Title

Childhood exposure to constricted living space: a possible environmental threat for myopia development

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Running title

Constricted living space and childhood myopia

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Abstract

Purpose: People in Hong Kong generally live in a densely populated area and their homes are smaller compared with most other cities worldwide. Interestingly, East-Asian cities with high population densities seem to have higher myopia prevalence, but the association between them has not been established. This study investigated whether the crowded habitat in Hong Kong is associated with refractive error among children.

Methods: In total, 1,075 subjects [Mean age (SD): 9.95 years (0.97), 586 boys] were recruited. Information such as demographics, living environment, and parental education and ocular status were collected using parental questionnaires. The ocular axial length and refractive status of all subjects were measured by qualified personnel.

Results: Ocular axial length was found to be significantly longer among those living in districts with a higher population density ($F(2,1072) = 6.15$, $p = 0.002$) and those living in a smaller home ($F(2,1072) = 3.16$, $p = 0.04$). Axial lengths were the same among different types of housing ($F(3,1071) = 1.24$, $p = 0.29$). Non-cycloplegic autorefraction suggested a more negative refractive error in those living in districts with a higher population density ($F(2,1072) = 7.88$, $p < 0.001$) and those living in a smaller home ($F(2,1072) = 4.25$, $p = 0.02$). After adjustment for other confounding covariates, the population density and home size also significantly predicted axial length and non-cycloplegic refractive error in the multiple linear regression model, while axial length and refractive error had no relationship with types of housing.

Conclusions: Axial length in children and childhood refractive error were associated with high population density and the small home size. A constricted living space may be an environmental threat for myopia development in children.

1. Introduction

Myopia, or short sightedness, which is the most common refractive error, can be regarded as a type of ocular disorder. It has been a global health concern costing not only optical corrections to obtain clear distant vision, but also costing medical burden as high myopes are predisposed to various ocular diseases such as cataract, glaucoma, macular degeneration and retinal detachment[1] which can cause severe or irreversible vision loss. As vision is crucial to our daily life, the vision loss can adversely affect the quality of life.[2]

"Emmetropisation" is a visually guided process for the eye to modify itself to obtain an optimum relationship between the axial length and other ocular components, such as cornea and lens, so that any infantile refractive error is corrected. However, there is an increasing number of children become myopic at an early age. Not only will this increase their risk of developing high myopia later in their lives, epidemic childhood myopia is also speculated to cause a shortage of certain labor forces as good uncorrected eyesight is a pre-requisite for some occupations such as pilots and firefighters, and thus lead to social burdens in coming decades.

East-Asian countries generally have an unexpectedly higher myopia prevalence compared with other parts of the world.[3] Among them, Hong Kong has long been a city with an extraordinary high prevalence of myopia.[4, 5]Studies have shown that myopia is more prevalent in Asians than in white European and African populations.[6, 7] Apart from genetic differences, these findings were found to be associated with the culture and lifestyle of East Asians, who are usually lacking in outdoor activities and engaged in a near-work-predominant education system.[6, 8] In addition, the crowded living habitat among the East-Asian cities may also be associated with this high prevalence of myopia.

Previous studies revealed that an urban environment is related to higher prevalence of myopia in children compared with sub-urban and rural environment.[9, 10] For example, the Sydney Myopia Study (SMS) suggested that the urbanicity of the living region was associated with childhood myopia,[11] in which the children living in a place of denser population were reported to have a higher prevalence of myopia. Some other studies attributed the association to the lack of outdoor activities and the excess of near work[12-14] for children living in urban area. The Sydney Myopia Study also reported that a flat-styled living, rather than house-styled, in urban area had an association with myopia prevalence. A recent study also suggested that the taller the building that the children were living in, the higher the chance that myopia would be observed.[15]

In 2004, Fan et al. conducted a population-based study on myopia prevalence in Hong Kong, which included 7560 schoolchildren.[4] From the results, 37% of the children were found to be myopic. They recruited one school from each of the 18 political districts in Hong Kong. However, among the 18 political districts, half of them had a population density lower than 10,000 persons per km^2, while only a few of them had a population density higher than 30,000 persons per km^2.[16] Their samples may have skewed towards the less populated areas and thus they may have underestimated the actual myopia prevalence of Hong Kong according to SMS.[11]

Hong Kong is one of the most densely populated cities in East Asia. The housing problem in Hong Kong has been intensely discussed, as the land supply is limited while the population is increasing.[16] In 2015, 45.7% of the Hong Kong population lived in public housing, and the internal floor area per person was only $13.1m^2$,[17] which is the highest among the same figure since 2005. While there are still hundreds of thousands of people queuing for the public housing, it was reported that around

171,000 people in Hong Kong live in substandard sub-divided flats.[18] Some children even have to live in flats with a total area of around 9m^2 with their whole family.[18]

In East Asian cities, people are generally living in relatively small flats in highly populated areas and the prevalence of myopia is high. However, the association between refractive error and size of living space has not been established. In the current study, we studied whether this crowded living environment is associated with refractive error among children in primary (elementary) school.

2. Methods

2.1 Subjects

Local primary school children were recruited between Jun 2015 and Feb 2016. Cluster sampling was used for the selection of schools. The 18 political districts in Hong Kong were divided into 3 clusters according to their population densities[16]- high: more than 30,000 persons per km^2; medium: 10,000 to 30,000 persons per km^2; and low: less than 10,000 persons per km^2. In each cluster, 4 schools were randomly selected (12 schools in total). Eight schools finally agreed to join the study (2 schools from the low density cluster, 3 schools from the medium density cluster, and 3 schools from the high density cluster). All their students, who fulfilled inclusion criteria, were examined in a vision screening which was held in their school. Inclusion criteria were students aged from 7 to 12 years and were a Hong Kong Chinese resident. In total, 1,235 students were invited for the study, and 1,173 students participated (95% response rate). Among them, 19 students exceeded the age limit and 15 mainland China residents were excluded from the study. Furthermore, we excluded 64 respondents from the analysis who had received different active myopia control interventions. As a result, 1,075 [Age (SD): 9.95 (0.97), 54.5% boys] students were included in the current study for the analysis. As all the subjects were local Chinese residents studying in government-supported schools with the same syllabus governed by the Education Bureau of The Hong Kong Government, we assumed that all subjects received similar education and it does not differ between groups. Informed consent and simple written assent were obtained from the parents and the students respectively. All procedures followed the tenet of Declaration of Helsinki and were approved by the Human Subjects Ethics Subcommittee of The Hong Kong Polytechnic University.

2.2 Data collection

The demographic data, ocular and family history, parental education level, and information regarding living environment were obtained by self-reported questionnaire, which were completed by the parents. For the living environment, information of the residential district, the home size and the physical type of housing were collected. Different home sizes were categorised as smaller than 27.87m^2 (300ft^2), from 27.87 to 55.74m^2 (from 300 to 600ft^2) and larger than 55.74m^2 (600ft^2), which were based on the common living style in Hong Kong. For the residential district, we grouped them according to their population densities[16] into low, medium and high population density which were defined as less than 10,000, from 10,000 to 30,000 and more than 30,000 persons per km^2 in the district respectively.

Ocular axial length (AL, length of eyeball) of the subjects was measured using partial coherence interferometry (Carl Zeiss Meditec, IOL Master, https://www.zeiss.com/meditec/int/products/ophthalmology-optometry/cataract/diagnostics/optical-biometry/iolmaster-500.html). A total of five measurements (signal-to-noise ratio greater than 2.0) were taken and the mean value was recorded. Their refractive status was evaluated by non-cycloplegic open-field auto-refraction (Shin-Nippon, NVision K5001, http://www.shin-nippon.jp/products/nvk5001/) while looking at a distant target at 6m. Cycloplegic agent, which paralyses accommodation (ability to focus at near), was not instilled because the data were collected on normal school days, and we did not want to interrupt the students' daily study. This is one of our limitations as the students may accommodate, resulting in a myopia over estimation in the auto-refraction results.[19] A total of five measurements within the published criteria were taken by an optometrist, and the representative value was recorded.[20] The recorded value was then transposed into spherical equivalent refraction (SER) by the following equation: SER = spherical refractive error + ½ cylindrical refractive error.

2.3 Statistical Analysis

Data analysis was performed using SPSS (IBM, ver. 22, https://www.ibm.com/analytics/us/en/technology/spss/). Axial length was the primary outcome and non-cycloplegic spherical equivalent refraction was the secondary outcome to assess the characteristics and trends between groups. Each independent variable was plotted against AL and SER, and the results were compared among groups using one-way ANOVA with Bonferroni correction. Multiple linear regression was used to assess the impact of population density, home size, and type of housing on AL and SER. Confounding covariates included age, gender, parental education level, and parental myopia. ~~All categorical covariates were transformed into dichotomous variables.~~ Missing data were treated using 10-time multiple imputation.[21] To ensure the absence of multicollinearity, only models showing the following signs (all collinearity tolerances larger than 0.8, all variance inflation factors less than 2 and all absolute Pearson's R of variables was smaller than 0.2) were analyzed. As data from right and left eyes were strongly correlated (AL: r = 0.96; SER: r = 0.92), only right eye data were analyzed. Significance level was set as $p < 0.05$.

3. Results

3.1 Descriptive characteristics of the sample

The subjects had a mean AL of 23.78mm (SD: 1.04) and SER of -1.21D (SD: 1.80). Table 1 shows the demographics and living environment of the participants, and the p values in Table 1 were from a univariate analysis of each variable. The age of the children did not significantly differ across all categories of population density ($F(2,1072) = 2.82$, $p = 0.06$), home size ($F(2,1072) = 2.10$, $p = 0.12$), and type of housing ($F(3,1071) = 1.60$, $p = 0.19$).

Table 1. Distribution of demographics and living environment factors.

	N (%)	Mean AL (SD)	*p* value†	Mean SER (SD)	*p* value†
All	1075 (100)	23.78 (1.04)		-1.21 (1.80)	
Gender			<0.001		0.935
Boys	586 (54.5)	24.02 (1.00)		-1.20 (1.80)	
Girls	489 (45.5)	23.49 (1.02)		-1.21 (1.80)	
Age			<0.001		<0.001
Lower third	358 (33.3)	23.53 (0.93)		-0.90 (1.64)	
Middle third	358 (33.3)	23.80 (1.06)		-1.34 (1.85)	
Upper third	359 (33.4)	24.02 (1.07)		-1.41 (1.87)	
Parental myopia			<0.001		<0.001
No parent is myopic	507 (47.2)	23.71 (1.02)		-1.00 (1.59)	
One parent is myopic	336 (31.3)	23.83 (1.07)		-1.37 (1.94)	
Both parents are myopic	152 (14.1)	24.09 (1.11)		-1.86 (2.01)	
Parental education level			0.110		0.513
Primary school or below	58 (5.4)	24.06 (1.07)		-1.53 (2.12)	
Junior secondary school	375 (34.9)	23.78 (1.05)		-1.22 (1.76)	
Senior secondary school	422 (39.3)	23.72 (1.02)		-1.17 (1.80)	
Tertiary education	163 (15.2)	23.83 (1.08)		-1.12 (1.65)	
Population density of the residential			0.002		<0.001
<10k persons per km^2	209 (19.4)	23.56 (0.93)		-0.89 (1.64)	
10k-30k persons per km^2	236 (22.0)	23.74 (1.07)		-1.01 (1.60)	
>30k persons per km^2	418 (38.9)	23.87 (1.09)		-1.46 (2.01)	
Home size			0.043		0.015
<27.87 m^2 (<300 ft^2)	305 (28.4)	23.85 (1.07)		-1.35 (1.88)	
27.87-55.74 m^2 (300-600 ft^2)	536 (49.9)	23.80 (1.10)		-1.26 (1.89)	
>55.74 m^2 (>600 ft^2)	152 (14.1)	23.59 (0.88)		-0.82 (1.38)	
Type of housing			0.293		0.156
Flat	913 (84.9)	23.77 (1.05)		-1.22 (1.81)	
Suite	38 (3.5)	24.00 (1.10)		-1.54 (1.83)	
House/Penthouse	29 (2.4)	23.52 (0.94)		-0.50 (1.65)	
Rooftop shack/Sub-divided unit	22 (2.0)	23.92 (1.27)		-1.16 (1.69)	

AL: Axial length; SER: Spherical equivalent refraction

†*p* values reported here were the significance level of univariate analysis between groups

3.2 Living environment - between group comparison

AL and SER were plotted across different groups of each variable individually. For AL, we observed significant difference in population density of the residential district ($F(2,1072) = 6.15$, $p = 0.002$, Figure 1) and home size ($F(2,1072) = 3.16$, $p = 0.04$, Figure 2). However, the difference in association of

AL in type of housing was not significant ($F(3,1071) = 1.24$, $p = 0.29$). Axial length increased as population density of the residential districts increased, but significant difference could only be observed in districts with low population density when compared with those with high population density ($p = 0.002$). There was also a decreasing trend of AL with home size. A significant difference was observed between those living in a larger home and those living in a smaller home ($p = 0.04$). For SER, we also observed significant difference in population density of the residential district ($F(2,1072) = 7.88$, $p < 0.001$, Figure 1) and home size ($F(2,1072) = 4.25$, $p = 0.02$, Figure 2). However, the difference in association of SER in type of housing was again insignificant ($F(3,1071) = 1.75$, $p = 0.16$). SER was more negative as population density of the residential districts increased. Significant difference could be observed in districts with low population density when compared with those with high population density ($p = 0.001$) and districts with medium population density when compared with those with high population density ($p = 0.009$). SER was less negative as home size increased. A significant difference was observed between those living in a large-sized home and those living in a small-sized home ($p = 0.02$), and between those living in a large-sized home and those living in a medium-sized home ($p = 0.03$)

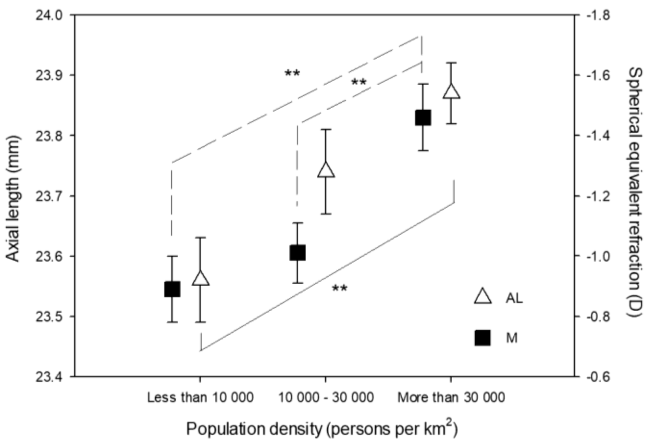

Figure 1. Association of population density of the residential district with axial length (AL) and non-cycloplegic spherical equivalent refraction (SER). The triangles and squares represent the mean ± standard error of AL and SER, respectively. Bonferroni correction: * p <0.05, ** p < 0.01.

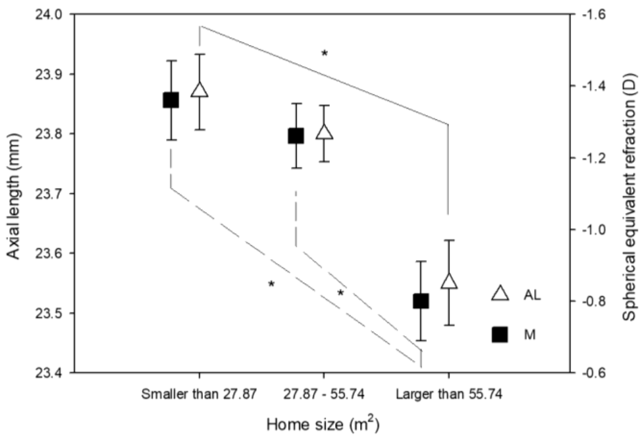

Figure 2. Association of home size with axial length (AL) and non-cycloplegic spherical equivalent refraction (SER). The triangles and squares represent the mean ± standard error of AL and SER, respectively. Bonferroni correction: * p <0.05, ** p < 0.01.

3.3 Living environment – multivariate analysis

The multiple linear regression models were overall significant (AL: $F(14,1060) = 10.26$, $p < 0.001$; SER: $F(14,1060) = 4.88$, $p < 0.001$) and the adjusted R^2 were 0.13 and 0.06 respectively. Table 2 summarises the effect of individual variable, and the p values were from a multivariate analysis of all variables, adjusted for gender, age, parental education level, and parental myopia. Among individual target covariates in the AL model, only population density of the residential district and home size made significant contribution. The *B* value (regression coefficient) for living in a district of high population density was 0.24 (95% CI 0.07 to 0.40), indicating that children living in districts with high population density were predicted to have a 0.24mm longer eye compared with those living in districts with low population density. However, the *B* value for medium population density was not significant ($p = 0.45$). The home size recorded a *B* value of 0.25 (95% CI 0.05 to 0.46) when comparing a large-sized and a small-sized home, predicting a 0.25mm longer eye for those living in a small-sized home. For a medium-sized home, the *B* value was 0.19 (95% CI 0.00 to 0.37) when compared to a large-sized home, indicating a 0.19mm longer eye for those living in a medium-sized home. Furthermore, type of housing did not significantly contribute to the model (Suite: $p = 0.17$; House/Penthouse: $p = 0.95$; Sub-divided unit/Rooftop shack: $p = 0.94$). In the SER model, only population density of the residential district and home size showed significant contribution. The *B* value for living in a district of high population density was -0.53 (95% CI -0.83 to -0.23), indicating that the SER of children living in districts with high population density were predicted to be 0.53D more myopic, or less hyperopic, compared with those living in districts with low population density. However, the *B* value for medium population density was not significant (p = 0.90). The home size recorded a *B* value of -0.47 (95% CI -0.86 to -0.08) when comparing a large-sized and a small-sized home, predicting the SER for those living in a small-sized home were 0.47D less, but the *B* value for medium-sized home was not significant (p = 0.06). Furthermore, type of housing did not significantly contribute to the model (Suite: p = 0.26; House/Penthouse: p = 0.63; Sub-divided unit/Rooftop shack: p = 0.72). The non-cycloplegic SER was similar to and supported the AL results.

Table 2. Multivariate analysis on axial length and spherical equivalent refraction

	B value (S.E.)	95% CI	*p* value
Axial length (mm)			
Population density of the residential district			
>30k persons per km^2	0.24 (0.08)	0.07 to 0.40	0.005
10-30k persons per km^2	0.07 (0.09)	-0.11 to 0.25	0.45
(ref = <10k persons per km^2)			
Home size			
<27.78 m^2	0.25 (0.10)	0.05 to 0.46	0.01
27.78-55.74 m^2	0.19 (0.09)	0.00 to 0.37	0.05
(ref = >55.74 m^2)			
Type of housing			
Suite	0.22 (0.17)	-0.10 to 0.55	0.17
House/Penthouse	-0.01 (0.18)	-0.37 to 0.35	0.95
Rooftop shack/Sub-divided unit	-0.02 (0.21)	-0.43 to 0.40	0.94
(ref = Flat)			
Spherical equivalent refraction (D)			
Population density of the residential district			
>30k persons per km^2	-0.53 (0.15)	-0.83 to -0.23	0.001
10-30k persons per km^2	-0.02 (0.16)	-0.33 to 0.29	0.90
(ref = <10k persons per km^2)			
Home size			
<27.78 m^2	-0.47 (0.20)	-0.86 to -0.08	0.02
27.78-55.74 m^2	-0.31 (0.17)	-0.64 to 0.02	0.06
(ref = >55.74 m^2)			
Type of housing			
Suite	-0.35 (0.31)	-0.95 to 0.25	0.26
House/Penthouse	0.17 (0.34)	-0.51 to 0.84	0.63
Rooftop shack/Sub-divided unit	0.14 (0.40)	-0.63 to 0.92	0.72
(ref = Flat)			

Confounding covariates included age, gender, parental myopia, and parental education level.

4. Discussion

The results of this study provide further support for an association between living environment and childhood refractive error. One of our major findings is that children living in districts of higher population density have a higher risk of having a longer eye and a more negative non-cycloplegic SER. Other research studies have also shown supporting results.[9-11] The Refractive Error Study in Children (RESC)[22] provided a standardised protocol to measure the prevalence of refractive error in school-aged children worldwide,[9, 23-26] enabling easy comparison as all the sampling and measurement protocols were the same. The RESC group found that studies conducted in urban areas revealed a higher myopia prevalence than those in rural areas.[27-29] Besides RESC, the Sydney Myopia Study[30] investigated many modifiable risk factors such as volume of near work,[14] time spent in outdoor activities,[31] and urbanicity of the residence.[11] For the living environment, Ip and co-workers found that children living in the inner city were more likely to have myopia than those living in outer suburban areas. In Hong Kong, the results were similar. We grouped the 18 political districts in Hong Kong into three clusters according to their population densities[16] and observed that population density was associated with the risk of having a longer eye (Figure 1). Similar trends were observed in both big and small cities, Sydney and Hong Kong, thus the effect of urbanicity ought not to be overlooked in considering factor that associates with childhood refractive error.

The second major observation of our study was the association of the home size with childhood refractive error. Children living in a home smaller than 27.87m^2 (300 ft^2) had a significantly longer eye when compared to those living in a home larger than 55.74m^2 (600 ft^2). Although myopia prevalence was thought to increase with socioeconomic status, which can partially be reflected by large home size and high parental education level, in our sample the small home size showed a stronger association with longer axial length and more negative SER than higher parental education level (AL: $F(3,1071) = 2.02$, $p = 0.11$; SER: $F(3,1071) = 0.77$, $p = 0.51$). One possible reason may be the constricted environment at home creating peripheral hyperopic defocus from the surroundings. Numerous studies had shown that peripheral hyperopic defocus accelerates, while peripheral myopic defocus retards, myopia progression.[32-35] In different visual environments, objects nearby produce various amount of defocus to the eye with regards to the plane of focus.[36, 37] Generally, an indoor environment creates more peripheral hyperopic defocus than an outdoor environment.[37] This condition may also apply to a constricted area in an indoor setting versus an open area, thus children in a smaller home would be exposed to stronger peripheral hyperopic defocus compared with those in a larger home.

The type of housing may be another factor associated with myopia prevalence. A recent nationwide population-based study in China evaluated the impact of living environment on myopia in school-aged children.[15] From their sizable sample, myopia was associated with the type of housing, in terms of the height of residential buildings. Higher myopia prevalence was observed in children living in taller buildings, which is independent of the residential region, age, gender and ethnicity. In the Sydney Myopia Study, myopia was more frequently observed in children living in apartments and terrace houses than those living in stand-alone or separate houses.[38] They suggested it was related to the nature of housing type, among which terrace houses and apartments are smaller and more confined. However, studies in Singapore did not show such relationship.[39, 40] Our study showed that home size was associated with axial length and refractive error instead of the type of housing. One possible reason for the insignificance may be the variation of housing type in Hong Kong was relatively too little, as the majority live in a flat-styled home. This could be a possible explanation why Asian children living in urban area are more likely to have myopia as they mostly live in flat-styled accommodation, yet it could not be reflected in our study.

The housing issue has been a complicated problem in Hong Kong. In 2015, the average living space per person in public housing was 13.1m^2.[17] Furthermore, according to a survey in 2009, Hong Kong had the lowest average residential floor space per person among 14 countries worldwide.[41] When compared to Australia, Hong Kong has only one fifth of the average residential floor space per person. For the average new home size built in 2009, Hong Kong again had the smallest area,[42] which was less than one fourth of those in Australia, Canada and the US. Our findings suggested that the small living space in Hong Kong is associated with a longer eye and a more minus refractive error. We speculate that the small home size and dense population may be two additional factors which are associated with the high prevalence of myopia in other East-Asian countries[43] apart from other known factors.

This study was strong in several aspects. The participation rate (95%) was high because this research project was also a community service project, which did not further filter subjects within the sampled groups. The sampling method was modified to recruit a proportional number of subjects from districts of different population densities, so that the sample would reflect the characteristics of the population. We set out to make the questionnaire as simple and straightforward as possible so that parents could easily provide valid data. Qualified optometric personnel conducted all measurements in the study to ensure the accuracy of the results.

Yet, our study was not without limitations. A cycloplegic agent was not instilled because the data were collected on normal school days, and we did not want to interrupt the students' daily study. This may affect the accuracy of the auto-refraction as the subjects may accommodate, resulting in a more minus SER.[19] However, the SER results were strongly correlated with the AL measurements (SER vs. AL: $r = -0.74$, $p < 0.001$), and hence could still identify the risk factors in the regression model. In addition, the data collection process adopted a self-reported questionnaire instead of an interview, which may hinder the data reliability to some extent. We tried to maximise the readability and ensure parents could understand the questionnaire without further explanation by inviting 10 laymen to answer the questionnaire. Our cross-sectional study could only establish the association between ocular parameters and living environment at a single time point. Further longitudinal studies shall be conducted to investigate the relationship between constricted living space and refractive error development.

5. Conclusion

In conclusion, there was an association between childhood refractive error and living environment, in terms of the size of home and the population density of the residential area. We speculate small homes and densely populated residential areas may be new types of "visual pollutants" that associate with the high prevalence of myopia.

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List of figure legends

Figure 1. Association of population density of the residential district with axial length (AL) and non-cycloplegic spherical equivalent refraction (SER). The triangles and squares represent the mean ± standard error of AL and SER, respectively. Bonferroni correction: * p <0.05, ** p < 0.01.

Figure 2. Association of home size with axial length (AL) and non-cycloplegic spherical equivalent refraction (SER). The triangles and squares represent the mean ± standard error of AL and SER, respectively. Bonferroni correction: * p <0.05, ** p < 0.01.