World Health Organization

THE IMPACT OF MYOPIA AND HIGH MYOPIA

Report of the Joint World Health Organization–Brien Holden Vision Institute Global Scientific Meeting on Myopia

University of New South Wales, Sydney, Australia
16–18 March 2015

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1. Executive summary

1.1 Introduction

The prevalence of myopia and high myopia is increasing globally at an alarming rate, with significant increases in the risks for vision impairment from pathological conditions associated with high myopia, including retinal damage, cataract and glaucoma. The impact of myopia is difficult to determine, because there are no standard definitions of myopia and high myopia, and recognition that myopia can lead to vision impairment is limited by the absence of a defined category of myopic retinal disease that causes permanent vision impairment. A further impediment to progress in this area is insufficient evidence of the efficacy of various methods for controlling myopia.

In view of concern about the current and future impact of myopia, the Minister of Health for Australia, the Right Honourable Mr Peter Dutton, contacted the Director-General of WHO, Dr Margaret Chan, to request the involvement of WHO in an international scientific meeting on myopia to be held by the Brien Holden Vision Institute (BHVI). As a result, a three-day joint WHO–BHVI meeting was convened on 16–18 March 2015 at the University of New South Wales in Sydney, Australia.

1.2 Summary

Scientific and clinical experts in myopia were invited from all six WHO regions (see Annex 1). Keynote presentations, working groups and plenary sessions were held to review the evidence on the major issues in myopia. The results of these deliberations were reported to plenary for discussion, and agreement was reached on a series of statements, definitions and priorities for research.

1.3 Agreed conclusions and recommendations

- The group agreed on definitions of myopia and high myopia and on a category for and description of the pathological consequences of myopia.
- The epidemiological surveys currently used to measure the status of vision (e.g. the WHO protocol and Rapid Assessment of Avoidable Blindness) do not allow the definition of high myopia as a possible cause of vision impairment, partly because these surveys do not include a description of this condition or any measurement of refractive error. The group agreed that action should be taken to include myopia and high myopia among the attributable causes of vision impairment in the surveys currently used.
- Measures for the detection and management of myopia should be an integral part of plans for the provision of eye-care services. They should be part of general health care for vision impairment due to (i) the uncorrected refractive error associated with (the increased prevalence of) myopia; and (ii) the pathological consequences of myopia.
- The term “myopic macular degeneration” (MMD) should be used clinically and in research to categorize the blinding retinal diseases associated with high myopia. Currently, a number of terms are used, including MMD, myopic maculopathy, myopic retinopathy and myopic choroidal neovascularization.

- Epidemiological data are lacking on the prevalence of myopia, high myopia and vision impairment associated with high myopia in Africa, central America, south America and Oceania. These areas should be priorities for future research.

1.4 Specific conclusions and recommendations

Definitions of myopia and high myopia

- The definition of myopia is "a condition in which the spherical equivalent objective refractive error is ≤ –0.50 diopter (–0.50 D) in either eye".
- The definition of high myopia is "a condition in which the spherical equivalent objective refractive error is ≤ –5.00 D in either eye".

Clinical definition of myopic macular degeneration

- The clinical definition of myopic macular degeneration (MMD) is "a vision-threatening condition in people with myopia, usually high myopia, which comprises diffuse, patchy macular atrophy with or without lacquer cracks, choroidal neovascularization and Fuchs spot".
- It was agreed that the direct ophthalmoscope lens power wheel should be used in rapid assessments of avoidable blindness and other surveys to record the power at which the fundus is clearest, to ensure that possible cases of high myopia are recorded.
- Clinical and epidemiological research on myopia
- A cycloplegia agent should be used in clinical or epidemiological studies of children under the age of 18 years.
- In surveys and studies, the continuous distribution of age and refractive errors should be reported for people up to the age of 25 years.
- The ocular history of individuals should include interventions such as refractive surgery and other procedures to reduce refractive error, but not necessarily the consequences of axial eye elongation.
- The use of cycloplegia investigation and its inclusion in survey protocols for both young adults and adults should be investigated further.

Attributing vision loss to high myopia or MMD in blindness surveys (rapid assessment of avoidable blindness, WHO survey protocol and others)

- It was agreed that the term "myopic macular degeneration" (MMD) should be used to define the retinal condition that causes vision impairment in myopia, because it is clearly defined and easily categorized for rapid assessment of avoidable blindness, in the WHO survey protocol and others.

Definition of MMD for the purposes of epidemiological surveys

- The definition of MMD for the purposes of epidemiological surveys (e.g. rapid assessment of avoidable blindness, WHO survey protocol) with limited resources and in remote settings was agreed to be:

"vision impairment and vision acuity that are not improved by pinhole and cannot be attributed to other causes, and direct ophthalmoscopy records a supplementary lens:

≤ –5.00 D and changes such as "patchy atrophy" in the retina, or ≤ –10.00 D".

Myopia correction

- Access to correction for myopia is essential to avoid vision impairment. All people with myopia should have access to appropriate, accurate refractive correction.

Myopia control

- Although there is a widely held clinical view that undercorrection of myopia is beneficial in preventing its progression, the available evidence does not support this idea. Recent reports show that undercorrection is associated with a higher rate of progression of myopia.
- Some initial published evidence indicates that time spent outdoors can delay the onset and perhaps reduce the progression of myopia, although more research is required, as it is also potentially a risk factor. If the evidence is proved correct, it will add beneficial eye care to the list of other health-promoting outdoor activities (e.g. reduction of childhood obesity through exercise, exposure to sunlight for vitamin D production, games for socialization).
- There is published evidence that excessive near work increases the risk of myopia.
- There is published evidence that multifocal spectacles can slightly reduce the rate of progress of myopia; executive bifocal lenses are associated with substantially larger reductions.
- Specially designed contact lenses that reduce peripheral hyperopia and/or create significant myopic defocus can slow the progress of myopia. It is important that contact lenses are appropriately cared for in order to avoid adverse effects.
- Orthokeratology can slow the progress of myopia, but overnight wear of contact lenses is associated with risks.
- Low-dose atropine has been shown to be effective in reducing the progression of myopia but not in slowing the rate of increase of axial length. A dose of 0.01% has few side-effects, but more research is required to determine the optimal regimen.
- Other agents have been suggested for the control of myopia, such as 7-methylxanthine; however, larger clinical trials are needed to establish their safety and efficacy.

Pathological consequences of myopia (pathological myopia)

- High myopia can cause serious, sight-threatening retinal damage. Hence, the following recommendations were agreed for the care and management of pathological myopia.
- Patients with complications from pathological myopia should have access to a full range of eye-care services.
- Myopic choroidal neovascularization is one of the consequences of high myopia that causes vision impairment; agents against vascular endothelial growth factor may be beneficial in the treatment of this condition, but the long-term prognosis for vision is unknown.
- Myopia increases the risk of glaucoma; glaucomatous optic neuropathy should be investigated in patients with high myopia.
- Myopia increases the risk of retinal detachment and cataract; a fundus and anterior segment examination is essential for people with high myopia.
- People with vision impairment that cannot be corrected to a level of vision that they find acceptable should have access to comprehensive eye-care services, including vision rehabilitation and appropriate devices and surgery if necessary.

2. Background and purpose of the consultation

It is estimated that over 285 million people in the world have vision impairment and that 42% of this is due to uncorrected refractive errors *(1).* Published estimates based on epidemiological studies indicate that myopia affects 1.89 billion people worldwide, and, if the current prevalence rates do not change, projections show that it will affect 2.56 billion people by 2020 *(2).* Uncorrected myopia is the leading cause of vision impairment, and MMD in higher myopia was reported as the major cause of new cases of blindness in Tajimi, Japan *(3)* and in Shanghai, China *(4, 5).* In the Beijing Eye Study, it was found that the major cause of vision impairment is cataract in older adults but pathological myopia in the younger cohort *(6)*. Myopia causes vision impairment not only by direct retinal damage *(7)* but also by increasing the risks for cataract *(8)* and the onset of glaucoma *(9).*

The meeting was called because the increasing prevalence of myopia and high myopia and the issue of vision impairment associated with myopia receive insufficient attention from a public health perspective in terms of assessment of prevalence, preventive interventions and possible treatment. Currently, there is no consensus on the thresholds for classifying myopia or high myopia. The terminology, classification and methods to be used in epidemiological studies should be defined in order to assess the extent and contribution of myopia to vision impairment.

A three-day joint WHO–BHVI global scientific meeting on myopia was convened on 16–18 March 2015 at the premises of the Institute, University of New South Wales, Sydney, Australia, in response to a communication from the then Minister of Health for Australia, Mr Peter Dutton, to the Director-General of WHO, Dr Margaret Chan, on the growing concern about myopia and the commitment of the Australian Government to discuss ways of addressing it. The participants were experts in myopia research (see Annex 1) drawn from all six WHO regions. The agenda included keynote presentations and working group sessions to share the most recent results from conclusive research on the core issues discussed, reviewing the published evidence, analysing and agreeing on definitions on the basis of scientific evidence and current medical practice, reviewing epidemiological data on morbidity and discussing the social and economic consequences for children, the elderly and society (for the programme of the meeting, see Annex 2). Particular attention was paid to the evidence on strategies for reducing the assessed and projected increase in myopia prevalence and their applicability in public health beyond research settings.

At the end of the meeting, the definitions and terminology were made available for consideration, in the framework of the 11th revision of the International Classification of Diseases *(10)*,and the conclusions for evidence-based public health policies and recommendations for additional research were presented as a contribution to World Health Assembly resolution WHA66.4 on a global action plan on universal eye health for 2014–2019 *(11).*

Professor Brien Holden was elected Chairperson of the meeting, and Professor Kovin Naidoo was elected Rapporteur. The draft agenda was adopted (for the programme of the meeting, see Annex 2).

3. Global prevalence of myopia

Myopia and high myopia were estimated to affect 27% (1893 million) and 2.8% (170 million) of the world population, respectively, in 2010. According to published studies, the prevalence of myopia is highest in east Asia, where China, Japan, the Republic of Korea and Singapore have a prevalence of approx. 50%, and lower in Australia, Europe and north and south America (2).

Preliminary projections based on these prevalence data and the corresponding United Nations population figures (12), and accounting for the effects of age and time, indicate that myopia and high myopia will affect 52% (4949 million) and 10.0% (925 million), respectively, of the world's population by 2050 (2) (Figs. 1 and 2).

Fig. 1. Numbers of cases (blue) and prevalence (red) of myopia worldwide between 2000 and 2050

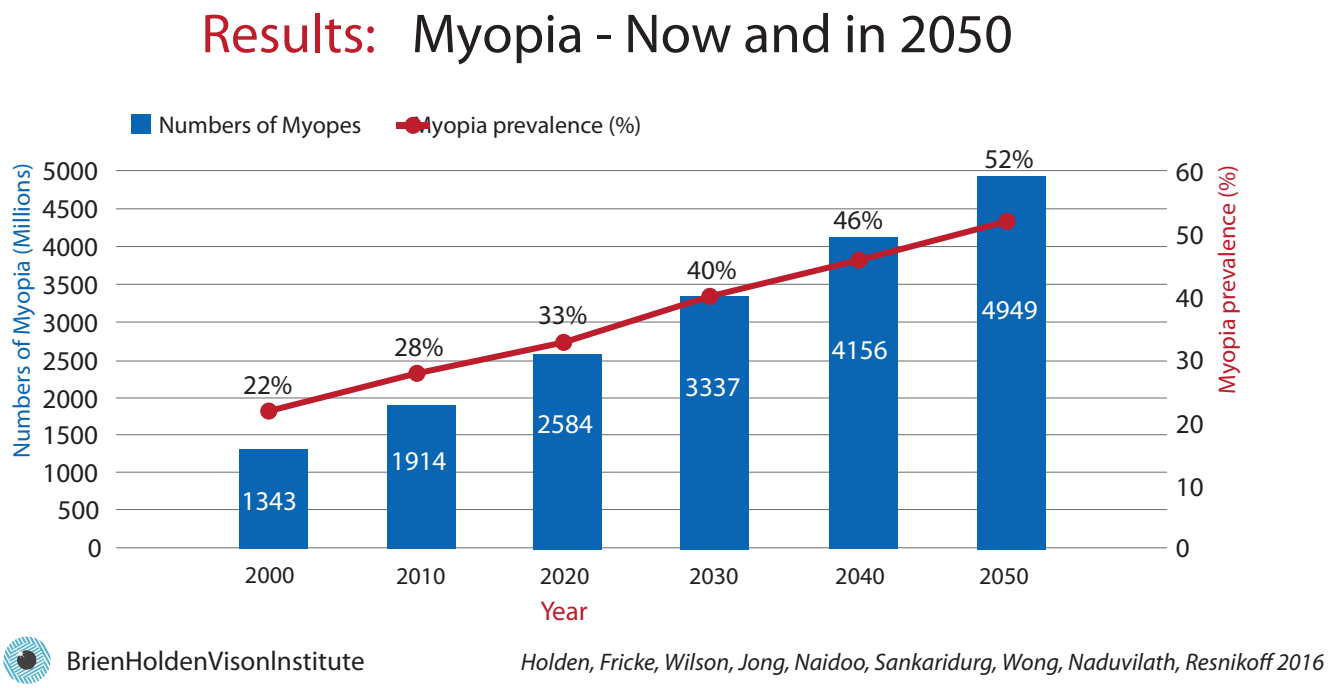
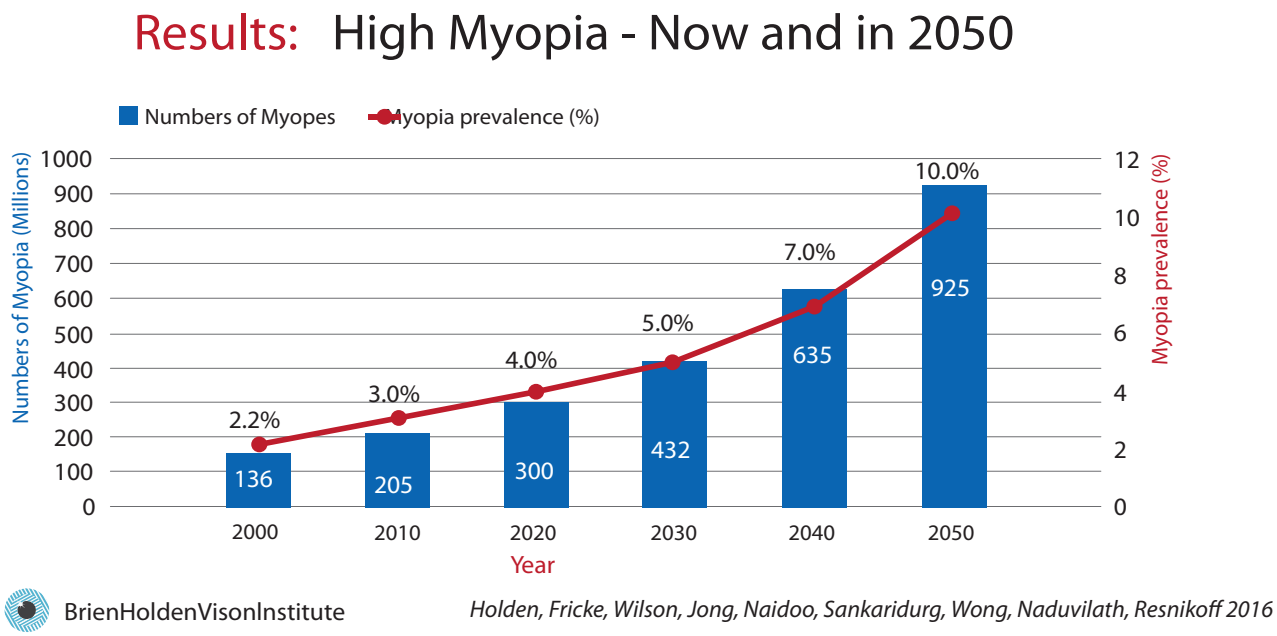


Fig. 2. Numbers of people worldwide with high myopia (blue) and prevalence (red) between 2000 and 2050



Countries were grouped according to the 21 regions of the WHO Global Burden of Disease programme (13) (see Annex 3) to determine regional differences in the prevalence of myopia and high myopia in smaller geographical areas than the large administrative and political WHO regions. The WHO regional structure will, however, be important for policy implementation. The model used to make projections (2) gave the results described below.

- In 2000, the prevalence of myopia did not exceed 50% in any of the regions but, by 2050, the prevalence will be ≥ 50% in 57% of the countries, if current trends continue.
- Countries in which the prevalence of myopia has been estimated and measured as low in the past (e.g. India) will have major increases by 2050.
- In 2050, the prevalence of myopia will be much higher in high-income regions of the Asia-Pacific, in east Asia and in south-east Asia, and the prevalence in high-income north America, southern Latin America, all of Europe, north Africa, the Middle East and about 30% of Africa will be similar to that in Asia today. The prevalence of high myopia is predicted to increase to 24% in all the Global Burden of Disease regions and in high-income Asia-Pacific countries by 2050.
- According to Global Burden of Disease estimates, uncorrected distance refractive error is the second largest cause of blindness (21%){Bourne, 2013 #1124} and the leading cause of moderate and severe vision impairment (53%) (1). The estimated cost of uncorrected refractive error in terms of direct and indirect loss of world productivity is 269 billion international dollars (I$) (14) (US$ 202 billion (15)),{Fricke, 2012 #1126} and the estimated cost of addressing the problem is US$ 28 billion over 5 years (15). On the basis of current estimates and demographic trends, myopia is the main cause of distance refractive error and will probably continue to be so in the future.
- Reducing the rate of myopia progression by 50% could reduce the prevalence of high myopia by up to 90%.

4. Myopia as a cause of vision impairment and blindness

Uncorrected refractive error has been reported to be the first cause of vision impairment in the world *(1)*, and undercorrected myopia is the most common cause of vision impairment, as judged by presentation for poor visual acuity.

MMD is the most common cause of visual impairment in patients with myopia, as 10% of people with pathological myopia develop MMD (due to choroidal neovascularization), which is bilateral in 30% of cases *(16)*.

Myopia is associated with higher risks of glaucoma and cataract but may be protective against age-related macular degeneration and diabetic retinopathy.

Approximately 1% of whites and 1–3% of Asians have pathological myopia (high myopia with signs of retinal atrophic changes) *(5)*. Pathological myopia causes more vision impairment or blindness in Asians (0.2–1.4%) than in Caucasians (0.1–0.5%). Overall vision impairment due to pathological myopia occurs in 2–15 Asian people per 1000 annually (Table 1). In this study, cut-offs according to the best-corrected visual acuity classification were used, based on WHO or United States criteria for vision impairment and blindness. Currently, choroidal neovascularization in MMD is managed by treatment with antivascular endothelial growth factor agents, but many questions remain regarding treatment regimens, monitoring, follow-up and long-term outcomes.

Table 1. Prevalence of blindness in pathological myopia

Disease stage	Parameter	Outcome	Reference
Pathological myopia	Prevalence in the general adult population		
	White	1%	17
	Asian	1–3%	18, 19, 20, 21
	Estimated prevalence of vision impairment due to pathological myopia		
	European	1–5 per 1000	22, 23, 24
	Asian	2–15 per 1000	3, 6, 25, 26, 27
	Other populations		28, 29
	Annual incidence of blindness due to pathological myopia		28, 30
	White	1–5 per 100 000	28, 31
	Asian	5–10 per 100 000	4
Myopic choroidal neovascularization	Prevalence of choroidal neovascularization		
	General population	0.05%	17, 21
	Patients with pathological myopia	5–10%	31, 32, 33
	Incidence of choroidal neovascularization in pathological myopia over 10 years	10%	16
Bilateral myopic choroidal neovascularization	Prevalence of bilateral choroidal neovascularization secondary to pathological myopia	15–30%	16, 31, 34

Source: Wong TY et al. *(5)*.

5. Terminology and classification

5.1 Myopia, high myopia and pathological myopia

There is currently no internationally agreed threshold for myopia or for high myopia. An operational definition for high myopia is necessary so that the results of population-based studies can be conducted with the same criteria in different countries, to determine the prevalence of high myopia, the prevalence of vision impairment and/or blindness attributable to high myopia and to determine whether high myopia progresses to pathological myopia in a similar way and in the same proportion in different countries, ethnic groups and socioeconomic environments. Longitudinal studies of high myopia and pathological myopia should be conducted to quantify the risk for sight-threatening conditions due to high myopia.

Currently, the definition of high myopia varies by study; it has been defined as: > –5.00 D myopia, ≥ –5.00 D myopia, > –6.00 D myopia, ≥ –6.00 D myopia and ≥ –8.00 D myopia. High myopia has also been defined on the basis of an axial length > 26 mm. Axial length, however, can be an inaccurate criterion because it can vary even in normal eyes. Overall eye power is derived from a combination of the lens, cornea and axial length, and some eyes with longer or shorter axial length have no refractive error. Furthermore, measurements using different instruments may vary.

The participants agreed that a classification of high myopia as ≤ –5.00 D is the best definition, as a person who has –5.00 D uncorrected myopia has a visual acuity of 6/172 *(10)*, which is much worse than the threshold for blindness (< 3/60 in the better eye) *(35)*.

Pathological myopia is also not well defined, with different descriptions in different studies of vision-threatening changes in the retina or the presence of posterior staphyloma,[1] and various criteria for axial length and spherical equivalents of refractive error. Pathological myopia has been reported as high myopia with myopia-related fundus abnormalities such as MMD and glaucoma.

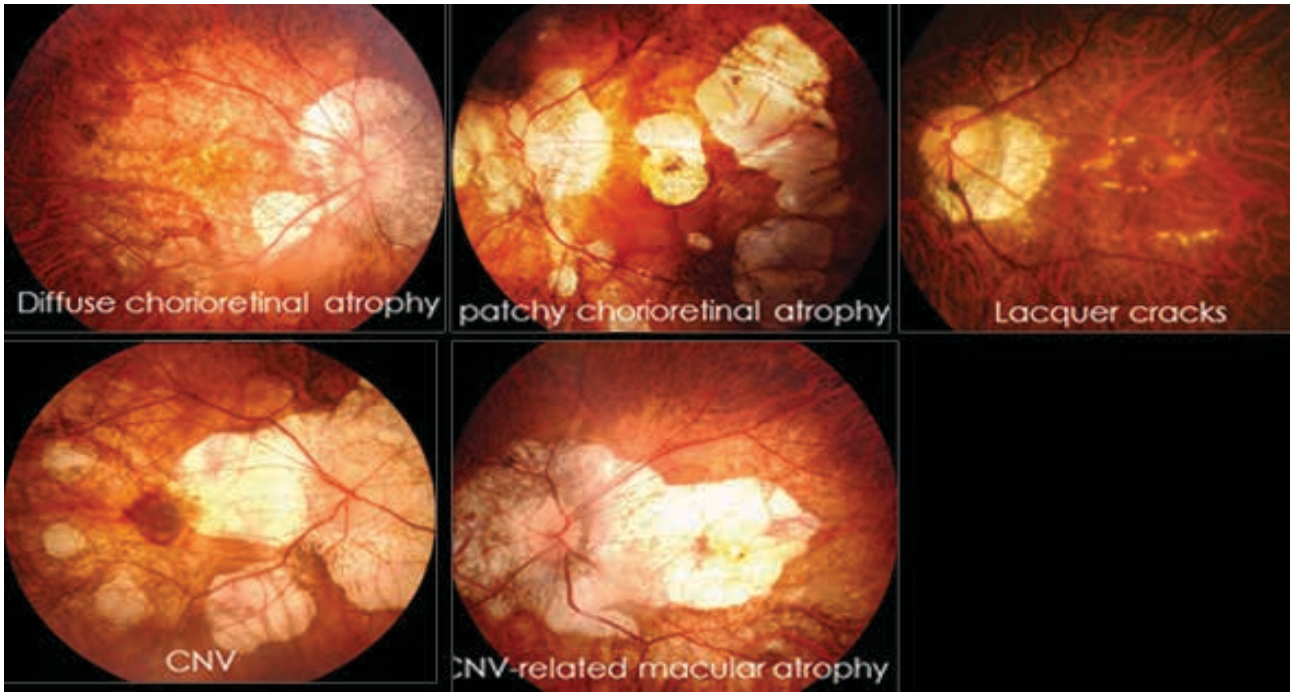
5.2 Myopic macular degeneration

MMD is a major cause of vision impairment in high myopia. A number of terms are used, including MMD, myopic maculopathy, myopic retinopathy and myopic choroidal neovascularization. Although other features of pathological myopia can cause vision impairment, the same term should be used in all studies and in clinical practice to ensure unequivocal classification and assessment of vision impairment due to high myopia.

MMD includes signs of diffuse chorioretinal atrophy, patchy chorioretinal atrophy, lacquer cracks, choroidal neovascularization and related macular atrophy in the presence of higher myopia (Fig. 3).

1 An outpouching of the wall of the eye with a radius of curvature that is less than that of the surrounding curvature of the wall of the eye; associated with a higher risk for degenerative changes in the retina.

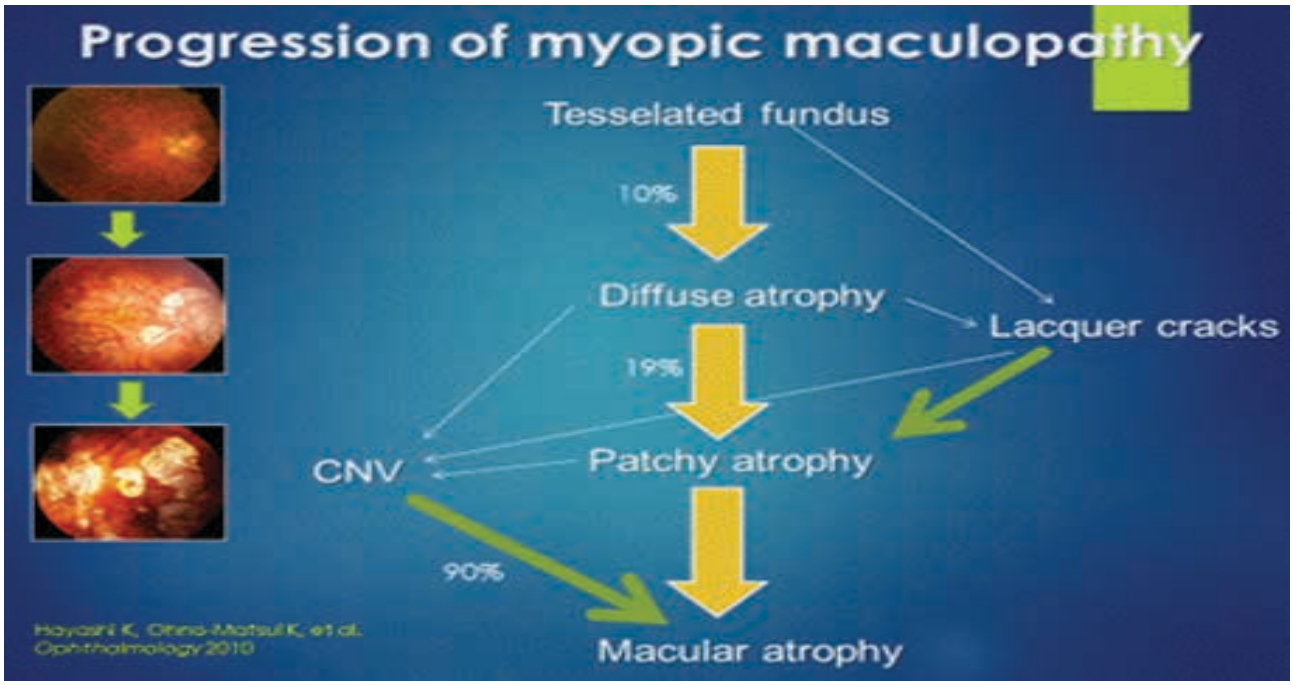
Fig. 3. Myopic macular degeneration



Source: Hayashi et al. *(33)*, presented by K. Ohno-Matsui during the meeting.

MMD develops in the presence of high myopia, with initial early retinal changes leading to a tessellated fundus, which may then develop into diffuse atrophy or lacquer cracks, patchy atrophy or choroidal neovascularization and finally MMD (Fig. 4).

Fig. 4. Progression of myopic macular degeneration in a group of people with high myopia (≤ –8.00 D)



Source: presented by K. Ohno-Matsui during the meeting, from a retrospective study of a group of Japanese people with myopia ≤ –8.00 D.

Table 2. A proposed international photographic classification and grading system for myopic macular degeneration

Category	Myopic maculopathy	Additional lesions
0	No macular lesions	
1	Tesselated fundus	Lacquer cracks
2	Diffuse chorioretinal atrophy	Choroidal neovascularization
3	Patchy chorioretinal atrophy	Fuchs spot
4	Macular atrophy	

Source: presented by K. Ohno-Matsui during the meeting.

No universal grading system for MMD is in use clinically. An international photographic grading system was proposed during the meeting (Table 2). It was noted, however, that the system is too complex for classifying vision impairment due to MMD in population-based surveys conducted by technicians and nurses.

6. Impact of myopia

Uncorrected distance refractive error was estimated in 2013 to affect 108 million people globally *(1)*. It is the leading cause of moderate and severe vision impairment (42%) and a major cause of blindness (3%) *(1)*. Uncorrected myopia as low as –1.50 D will result in moderate vision impairment, and uncorrected myopia of –4.00 D is sufficient refractive error to be classified as blindness *(36)*. Most distance refractive error is caused by myopia; the global prevalence of myopia is expected to increase from 27% of the world's population in 2010 to 52% by 2050 *(2)*. In raw numbers, this would correspond to a 2.6-fold increase in the number of people with myopia, allowing for the predicted increase in the global population. If the increasing prevalence of myopia is not addressed, a similar increase in uncorrected refractive error can be expected. These projections are based on conservative assumptions and, given the published relationship between level of education and myopia, increased provision of education could markedly increase these trends. Furthermore, uncorrected distance refractive error has been estimated to result in a global loss of productivity of I$ 269 billion *(14)* (US$ 202 billion *(15)*), which will also increase if there is a significant increase in uncorrected myopia.

The cost of care is also likely to increase significantly, and will be exacerbated by an even greater increase in the prevalence of high myopia, from 2.8% (190 million people) to 9.7% (924 million people) by 2050 *(2)*, representing a 4.9-fold increase in high myopia. In some populations of young adults in Asia, the prevalence of high myopia has already reached 38% *(37)*. The annual direct cost of optical correction of myopia for Singaporean adults has been estimated at US$ 755 million. SM Saw et al., in a presentation shared at the meeting, estimated that, if the available data were extrapolated to all cities in Asia in which the prevalence of myopia is approximately equal to the rates in Singapore, the estimated direct cost would be US$ 328 billion. Lim et al. *(38)* estimates that the direct cost of myopia in Singaporean children was US$ 148 per child per year. {Wang, 2008 #1448}

The impact of myopia is not only financial; it also affects quality of life and personal development. A study of Singaporean adolescents found that those with vision impairment, measured in terms of presenting vision (i.e. wearing their habitual correction), had statistically significantly

lower scores for total quality of life (P = 0.03), psychosocial functioning (P = 0.03) and school functioning (P = 0.02) *(39)*. Another study indicates that correction of refractive errors by the provision of spectacles in low socioeconomic areas in China would markedly improve educational outcomes since the major medium of instruction is the blackboard *(40)*. The increase in the prevalence of high myopia will eventually lead to an increase in pathological myopia and hence blindness and permanent vision impairment, with an associated increased pressure on ophthalmological and low-vision services.

The participants agreed on the basis of the evidence that myopia warrants national and international synergistic efforts, as the costs and public health implications are huge and often underestimated.[2]

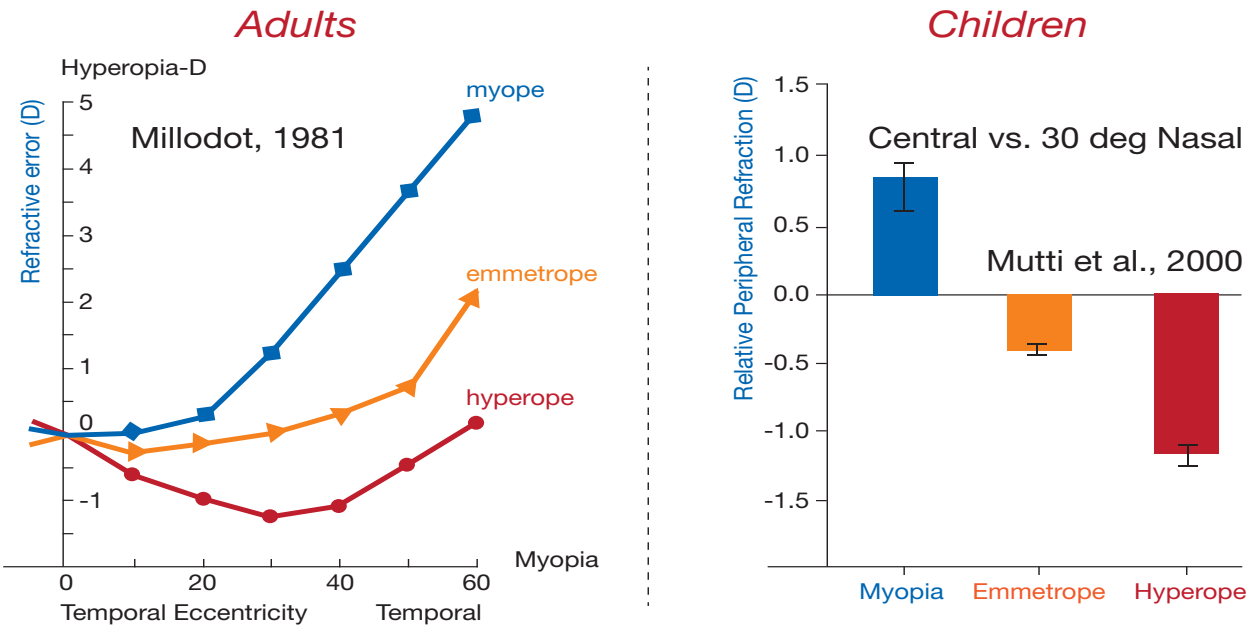
7. Evidence for causes of myopia

7.1 Optical and environmental influences

Several optical and environmental factors have been identified as possible causes of the onset and progression of myopia, acting either individually or in combination.

Peripheral hyperopic defocus in a corrected myopic eye *(41)*:[3] According to Smith et al. *(42)*, experimentally imposed hyperopic defocus, which is common in corrected myopic eyes, can increase ocular growth; whereas myopic defocus, especially when it is imposed over a large area of the retina, can slow axial elongation (Fig. 5).

Fig. 5. Association between central and peripheral refraction



Source: presented by EL Smith III during the meeting.

2 SM Saw et al., presentation to the meeting.

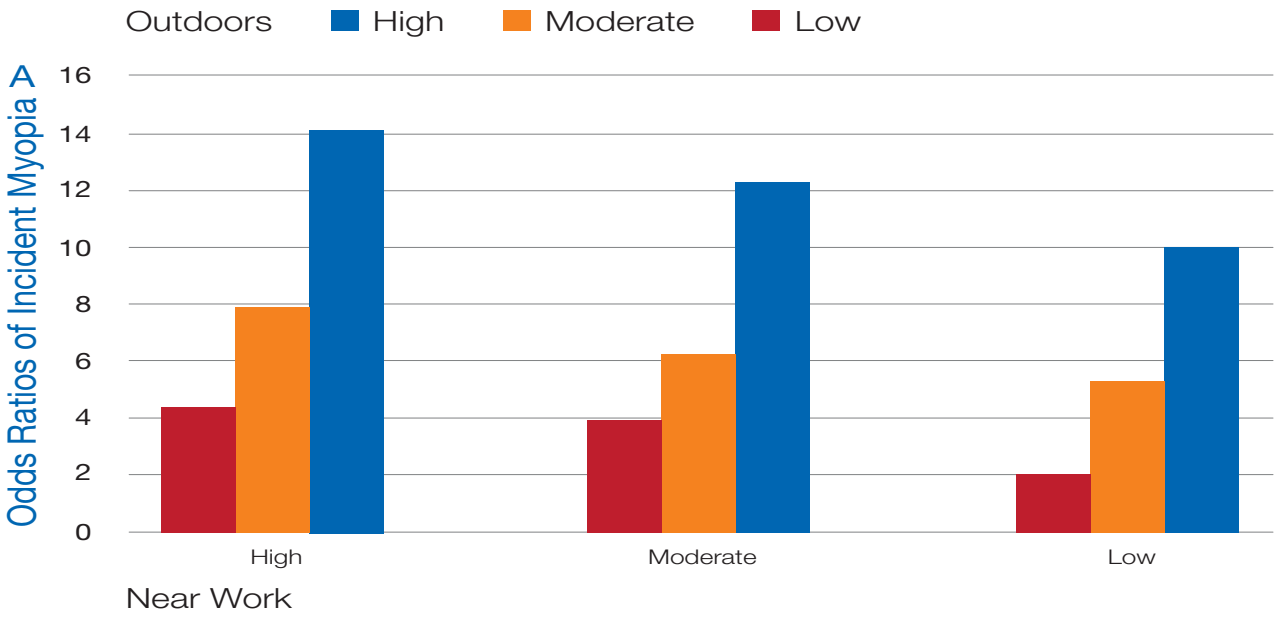
3 EL Smith III, presentation to the meeting.

The pattern of peripheral refraction varies with central refraction. People with myopia typically have relative hyperopia in the periphery, whereas those with hyperopia have relative myopia in the periphery *(43,44).*

Intensive near work (*45,45):4* Ghosh et al. *(45)* suggested that the mechanism by which near work increases axial length is the combined influence of biomechanical factors (i.e. extraocular muscle forces, ciliary muscle contraction) associated with near tasks in downward gaze.

Time spent outdoors (36): I. Morgan informed the meeting that the epidemic of myopia in east Asia is primarily due to changes in environmental (social) factors, specifically intensive education and less time spent outdoors (Fig. 6). Observed seasonal variation in the progression of myopia adds weight to the argument that time spent outdoors slows the progression of myopia.

Fig. 6. Five-year risk of incident myopia among six-year-old Australian children



Source: French et al., 2013 *(37)*.

Successive and simultaneous hyperopic defocus: As indoor scenes have highly heterogeneous dioptric topography, eyes are more likely to experience hyperopic defocus, which has been shown to be a strong stimulus for myopic growth in laboratory animals *(38)*.

7.2 Genetics and parental history

Genetics and the environment play a role in the development and progression of myopia, but the genetic contribution is considered small, and there is consensus that genes may determine susceptibility to environmental factors *(39).* In other words, genes determine where an individual comes in the distribution of refractive errors, but the mean is probably determined by environmental factors.

Genes for myopia and high myopia development have been identified in familial studies and twin studies and by linkage analysis. The 19 loci for myopia are MYP1–MYP19 *(1).* Large-scale

4 I Morgan, presentation to the meeting.

genome association studies have been conducted on single nucleotide polymorphisms. Two of the largest studies are that of the Consortium for Refractive Error and Myopia (CREAM), with almost 46 000 participants *(40)*, and the 23andME study, with over 59 000 participants, which found genes associated with myopia and high myopia *(41)*.

As M. He reported during the meeting, twin studies have shown that genetics can explain 60–80% of variance in spherical equivalent refractive error and axial length. Other studies, however, have indicated that the genetic contribution is far less and does not explain the majority of cases of high myopia *(42)*. Studies of the genetic contribution should include evaluation of environmental aspects, as factors such as time spent outdoors time and near work vary by family. The rapid increase in the prevalence of myopia seen over a short time in east Asia *(43, 44, 45)* cannot be explained by genetics, thus indicating that environmental factors associated with more widespread education and urbanization play a larger role. Furthermore, the higher prevalence of myopia is not limited to a single race: it is higher in people of Chinese, Indian and Malay origin in Singapore *(56)* than in Indians in India *(46)* and rural Chinese in China *(54)*.

In the twin study by M. He et al., reported during the meeting, baseline refraction and parental myopia were found to be risk factors, while near work intensity and outdoor exposure were possible risk factors. Other studies have found that the children of myopic parents have a higher prevalence of myopia, but the relative risk varies and is lower where the prevalence of myopia is high, as in east Asia *(47, 48, 49, 50).*

8. Control of myopia

8.1 Optical control

Various optical approaches to the control of myopia progression have been evaluated over the past few decades. These are based on different hypotheses of myopia progression, such as accommodative lag associated with myopia and peripheral defocus. The spectacle methods evaluated include undercorrection, progressive addition lenses, executive bifocals, peripheral defocus correction and peripheral defocus plus a bifocal aid. Contact lens methods include rigid gas-permeable lenses, bifocal contact lenses, peripheral plus contact lenses, orthokeratology and extended depth-of-focus lenses. Executive bifocal spectacles, orthokeratology and peripheral plus contact lenses appear to be the most effective, reducing the rate of myopia progression by 57% *(51)*, 45% *(52)* and 50% *(53)*, respectively. Extended depth-of-focus lenses are a promising means of myopia control, but longer-term studies are required. The details of these optical methods are outlined below.

8.1.1 Spectacle methods

Leaving myopia uncorrected did not reduce the rate of progression in comparison with full correction or undercorrection in a 12-month prospective, randomized study in children aged 9–12 years *(54)*. Undercorrection has been shown to increase myopia progression; it has been suggested that this is due to peripheral and central blur, stimulating axial length growth *(55)*. Undercorrection is therefore not advocated *(56)*. Progressive addition lenses have been shown to have a small, statistically significant but not clinically significant effect, although clinical significance was found in subgroups, such as people with excess convergence or

accommodative lag *(57)*. The reduction in the rate of myopia progression was correlated with the degree of relative myopia produced in the superior retina by near addition *(58)*.

Executive bifocals with a +1.50 addition and 3 D base-in prism reduced the rate of myopia progression by 57% after three years *(62).* These lenses are thought to reduce the stimulus for axial elongation, either by reducing the accommodative lag in myopia (although this association has not yet been demonstrated) or by imposing myopic focus in the superior peripheral retina. Spectacle lenses with peripheral plus that are intended to reduce the degree of relative peripheral hyperopic defocus in people with myopia were investigated in a 12-month trial. The reduction in myopia progression was not statistically significant. In a subgroup of children with myopic parents, the rate of myopic progression was 30% less than in controls (–0.68 ± 0.48 D vs –0.97± 0.48 D, $P = 0.033$) *(59)*. A lens with peripheral plus and a progressive addition lens-like near addition resulted in a small but statistically significant reduction in myopia progression, which was similar to that observed with spectacles with peripheral plus *(60)*. This study showed that executive bifocals provide good clinical myopia control and that other forms of spectacle correction have limited or no effect on myopia progression.

The factors that may limit the success of spectacle myopia control methods are eye movements behind the lens (which affect the position of the optical treatment zone relative to the visual axis), compliance, the maintenance of a large non-treatment zone in order to minimize effects on central vision, and "swim" produced by eccentricity-dependent variations in magnification that can be produced by either eye or head movements *(71).*

8.1.2 Contact lens methods

Standard rigid gas-permeable lenses do not reduce the rate of myopic axial elongation and can lead to some corneal flattening *(61)*.

Bifocal contact lenses significantly reduce the rate of myopia progression, in terms of both the spherical equivalent of refractive error and axial length. It has been suggested that bifocal contact lenses act by reducing accommodative lag *(62)*; however, it is more likely that they act by reducing peripheral hyperopic defocus or imposing myopic defocus *(63)*. Peripheral defocus correction by peripheral-plus contact lenses results in a 50% reduction in the rate of myopic progression, in terms of both spherical equivalent and axial length *(64)*.

A dual-focus contact lens with multiple rings of plus power that produce relative myopic defocus over a large part of the retina resulted in a 36% reduction in the progression of myopia and a 49% reduction in the rate of change in axial length: however, long-term studies are still required *(41).*

Orthokeratology involves wearing rigid gas-permeable lenses overnight to flatten the cornea. Use of these lenses led to a consistent reduction in myopia progression of approximately 45% over a two-year period and 30% over five years, when measured in terms of axial length *(63)*.

Extended depth-of-focus lenses prove the myopic defocus hypothesis by reducing the signals that are thought to increase axial growth *(65)*. Preliminary results showed a 35% reduction in the rate of progression of the spherical equivalent of refractive error and a reduction of up to 45% in the rate of progression in axial length.

8.2 Time spent outdoors and behavioural influences

A number of studies have been conducted to determine the effects of the amount of time spent outdoors and behavioural changes on myopia progression in children *(66, 67, 68)*. Evidence is emerging that spending more time outdoors can protect against the onset of myopia, the effect of near work and the effect of parental myopia and possibly slow the rate of progression of myopia.

It was reported that, when children spend sufficient time outdoors (more than two hours/day), the risk of myopia was reduced, even when they had two myopic parents and continued to perform near work *(77)*. The total time spent outdoors appeared to be the important factor, rather than time playing sports, because time spent indoors playing sports was not beneficial. Thus, the nature of the outdoor activities does not seem to be critical *(77).*

Wu et al. *(79)* reported that the incidence of new cases of myopia over one year was significantly reduced, by approximately 50%, when the time spent outdoors was increased by an additional 80 minutes/day, compared with a control group (8.4% versus 17.6%). The rate of progression of myopia in the children who spent additional time outdoors was also significantly reduced (0.25 D versus 0.38 D). In the Guangzhou outdoor activity longitudinal study *(69)*, a 23% reduction in the number of cases of incident myopia was found after an additional 40 minutes/day outdoors for three years. A small, statistically significant reduction in the spherical equivalent refractive error was found but no statistically significant reduction in the rate of axial length elongation.

The mechanism of action of time spent outdoors remains unknown and requires further investigation. Rose et al. *(77)* hypothesized that the brighter light outdoors stimulates the release of dopamine from the retina, which is reported to inhibit axial elongation in animal models of form deprivation myopia *(70, 71)*. Seasonal differences in the rates of myopic progression, which are faster in winter and slower in summer, support this hypothesis *(72)*.

Increasing children's time outdoors may be difficult, particularly during school time, because of a cultural commitment to educational success in many parts of the world, as well as weather conditions.5 Outdoor activity could be made part of obesity reduction campaigns for children, and schoolchildren in particular.

Further studies should be conducted on the effect of time spent outdoors, with better, simpler survey methods. Work is also needed to address the social, cultural and educational barriers to spending more time outdoors. For example, children in Guangzhou and their parents are committed to intense, lengthy extracurricular study with a daily two-hour afternoon nap, and they often do not leave their classrooms during school hours.6

8.3 Pharmacological and therapeutic control

A number of therapeutic interventions for myopia control have been investigated. Use of 0.01% atropine is the most common treatment regimen for the management of myopia in children in a number of Asian countries, such as Singapore and Taiwan, China. One experimental intervention that is being tested in Denmark is 7-methylxanthine; it shows promise, but its long-term safety still needs to be studied.

5 SM Saw, presentation to the meeting.

6 I Morgan, presentation to the meeting.

8.3.1 Atropine

Atropine eye-drops are antimuscarinics, blocking the muscarinic receptors from stimulation by the neurotransmitter acetylcholine. These receptors are found in the central nervous system and in many parts of the eye, where they can, for example, cause pupil dilatation and block accommodation *(73)*. Atropine reduces myopia progression in children in a dose-related manner, but a rebound effect ("catch-up") occurs with higher doses *(74)*.

Atropine eye-drops are generally considered to be safe, although a high percentage of products have substantial side-effects, such as allergic reactions, fixed dilated pupils requiring sunglasses to be worn, accommodative paralysis necessitating bifocal spectacles, papillary conjunctivitis and, in some cases, nausea and vomiting. Lower doses, such as 0.01% (as opposed to the usual clinical concentration of 1.0%), reduce the common side-effects observed with the higher dose, including pupil dilatation, loss of accommodation and reduced near vision. Atropine at 0.01% resulted in a 59% reduction in the rate of progress of myopia, with minimal adverse effects; however, controversially, it had no effect on axial elongation *(85).* During a seven-year observation period after treatment for two years, atropine at 0.01% slowed myopia progression by 50% in children aged 6–9 years, with no apparent effect on axial elongation rates.[7]

Clinical guidelines are needed on who should be treated, when treatment should begin and cease and the duration of treatment. Table 3 lists potential clinical guidelines based on the ATOM2 study.

Atropine eye-drops were recently approved by the United States Food and Drug Administration for long-term amblyopia therapy in children. There is currently no regulatory approval for the use of atropine to slow myopia progression.

Table 3. Clinical guidelines for children aged 6–10 years with myopia > 1.0 D and documented myopia progression > 0.5 D per year

Treat with atropine 0.01% for two years		
Good response: almost no myopic progression (< 0.5 – in second year)	Moderate response: Myopic progression of 0.5 D–1.0 D in second year	Poor response: Myopic progression > 1.0 D in second year
Taper off and stop atropine	Continue atropine 0.01% for a further 1–2 years, then taper off and stop atropine	May be a non-responder. Consider tapering off and stopping atropine
Follow child for one year after stopping atropine		
Recommence atropine if there is significant rebound, and continue monitoring		

Source: modified from the ATOM2 study *(85)*.

8.3.2 7–methylxanthine

7-methylxanthine is a non-selective adenosine antagonist that affects the release of neurotransmitters such as dopamine, norepinephrine, acetylcholine, glutamate and serotonin *(75)*. It is a metabolite of caffeine and theobromine, and its half-life after oral ingestion is 3.5 hours. 7-methylxanthine is thought to penetrate the blood–brain barrier only minimally and to be relatively non-toxic; it is excreted predominantly through the kidneys.

7 TY Wong, presentation to the meeting.

During eight years of follow-up of 750 myopic Danish children who were treated with various systemic dosages of 7-methylxanthine, no side-effects were reported. The dose of 400 mg twice a day reduced myopia progression and excessive eye elongation by 60% *(70).*

9. Research

There is a large body of research on myopia, but the epidemiology, myopigenesis, myopia control, risk factors and pathophysiology of the condition require further research to improve evidence-based management. Areas where further research is required are detailed below.

9.1 Epidemiology of myopia

Epidemiological studies are essential for defining priorities in planning and targeting resources for eye care. Management of myopia and prevention of vision impairment from uncorrected myopia must be optimized in view of the projected increases in the global prevalence of the condition. Participants agreed that MMD should be included in epidemiological studies on the prevalence and causes of vision impairment, including rapid assessments of avoidable blindness and WHO surveys on vision impairment and causes.

Few data are available on the prevalence of vision impairment due to conditions associated with high myopia, such as cataracts, glaucoma and MMD. Higher-quality data should be produced on the prevalence of myopia in various countries, especially developing countries in Africa, the Americas and the WHO Western Pacific Region.

9.2 Myopigenesis and genetic, environmental, optical and therapeutic factors

9.2.1 Environmental factors

Strategies should be devised to increase the amount of time children spend outdoors, particularly in preschool and primary school.

Although it is clear that increased time outdoors reduces the risk of myopia, the aspect that imparts a protective effect is not known. The potential roles of ambient lighting and differences in the spectral composition of light, dioptric topography and spatial scale should be clarified to optimize any therapeutic benefit. Controlled parametric studies involving experimental animal models of myopia would be useful.

Randomized clinical trials with at least three years of follow-up should be conducted to determine the optimum time required to control the development and progression of myopia.

9.2.2 Optical and pharmaceutical approaches

A variety of interventions, from spectacles to contact lenses to pharmaceuticals, appear to be effective in reducing the progression of myopia in children. Best-practice clinical trials (randomized trials that are blinded when appropriate, with adequate power and use of cycloplegic agents, for a minimum of 12 months and preferably longer) should be conducted to optimize strategies.

Clinical trials should include an intention-to-treat analysis, assessment and analysis of the effect of compliance and documentation of any adverse events.

9.2.3 Near work

It is widely recognized that near work in formal education is associated with myopia. Studies should be conducted to identify and characterize the components of near work and formal education, e.g. contrast and spatial components, that could cause myopia.

9.2.4Combination therapy

The effect of combining the various types of preventive and control strategies is unknown. Knowing how the different therapies and strategies work together is important, as patients are unlikely to use one method in isolation.

9.3 Risk factors and individual heterogeneity

Individual differences in susceptibility and behaviour are likely to play a role in determining the occurrence of myopia and, probably, the ultimate degree of myopia. There are significant gaps in understanding of refractive development from approximately two years of age until the start of formal education and between the end of secondary education and middle age (approx. 40 years). Studies on refractive development and the prevalence of refractive errors from approximately two years of age up to and including 25 years are encouraged. These would benefit from methods for documenting behaviour quantitatively, such as validation of questionnaires and objective measurement of exposure to light.

9.4 High myopia, pathological myopia and comorbid conditions

It is not understood whether high myopia develops into pathological myopia or whether they are two conditions with different underlying causes. Retrospective case-control studies, population-based studies or meta-analyses are needed to determine whether and what proportion of people with high myopia develop pathological myopia. The natural history, including age at onset of pathological myopia, and the risk factors and factors associated with vision impairment should be studied. The causes of high myopia and pathological myopia must be identified, including genetics and the environment, near work and time spent outdoors.

The proportion of people with myopia who will develop ocular complications is not known, nor the age or level of myopia at which complications typically develop. Research is required to understand the causes of the comorbid conditions associated with myopia and their risk factors.

9.5 Eye examinations in myopia

The use of cycloplegic agents in eye examinations should be standardized, as there are no guidelines on use of these agents in myopia. Studies show that the measured level of refractive error in people with myopia differs when cycloplegics are used. Studies are required to determine the optimal cycloplegic regimen for studying myopia progression in children and adults of different ethnic backgrounds, including the cycloplegic agent, the concentration (number of drops) and time before measurement.

10. Conclusions

Documented increases in the prevalence of myopia and high myopia worldwide are a serious public health concern. Data to inform research, clinical practice and public health policy must be produced urgently. The participants in this joint consultation agreed on recommendations for consistent use of international terminology for obtaining internationally comparable, accurate data on the prevalence of myopia and high myopia. They agreed on definitions of myopia and high myopia and a description of the pathological consequences of myopia. They further agreed that myopia and high myopia should be included as attributable causes of vision impairment in epidemiological surveys, and that the term “myopic macular degeneration” should be used to categorize the blinding retinal diseases associated with high myopia, in preference to the many other terms in current use. The consultation provided an opportunity to categorize myopic defects, evaluate the evidence on myopia control strategies and identify gaps in knowledge that must be filled urgently as a basis for evidence-based strategies to reduce the prevalence of high myopia and associated vision impairment.

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Annex 1. Participants

Professor Mingguang He, Centre for Eye Research Australia Melbourne, Australia, and Zhongshan Ophthalmic Centre, Guangzhou, China mingguanghe@gmail.com	Dr Solange R. Salomão, Federal University of São Paulo, São Paulo, Brazil ssalomao@unifesp.br
Professor Brien Holden, Brien Holden Vision Institute, Sydney, Australia b.holden@brienholdenvision.org	Professor Padmaja Sankaridurg, Brien Holden Vision Institute, Sydney, Australia p.sankaridurg@brienholdenvision.org
Professor Jost B. Jonas, Ruprecht Karl University of Heidelberg, Heidelberg, Germany jost.jonas@medma.uni-heidelberg.de	Professor Seang Mei Saw, National University of Singapore, Singapore seang_mei_saw@nuhs.edu.sg
Dr Monica Jong, Scientific Secretary, Brien Holden Vision Institute, Sydney, Australia m.jong@brienholdenvision.org	Professor Earl L Smith III, University of Houston, Houston, Texas, USA esmith1@Central.UH.EDU
Professor Jafer Kedir, Jimma University, Jimma, Ethiopia jafked@yahoo.com	Dr Klaus Trier, clinical practice, Hellerup, Denmark ktrier@dadlnet.dk
Dr Ivo Kocur, World Health Organization, Geneva, Switzerland kocuri@who.int	Dr Susan Vitale, National Institutes of Health, Washington DC, USA sev@nei.nih.gov
Dr Silvio Paolo Mariotti, World Health Organization, Geneva, Switzerland mariottis@who.int	Professor Tien Y. Wong, National University of Singapore, Singapore wong.tien.yin@snec.com.sg
Dr Hasan Minto, Brien Holden Vision Institute, Islamabad, Pakistan h.minto@brienholdenvision.org	Professor Abbas Ali Yekta, Mashhad University of Medical Sciences, Mashhad, Islamic Republic of Iran YektaA@mums.ac.ir
Professor Ian Morgan, Australian National University Canberra, Australia Ian.Morgan@anu.edu.au	Professor Kovin Naidoo, Brien Holden Vision Institute, Durban, South Africa k.naidoo@brienholdenvision.org
Professor Kyoko Ohno-Matsui, Tokyo Medical and Dental University, Tokyo, Japan k.ohno.oph@tmd.ac.jp	Professor Olavi Pärssinen, University of Jyvaskyla, Jyvaskyla, Finland olavi.parssinen@top.fimnet.fi

Observers

Dr Adriana Berezovsky, Federal University of São Paulo, São Paulo, Brazil aberezovsky@unifesp.br
Mr Tim Fricke, Brien Holden Vision Institute, Sydney, Australia t.fricke@optusnet.com.au
Dr David Wilson, Brien Holden Vision Institute, Sydney, Australia d.wilson@brienholdenvision.org

Annex 2. Programme

Day 1. Monday 16 March 2015 – Chairs: Professor Serge Resnikoff and Dr Ivo Kocur

09:00	Welcome	Professor Brien A. Holden
09:20	Welcome – The scope and purpose of the meeting	Dr Ivo Kocur and Dr Silvio Mariotti
09:45	The magnitude of myopia The prevalence of myopia and higher levels of myopia at global and regional levels and projected increase to 2050	Professor Brien A. Holden
10:15	Vision impairment and blindness in myopia Vision impairment in myopia and comorbid conditions Permanent vision impairment caused by myopia Prevalence of vision impairment and blindness associated with myopia Prevalence and risks for comorbidity with myopia	Professor Tien Y. Wong
11:00	Morning tea	
11:30	Terminology and classification of high myopia and pathological myopia Definition, classification and terminology of myopia and higher myopia, including the vision impairment	Professor Kyoko Ohno-Matsui
12:00	Myopic macular degeneration Definition, description, characteristics and effects	Professor Jost B. Jonas
12:30	Impact of myopia on society Myopia and complications of myopia and social and economic impacts	Professor Seang Mei Saw
13:00	Lunch	
14:00	Breakout sessions – Definitions	
	Group 1. Definitions and methods for prevalence studies of myopia and high myopia and data (to include refractive error and vision impairment due to higher levels of myopia) – current state of surveys of WHO and rapid assessment of avoidable blindness	
	Group 2. Definition of myopic macular degeneration (MMD) for surveys and future publications, protocol for measuring the prevalence of MMD in epidemiological surveys and future publications, including a grading scale and quantification of MMD. Terminology, classification, survey methods and protocols	
15:30	Afternoon tea	
16:00	Plenary session: Definitions, review of outcomes	
17:30	Close Day 1	

Group 1

Facilitator: Professor Kovin Naidoo

Reporter: Mr Tim Fricke (observer)

Participants: Professor Jafer Kedir, Dr Ivo Kocur, Dr Hasan Minto, Professor Ian Morgan, Professor Olavi Pärssinen, Dr Solange R. Salomão, Professor Padmaja Sankaridurg

Professor Seang Mei Saw, Professor Earl L. Smith III, Dr Susan Vitale, Dr David Wilson (observer), Professor Abbas Ali Yekta

Group 2

Facilitator: Professor Serge Resnikoff

Reporter: Dr Monica Jong

Participants: Dr Adriana Berezovsky (observer), Professor Mingguang He, Professor Brien Holden, Professor Jost B. Jonas, Dr Silvio Mariotti

Professor Kyoko Ohno-Matsui, Professor Gullipalli (Nag) Rao, Dr Klaus Trier, Professor Tien Y. Wong, Professor Jiangling Zhao

Day 2. Tuesday 17 March 2015 – Chairs: Professor Mingguang He and Dr Silvio Mariotti

09:00	The day's activities	Chair
09:10	Evidence related to the causes of myopia: optical and environmental Evidence on the causes of myopia progression, e.g. retinal image profile, and the role of the macula and the periphery in the induction of myopia, environment (light), myopia induction models	Professor Earl L. Smith III
09:25	Evidence related to the causes of myopia: genetics, parental history, other Relation of genetics and parental myopia with myopia, Singapore study and CREAM consortium	Professor Seang Mei Saw
09:40	Evidence related to the causes of myopia: genetics and environmental risk factors for onset and progression of myopia Nine years of follow-up data from the Guangzhou Twin Cohort Study	Professor Mingguang He
09:55	Discussion	
10:10	Evidence for myopia control: optical Review of the evidence on the effects of optical intervention: peripheral plus, extended depth of focus, orthokeratology, bifocal spectacles	Professor Padmaja Sankaridurg
10:35	Evidence for myopia control: outdoors, behavioural Review of the evidence on the effects of environmental and behavioural interventions Examples of health policy and possible myopia control activities and interventions implemented – e.g. Chinese Taipei considering laws to monitor the time spent on near devices, and "and or the time" in Wuhan, China	Professor Ian Morgan
11:00	Morning tea	
11:30	Evidence for myopia control: lessons for atropine Review of the evidence on the effects and use of atropine	Professor Tien Y. Wong
12:00	Evidence for myopia control: therapeutic 7-methylxanthine Review of the evidence on the effects and use of 7-methylxanthine	Dr Klaus Trier
12:30	Lunch	
13:30	Breakout session: Future research needed **Group 1.** Epidemiological research on the prevalence of myopia, high myopia, blindness and vision impairment due to myopia (cataracts, glaucoma, MMD) **Group 2.** Definition of MMD for surveys and future publications, protocol for measuring the prevalence of MMD in epidemiological surveys and future publications, including a grading scale and quantification of MMD. Terminology, classification, survey methods and protocols **Group 3.** Vision impairment and blindness due to myopia **Group 4.** Draft recommendations on the public health implications of interventions	
15:30	Afternoon tea	
16:00	Plenary session: Future research review and outcomes	Group reporters Moderator: Dr Silvio Mariotti
17:30	Close of day 2	

Breakout groups

Group 1

Facilitator: Dr Susan Vitale

Reporter: Dr Hasan Minto

Participants: Mr Tim Fricke (observer), Professor Jafer Kedir, Dr Ivo Kocur, Dr David Wilson (observer), Professor Olavi Pärssinen

Group 2

Facilitator: Professor Earl Smith III

Reporter: Professor Padmaja Sankaridurg

Participants: Dr Silvio Mariotti, Professor Seang Mei Saw, Dr Klaus Trier, Professor Jialiang Zhao

Group 3

Facilitator: Professor Nag Rao

Reporter: Dr Monica Jong

Participants: Professor Jost B. Jonas, Professor Kyoko Ohno-Matsui, Dr Solange R. Salomão, Professor Abbas Ali Yekta, Dr Adriana Berezovsky (observer)

Group 4

Facilitator: Professor Tien Wong

Reporter: Professor Kovin Naidoo

Participants: Professor Brien Holden, Dr Silvio Mariotti, Professor Serge Resnikoff, Professor Mingguang He

Day 3. Wednesday 18 March 2015 – Chair: Professor Brien A. Holden

09:00	Brief outline of the morning Housekeeping: transfers to the airport, lunch, luggage storage	Chair
09:10	Plenary session: conclusions and recommendations • Action plan/roadmap for establishing definitions of myopia, high myopia and MMD, further research needed • Conclusions and recommendations and next steps, i.e. creating a category for MMD in blindness surveys, dealing with myopia progression at clinical level Follow-up meeting and agreed timelines	Presenter: Dr Ivo Kocur Moderator: Dr Silvio Mariotti
12:00	Close	
12:10	Lunch	

Annex 3. Regions defined in the WHO Global Burden of Disease programme

Subregion	Countries
High-income region	
Asia-Pacific, high income	Brunei Darussalam, Japan, Republic of Korea, Singapore
Australasia	Australia, New Zealand
North America, high income	Canada, United States of America
Western Europe	Andorra, Austria, Belgium, Cyprus, Denmark, Finland, France, Germany, Greece, Iceland, Ireland, Israel, Italy, Luxembourg, Malta, Netherlands, Norway, Portugal, Spain, Sweden, Switzerland, United Kingdom of Great Britain and Northern Ireland
South Asia region	
South Asia	Afghanistan, Bangladesh, Bhutan, India, Nepal, Pakistan
Sub-Saharan Africa region	
Central Africa	Angola, Central African Republic, Congo, Democratic Republic of the Congo, Equatorial Guinea, Gabon
East Africa	Burundi, Comoros, Djibouti, Eritrea, Ethiopia, Kenya, Madagascar, Malawi, Mauritius, Mozambique, Rwanda, Seychelles, Somalia, Sudan, Uganda, United Republic of Tanzania, Zambia
Southern Africa	Botswana, Lesotho, Namibia, South Africa, Swaziland, Zimbabwe
West Africa	Benin, Burkina Faso, Cameroon, Cape Verde, Chad, Côte d'Ivoire, Gambia, Ghana, Guinea, Guinea-Bissau, Liberia, Mali, Mauritania, Niger, Nigeria, Senegal, Sierra Leone, São Tomé and Príncipe, Togo
Other regions	
Central Asia	Armenia, Azerbaijan, Georgia, Kazakhstan, Kyrgyzstan, Mongolia, Tajikistan, Turkmenistan, Uzbekistan
East Asia	China, Hong Kong SAR (China), Macau SAR (China), Democratic People's Republic of Korea, Taiwan (China)
South-east Asia	Cambodia, Indonesia, Lao People's Democratic Republic, Malaysia, Maldives, Myanmar, Philippines, Sri Lanka, Thailand, Timor-Leste, Viet Nam
Oceania	Fiji, Kiribati, Marshall Islands, Micronesia (Federated States of), Papua New Guinea, Samoa, Solomon Islands, Tonga, Vanuatu
Central Europe	Albania, Bosnia and Herzegovina, Bulgaria, Croatia, Czech Republic, Hungary, Montenegro, Poland, Romania, Serbia, Slovakia, Slovenia, the former Yugoslav Republic of Macedonia
Eastern Europe	Belarus, Estonia, Latvia, Lithuania, Republic of Moldova, Russian Federation, Ukraine
Andean Latin America	Bolivia (Plurinational State of), Ecuador, Peru
Central Latin America	Colombia, Costa Rica, El Salvador, Guatemala, Honduras, Mexico, Nicaragua, Panama, Venezuela (Bolivarian Republic of)
Southern Latin America	Argentina, Chile, Uruguay
Tropical Latin America	Brazil, Paraguay
Caribbean	Antigua and Barbuda, Bahamas, Barbados, Belize, Cuba, Dominica, Dominican Republic, Grenada, Guyana, Haiti, Jamaica, Saint Lucia, Saint Vincent and the Grenadines, Suriname, Trinidad and Tobago
North Africa and Middle East	Algeria, Bahrain, Egypt, Iran (Islamic Republic of), Iraq, Jordan, Kuwait, Lebanon, Libya, Morocco, Occupied Palestinian Territory, Oman, Qatar, Saudi Arabia, Syrian Arab Republic, Tunisia, Turkey, United Arab Emirates, Yemen

For more information, please contact:

Department for Management of NCDs, Disability, Violence and Injury Prevention (NVI)

World Health Organization

20, avenue Appia
CH-1211 Geneva 27
Switzerland
Tel: +41 22 791 2111
Fax: +41 22 791 3111
www.who.int/blindness

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