REVIEW

Title

Effect of spatially-related environmental risk factors in visual scenes on myopia

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ABSTRACT

Myopia, the most common refractive error, is estimated to affect over two billion people worldwide, especially children from East Asian regions. Children with early onset myopia have an increased risk of developing sight threatening complications in later life. In addition to the contribution of genetic factors, of which expression is controversially suggested to be subject to environmental regulation, various environmental factors, such as near-work, outdoor, and living environment, have also been determined to play significant roles in the development of refractive error, especially juvenile myopia. Cues from daily visual scenes, including lighting, spatial frequency, and optical defocus over the field of visual stimuli, are suggested to influence emmetropisation, thereby affecting myopia development and progression. These risk factors in visual scenes of the everyday life may explain the relationship between urbanicity and myopia prevalence. This review first summarises the previously reported associations between myopia development and everyday-life environments, including schooling, urban settings, and outdoors. Then, there is a discussion of the mechanisms hypothesised in the literature about the cues from different visual scenes of urbanicity in relation to myopia development.

INTRODUCTION

Myopia is the most common refractive error, which has been predicted to affect more than two billion of the global population by the end of 2020.[1] The childhood myopia pandemic is particularly severe in East Asian regions, such as Hong Kong, where the myopia prevalence of 12-year-old children has reached over 50%.[2,3] Myopia progression is predominantly associated with axial elongation, and, thus, posterior ocular stretching. This structural change, which happens in myopic children, especially those with high myopia, has been reported to be associated with an increased risk of retinal detachment, glaucoma, and macular degeneration,[4] leading to an estimated economic loss in gross domestic product of six billion USD annually due to myopic macular degeneration alone.[5]

While genetics is arguably a risk factor, which increases the susceptibility to myopia development in children, the high incidence of myopia may be more justifiably due to environmental exposures.[6] Although myopia affects only about 5% of children aged less than 6 years, substantial amounts of myopia develop in older children exposed to certain myopiagenic risk factors after a few years of schooling. With the rapid increase in myopia prevalence in recent decades, association has been established between increased myopia prevalence and various environmental factors in modern human life, including near work, time spent outdoors, and urbanisation. These risk factors will be reviewed in Part One. Speculation about the reasons for the contribution of such environmental factors, particularly cues from visual scenes in the urbanised world, to myopia development will be discussed in Part Two with the supportive evidence from human and animal studies.

PART ONE – Environmental risk factors in modern everyday life on myopia

Near work

For many years, researchers have noted an association between refractive error and near work, which has been considered as fundamental evidence of environmental risk for myopia development. Increased myopia prevalence with higher levels of education,[7-9] which is reasonably related to increased amount of studying, also reflected the role of near work in myopia development. With respect to the role of near work in myopia, Huang and co-workers[10] performed a systematic review and meta-analysis, which reported that near work was associated with myopia prevalence, but not the risk of developing myopia. Cross-sectional epidemiological studies revealed myopic children were likely to spend more time reading and studying.[11,12] Vice versa, children with greater reading exposure were more likely to become myopic.[13,14] Faster axial elongation was also significantly associated with the number of books read in a week and the total reading time reported in another three-year longitudinal study.[15] As well as reading time and exposure, close reading distance was also reported to be associated with higher odds of myopia, more myopic refractive error, incident myopia, and myopic shift in refraction.[16-18] Participation in near-work-rich cramming schools, which are popular in East Asian countries, was also suggested to contribute to the increase in myopia prevalence in these countries. This hypothesis was later supported by a four-year longitudinal study in Taiwan,[19] in which attendance at cramming school for over two hours per day increased the odds ratio of myopia incidence.

In contrast, some studies showed inconclusive results. A five-year longitudinal study reported that extensive near work was associated with myopia incidence in the younger, but not the older cohort.[20] Every one hour less in near work activity was shown to contribute to myopia stabilisation by age fifteen in a univariate, but not multivariate analysis.[21] In a recent four-year longitudinal study, longer daily reading time was associated with a higher myopia prevalence, but not incidence.[19]

On the other hand, some studies did not demonstrate this effect of near work on myopia, with progression not significantly differing in children having various intensities of near work.[22] Near work tasks, including school homework, leisure reading, and handheld console games, correlated poorly with refractive error in the children.[16] The amount of near work was also reported to be independent of myopia incidence, in which baseline near work undertaken by future-myopes did not differ from that of participants who remained emmetropic.[23] The effect of near work on myopia remains controversial, thereby the pro-, against-, and inconclusive results of near work are summarised in Table 1.

The emergence and penetration of electronic devices has made device screen time more important for studies investigating near work, as electronic devices for in gaming, social media, and digital entertainment have now heavily infiltrated daily life.[24] Myopic children

are more likely to spend more than two hours per day watching television / video, using computers, and playing mobile games.[12] These digital screen activities were also reported to be significant risk factors for myopia progression.[25] A longitudinal study showed computer use was moderately associated with myopia development, in particular, at a very young age.[26] However, a later study did not find any association between computer / internet / video games and either prevalence or incidence of myopia.[19] As the prevalence of childhood myopia was already high in East-Asia, including Hong Kong, Taiwan, and Singapore, before the digital era, the widespread screen use may only represent a new form of near work, shifting book reading to digital reading, or a factor keeping children from OA, given the myopia prevalence maintained relatively stable.[3]
Despite the controversy, in addition to the cross-sectional relationship that myopes perform more near work, more near work can also lead to increased incidence of myopia. Consolidating the findings from different studies, near work is believed to be a myopiagenic factor, but the current methods in quantifying near work characteristics are limited. With advances in technology, quantifying the amount of near work in myopia research needs to be more sophisticated and holistic, rather than merely recording the distance, duration, or types of near tasks.

Outdoor environment and activities

In contrast to the controversy surrounding the effect of near work on myopia development, researchers have reached a consensus that time spent outdoors are protective against myopia development.[27-29] A representative study, the Sydney Myopia Study (SMS), demonstrated an association between high levels of outdoor activities (OA) and lower myopia prevalence, as well as a more hyperopic spherical equivalent refraction (Table 2).[30] They also reported that, regardless of the amount of near work, the amount of OA was always negatively associated with the odds ratio of having myopia. An analogous study, the Singapore Cohort study Of Risk factors for Myopia (SCORM) conducted in Asian children, who have a significantly higher myopia prevalence, yielded similar results.[31] A follow-up of SMS, the Sydney Adolescent Vascular and Eye (SAVE) study, reported that a lack of OA was associated with myopia incidence over 5 - 6 years.[20]

Instead of directly reporting the time spent outdoors, the effect of outdoors was also reflected in some other measures. The Orinda Longitudinal Study of Myopia (OLSM) reported more sports and outdoor hours were associated with a lower myopia prevalence,[11] as well as a lower myopia incidence over 5 years.[32] Notably, the OLSM did not separate OA from sports activities. Although hours spent in sports were associated with total OA time, later studies suggested sports alone could not provide protective effect against myopia.[30,33] Eastern and Western styles of education differ significantly in terms of proportion of outdoor classes, e.g., Singaporean versus Australian,[34] international- versus local-styled schools in Hong Kong,[35] and academically selective versus comprehensive schools in Sydney.[16] This difference in education modality was suggested to contribute to the myopia prevalence in such groups of students.[34] The more intense education modality and higher academic performance were always associated with longer time spent in studying and less time in OA, which are both risk factors for myopia. A cohort study reported a higher level of OA could decrease the effect of combined near work activities on myopia development.[26] This study reported the protective effect of time outdoors against the impact of an increased level of near work, and supported the findings of the SMS,[30] which was the first to report that students with combined higher levels of OA and low levels of near work resulted in more hyperopic refraction.

The negative association between OA and myopia prevalence and incidence was also demonstrated in observational studies. Hence, later clinical trials shifted the focus to the protective effect of treating children with OA (Table 2). In Taiwan, two nearby schools were recruited, in which one implemented a recess-outside-classroom program for the students, which emptied classrooms during recess, while the second school served as a control without any intervention.[36] After twelve months, the students in the school with the intervention had both significantly lower myopia incidence in non-myopic children and slower myopic progression in myopic children than those in the control school. The same research group later extended the study to a multi-area, cluster-randomized controlled trial with a larger sample size of approximately 600 children.[37] In this trial, the intervention group was also encouraged to participate more in OA via various campaigns, such as educational promotions, family events, and reward programs. The results indicated a protective effect of OA against myopia, with an odds ratio of myopia incidence in the intervention group of 0.46 compared with control group. Another three-year randomised clinical trial, which included approximately 2,000 children in six intervention and six control schools, was conducted in China.[38] In this study, one extra forty-minute OA class was added to the schedule every school day in the intervention schools, which lowered the myopia incidence after three years in these schools. However, although myopic shift in spherical equivalent refraction was also less in the intervention schools, axial elongation was not different from the controls. It is also worth noting that the myopic shift in refraction before and after the onset of myopia should be distinguished, as they may be regulated separately.[39] Additionally, an OA promotional campaign might not always have high compliance unless incentives are given,[40] as teachers and parents may prefer more study time for the children.

There are several theories suggesting the mechanism of time spent outdoors preventing myopia development. The most widely accepted is the light intensity of the outdoor environment.[41] In clinical observational studies, Read and co-workers measured light exposure using a wrist-worn actigraphy device in emmetropes and myopes.[42] Their findings showed that emmetropes had significantly higher light exposure than age-matched myopes over two weeks within the school term. Furthermore, in another clinical trial carried out in China, elevated light intensity, achieved by improving the lighting system in classrooms, also lowered myopia incidence and the myopia progression rate over one year.[43] As suggested in animal studies, higher light intensity can retard form deprivation and lens induced myopia,[44-47] in which dopamine upregulation is the widely accepted mechanism. In addition, suppression of experimental myopia was associated with an increase in dopamine receptor activities,[48,49] while in contrast, dopamine antagonists abolished the protective effect of bright light against experimental myopia.[45] In the OA promotion campaign in Taiwan mentioned earlier,[37] collar light meters were used to measure light exposure for seven days. The results suggested, rather than high light intensity (up to 10,000 lux), more time spent in even a relatively dimmer outdoor environment (1,000 to 3,000 lux, e.g., hallways with big windows, under tree shade) was also sufficient to be protective against myopia. The light intensity measured using a child-sized mannequin head light meter was

comparable to that measured using light metres on children's collars.[50] Even with sunlight protective equipment, e.g. sunglasses and hats, the outdoor light intensity, which was eleven- to forty-three-fold greater than indoor lighting, was adequate for myopia protection. Hence, a custom-made glass classroom was designed and built for students to increase their light exposure during school time.[51] The light intensity was significantly increased and both teachers and students gave more positive feedback of the glass classroom than a traditional classroom. However, neither refractive nor biometric data was measured in the study.
While experimental myopia required up to 10,000 lux to be counteracted, the success with lower light intensities (1,000 to 3,000 lux) in clinical studies may suggest the disparity of constant versus intermittent myopiagenic stimuli, contributing differently to eye growth in lab-based experimental setups and the real-life environment, respectively.
While the general belief of the protective mechanism of OA against myopia is the light intensity in the environment, other theories regarding the mechanism of OA protection concern the properties of the outdoor visual stimuli, including 1) spatial details[52-54] - as myopisation was inhibited by high spatial frequency stimuli, which are abundant in outdoor natural environments, and 2) defocus over the visual field[55,56] - the distribution uniformity is more favourable for emmetropisation in an outdoor environment, while the distribution is more dispersed in an indoor environment. These relatively less popular theories regarding the cues of visual stimuli in different scenes will be discussed in Part Two.

Living environment

In addition to vision-related activities, the living environment may be associated with myopia prevalence. In Eastern countries, children and adolescents spend most after-school time at home, doing homework and studying unless they attend cramming schools or tutorial classes. Common leisure activities are most likely to take place at home (e.g., watching television, playing computer games, and leisure reading) or in the neighbourhood (e.g., going out for a walk, window shopping, and playing sports). While the eyes are constantly exposed to surrounding stimuli, including various spatial and temporal contents, the living environment could therefore be an important contributor to children's refractive development.

Urbanicity, which is the degree of how urban an area is, has been also reported to be associated with myopia prevalence. The Refractive Error Study in Children (RESC) is a multi-national study, which unified the sampling and measurement protocol for ease of comparison of childhood refractive error among countries.[57] Interestingly, the study reported a consistently higher myopia prevalence in more urbanised regions.[58-67] Even within a country, a higher myopia prevalence was reported in urbanised regions in India [New Delhi vs. Mahabubnagar[61,62]] and China [Guangzhou vs. Shunyi vs. Yangxi[60,64,65]], which was independent of age, gender, and parental myopia.[68] In Australia, the SMS also reported the amount and prevalence of myopia in the greater Sydney region.[69] The region was divided into 14 areas according to the statistical bureau, then classified into five levels based on the population density from region 1 (outer suburban) to region 5 (inner city). There was an increasing trend of myopia prevalence, and a myopic shift in refractive error, from low to high population densities in the outer suburban area to the inner city. China is rapidly urbanising, with millions migrating from the countryside to cities. With increasing population densities and socioeconomic status, the urbanised area within a town was also reported to impose a higher risk of myopia compared with the rural area.[70] In Barcelona, researchers investigated the effect of green space exposure on spectacle usage in children,[71] inferring myopia prevalence, in the city. Green space near the children's home, schools, and commuting routes were characterised using satellite data. The results showed that increased exposure to green space was associated with a lower percentage of spectacle use, as well as the spectacle requirement incidence over three years. However, a longitudinal study in the United Kingdom found no strong evidence for an association between urban and rural status with incidence of myopia, while the small amount of variation in myopia incidence were suggested to be related to other underlying factors rather than geographical differences or population density itself.[72]

In addition to the surrounding environment, the effect of housing is a controversial issue regarding its association with myopia prevalence. A study in Singapore classified the type of housing based on the number of rooms in government apartments and private housing and reported that it did not appear to affect either the prevalence or the amount of myopia.[22] Another study, also from Singapore, showed the prevalence of myopia increased with better housing. The myopia prevalence was higher in children living in larger than smaller public apartments, and was the highest in those living in private and condominium housing.[73] In contrast, the SMS reported that children living in smaller, confined housing types, such as apartments (26.3%) and terraced houses (21.4%), had a higher risk of having myopia than those living in stand-alone and separate houses (11.3%).[69] In China, the height of the building was reported to be associated with myopia, with higher odds for the children to have myopia in taller buildings.[74] Children living in a rental home were also reported to be at higher risk of myopia than those living in a private property.[75] Rather than being an independent factor, the housing type and home size were often regarded as an indicator of socioeconomic status, in which higher parental education and household income were reported to be associated with higher myopia prevalence.[20,22,76] A study conducted by the authors reported that Hong Kong children living in smaller homes had longer axial length and more negative refractive error than those living in a larger home.[77] Recently, it was reported that greater myopia progression occurred in children living in small-sized apartments, compared to those living in medium-sized and large-sized homes.[78] Table 3 summarises the results from different locations, reporting the associations between living environment and refractive error, in terms of various measures, including urbanicity, population density, type of household, and home size.

Therefore, higher population density and more constricted homes may increase the risk of myopia. The more constricted environment in smaller homes tends to result in more relative hyperopic defocus created by the closer household objects, which was shown in other studies to increase myopia progression.[79,80] However, given that the results from these epidemiology studies are highly confounded with other factors, including, but not limited to school performance, amount of near work and OA, and parental myopia, cautious interpretations of these results on myopia development are warranted. A more comprehensive investigation of the effect of environmental influence on myopia, such as the use of hypothesis-driven sequential testing for interactions between variables, is believed to be a useful alternative direction for study.

PART TWO – Cues for directing eye growth in daily visual scenes

Spatial characteristics of the visual stimuli in the scene

The efficacy of emmetropisation has been suggested to depend on the spatial contrast and frequency of the visual stimuli. Mid to high spatial contrast and frequency were shown to be effective in preventing form-deprivation myopia (FDM),[52] and were critical cues in compensational eye growth in response to myopic defocus.[81] In a recent chick study, high spatial frequency minimised myopisation induced by negative lenses, when compared with low spatial frequency stimuli.[82] This effect was also found to be a graded response, in that myopisation retardation was more obvious when the constituent of high spatial frequency increased. Exposure to mid and high spatial frequencies was also reported to promote a more accurate emmetropisation in chicks.[53] Compared with animal studies, only one study on human retinal electrophysiology investigated the effect of spatial frequency on response to optical defocus.[54] Positive defocus increased, while negative defocus decreased, the retinal responses measured by multifocal electroretinogram. However, this phenomenon only appeared under low spatial frequency stimulus, but not high spatial frequency stimulus, indicating that spatial frequency composition can influence the response from the human retina to different optical defocus. Summarising these findings, low spatial frequency appeared to favour, whereas high spatial frequency appeared to inhibit myopisation (Table 4).

Unlike in an experimental setup, real world visual scenes consist of a spectrum of spatial contrasts and frequencies, combining the highs and lows. In natural scenes, the mid to high spatial frequency constituents were found to be richer, whereas low spatial frequency was lacking.[53] Another study also compared spatial frequency content in pictures of artificial versus natural scenes,[83] showing that low spatial content was increasingly richer in an urban environment (e.g., traffic, skyscrapers), especially in indoor settings, when compared with natural scenes. This artificial content was suggested to share similar characteristics to those known to induce FDM in animal models, i.e., having richer low spatial frequencies and contrasts which favour myopisation. It is therefore speculated that the low spatial frequency properties of urban artificial and indoor environments may be a contributing factor to myopia development in children, leading to a higher myopia prevalence in urbanised regions.

Dioptric distance of objects in the visual scene

Within a visual scene, objects close-up to the eye would trigger an accommodative response. Whether the lag of accommodation, which produces hyperopic defocus to the eye, would worsen myopia has been extensively discussed in the literature,[84-86] and to date remains controversial. Despite the accuracy of on-axis accommodation, objects away from the visual axis project defocused images on the visual field based on the refractive profile along the eccentricity. Similarly, whether peripheral refraction is an essential contribution to myopia development remains controversial because of the contradictory results obtained from animal experiments,[80] epidemiological studies,[87,88], and myopia-control clinical trials.[89,90]

It was suggested that relative peripheral hyperopia was associated with on-axis myopia progression,[91] as the peripheral retina could recognise hyperopic defocus for the eye to elongate and match with the focal length. Evidence from human electrophysiological studies also supported the suggestion that the peripheral retina could distinguish the sign, and possible magnitude of defocus.[54,92] However, in addition to peripheral refraction itself, another proposal for the role of the peripheral retina in modulating emmetropisation is the dioptric uniformity hypothesis.[55,56] Although the beneficial effects of OA in lowering the risk of myopia are usually attributed to the light intensity,[41] others have suggested that the difference between outdoor and indoor defocus profile may also contribute to myopia development.[56,93-95] In an outdoor environment, objects are usually far away, creating a more uniform vergence to the eye. In contrast, indoor objects are usually closer to the eye, resulting in the visual field experiencing a widely varied vergence across the retina.[94,96] A recent longitudinal study demonstrated the association between defocus profile in near-work environment at home and myopia progression in schoolchildren, supporting the dioptric uniformity hypothesis.[78] In the study, three-dimensional images of the near-work environment were captured by a depth sensing camera to mimic the child's view as if they were performing a near task in the visual scene. The scene defocus of the objects in the visual scene was calculated with respect to the child's working distance, i.e., the objects further than working distance would create myopic scene defocus, and vice versa for closer objects creating hyperopic scene defocus. The scene characteristics were represented by the dispersion of the scene defocus values (dioptric uniformity), and the net amount of scene defocus (peripheral defocus). The results showed that greater dispersion of the defocus over the central 30° visual field and more hyperopic scene defocus at paracentral eccentricity were associated with greater progression in myopia (Table 4). Hence, in a more defocus-dispersed environment, a more rapid change in defocus profile would result and interrupt the defocus signal integration in the retina,[56] leading to failure in emmetropisation and excessive myopia progression. Despite the supportive results, a major issue of the dioptric uniformity hypothesis is a lack of an established mechanism to detect such defocus variations, which is also incompatible with the evidence of a regional response of compensatory eye growth under local defocus stimulus.

SPECULATIONS and CONCLUSIONS

Emmetropisation is a visually guided process, in which the eye modulates its refractive components to achieve emmetropia. "Visually guided" implies that the cues in the visual scene are complex and multifactorial, and each may have its own as well as interactive contributions to refractive error development. Despite the widely discussed role of lighting (in terms of intensity and chromaticity), the current review suggests other spatial cues, including spatial frequency and dioptric distribution, are related to myopia development. Studies have suggested these visual cues are in opposition – natural versus artificial; high versus low spatial frequency, indoors versus outdoors; dioptric varying versus uniform. While existing studies are mainly animal experiments with well-controlled environmental settings, further research could point to the relationship between these visual cues and myopia development in children.

The environment in the modern human habitat is related to refractive error and its development. In daily life, different environmental risk factors, such as substantial near work and lack of time spent outdoors, could exert myopiagenic effects on children, which may be associated with the increasing myopia prevalence in urbanised regions. These myopiagenic stimuli may be more abundant in certain environments, for example, a constricted near work environment, which is dioptric non-uniform and rich in components of low spatial frequencies, possibly leading to more rapid myopia progression. To alleviate the future extreme prevalence of myopia, in addition to promoting active myopia control strategies, such as atropine and orthokeratology, design and modification of the living environment could be another approach deserving attention.

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Table 1. Pro- and against- nearwork (Time, working distance, and screen time) evidence for myopia

Author	Study design (location)	Sample size	Nearwork parameter	Findings
Pro				
Mutti et al.[11] Saxena et al.[12]	Cross-sectional (USA) Cross-sectional (India)	366 9,884	Reading and studying time	Myopic children spent more time to do so
Saw et al.[14]	Cross-sectional (Singapore)	1,453	Number of books	Reading exposure of more than 2 books a week significantly increased the odds of being myopic in children of 7-9 years old
Tideman et al.[15]	Longitudinal (Netherlands)	4,734	Number of books reading time	Both parameters were significantly associated with axial elongation
Ip et al.[16] Li et al.[17]	Cross-sectional (Australia) Cross-sectional (China)	2,353 2,267	Reading distance	Close reading distance was associated with a greater odd of having myopia / more myopic refractive error
Huang et al.[18]	Longitudinal (Taiwan)	10,743	Reading distance	Longer reading distance was protective against incident myopia and myopic shift in refractive error
Inconclusive				
French et al.[20]	Longitudinal (Australia)	2,103	Near work hours and dioptre hours	Extensive near work increased the risk of incident myopia in the younger cohort, but not the older cohort
Scheiman et al.[21]	Clinical trial (USA)	233	Near work hours	Reduced near work hours could enhance the odds of myopia stablisation by the age of 15 in univariate analysis, but not multivariate analysis
Ku et al.[19]	Longitudinal (Taiwan)	1,958	Reading time	Long reading time was associated with high myopia prevalence, but not incidence; medium reading time was associated with both myopia prevalence and incidence
Against				
Ip et al.[16]	Cross-sectional (Australia)	2,353	Near work time (school homework, leisure reading, and combined nearwork activities)	Significant but weak correlations between hours of near work and refractive error in children
Saw et al.[22]	Longitudinal (Singapore)	153	Near work time Reading distance	Both parameters were independent of myopic shift in refractive error
Jones-Jordan et al.[23]	Longitudinal (USA)	731	Reading and studying time	Reading and studying time did not significantly differ between myopes and emmetropes before the onset of myopia

Table 2. Effect of outdoor environments on myopia

Author	Study design (location)	Sample size	Outdoors parameter / intervention	Findings
Mutti et al.[11]	Cross-sectional (USA)	366	Sports activity engagement	Children spent more time engaged in sports had lower odds of being myopic
Rose et al.[30] Enthoven et al.[26] Dirani et al.[31]	Cross-sectional (Australia) Cohort study (Netherlands) Cross-sectional (Singapore)	1,765 5,074 1,249	Times spent outdoors	More time spent outdoors was associated with lower odds of being myopic and a more hyperopic refractive error
French et al.[20] Guggenheim et al.[33]	Longitudinal (Australia) Longitudinal (UK)	2,103 9,109	Times spent outdoors	More time spent outdoors was associated with lower odds of incident myopia
Wu et al.[36] Wu et al.[37]	Interventional (Taiwan) Cluster-randomised trial (Taiwan)	571 693	Recess outside classroom	The intervention group had lower odds of incident myopia and less myopic shift in refractive error
He et al.[38]	Cluster-randomised trial (China)	1,903	Extra 40-minute outdoor class	The intervention group had lower odds of incident myopia and less myopic shift in refractive error

Table 3. Evidence for the association between living environment and myopia

Author	Study design (location)	Sample size	Living environment parameter	Findings
Dandona et al.[61] Murthy et al.[62] Zhao et al.[60] He et al.[64]	Cross-sectional (India) Cross-sectional (China)	4,074 6,447 6,134 4,364 2,454	Urban versus rural cities/county/district in a country	Myopia prevalence was reported to be higher in urban areas than semi-rural and rural areas
Ip et al.[69]	Cross-sectional (Australia)	2,367	Outer suburban to inner city regions in a metropolitan	Children living in areas of higher population density had higher odds of myopia and a more myopic refractive error; a more confined housing type was also associated with myopia prevalence
Zhang et al.[70]	Cross-sectional (China)	2,480	Population density	Population density was negatively correlated with refractive error
Dadvand et al.[71]	Cross-sectional (Spain)	2,727	Green space surrounding home, school, and commuting route between home and school	Exposure to surrounding green space was negatively associated with spectacle use in children
Morris et al.[72]	Cohort study (UK)	3,512	Population density	Population density was associated with incident myopia, but which was attributed to other individual parameters, e.g., lifestyle
Quek et al.[73]	Cross-sectional (Singapore)	946	Type of housing (in terms of number of rooms and ownership)	Myopia prevalence increased with "better" type of housing in teenagers
Wu et al.[74]	Cross-sectional (China)	43,771	Type of housing (in terms of building height)	Children living in taller building had increased odds of being myopic
Tideman et al.[75]	Cross-sectional (Netherlands)	5,711	Type of housing (in terms of ownership)	Children living in a rental home had increased odds of being myopia than those living in a privately owned home, but which was possibly confounded by lifestyle
Choi et al.[77]	Cross-sectional (Hong Kong)	1,075	Home size	Small home size was a significant risk factor for more myopic refractive error and longer axial length
Choi et al.[78]	Longitudinal (Hong Kong)	50	Home size	Small home size was a significant risk factor for myopic shift in refractive error

Table 4. Spatial characteristics of visual stimuli (spatial frequency and dioptric distribution) in relation to myopia

Author	Subjects	Properties of the visual stimuli	Findings
Spatial frequency (SF)			
Schmid & Wildsoet[52]	Chicks	SF on vertical sine wave grating patterns	Mid and mixed SF were more effective in preventing form-deprivation myopia than high, low, or high + low SFs
Hess et al.[53]	Chicks	Spectral slope on phase-scrambled targets	Steeper spectral slope (low SF rich) was associated with more myopic shift in refractive error under in-focus condition
Diether & Wildsoet[81]	Chicks	Standard and striped (spatial-rich) Maltese crosses (MC)	Striped MC better-compensated the induced myopic defocus compared with standard MC; both MCs near-fully compensated induced hyperopic defocus; striped MC induced transient hyperopic shift under competing defocus
Chin et al.[82]	Chicks	SF on checkers	High SF hindered vitreous chamber elongation under hyperopic defocus when compared with low SF
Chin et al.[54]	Human (young adults)	SF on gratings, covering multifocal electroretinogram (mfERG) stimulus	Low SF generated greater defocus-induced change in mfERG when compared with high SF
Dioptric distribution			
Choi et al.[78]	Human (schoolchildren)	Net amount and dispersion of defocus	Less uniform dioptric profile in the scene and more hyperopic scene defocus in the paracentral region were associated with faster myopia progression in schoolchildren