

# Trends in the Prevalence of Myopia and Myopic Maculopathy in a Japanese Population: The Hisayama Study

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Submitted: January 9, 2019

Accepted: June 5, 2019

Citation: Ueda E, Yasuda M, Fujiwara K, et al. Trends in the prevalence of myopia and myopic maculopathy in a Japanese population: the Hisayama study. *Invest Ophthalmol Vis Sci.* 2019;60:2781-2786. <https://doi.org/10.1167/iops.19-26580>

**PURPOSE.** To examine trends in the prevalence of myopia and myopic maculopathy in a general Japanese population.

**METHODS.** Residents of a Japanese community aged 40 years and older participated in surveys conducted in 2005, 2012, and 2017. Each participant underwent comprehensive eye examinations that included measurements of refractive error, axial lengths, and color fundus photography. Myopic maculopathy was defined according to the criteria of the Meta-analysis of Pathologic Myopia Study Group classification system. Trends in the prevalence of myopia and myopic maculopathy were tested by using a logistic regression analysis fitted by generalized estimating equations to account for individuals submitting to repeated examination.

**RESULTS.** The age-adjusted frequencies of myopia increased significantly from 2005 to 2017 (myopia, 37.7%–45.8%; high myopia 5.8%–9.5%; all *P* for trend <0.001). The age-adjusted frequency of an axial length level of 26.5 mm or more increased significantly from 2005 to 2017 (3.6%–6.0%; *P* for trend <0.001). The age-adjusted prevalence of myopic maculopathy also increased significantly with time (1.6% in 2005, 3.0% in 2012 and 3.6% in 2017; *P* for trend <0.001). Upward trends were observed in the prevalence of diffuse chorioretinal atrophy and patchy chorioretinal atrophy (all *P* for trend <0.05).

**CONCLUSIONS.** Our findings suggest that the prevalence of myopia and myopic maculopathy, especially diffuse chorioretinal atrophy and patchy chorioretinal atrophy, increased significantly over the past 12 years in a general Japanese population.

Keywords: epidemiology, myopia, myopic maculopathy

Myopia is increasing worldwide and has become an extensive public health problem.<sup>1</sup> The prevalence of myopia in the east Asian region has been acknowledged to be higher than that in other regions,<sup>1</sup> possibly due to increasing educational pressures, combined with lifestyle changes, which have reduced the time children spend outside.<sup>2,3</sup> In Japan, myopia has become a common ocular disorder among school children in the past 50 years,<sup>4,5</sup> partly due to the prevalence of high-pressure educational systems<sup>6–8</sup> since the 1960s, and partly to the excessive use of near electronic devices in more recent decades.<sup>9</sup>

Myopic maculopathy is one of the most important complications of myopia for middle-aged and older people, and often causes significant visual impairment in both Asian<sup>10,11</sup> and Western<sup>12,13</sup> populations. Several epidemiologic studies have examined the prevalence of myopic maculopathy.<sup>14–21</sup> However, the definition of myopic maculopathy has not been consistent across studies owing to the lack of a common classification scheme. To address this issue, the Meta-Analysis of Pathologic Myopia (META-PM) study group proposed a new classification system for myopic maculopathy,<sup>22</sup> and their

standardized diagnostic criteria have made it possible to directly compare the prevalence and subtypes of individual myopic lesions, and to examine trends more accurately.

It is generally assumed that myopic maculopathy will increase dramatically among middle-aged and elderly individuals along with the aging of recent generations of young adults, who have a high prevalence rate of myopia.<sup>1</sup> However, there have been no studies examining trends in the prevalence of myopia and myopic maculopathy in these age groups. The purpose of this study was to investigate trends in the prevalence of myopia and myopic maculopathy over the last decade among a general Japanese population aged 40 years or older.

## MATERIALS AND METHODS

### Study Population

The Hisayama Study is an ongoing, long-term, population-based study on cardiovascular disease and its risk factors in the town of Hisayama, which is adjacent to the Fukuoka metropolitan



**TABLE 1.** Trends in Mean Values or Median Values of Myopia-Related Factors From 2005 to 2017

Variables	2005, <i>n</i> = 1892	2012, <i>n</i> = 2874	2017, <i>n</i> = 2936	<i>P</i> for Trend
Age, y*	63 (11)	63 (12)	64 (13)	0.37
Sex (women %)	59.0	56.2	55.8	0.37
Height, cm*	156.4 (8.9)	157.8 (9.3)	155.8 (9.5)	<0.001
SE refraction, D†‡	−0.1 (−1.3 to 1.0)	−0.1 (−2.0 to 0.9)	−0.4 (−2.4 to 0.8)	<0.001
Axial length, mm†‡	23.4 (22.7 to 24.2)	23.6 (22.9 to 24.5)	23.8 (23.0 to 24.8)	<0.001

\* Values are expressed as unadjusted means (standard deviations).

† Values are expressed as medians (interquartile ranges).

‡ Data from right eyes.

area in southern Japan.<sup>23</sup> As a part of the study, an epidemiologic study of eye disease among the residents aged 40 years or older has been underway since 1998.<sup>24</sup> For the present study, we performed a series of three cross-sectional surveys for myopic maculopathy in 2005, 2012, and 2017, which included available data on objective refraction and axial length.

In 2005, all residents of the town of Hisayama who were aged 40 years or older on April 1<sup>st</sup> (*n* = 4439) were encouraged to participate in eye examinations in conjunction with health check-ups conducted by home visits of the study team and staff members of the town's Health and Welfare Office. Among them, a total of 1895 subjects (participation rate, 42.7%) consented to participate in the eye examinations. In the same manner, we performed eye examinations on 2948 of 4624 residents (participation rate, 63.8%) in 2012 and 3246 of 4938 residents (participation rate, 65.7%) in 2017. In addition, we excluded subjects who had missing or ungradable photographs in both eyes from the examined population for each survey year (3 subjects in 2005, 74 subjects in 2012, and 310 subjects in 2017). As a consequence, we enrolled 1892 subjects in 2005, 2874 subjects in 2012, and 2936 subjects in 2017 in the present study. In the additional analysis using spherical equivalent (SE) refraction data, subjects with a history of cataract surgery or unavailable SE refraction data were also excluded; there were 241 such subjects in 2005, 529 in 2012, and 529 in 2017.

### Ophthalmic Examination and Other Myopia-Related Factor Measurements

Ophthalmic examinations and clinical evaluations were carried out in a similar manner among the three surveys included in this study. In the ophthalmic examination, the measurements of objective refraction, axial lengths, and noncontact tonometry, and the color fundus photography of both eyes were performed for each participant. Objective refraction was measured using an AR-660 automatic refractometer (Nidek, Aichi, Japan) without cycloplegia. A SE refraction was used to calculate refractive error. The SE refraction was defined as a sphere plus half of the cylindrical refraction. Myopia and high myopia were defined as SE refraction <−0.5 diopters (D) and SE refraction <−5.0 D, respectively. Axial length measurements were performed with noncontact partial coherence laser interferometry using an IOL Master (Carl Zeiss, Hennigsdorf, Germany) in 2005 and 2012 or an OA-2000 (Tomey GmbH, Nagoya, Japan) in 2017. Nonstereoscopic fundus photographs (45°) were taken using a nonmydriatic digital fundus camera (TRC NW-200 in 2005 and 2012, DRI-OCT Triton in 2017; Topcon Corporation, Tokyo, Japan). We photographed one field, centered at a point midway between the temporal edge of the optic disc and the fovea in both eyes.

In the clinical evaluation, body height was measured in light clothing without shoes.

### Definition of Myopic Maculopathy

The presence of myopic maculopathy was determined based on the grading of the color fundus photographs. All photographs were evaluated independently by two experienced ophthalmologists (EU and SH). When their judgments disagreed, the photographs were reexamined by three retinal specialists (EU, SH, and MY) and the final judgment was determined after discussion. Graders were blinded to the clinical data of participants in the process of the photograph evaluation. The level of agreement between the graders was moderate (the  $\kappa$  statistic: 0.86) to substantial for most features.

Based on the META-PM study group classification system, myopic maculopathy was graded into the following three categories: diffuse chorioretinal atrophy (category 2), patchy chorioretinal atrophy (category 3), and macular atrophy (category 4).<sup>22</sup> To supplement this categorization, lesions with any of three additional features—lacquer cracks, myopic choroidal neovascularization, and Fuchs spot—were defined as plus lesions. An eye was considered to have myopic maculopathy if category 2, 3, 4, or any plus lesion was observed according to fundus photograph grading.<sup>22</sup> When a participant had different categories for each eye, the eye with the more severe myopic maculopathy category was chosen for analysis.

### Statistical Methods

The SAS software package version 9.4 (SAS Institute, Cary, NC, USA) was used to carry out all statistical analyses. The frequencies of each SE refraction and axial length, and the prevalence of myopic maculopathy were adjusted for age and calculated by using the generalized estimating equations (GEE).<sup>25,26</sup> Because some subjects participated in two or all three of the surveys, the trends in the prevalence of each factor across survey years were assessed by the logistic or linear regression analysis fitted by GEE to account for individuals who submitted to more than one examination. A two-tailed value of  $P < 0.05$  was considered statistically significant in all analyses.

### Ethical Considerations

This study was approved by the Kyushu University Institutional Review Board for Clinical Research, and was carried out in accordance with the Declaration of Helsinki. Informed consent was obtained from all participants.

### RESULTS

Among the surveys, the mean age of the participants was approximately 65 years. The proportion of women was approximately 60% over the study period.

The mean values, median values, and frequencies of myopia-related factors are summarized in Tables 1 and 2. The

**TABLE 2.** Trends in the Age-Adjusted Frequencies of Myopia-Related Factors From 2005 to 2017

Variables	2005, <i>n</i> = 1892	2012, <i>n</i> = 2874	2017, <i>n</i> = 2936	<i>P</i> for Trend
SE refraction level				
<−0.5 D	37.7 (35.5–40.0)	40.6 (38.7–42.5)	45.8 (43.9–47.7)	<0.001
<−1.0 D	27.7 (25.8–29.8)	32.6 (30.9–34.4)	38.0 (36.2–39.8)	<0.001
<−5.0 D	5.8 (4.9–6.8)	8.0 (7.0–9.0)	9.5 (8.5–10.6)	<0.001
<−8.0 D	1.5 (1.1–2.1)	2.5 (2.0–3.1)	3.0 (2.5–3.7)	<0.001
Axial length level				
<23.5 mm	55.0 (53.1–57.0)	46.2 (44.5–47.9)	41.8 (40.1–43.5)	<0.001
23.5–24.9 mm	32.2 (30.4–34.3)	35.2 (33.7–36.8)	36.0 (34.4–37.6)	<0.001
25.0–26.4 mm	7.9 (6.9–9.0)	10.6 (9.6–11.7)	12.9 (11.8–14.1)	<0.001
≥26.5 mm	3.6 (3.0–4.5)	5.1 (4.4–5.9)	6.0 (5.3–6.9)	<0.001

Data from right eyes. Values are expressed as the percentages (95% confidence interval).

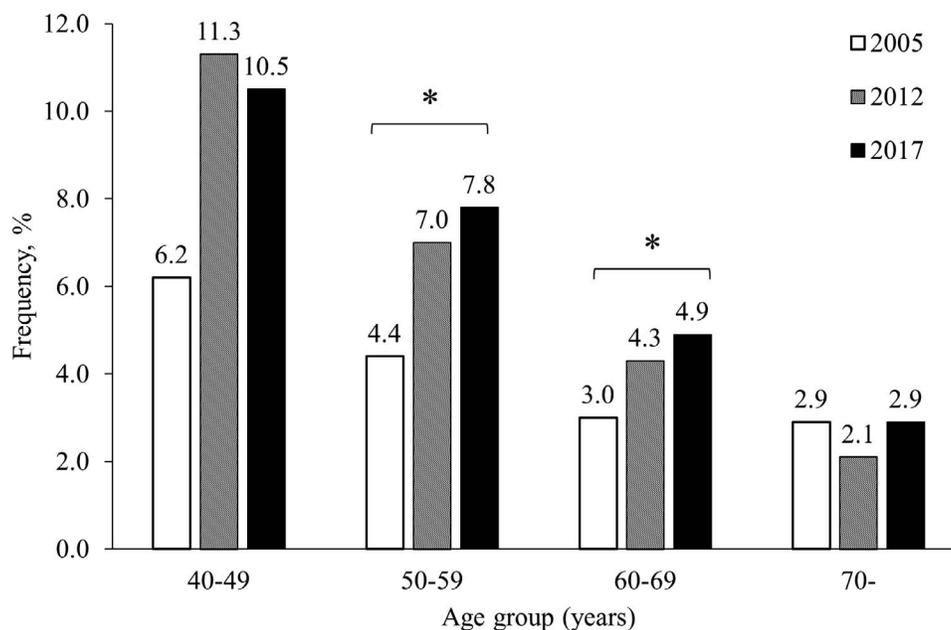
mean value of body height increased significantly with time. The age-adjusted frequencies of myopia increased from 37.7% in 2005 to 45.8% in 2017 (*P* for trend < 0.001). Similarly, there were increasing trends in the prevalence of high myopia from 5.8% to 9.5% with time (*P* for trend < 0.001). The age-adjusted frequency of an axial length level of less than 23.5 mm decreased significantly, whereas the frequencies of the axial length levels of 25.0 to 26.4 and 26.5 mm or more increased significantly from 2005 to 2017 (all *P* for trend < 0.001). The age-specific frequency of an axial length level of 26.5 mm or more is shown in Figure 1. The frequency of longer axial length (≥26.5 mm) increased in the age groups of 50 to 59 and 60 to 69 years from 2005 to 2017.

Next, we compared the age-adjusted prevalence of myopic maculopathy among the three surveys (Table 3). The age-adjusted prevalence of myopic maculopathy increased significantly with time (1.6% in 2005, 3.0% in 2012, and 3.6% in 2017; *P* for trend < 0.001). Similar trends were observed for the prevalence of myopic maculopathy in both sexes (Supplemental Fig. S1). With regard to the categories of myopic maculopathy defined by the META-PM study group, the prevalence of diffuse chorioretinal atrophy (category 2) and patchy chorioretinal atrophy (category 3) increased (diffuse

chorioretinal atrophy: *P* for trend = 0.004; patchy chorioretinal atrophy: *P* for trend < 0.001) with time. Conversely, the prevalence of macular atrophy (category 4) did not change across the surveys (*P* for trend = 0.51). In addition, the prevalence of all plus lesions did not change over the study period (Lacquer cracks: *P* for trend = 0.41; myopic choroidal neovascularization: *P* for trend = 0.92; Fuchs spot: *P* for trend = 0.65). The age-specific prevalence of myopic maculopathy increased significantly from 2005 to 2017 in the 50- to 59-, 60- to 69-, and 70-years or older age groups (all *P* for trend < 0.05), but it did not reach the statistically significant level in the 40- to 49-years group (*P* for trend = 0.08) (Fig. 2).

## DISCUSSION

The present study demonstrated that the age-adjusted frequency of myopia and high myopia increased significantly from 2005 to 2017 in a general Japanese population. The age-adjusted frequency of the axial length levels of 26.5 mm or more increased over time. The age-adjusted prevalence of myopic maculopathy, determined by the META-PM study group classification system, increased progressively with time. In addition, significant increases in the prevalence of diffuse



**FIGURE 1.** Trends in the age-specific frequency of axial length ≥26.5 mm from 2005 to 2017. The frequency of longer axial length (≥26.5 mm) increased in the age groups of 50 to 59 and 60 to 69 years from 2005 to 2017. \**P* < 0.05.

TABLE 3. Age-Adjusted Prevalence of Category for Myopic Maculopathy From 2005 to 2017

Variables	2005, n = 1892		2012, n = 2874		2017, n = 2936		P for Trend
	n	% (95%CI)	n	% (95%CI)	n	% (95%CI)	
Myopic maculopathy	33	1.6 (1.2-2.2)	81	3.0 (2.5-3.6)	109	3.6 (3.0-4.3)	<0.001
Diffuse atrophy (category 2)	21	1.1 (0.7-1.6)	40	1.5 (1.1-2.0)	55	1.9 (1.4-2.4)	0.004
Patched atrophy (category 3)	5	0.3 (0.1-0.6)	30	1.0 (0.7-1.4)	41	1.3 (0.9-1.7)	<0.001
Macular atrophy (category 4)	7	0.3 (0.1-0.5)	11	0.3 (0.2-0.6)	13	0.4 (0.2-0.7)	0.51
Plus lesions							
Lacquer cracks	3	0.1 (0.04-0.4)	9	0.2 (0.1-0.6)	9	0.2 (0.1-0.5)	0.41
Myopic choroidal neovascularization	2	0.1 (0.02-0.3)	5	0.1 (0.04-0.4)	4	0.1 (0.04-0.4)	0.92
Fuchs spot	2	0.1 (0.02-0.3)	11	0.2 (0.1-0.5)	6	0.2 (0.04-0.4)	0.65

Values are expressed as the percentages (95% confidence interval).

chorioretinal atrophy (category 2) and patchy chorioretinal atrophy (category 3) were found over the study period. To the best of our knowledge, this is the first population-based study to examine trends in the prevalence of myopia and myopic maculopathy among both middle-aged and elderly participants in a general Japanese population.

There have been only a few community-based epidemiologic studies addressing the trend in myopia among adults. One of these, the National Health and Nutrition Examination Survey,<sup>27</sup> reported that the incidence of myopia among adult participants increased from 24.8% to 44.8% between 1971 and 1999, which is consistent with our findings. Several epidemiologic studies have reported an increasing trend in the prevalence of myopia in adolescence among several developed countries as well as Japan.<sup>4,5,28</sup> The Japanese Ministry of Education, Science, and Culture reported that the prevalence of myopia increased rapidly from 11.6% to 62.3% between 1949 and 2017 among high school students in all 47 prefectures throughout Japan.<sup>5</sup> The other population-based

study was conducted in 17-year-old Japanese students and showed that the prevalence of myopia increased from 49.3% to 65.6% over a 13-year period from 1984 to 1996.<sup>4</sup> Because adolescents have consistently exhibited high rates of myopia over the last 5 decades in Japan,<sup>4,5</sup> it is reasonable to consider that, as these adolescents grow older, the prevalence of myopia among adults will increase.

The present study demonstrated an increasing trend in the prevalence of myopic maculopathy in Japan. The age-adjusted prevalence of myopic maculopathy was 3.0% in our 2012 survey and 3.6% in our 2017 survey. Since 2011, there have been two population-based studies on the prevalence of myopic maculopathy defined using the META-PM study group classification system as follows: the 2013 Chinese American Eye Study,<sup>17</sup> which reported a prevalence of 2.5%, and the 2011 Singapore Epidemiology of Eye Diseases study,<sup>21</sup> which found a prevalence of 3.8%. The frequency of myopia (SE refraction < -0.5 D) in our 2012 study was 40.6%, which is higher than that in the Singapore Epidemiology of Eye Diseases

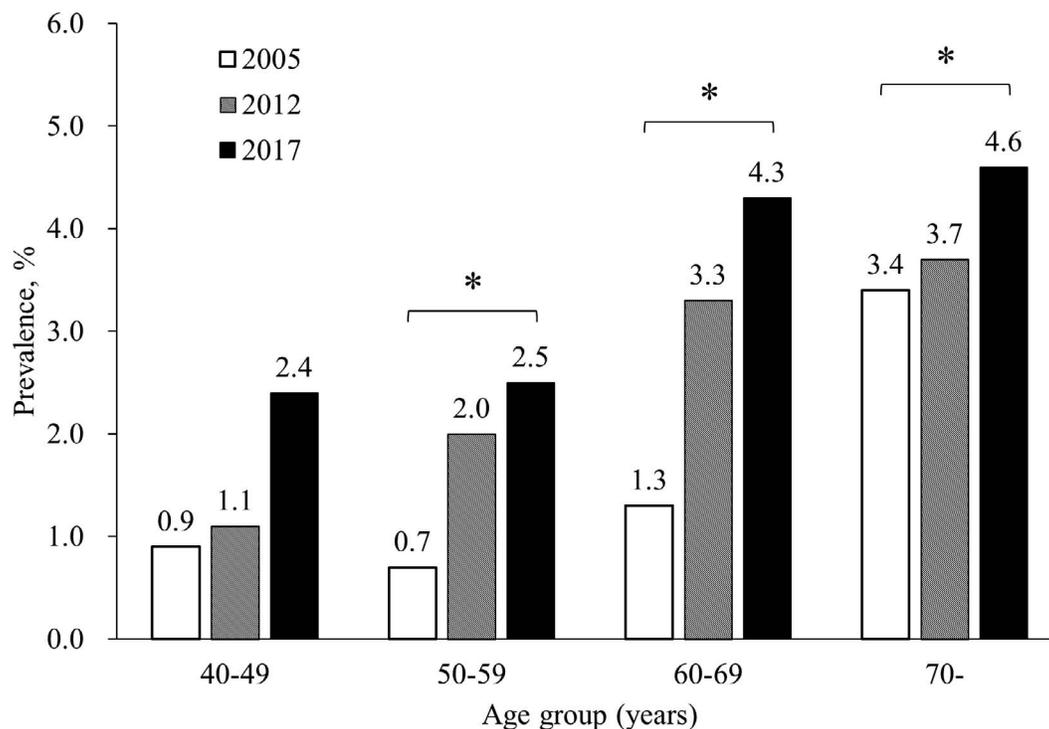


FIGURE 2. Trends in the age-specific prevalence of myopic maculopathy from 2005 to 2017. The age-specific prevalence of myopic maculopathy increased significantly in the 50- to 59-, 60- to 69-, and 70-years or older age groups from 2005 to 2017. \* $P < 0.05$ .

study (35.6%) and that in the Chinese American Eye study (36.8%). The prevalence of myopic maculopathy may be higher in Singapore than in Japanese and Chinese American populations. The precise reason for the racial differences in the prevalence of myopic maculopathy is unknown, but it could be related to differences in the characteristics of study participants (e.g., the age and proportion of either sex), or perhaps to genetic factors.

In the present study population, the age-adjusted frequency of the axial length level of 26.5 mm or more increased with time. The elongation of axial length is known to be the major structural cause of myopia. As to the possible mechanism underlying the increase in myopic maculopathy, axial elongation due to thinning of the choroid may be the most likely candidate.<sup>29-31</sup> Several epidemiologic studies have reported a significant association between longer axial length and the presence of myopic maculopathy.<sup>14-21</sup> Similarly, we previously reported<sup>20</sup> that longer axial length was one of the risk factors for myopic maculopathy in our study subjects. In addition, several studies have shown that axial length was correlated negatively with choroidal thickness.<sup>29-31</sup> A prospective observational study found that macular choroidal thickness is an indicator of the severity of myopic maculopathy.<sup>31</sup> The authors of that report conjectured that marked thinning of the choroid may lead to pathological fibrotic changes and macular degeneration.<sup>31</sup> In light of these findings, the elongation of axial length may contribute to the trend of increased prevalence of myopic maculopathy. Prospective longitudinal studies are needed to confirm the influence of axial length on the development of myopic maculopathy.

In the present study, we investigated the trends in the prevalence of subcategories of myopic maculopathy defined based on the disease-progression patterns according to the criteria of the META-PM study group. The increase was prominent in the subgroups with diffuse chorioretinal atrophy (category 2) and patchy chorioretinal atrophy (category 3). The reason for these increases in diffuse chorioretinal atrophy and patchy chorioretinal atrophy is not precisely clear, but the elongation of axial length may have played a role. On the other hand, macular atrophy (category 4) was unchanged over the study period. Importantly, macular atrophy is significantly associated with worse vision than either diffuse chorioretinal atrophy or patchy chorioretinal atrophy.<sup>21,32</sup> Therefore, further ongoing studies will be needed to confirm that macular atrophy will increase as younger individuals, who seem to be more dependent on the relevant environmental parameters, advance in age.

The strengths of our study include the use of a novel unified system of myopic maculopathy diagnosis across all three cross-sectional surveys. Several limitations of our study should also be mentioned. First, the participation rates were not very high at the three cross-sectional examinations, which likely meant there was a selection bias present at all three visits, possibly resulting in an underestimation of the prevalence of either myopia or myopic maculopathy. This was particularly true of the examination in 2005, which had much lower participation than the other two examinations. However, the prevalence of myopia and myopic maculopathy increased substantially from 2012 to 2017, despite these surveys having similar participation rates. In addition, we compared axial lengths measured in the 2012 survey between subjects who participated in both the 2005 and 2012 surveys and those who participated in only the 2012 survey and not the 2005 survey. As a consequence, we found that there was no difference in axial length in 2012 between these subjects ( $P = 0.33$ ), which suggests that the influence of any selection bias on the present findings was probably modest. Second, a

total of 2561 (64.9%) subjects participated in two or more of three surveys. In order to overcome this problem, the trends in myopia and myopic maculopathy across the three time periods were assessed using GEE with a logit link function in the present study. The GEE approach, which was developed by Zeger et al.,<sup>25</sup> considers the correlation among repeated participation of the same individuals.<sup>26</sup> A significant rise in the age-adjusted prevalence of myopic factors and myopic maculopathy was observed in the GEE analysis, and we therefore believe that the findings of the present study reflect the rising trends in the prevalence of myopic maculopathy with time in a Japanese community. Third, the detection and classification of myopic chorioretinal atrophy was performed using only fundus photographs, not optical coherence tomography or fluorescein and indocyanine green angiograms, and this could have led to an underestimation of the true prevalence. However, we consider that this limitation may not have exerted a meaningful influence on our findings of increase in the prevalence of diffuse chorioretinal atrophy and patchy chorioretinal atrophy. Fourth, we could not discuss the trends in the prevalence of plus lesions due to the very small numbers of plus lesions. Large-scale studies are required to elucidate this issue.

In conclusion, the present findings indicated that the prevalence of myopia and myopic maculopathy, particularly diffuse chorioretinal atrophy and patchy chorioretinal atrophy, increased significantly from 2005 to 2017. Because the prevalence of myopia among the world population is expected to continue to rise over the next 30 years, further investigations using standardized definitions of myopic maculopathy will be needed to predict how this condition will change and progress.

### Acknowledgments

The authors thank the residents of the town of Hisayama for their participation in the survey and the staff of the Division of Health and Welfare of Hisayama for their cooperation with this study. The statistical analyses were carried out using the computer resource offered under the category of General Projects by Research Institute for Information Technology, Kyushu University.

Supported by Grants-in-Aid for Scientific Research (Tokyo, Japan) (A; JP16H02644 and JP16H02692), (B; JP16H05850, JP16H05557, JP17H04126, and JP18H02737) and (C; JP16K09244, JP17K09114, JP17K09113, JP17K01853, JP18K07565, and JP18K09412) and Grants-in-Aid for Early-Career Scientists (Tokyo, Japan) (JP18K17925, JP18K17382, and JP18K16960) from the Ministry of Education, Culture, Sports, Science and Technology of Japan; by Health and Labour Sciences Research Grants of the Ministry of Health, Labour and Welfare of Japan (Tokyo, Japan) (H29-Junkankitou-Ippan-003 and H30-Shokuhin-[Sitei]-005); and by Grants-in-Aid from the Japan Agency for Medical Research and Development (Tokyo, Japan) (JP18dk0207025, JP18ek0210082, JP18gm0610007, JP18ek0210083, JP18km0405202, JP18ek0210080, and JP18fk0108075).

Disclosure: E. Ueda, None; M. Yasuda, None; K. Fujiwara, None; S. Hashimoto, None; K. Ohno-Matsui, None; J. Hata, None; T. Ishibashi, None; T. Ninomiya, None; K.-H. Sonoda, None

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