Review: Highlights from the 2019 International Myopia Summit on 'Controversies in Myopia'

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Abstract

Myopia is an emerging public health issue with potentially significant economic and social impact in populations especially from East Asia. However, many uncertainties around myopia and its clinical management. The International Myopia Summit workgroup was convened by the Singapore Eye Research Institute, the World Health Organization (WHO) Regional Office for the Western Pacific and the International Agency for the Prevention of Blindness (IAPB) in 2019. The aim of this workgroup was to summarise available evidence, identify gaps or unmet needs, and provide consensus on future directions for clinical research in myopia. In this review, amongst the many 'controversies in myopia' discussed, we highlight three main aspects: First, development of clinical interventions for the prevention of ocular elongation and pathologic myopia are needed, and may require multifaceted research targeting multiple sites, including the Bruch's membrane, choroid and sclera. Second, clinical myopia management requires cooperation between optometrists and ophthalmologists to provide patients with holistic care, and a tailored approach that balances risks and benefits of treatment by utilising both optical and pharmacological interventions. Third, the diagnosis and management of myopia complications may be improved through collaboration between clinicians, researchers and industry. There is an unmet need to develop new imaging modalities for both structural and functional analyses and to establish normative databases for myopia in the long term. In conclusion, the workgroup's call to action advocated for a paradigm shift towards a collaborative approach in the holistic clinical management of myopia.

Introduction

Myopia is increasingly recognised as an emerging public health issue with significant economic burden particularly in East Asia.[1-5] The awareness of myopia and it impact has led to the implementation of public health interventions, the study of myopia control therapies and research into the treatment of myopia-related complications.[6] However, there are several unresolved questions with regards to the clinical management of myopia and pathologic myopia. Thus, the International Myopia Summit (IMS) workgroup was convened in 2019, supported by the World Health Organisation (WHO) and the International Agency of Prevention of Blindness (IAPB).

The main aim of this workgroup was to discuss 'controversies' surrounding myopia, identify unmet needs in myopia research and its clinical management, and provide suggestions for future development in the field of myopia – **Supplementary Table 1**. The composition of the workgroup consisted of representatives from 20 international organizations renowned for myopia prevention, research and/or clinical management. Members of the workgroup comprised public health officials, optometrists, ophthalmologists and researchers – **Supplementary Table 2**. The definitions of myopia used followed recent consensus,[6-9] to ensure consistency for this workgroup meeting – **Table 1**.

In this review, we included published literature from a non-systematic review of available evidence from the last 20 years up to July 2019 in MEDLINE, EMBASE and Cochrane Library, using the search terms "myopia","high myopia", "pathologic myopia" alone or in combination with "prevalence", "epidemiology", "diagnosis", "treatment", "imaging", "control","prevention", "optical", "spectacles", "atropine", "contact lens" and "orthokeratology". The reference lists from articles identified by this search strategy were also used to include other relevant publications. While publications on randomized clinical trials were prioritized, we also included highly regarded or highly-cited publications, such as review articles and meta-analyses. Here, we present discussions on three 'controversies' in the clinical management of myopia, highlighted by the workgroup as aspects that may require further collective focus – **Figure 1**.

Table 1: Definitions of Myopia used in this review as previously defined [6-9]

Term	Definition
Myopia	Spherical equivalent refractive error ≤ –0.50 diopter
High myopia (without pathology)	Spherical equivalent refractive error ≤ –5.0 diopter
Myopic macular degeneration	A vision-threatening condition occurring in people with myopia, usually high myopia that comprises diffuse or patchy macular atrophy with or without lacquer cracks, macular Bruch's membrane defects, myopic choroidal neovascularisation and Fuchs spot.
Pathologic myopia	Excessive axial elongation associated with myopia that leads to structural changes in the posterior segment of the eye (including posterior staphyloma, myopic macular degeneration, myopic traction maculopathy, and high myopia-associated optic neuropathy) and that can lead to loss of best-corrected visual acuity.

Controversy 1: Should research in myopia treatments focus on preventing the development of pathologic myopia rather than prevention of myopia progression?

There is increasing awareness that myopia is not just a refractive error that can be “reversed” by optical aids or refractive surgery. Myopia may progress to pathologic myopia, a potentially blinding condition due to complications such as retinal detachment, myopic maculopathies and glaucoma.[10] However, current clinical management of myopia is focused on its control and reducing myopia as a refractive error, rather than interventions to prevent the development of pathologic myopia and its complications.[10 11] Given this context, two important aspects were highlighted and discussed:

<u>‘Does controlling myopia in childhood, prevent the development of pathologic myopia in adulthood?’</u>

Pathologic myopia (PM) is a sight threatening condition that includes myopia macular degeneration (MMD), myopic traction maculopathy, myopic choroidal neovascularization (mCNV) and myopia-associated optic neuropathy.[8 10] Posterior staphyloma (PS), an outward protrusion of all layers of the posterior eye globe, is a hallmark lesion of PM.[11] The prevalence of PM is closely correlated with the severity of myopia.[12] The Guangzhou twin eye study demonstrated that earlier age at myopia onset was associated with higher myopic refractive error at 18 years old .[13] Current myopia control options can reduce progression by 50% and specifically, among children with age of onset at 8 years old, myopia control would reduce their mean refractive error from -6D to -3D. This level of myopia control would significantly reduce the risk of PM from 30% to 5%.[14]

Conversely, PM is a complex condition with multiple non-modifiable risk factors other than axial length (AL), such as age, gender and genetics.[10] With pharmaceutical treatments, AL reduction is limited. Specifically in the ATOM and LAMP studies, AL increased by +0.41mm and +0.36mm in the 0.01% atropine groups, respectively, compared to +0.38mm and +0.4mm with placebo.[15-18] The second year follow up of LAMP Study did however report significant reduction in axial elongation when children on placebo, were switched to 0.05% Atropine in the second year (0.15 vs 0.43 mm, $P< 0.001$ in year 2 and year 1, respectively.[19] Furthermore, eyes with shallow PS may have a higher frequency of mCNV[20], suggesting that the risk of mCNV may not be closely correlated with AL. Age is another important risk factor. PM and PS do not occur in children with high myopia without pathology.[21 22] Men in general have longer AL than women[23], but a higher prevalence of MMD and mCNV is observed in females in multivariable analyses.[24 25] Lastly, genome wide association studies have identified single nucleotide polymorphisms (SNPs) for refractive error[26], while the SNPs specific for PM are still unknown.[27] However, it remains unclear if slowing myopia progression in individuals with high genetic risk will be effective in preventing PM.

‘A potential treatment target: Is the Sclera and choroid, or Bruch’s membrane a primary site of pathogenesis in pathologic myopia?’

Ophthalmoscopic features of axial myopia suggest a significant contribution of the Bruch’s membrane (BM) to several pathologic features including lacquer cracks (cracks in the BM), patchy/macular atrophy (both are BM defects), mCNV (which arise from a break of the BM) and parapapillary gamma zone (a result of the temporal shift and widening of the optic nerve head–related BM opening). Histologically, BM defects in congenital colobomata and toxoplasmotic scars are associated with scleral staphyloma.[28] Both choroidal and scleral volume are not associated with AL, but BM increases in volume with AL.[29] This suggests that BM may have an active role in the process of axial elongation. A hypothesis for the role of BM in the process of myopization states that axial elongation occurs by the production of and elongation of the BM in the equatorial region.[30] This explains the decrease in retinal pigment epithelium density and retinal thinning at the equator.[31 32] Also, the compression of the choroid against the sclera by the expanding BM results in choroidal thinning.[30] Enlargement of the BM opening and development of macular BM defects may be explained by the tension in BM in the coronal direction.[30] Thus, BM may be more than just an almost invisible double basal membrane with some collagen and elastin in between. Further evidence to support this hypothesis was demonstrated in a guinea pig model of myopia, in which intraocular injection of antibodies to amphiregulin, a member of the epithelial growth factor family that regulates the production of BM, was shown to decrease axial elongation in a dose dependent manner.[33 34]

There is equally strong evidence for the sclera and choroid as the primary sites of pathology in PM. In both mammalian models and in human studies, myopia development is associated with rapid scleral thinning and tissue loss.[35-37] Remodelling of the sclera is a major feature in the guinea pig model of myopia in particular.[38] In terms of biomechanics, scleral biomechanical properties varies with the severity of myopia, and focal areas of weakness in the sclera can be found in the myopic eye.[39] Choroidal thinning is closely associated with increasing levels of myopia and MMD[40 41] and in the chicken myopia model, choroid thickness is negatively correlated with myopia.[42] Scleral

crosslinking as a means to stop scleral growth has been extensively investigated, but clinical application has been limited by a lack of safe and effective methods for applying ultraviolet A radiation and chemicals to the posterior sclera.[43 44] Lastly, scleral regenerative therapy is an approach whereby human fibroblasts transplanted onto the posterior sclera may strengthen the sclera by producing type I collagen, and has been shown to significantly reduce axial elongation in a rat myopia model.[45]

Conclusion:

There is currently no definitive evidence to suggest that myopia control in childhood could prevent PM development later in life, and as such, long-term prospective studies are needed to answer this question. Research in myopia treatment would benefit from a shift in focus towards devising clinical therapies targeted at preventing AL elongation and PM. However, there is currently insufficient evidence to support a primary site of pathology in PM. Thus research into possible strategic targets for therapies may require focus on multiple sites, as current evidence suggest the possibility of Bruch's membrane, choroid and sclera all playing a role in PM development.

Controversy 2: There is currently no "gold standard" intervention in the clinical management of myopia control.

Atropine eyedrops, orthokeratology, defocus multizone soft contact lens[46] and defocus incorporated multiple segments (DIMS) spectacle lenses[47] have been reported to be effective options for reducing myopia progression. Soft contact lenses and DIMS spectacles are recent innovations that have shown great promise for myopia control. A 3 year randomized clinical trial of MiSight dual focus contact lens (CooperVision, Pleasanton, CA, USA) (n=109) showed that myopia progression and axial elongation were 59% and 52% less in the MiSight arm than the single vision contact lens arm.[46] In the 2 year randomised clinical trial of DIMS spectacles (n=160), children on DIMS spectacles had significantly slower myopia progression and axial elongation (52% and 62%

respectively) over 2 years when compared with those wearing single vision spectacle lenses. [48] However, variations between studies and individuals are large in the former and only one study in the later, further studies is warranted. There is also growing interest in combining pharmaceutical and lens based interventions.[49] A recent study (n=60) evaluated the efficacy of atropine 0.01% eyedrops as an adjunctive treatment for children who have already been on ortho-k treatment for a year. While on Ortho-k treatment in the first year, axial elongation was 0.46 ± 0.16 mm/yr, decreasing significantly to 0.14 ± 0.14 mm/yr ($p<0.001$) when atropine was added in the second year.[50] The potential synergistic effects from combination therapy may be of benefit particularly for rapid myopia progressors

These treatment options are usually offered to patients based on the expertise of the eye care professional, influenced by a wide range of practice patterns around the world.[6] However, the clinical management of myopia ideally should be evidence-based, selected to provide the best risk-benefit profile for that individual or child. Recently, two interventions have emerged with greatest potential for myopia control:

<u>'Should orthokeratology be the treatment of choice for controlling myopia progression in children?'</u>

Orthokeratology (Ortho-K) has been reported to be effective in controlling myopia progression (30-56% reduction)[51-56] Ortho-K may have different treatment effects depending on the age and degree of myopia. In the Retardation of Myopia in Orthokeratology (ROMIO) study, the effectiveness of ortho-k on myopia control was observed to be better in younger children less than 9 years than in older subjects.[56] In another retrospective study, AL elongation was slower by 49%, 59% and 46% in the low, moderate and high myopia subgroups respectively. While significant differences between orthokeratology and control groups were observed in both the first and second year of follow up in the low and moderate myopia groups, a significant difference was only observed in the first year within the high myopia group.[57] In comparison, atropine's efficacy depending on concentration, ranges between 60 to 80% reduction.[15-17 58-60]. However, higher doses are associated with increased side effects such as photophobia and a decrease in accommodation amplitude which may result in the need

for photochromic, progressive or bifocal addition spectacles. Furthermore there is a need for concurrent spectacle or contact lens usage.[59] On the other hand, the main risk associated with Ortho-K would be infectious keratitis. While the estimated incidence of infectious keratitis in Ortho-K wearers is rare at 7.7/10000 patient eye years, this increases to 13.9/10,000 patient-years in children, which make up the brunt of Ortho-K wear for myopia progression treatment.[61 62] A 10-year retrospective study of 104 eyes of 53 children who underwent orthokeratology treatment observed adverse events in 53 eyes (51%). Of these, conjunctival complications such as allergic conjunctivitis were the most frequent, while corneal infiltration and keratitis occurred in 8 eyes (7.7%).[63] To put the figures in perspective, the estimated incidence of infectious keratitis in daily-wear rigid-gas-permeable (RGP) lens wearers is 1.2/10,000, while in extended wear soft lens wearers, the incidence ranges from 13.3 – 19.5/10,000. This suggests that Ortho-K wear risk in children is essentially similar to that of extended wear soft contact lens wear.[64] Risk factors for infectious keratitis include overnight wear, insufficient training of practitioners and wearers, non-professional fitting procedures, poor compliance with lens hygiene, or inadequate follow-up.[65] These infections can be severe and may result in visual loss or the need for corneal transplantation. Importantly, parents should be counseled as to the risk of infectious keratitis and eye care professionals should undergo rigorous training and accreditation before prescribing Ortho-K to ensure quality control. Besides microbial keratitis, other side effects of Ortho-K include induced astigmatism, third and fourth order spherical aberrations, recurrent corneal erosion, corneal staining, edema and haze.[61 62]

Rebound upon discontinuation is an important issue emphasized in atropine but this has been less widely studied in Ortho-K.[16 58 66] In terms of vision, Ortho-K provides the best uncorrected visual acuity, whereas atropine may cause poor near visual acuity especially with higher doses and spectacles are still required. Quality of life and subjective ratings from multiple studies show an improvement with Ortho-K compared to wearing single vision spectacles.[67-69] The cost effectiveness of Ortho-K requires further study. Ortho-K lenses in general are more expensive than other optical interventions, costing annually on an average, USD$1000-2000[70], requiring

individualised design and fitting, and intensive review to detect complications. Additionally, they are usually not covered by most health reimbursement or insurance plans.[70]

'Should atropine eye drops be used in children with low or no myopia to prevent myopia progression?'

Both the Meta-analysis of Interventions for Myopia Control (30 RCTs. 5,422 eyes) and the Meta-analysis of Atropine Studies for Myopia Control (19 studies, 3,137 children) concluded that atropine markedly slowed myopia progression.[60] [59] While there is currently only one small study providing evidence for the effectiveness of atropine in children with no myopia[71], it is known that younger age of myopia onset is associated with high myopia. It can be safely predicted that 5-year-old children, whose refraction are between +0.75D to -0.49D will soon develop myopia. These may be the at-risk group (pre-myopes) that is likely to benefit from low dose atropine use. ATOM3 is an ongoing double-blind randomized placebo-controlled clinical trial initiated in June 2017 to evaluate the use of atropine 0.01% in the prevention and control of myopia in pre-myopes.[72]

The main concern against using atropine in children with no myopia is the risk of side effects. In the LAMP study, 30-34% of children on atropine required photochromatic glasses and 2.8-6.4% developed allergic conjunctivitis.[18] 70% and 61% of subjects receiving 0.5% and 0.1% atropine, respectively, requested progressive glasses for reading in the ATOM 2 study.[16] In the LAMP study, even 0.01% atropine was associated with accommodation paralysis in 1.8% of subjects.[18] Hence, some children may paradoxically require spectacles after commencing atropine. Although extremely rare, there is a risk of more severe systemic side effects such as palpitations, confusion, dry mouth and high fever. In addition, the long term side effects of atropine eyedrops are still unclear. In children, a rebound effect was observed upon abrupt cessation of treatment, where the rate of myopia progression increased. When higher atropine was stopped for 12 months after 24 months of treatment (phase 2 of ATOM2), there was a rapid increase in myopia in children originally treated with higher concentrations of atropine, whereas those receiving the lowest concentration of 0.01% showed

minimal change.[16 66] This rebound phenomenon can significantly reduce the effectiveness of atropine eyedrops for myopia control, compared to optical treatments. Importantly, atropine is largely used as an off-label treatment for myopia in most countries. Where low dose atropine eyedrops unavailable commercially, the use of low dose atropine may bear significant risks from patients diluting down higher doses and inconsistencies from compounding pharmacies.

Conclusion:

Overall, optimizing the clinical management of myopia would benefit from an alignment of best practice patterns, with a tailored approach that can only be achieved with close collaboration amongst eye care practitioners. While current evidence suggests that low-dose atropine is a good option, potential side-effects and the lack of availability in certain healthcare settings needs to be considered. However, the use of atropine in children with low or no myopia requires further evidence from clinical trials prior to any recommendation. There are other emerging treatment options that are effective such as orthokeratology, contact lens, and spectacles, which should be considered in the holistic management pathway of myopia. Finally, there is growing interest in combining interventions,[49] such as atropine and orthokeratology which may have a synergistic effect while balancing the risks and benefits of both therapies.[50]

Controversy 3: Current technology is inadequate for the diagnosis and monitoring of myopia related complications.

The burden of visual impairment arising from myopia comes primarily from PM and its complications such as MMD, which is now a leading cause of blindness in developed nations.[73] Thus, the early detection and monitoring for myopia-related complications is important for timely intervention and prevention of visual impairment.[74] The detection and evaluation of two major complications of PM, myopic choroidal neovascularisation and myopia-associated optic neuropathy, are discussed:

‘Is optical coherence tomographic angiography (OCTA) adequate for the evaluation of myopic choroidal neovascularisation?’

Optical coherence tomographic angiography (OCTA) is a relatively new imaging technology that has emerged as a potential alternative to more invasive imaging modalities, namely fundus fluorescein angiography (FFA) for the evaluation of myopic choroidal neovascularisation (CNV). The pooled diagnostic accuracy of OCTA was reported in 2 separate meta-analyses to have a sensitivity of 0.87-0.90, specificity of 0.97 and an area under the curve of 0.96 for detecting CNV.[75 76] OCTA, in conjunction with OCT, can be utilized for the monitoring of treatment response and activity. On OCT, the resolution of subretinal hyper-reflective material, subretinal fluid and a well-defined border to the CNV lesion are reliable signs of inactivity. On OCTA, the CNV lesion typically decreases in size although the vascular network persists, regular monitoring of the vascular network size on OCTA is useful for assessing for recurrence.[74]

However, several limitations of OCTA remain. First, OCTA informs of perfusion through the vascular complex but offers no information on vascular leakage, which is a key treatment indicator. Relying on OCTA alone may result in over-treatment of inactive mCNV. Second, artefacts and poor scan quality are common in patients with poor vision and who are thus unable to sustain fixation long enough for scan acquisition. Third, segmentation errors are particularly prevalent in highly myopic eyes with long axial lengths, steep retinal contours and posterior staphyloma. Moreover, poor fixation and motion artefacts are common causes of uninterpretable scans (**Figure 2**).

‘Can current diagnostics adequately diagnose and monitor glaucoma or myopia-associated optic neuropathy in high myopes?’

There are several challenges for the adequate diagnosis and monitoring of glaucoma or myopia-associated optic neuropathy in high myopes. Anatomically, the three layers of the optic nerve head, namely the BM opening, the choroidal opening, and the opening in the peripapillary scleral flange covered by the lamina cribrosa get misaligned by a shift of the BM opening usually into the temporal

inferior direction.[77] This leads to an overhanging of BM into the intrapapillary region at the nasal disc border, and to an absence of BM in the temporal parapapillary region, i.e. the temporal gamma zone.[77 78] With an axial length of more than 26.5mm, the BM opening additionally enlarges, eventually leading to a circular gamma zone, In addition, the colour contrast and spatial contrast between the optic cup and neuroretinal rim decrease with longer axial length. This complicates the assessment of cup to disc ratio and measurements of retinal nerve fibre layer (RNFL) thickness with OCT. Functionally, these eyes often have macular pathology and these may confuse the assessment of glaucomatous visual field defects on perimetry. The decreased scleral rigidity in highly myopic eyes may also result in underestimation of the intraocular pressure in these eyes.[79 80]

Regardless, there are clinical indicators and clues that can aid a physician in diagnosing and monitoring glaucoma in these patients. First, glaucoma is a progressive disease in which longitudinal analysis is key. By comparing the same eye over time, the impact of ambiguous anatomy on diagnosis and monitoring will be reduced. Second, assessing the macular ganglion cell-inner plexiform layer (GC-IPL) thickness measurements in areas without BM defects for vertical asymmetry is also a useful method for diagnosis and monitoring glaucoma because most eyes with MMD tend to have preservation of the inner retinal thickness at least in the earlier stages.[81]

However, none of the current imaging modalities currently used for glaucoma assessment has been optimized for use in high myopes. RNFL measurements with OCT is problematic due to an indistinct BM edge which tends to shift temporally in high myopes. The superior and inferior RNFL converge more temporally than in a non-highly myopic eye, and signal loss around optic disc can occur in the presence of a posterior staphyloma. GC-IPL measurements can be inaccurate when there is co-existing myopic traction maculopathy (**Figure 3**) or underlying BM defects. An overarching limitation of structural analysis is the lack of a normative database for the highly myopic population, which is likely to differ significantly from a database of non-highly myopic eyes due to the above-mentioned anatomical differences. Lastly, objective visual field assessment such as the Humphrey

Visual Field (HVF) is often unable to differentiate between deterioration due to glaucoma or myopic maculopathy.[79 82]

Conclusion:

The structure of the myopic eye adds complexity to the evaluation and early detection of sight threatening complications such as MMD and myopia-associated optic neuropathy, that cannot be bridged with current diagnostics. Collaboration between clinicians, researchers and industry is needed to optimize diagnostic and imaging technologies specifically for the myopic eye. Currently, OCTA imaging alone may be inadequate for evaluating myopic CNV, while the evaluation of myopia-associated optic neuropathy requires further research to accurately evaluate optic nerve damage in PM. Overall, there is an unmet need to explore and develop new imaging modalities for both structural and functional analyses and to establish normative databases for myopia in the long term.

Summary and Conclusions

The aim of this review is to highlight various aspects of clinical myopia discussed during the International Myopia Summit in 2019, including gaps in myopia research that require further study, consensus where evidence is not well established, and a call to action for stakeholders to collaborate in the management of myopia. We acknowledge that the views presented are limited to that of the workgroup, which comprised an international panel from diverse backgrounds, all involved in myopia prevention or research. There are also potential biases arising from the representation of myopia experts mainly from Asia, but we have included a comprehensive review of the available published evidence to provide an objective summary in this article. Nonetheless, we have highlighted three key areas with regards to the clinical management of myopia, which may benefit from further research and development. First, controlling childhood myopia is theoretically preventing futher high myopia in adulthoor. However, as controlling childhood myopia alone may not be enough to prevent the development of PM in adulthood, there is an unmet need to search for potential treatment targets and to develop therapies interventions that prevent progression to PM. Second, the clinical management of

myopia will benefit from co-management from eye care professionals, such that the treatment plan may be tailored to patient needs while weighing the relative costs and benefits of each intervention. Third, evaluation of myopia complications using current technologies present limitations that require collaboration between clinicians, researchers and industry partners to overcome in the long term. The workgroup advocated a paradigm shift in our approach to clinical management of myopia - one that necessitates coordinated action among the eye care community in our fight against the 'myopia epidemic'.

Supplementary Table 1: A summary of debated topics and consensus achieved at the International Myopia Summit

Motion	**Consensus**
Myopia Prevention and Public Policy	
Are current myopia definitions to inform public policy currently adequate?	There is overemphasis on cut-off values for myopia. Myopia as a refractive error is a continuous measure with multifactorial risk for developing complications.[12 83]
Should myopia be a primary priority for health ministries in Asia?	Advocates require more data on cost effectiveness and societal impact, (which includes workforce productivity, education and national defense), to justify and empower ministries to act.[84-96]
Should outdoor time be mandated for all school-going children?	This is considered the most cost-effective myopia prevention strategy, but there are challenges in its implementation. There is a need to engage stakeholders, such as parents, health and

	education ministries to address these challenges.[87 97-100]
Myopia Control	
Should “breaks” in near work activities be mandated for all school-going children?	More evidence is needed to support this intervention. The causal relationship between myopia and near work, the relative contribution of near work vs outdoor activity, and the effect of different types of near work on myopia require further study.[101-107]
Is orthokeratology the treatment of choice for controlling myopia progression in children?	Careful patient selection and stringent follow up with close co-management between optometrists and ophthalmologists are important to maximize efficacy and minimize the risk of blinding complications.[51-61 63-70]
Should atropine be used in children with low or no myopia to prevent myopia progression?	Low dose atropine is effective for myopia control in children with low myopia, but the exact dosage to minimise side effects whilst retaining efficacy is still to be determined. Further evidence from clinical trials for the safety and efficacy of low dose atropine in children without myopia is needed.[16 18 59 60 66 71]
Myopia myths	
Are environmental factors more important than genetics as a determinant of myopia?	The effectiveness of environmental interventions should be considered in the context of different genetic risk determinants.[108-112]
Are near work and increased screen time related to myopia progression?	Near work is related to myopia onset and progression, but this is less clear for increased

	screen time. More studies are needed to investigate the effect of increased screen time on increased near work and reduced time spent outdoors.[98 102 113 114]
Does controlling myopia in childhood prevent pathologic myopia in adulthood?	Pathologic myopia is a multifactorial disease with additional risk factors besides refractive error, such as age, gender and genetics. Controlling refractive error alone may not be enough to prevent pathologic myopia. Long term studies are needed to assess the effectiveness of myopia control in childhood on the prevention of pathologic myopia in adulthood.[10-27]
Industry and regulation of myopia treatment	
Should spectacles be reimbursed by health insurance and/or public health care providers?	WHO has included spectacles in the list of Priority Assistive Products, and spectacle coverage is now an indicator for Universal Health Coverage. However, there are barriers to implementation that need to be overcome, including the lack of integration of refractive and optical services in health systems, regulatory hurdles and issues of equitability.[115]
Should orthokeratology be regulated as a medical device?	Orthokeratology is regulated as a medical device by many government agencies. More stringent regulations may be required, such as a requirement for eyecare professionals to be trained and certified before they can prescribe orthokeratology. Co-management between

	optometrists and ophthalmologists is important to minimize the risk of complications such as corneal infections.[62 116 117]
Should refractive surgery be considered a medical treatment for adult high myopia?	Refractive surgery should not be considered a medical treatment because of issues with efficacy and predictability of excimer laser treatments, side effects of phakic intraocular lenses, risk of malpractice litigation and lack of evidence for cost effectiveness compared to spectacles or contact lenses.[118-122]
Pathologic myopia	
Is wide field imaging mandatory to screen for pathologic myopia in adult high myopes?	The cost, affordability, quality and accuracy of wide field imaging requires further study. Wide field imaging cannot replace good history taking and a dilated fundal examination. Guidelines on who to screen and what to screen for are needed.[123 124]
Is retinal detachment in high myopes best managed with combined scleral buckling and vitrectomy?	High myopes with rhegmatogenous retinal detachment are typically younger, phakic patients that can be adequately managed with scleral buckling alone. In more complex cases requiring vitrectomy, adding an encircling scleral buckle to support the vitreous base may optimise single surgery success rates.[125-128]
Should myopic traction maculopathy be treated early before vision deteriorates?	There is significant risk of visual loss from macular hole associated with surgery for myopic traction maculopathy. Surgery should be reserved

	for patients with foveal detachment or worsening vision, and monitoring is advised for patients with early stages of myopic traction maculopathy.[129-133]
Is optical coherence tomographic angiography adequate for starting treatment in and monitoring of myopic choroidal neovascularisation?	The structural abnormalities of the highly myopic eye present significant difficulty for current imaging technology, including optical coherence tomographic angiography. Collaboration between clinicians, researchers and industry partners is needed to improve and optimize imaging modalities for the myopic eye.[74-76]
Is Bruch's membrane the primary site of pathology in pathologic myopia?	There is insufficient evidence to support a primary site of pathology in pathologic myopia. Further research is required to elucidate the pathogenesis to guide the development interventions for pathologic myopia.[28-32 35-42]
Can glaucoma in high myopes be adequately diagnosed and monitored with current diagnostics?	There is a need to explore and develop other new imaging modalities and to build normative databases for both structural and functional analyses. This requires close collaboration between clinicians, researchers and industry partners.[79-82]

Supplementary table 2: Organisations represented at the International Myopia Summit Workgroup 2019.

Organisations	1. World Health Organisation (Western Pacific Region) 2. International Agency for Prevention of Blindness 3. International Myopia Institute 4. World Optometry Council 5. Centre for Eye Research Australia, Australia 6. Brien Holden Vision Institute, Australia 7. School of Optometry and Vision Science, University of New South Wales 8. School of Optometry and Vision Science, Queensland University of Technology, Australia 9. Research School of Biology, Australian National University, Australia 10. Shanghai Eye Diseases Prevention & Treatment Centre, China 11. Department of Ophthalmology, Wenzhou Medical College, China 12. Medical Faculty Mannheim, Heidelberg University, Germany 13. Singapore Eye Research Institute, Singapore 14. National University Hospital, Singapore 15. National Healthcare Group Eye Institute, Singapore 16. Institute of Molecular and Cell Biology (IMCB), Agency for Science, Technology and Research (A*STAR), Singapore 17. Kaohsiung Chang Gung Memorial Hospital, Chinese Taipei 18. Chang Gung University College of Medicine, Chinese Taipei 19. International Centre for Eye Health, London School of Hygiene and Tropical Medicine, United Kingdom 20. Department of Ophthalmology, Columbia University, USA

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Figure legends

Figure 1: The future of research in myopia.

Figure 2: 12x 12mm Swept source optical coherence tomographic angiography scans of the choroid in a patient with good fixation (A) and a patient with poor fixation (B) Note the presence of motion artefacts (white arrowheads) and artefactual dropout of vascular flow signal due to from segmentation error (white arrow).

Figure 3: Ganglion cell- inner plexiform layer (GC-IPL) thickness analysis using spectral domain optical coherence tomography (SD-OCT) in a patient with high myopia and normal tension glaucoma. Red and yellow lines on the OCT B scan image define the anterior and posterior boundaries of the GC-IPL layer respectively. Segmentation error is seen on the OCT B scan in the right eye (white arrow) due to myopic traction maculopathy.