and towards myopia.[3] The regulation of axial elongation is thus the main focus of controlling and preventing myopia.[3]

Compared with full-term children, preterm children have been reported to show different growth mechanisms. In a study by Yang *et al*[21] and our prior study,[16] the authors explored refractive and structural outcomes in treated ROP children evaluated at a mean age of 9–10 years. These eyes with ROP were noted to have shallower ACDs, thicker lenses and steeper corneas. Interestingly, their ALs were similar to those of full-term children. These results led to the conclusion that the development of myopia in preterm infants is related to the changes that occur

Table 2 Functional and structural characteristics of the eyes of the myopic and non-myopic preterm children

Variables	Myopic group (n=23)	Non-myopic group (n=76)	*P* value*
UDVA (n=92), mean (SD), logMAR	0.6 (0.5)	0.1 (0.2)	<0.001
BCVA (n=87), mean (SD), logMAR	0.06 (0.11)	0.01 (0.05)	0.013
Strabismus, No. (%)	4 (17)	4 (5)	0.082
Amblyopia, No. (%)	7 (31.8)	8 (11.9)	0.047
SE, mean (SD), D	−3.2 (3.5)	0.8 (0.8)	<0.001
Spherical power (n=95), mean (SD), D	−2.2 (3.5)	1.3 (1.0)	<0.001
Cylindrical power (n=95), mean (SD), D	−1.9 (1.2)	−0.9 (0.8)	<0.001
Keratometry (n=94), mean (SD), D			
K1 horizontal	43.7 (2.1)	43.5 (1.7)	0.702
K2 vertical	45.6 (1.7)	44.7 (2.2)	0.095
K1–K2 average	−1.9 (1.3)	−1.4 (0.7)	0.013
Corneal size† (n=26), mean (SD), mm	11.8 (0.4)	11.9 (0.4)	0.535
Axial length (n=92), mean (SD), mm	23.0 (1.0)	22.2 (0.9)	<0.001
ACD (n=85), mean (SD), mm	3.2 (0.3)	3.1 (0.3)	0.052

*Compared by t-test or Fisher's exact test.
†Measured by corneal white-to-white distance.
ACD, anterior chamber depth; BCVA, best-corrected visual acuity; D, diopters; logMAR, logarithm of the minimum angle of resolution; SE, spherical equivalence; UDVA, uncorrected distant visual acuity.

Table 3 Serum 25(OH)D concentration in all participants, myopic and non-myopic groups*

Variables	All participants	Myopic group	Non-myopic group	P value†
Serum 25(OH)D concentration (nmol/L), mean (SD)	49.0 (13.8)	49.7 (13.6)	48.8 (14.0)	0.806
Serum 25(OH)D status, No. (%)				
Deficient (<30 nmol/L)	5 (6)	2 (10)	3 (4)	0.182
Insufficient (30–50 nmol/L)	45 (51)	7 (35)	38 (56)	
Optimal (51–249 nmol/L)	38 (43)	11 (55)	27 (40)	
Serum 25(OH)D, tertile, No. (%)				
First tertile	36 (41)	7 (35)	29 (43)	0.767
Second tertile	29 (33)	8 (40)	21 (31)	
Third tertile	23 (26)	5 (25)	18 (27)	

*The valid sample size was 88 (20 in the myopic group and 68 in the non-myopic group).
†Compared by t-test or Fisher's exact test.
25(OH)D, 25-hydroxyvitamin D.

in the anterior segment and not to the elongation of the AL, indicating a different mechanism than that observed in full-term infants.

However, the baseline dimensions of preterm and full-term infants are different. Cook *et al*[22] reported that at 52 weeks' postmenstrual age, compared with full-term infants, preterm infants without ROP had shorter ALs, shallower ACDs and steeper corneas. In this study, we directly compared the optical components between preterm myopic and non-myopic eyes and found that myopic preterm children had significantly longer ALs than non-myopic preterm children. This observation is in accordance with the findings of other investigators[23] and implies that in preterm eyes, elongation of the AL is still an important factor in the development of myopia. Thus, when attempting to control myopia, similar measures might be beneficial for both preterm and full-term eyes. The reason that prior investigations found that AL was similar between preterm and full-term eyes was likely the high prevalence of myopia in preterm subjects, which caused the AL to be longer in preterm subjects than in their non-myopic preterm peers and thus was similar to that of emmetropic full-term children.

Apart from increasing outdoor activities, atropine drops have also been demonstrated to be useful in slowing the progression of myopia.[24] However, adverse effects are not uncommon and might cause complications in susceptible eyes. For example, acute-angle closure glaucoma attacks were reported in infants with ROP.[25] These attacks were also reported in ROP patients later in life, with one attack directly following pupillary dilatation during a routine clinical examination.[26] Our recent report[27] demonstrated that ROP eyes have a crowded anterior chamber angle, which might predispose these eyes to angle-closure glaucoma. Due to these potential side effects of atropine therapy, increasing outdoor time with a moderate light intensity[28] should be considered as a safe and non-invasive method for myopia treatment in preterm children.

Table 4 Multivariable-adjusted logistic regression analysis for factors associated with myopia in preterm children*

Predictor	OR (95% CI)	*P* value
Age (years)	2.35 (0.84–6.60)	0.104
Boy	0.78 (0.22–2.73)	0.697
ROP severity		
No ROP/mild or type 2 ROP	Reference	
Type 1 ROP	3.82 (1.14–12.81)	0.030†
No. of myopic parents		
0–1	Reference	
2	1.44 (0.39–5.31)	0.584
Time spent outdoors (hours/day)	0.13 (0.02–0.98)	0.048†
Near-work time (hours/day)	0.73 (0.48–1.10)	0.131
Serum 25(OH)D concentration (nmol/mL)	0.99 (0.95–1.04)	0.765

*The valid sample size was 81.
†*P*<0.05.
25(OH)D, 25-hydroxyvitamin D; ROP, retinopathy of prematurity.

In our study, serum 25(OH)D concentrations were similar between the myopic and non-myopic groups and were not correlated with the SE. Several studies have also failed to associate myopia with serum 25(OH)D levels or genes related to vitamin D metabolism.[29–31] These data suggest that vitamin D might not be directly involved in the regulation of myopia in either full-term or preterm children.

Infants born at lower gestational ages have been reported to have a greater risk of vitamin D deficiency in infancy.[15 32] In accordance with our study, a previous study also showed that in Taiwanese children, the prevalence of vitamin D deficiency was 51.0%,[33] and the worldwide vitamin D deficiency prevalence is also estimated to be as high as 30%–60%.[34] A vitamin D-deficient state influences not only bone growth but also several extraskeletal functions. There is global awareness and effort to manage the high prevalence of vitamin D deficiency; however, the true implications of the high prevalence of vitamin D deficiency in our study group and its relationship with ocular health and development remain to be determined.

There are several limitations to our study. The first limitation is that the measurements of time spent outdoors/on near-work were indirect and semiquantitative. Nevertheless, the average outdoor time was 5–6 hours/week in our study, which is in accordance with a previous study in Chinese children.[3] In future studies, the use of quantitative tools such as a light metre could provide a more precise study approach.

The second limitation is the lack of a detailed evaluation of dietary vitamin D intake and sun-protective measurements. In response to the questionnaire, 19% of the parents stated that they let their child use sunglasses. These parents might be more cautious about sunlight exposure and might therefore adopt other sun protection measures for their child, thus affecting vitamin D levels. We speculated that these limitations also contributed to the fact that we failed to observe a positive correlation between serum 25(OH)D concentrations and outdoor time. To overcome this problem, a more detailed survey of daily diet and supplements should be implemented, or a larger study population should be used to reduce this bias. However,

the latter is more difficult, especially given the relatively small population with ROP.

The third limitation is the method used to treat ROP. Fifty-three per cent of the children were treated with IVB alone, and 47% were treated by IVB + laser. Researchers have noted that the structural dimensions of the anterior segment are different between laser-treated and IVB-treated eyes, and we also found similar results (online supplementary table 3).[35] It has been speculated that the laser limits the growth of vessels towards the periphery, resulting in more immature anterior structural dimensions. In comparison, IVB-treated eyes have less damage and might attain relatively normal development. These differences in the structures that affect refraction status imply that potentially different underlying mechanisms are involved. Groups consisting of subjects with laser or IVB monotherapy could offer more precise information.

In conclusion, this study demonstrates an association between increased time spent outdoors and a lower prevalence of myopia in school-aged children with preterm birth with or without a history of ROP. Serum 25(OH)D levels seemed not to be correlated with myopia in this population, although a high proportion of these preterm children had vitamin D insufficiency.

Contributors Chou HD drafted the manuscript and organised the data for analysis. Yao TC, Huang YS and Wu WC provided the idea of the study. Yao TC, Huang YS, Huang CY, Lai CC and Wu WC planned the study and obtained grants. Huang CY, Yang ML, Sun MH, Chen HC, Liu CH, Chu SM, Hsu JF, Chen KJ, Hwang YS and Wu WC conducted the study. Wu WC revised the manuscript and reviewed the article. All authors read and approved the final manuscript.

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Competing interests None declared.

Patient consent for publication Not required.

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ORCID iDs
Hung-Da Chou http://orcid.org/0000-0002-1561-3059
Chun-Hsiu Liu http://orcid.org/0000-0003-2352-5734
Wei-Chi Wu http://orcid.org/0000-0003-3760-7255

REFERENCES

1 Ikuno Y. Overview of the complications of high myopia. *Retina* 2017;37:2347–51.
2 Rose KA, French AN, Morgan IG. Environmental factors and myopia: paradoxes and prospects for prevention. *Asia Pac J Ophthalmol* 2016;5:403–10.
3 Morgan IG, French AN, Ashby RS, *et al*. The epidemics of myopia: aetiology and prevention. *Prog Retin Eye Res* 2018;62:134–49.
4 Wu P-C, Tsai C-L, Wu H-L, *et al*. Outdoor activity during class recess reduces myopia onset and progression in school children. *Ophthalmology* 2013;120:1080–5.
5 Guggenheim JA, Northstone K, McMahon G, *et al*. Time outdoors and physical activity as predictors of incident myopia in childhood: a prospective cohort study. *Invest Ophthalmol Vis Sci* 2012;53:2856–65.
6 Jones LA, Sinnott LT, Mutti DO, *et al*. Parental history of myopia, sports and outdoor activities, and future myopia. *Invest Ophthalmol Vis Sci* 2007;48:3524–32.
7 Huang H-M, Chang DS-T, Wu P-C. The association between near work activities and myopia in children-a systematic review and meta-analysis. *PLoS One* 2015;10:e0140419.
8 Rose KA, Morgan IG, Ip J, *et al*. Outdoor activity reduces the prevalence of myopia in children. *Ophthalmology* 2008;115:1279–85.
9 Zhou X, Pardue MT, Iuvone PM, *et al*. Dopamine signaling and myopia development: what are the key challenges. *Prog Retin Eye Res* 2017;61:60–71.
10 Choi JA, Han K, Park Y-M, *et al*. Low serum 25-hydroxyvitamin D is associated with myopia in Korean adolescents. *Invest Ophthalmol Vis Sci* 2014;55:2041–7.
11 Tideman JWL, Polling JR, Voortman T, *et al*. Low serum vitamin D is associated with axial length and risk of myopia in young children. *Eur J Epidemiol* 2016;31:491–9.
12 Lind A, Dahlgren J, Raffa L, *et al*. Visual function and fundus morphology in relation to growth and cardiovascular status in 10-year-old moderate-to-late preterm children. *Am J Ophthalmol* 2018;195:121–30.
13 Page JM, Schneeweiss S, Whyte HE, *et al*. Ocular sequelae in premature infants. *Pediatrics* 1993;92:787–90.
14 Ruan L, Shan H-D, Liu X-Z, *et al*. Refractive status of Chinese with laser-treated retinopathy of prematurity. *Optom Vis Sci* 2015;92:S3–9.
15 Burris HH, Van Marter LJ, McElrath TF, *et al*. Vitamin D status among preterm and full-term infants at birth. *Pediatr Res* 2014;75:75–80.
16 Wu W-C, Lin R-I, Shih C-P, *et al*. Visual acuity, optical components, and macular abnormalities in patients with a history of retinopathy of prematurity. *Ophthalmology* 2012;119:1907–16.
17 Early Treatment For Retinopathy Of Prematurity Cooperative Group. Revised indications for the treatment of retinopathy of prematurity: results of the early treatment for retinopathy of prematurity randomized trial. *Arch Ophthalmol* 2003;121:1684–94.
18 Egashira SM, Kish LL, Twelker JD, *et al*. Comparison of cyclopentolate versus tropicamide cycloplegia in children. *Optom Vis Sci* 1993;70:1019–26.
19 Munns CF, Shaw N, Kiely M, *et al*. Global consensus recommendations on prevention and management of nutritional rickets. *J Clin Endocrinol Metab* 2016;101:394–415.
20 Kim SJ, Port AD, Swan R, *et al*. Retinopathy of prematurity: a review of risk factors and their clinical significance. *Surv Ophthalmol* 2018;63:618–37.
21 Yang C-S, Wang A-G, Shih Y-F, *et al*. Long-Term biometric optic components of diode laser-treated threshold retinopathy of prematurity at 9 years of age. *Acta Ophthalmol* 2013;91:e276–82.
22 Cook A, White S, Batterbury M, *et al*. Ocular growth and refractive error development in premature infants without retinopathy of prematurity. *Invest Ophthalmol Vis Sci* 2003;44:953–60.
23 Choi MY, Park IK, Yu YS. Long term refractive outcome in eyes of preterm infants with and without retinopathy of prematurity: comparison of keratometric value, axial length, anterior chamber depth, and lens thickness. *Br J Ophthalmol* 2000;84:138–43.
24 Yam JC, Jiang Y, Tang SM, *et al*. Low-concentration atropine for myopia progression (LAMP) study: A randomized, double-blinded, placebo-controlled trial of 0.05%, 0.025%, and 0.01% atropine eye drops in myopia control. *Ophthalmology* 2019;126:113–24.
25 Trigler L, Weaver RG, O'Neil JW, *et al*. Case series of angle-closure glaucoma after laser treatment for retinopathy of prematurity. *J Aapos* 2005;9:17–21.
26 Wu S-C, Lee Y-S, Wu W-C, *et al*. Acute angle-closure glaucoma in retinopathy of prematurity following pupil dilation. *BMC Ophthalmol* 2015;15:96.
27 Chang SHL, Lee Y-S, Wu S-C, *et al*. Anterior chamber angle and anterior segment structure of eyes in children with early stages of retinopathy of prematurity. *Am J Ophthalmol* 2017;179:46–54.
28 Wu P-C, Chen C-T, Lin K-K, *et al*. Myopia prevention and outdoor light intensity in a school-based cluster randomized trial. *Ophthalmology* 2018;125:1239–50.
29 Williams KM, Bentham GCG, Young IS, *et al*. Association between myopia, ultraviolet B radiation exposure, serum vitamin D concentrations, and genetic polymorphisms in vitamin D metabolic pathways in a multicountry European study. *JAMA Ophthalmol* 2017;135:47–53.
30 Guggenheim JA, Williams C, Northstone K, *et al*. Does vitamin D mediate the protective effects of time outdoors on myopia? findings from a prospective birth cohort. *Invest Ophthalmol Vis Sci* 2014;55:8550–8.
31 Cuellar-Partida G, Williams KM, Yazar S, *et al*. Genetically low vitamin D concentrations and myopic refractive error: a Mendelian randomization study. *Int J Epidemiol* 2017;46:1882–90.
32 Monangi N, Slaughter JL, Dawodu A, *et al*. Vitamin D status of early preterm infants and the effects of vitamin D intake during hospital stay. *Arch Dis Child Fetal Neonatal Ed* 2014;99:F166–8.
33 Yao T-C, Tu Y-L, Chang S-W, *et al*. Suboptimal vitamin D status in a population-based study of Asian children: prevalence and relation to allergic diseases and atopy. *PLoS One* 2014;9:e99105.
34 Hossein-nezhad A, Holick MF. Vitamin D for health: a global perspective. *Mayo Clin Proc* 2013;88:720–55.
35 Geloneck MM, Chuang AZ, Clark WL, *et al*. Refractive outcomes following bevacizumab monotherapy compared with conventional laser treatment: a randomized clinical trial. *JAMA Ophthalmol* 2014;132:1327–33.