Special Issue

IMI – Defining and Classifying Myopia: A Proposed Set of Standards for Clinical and Epidemiologic Studies

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Purpose. We provide a standardized set of terminology, definitions, and thresholds of myopia and its main ocular complications.

Methods. Critical review of current terminology and choice of myopia thresholds was done to ensure that the proposed standards are appropriate for clinical research purposes, relevant to the underlying biology of myopia, acceptable to researchers in the field, and useful for developing health policy.

Results. We recommend that the many descriptive terms of myopia be consolidated into the following descriptive categories: myopia, secondary myopia, axial myopia, and refractive myopia. To provide a framework for research into myopia prevention, the condition of "pre-myopia" is defined. As a quantitative trait, we recommend that myopia be divided into myopia (i.e., all myopia), low myopia, and high myopia. The current consensus threshold value for myopia is a spherical equivalent refractive error ≤ -0.50 diopters (D), but this carries significant risks of classification bias. The current consensus threshold value for high myopia is a spherical equivalent refractive error ≤ -6.00 D. "Pathologic myopia" is proposed as the categorical term for the adverse, structural complications of myopia. A clinical classification is proposed to encompass the scope of such structural complications.

Conclusions. Standardized definitions and consistent choice of thresholds are essential elements of evidence-based medicine. It is hoped that these proposals, or derivations from them, will facilitate rigorous, evidence-based approaches to the study and management of myopia.

Keywords: myopia, myopia classification, myopia definitions, high myopia, myopia thresholds, high myopia, pathologic myopia

1. Introduction

Myopia currently is widely recognized as a significant public health issue causing significant visual loss and a risk factor for a range of other serious ocular conditions.[1] The prevalence of this condition is increasing on a global basis, for reasons that still are not understood.[2] Although partial reductions in progression rates have been observed from pharmacologic therapies, optical treatments, and behavioral modifications[3] (see also accompanying paper IMI – Interventions for Controlling Myopia Onset and Progression Report),[4] we are a long way from being able to reverse the temporal trends of the last few decades. This makes myopia, and its associated complications, a high research priority.

Myopia has been the subject of scientific study since the work of Johannes Kepler in 1604, and a topic of philosophic discussion from the time of Aristotle. Over the intervening centuries, myopia has been defined in a wide variety of ways: presumed etiology, age of onset, progression pattern, amount of myopia (in diopters [D]) and structural complications. This has led to an excessive and confusing accumulation of terms. Table 1 lists some of the terms and concepts that have been used in classifying myopia as a function of these five categories. As shown in this table, several terms have been used in ways that relate to more than one category; that is, to describe the presumed etiology as well as the severity or amount of myopia. Transient forms of myopia that often are termed pseudo myopia (e.g., instrument myopia, night myopia, or accommodative spasm) are not included in this Table.

The extensive literature regarding the etiology of refractive errors has revealed a complex picture. It is clear that myopia is a multifactorial condition, and that any classification based on

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Table 1. Descriptive Terms Used to Describe Various Subtypes of Myopia According to Classification Based on Presumed Etiology, Age of Onset, Progression, Amount of Myopia and Structural Complications

Basis of Classification	Associated Descriptive Terms for Different Types of Myopia
Presumed etiology	Axial, benign, component, correlational, curvature, index, lenticular, physiologic, physiological, refractive, school, simple, syndromic
Age at onset	Childhood, congenital, acquired, juvenile onset, youth onset, school, adult, early adult onset, late adult onset
Progression pattern	Permanently progressive, progressive, progressive high, progressive high degenerative, stationary, temporarily progressive
Amount of myopia	Low, medium, intermediate, moderate, high, pathologic, pathological, physiologic, physiological, severe, simple
Structural complications	Degenerative, degenerative high, malignant, pathologic, pathological, pernicious, progressive, progressive high, progressive high degenerative

simple etiologic factors is likely to be an over-simplification at best and misleading at worst. Time of onset also is of questionable value, since we do not yet know whether the biological processes underlying myopia at age 7 differ from those in myopia that develop in early adults. There also is considerable variation in the age at onset of myopia and its progression in different geographic regions.[5] Terms that are used commonly to describe the anatomic complications,[6] notably "pathologic myopia" or its alternative spelling "pathological myopia," also are used to describe higher degrees of myopia based on refractive error, even in the absence of structural complications.[7] Furthermore, the structural complications of high myopia have been demonstrated to be highly age-dependent,[8] so relying on a dioptric threshold for pathologic myopia is problematic. Such terms as "physiologic myopia" also are used in relation to etiology and severity of myopia. In addition, this term carries the implication that such myopia, being physiologic, is devoid of any adverse consequence, which is a misleading inference.[9]

In this era of evidence-based medicine, the accumulation of different terms and classifications is a significant hindrance. There also is considerable variation in defining myopia in terms of dioptric error. Such inconsistency creates challenges when comparing epidemiologic studies. Meta-analysis of randomized controlled trials can be weakened by variations in the inclusion criteria and definitions. Standardized, international classifications are an essential feature of the evidence-based approach, as demonstrated in fields, such as retinopathy of prematurity and diabetic retinopathy. To date, the myopia field has lacked a similar set of internationally agreed standards. We propose a set of definitions for myopia that are evidence-based, statistically sound, and clinically relevant.

This initiative arose from the work of the International Myopia Institute (IMI) and the international committee responsible for producing this study includes researchers in a wide range of fields: pediatric ophthalmology, epidemiology, public health, optometry, clinical myopia research, and medical retina. Input also was received from a large number of researchers within this field who are affiliated with the IMI. It is hoped that these proposals, or derivations from them, will facilitate rigorous, evidence-based approaches to the study and management of myopia.

Table 2. Summary of Proposed General and Quantitative Thresholds for Myopia

Term	Definition
Qualitative definitions	
Myopia	A refractive error in which rays of light entering the eye parallel to the optic axis are brought to a focus in front of the retina when ocular accommodation is relaxed. This usually results from the eyeball being too long from front to back, but can be caused by an overly curved cornea and/or a lens with increased optical power. It also is called nearsightedness.
Axial myopia	A myopic refractive state primarily resulting from a greater than normal axial length.
Refractive myopia	A myopic refractive state that can be attributed to changes in the structure or location of the image forming structures of the eye, i.e. the cornea and lens.
Secondary myopia	A myopic refractive state for which a single, specific cause (e.g., drug, corneal disease or systemic clinical syndrome) can be identified that is not a recognized population risk factor for myopia development.
Quantitative definitions	
Myopia	A condition in which the spherical equivalent refractive error of an eye is ≤ -0.50 D when ocular accommodation is relaxed.
Low myopia	A condition in which the spherical equivalent refractive error of an eye is ≤ -0.50 and > -6.00 D when ocular accommodation is relaxed.
High myopia	A condition in which the spherical equivalent refractive error of an eye is ≤ -6.00 D when ocular accommodation is relaxed.
Pre-myopia	A refractive state of an eye of $\leq +0.75$ D and > -0.50 D in children where a combination of baseline refraction, age, and other quantifiable risk factors provide a sufficient likelihood of the future development of myopia to merit preventative interventions.

2. Rationalization of Myopic Terminology

We propose that many of the descriptive terms within Table 1 should be abandoned, and a simpler set of terms be adopted, as shown in Tables 2 and 3. Five fundamental aspects of myopia should be covered by any set of terminology: optics, etiology (if known), diagnostic thresholds, progression, and structural complications.

There is wide consensus in defining myopia optically in relation to the formation of the retinal image, though the precise choice of words does vary. The current version of the World Health Organization's (WHO) International Classification of Disease (ICD-10) provides the following definition for myopia:

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Table 3. Definitions for the Structural Complications of Myopia

Term	Definition
Descriptive definitions	
Pathologic myopia	Excessive axial elongation associated with myopia that leads to structural changes in the posterior segment of the eye (including posterior staphyloma, myopic maculopathy, and high myopia-associated optic neuropathy) and that can lead to loss of best-corrected visual acuity.
Myopic macular degeneration (MMD)	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, CNV and Fuchs spot.
Diagnostic subdivisions of MMD	
Myopic maculopathy	Category 0: no myopic retinal degenerative lesion. Category 1: tessellated fundus. Category 2: diffuse chorioretinal atrophy. Category 3: patchy chorioretinal atrophy. Category 4: macular atrophy. "Plus" features (can be applied to any category): lacquer cracks, myopic choroidal neovascularization, and Fuchs spot.
Presumed myopic macular degeneration	A person who has vision impairment and vision acuity that is not improved by pinhole, which cannot be attributed to other causes, and: • The direct ophthalmoscopy records a supplementary lens < -5.00 D and shows changes such as "patchy atrophy" in the retina or, • The direct ophthalmoscopy records a supplementary lens < -10.00 D.
Specific clinical conditions characteristic of pathologic myopia	
Myopic traction maculopathy (MTM)	A combination of macular retinoschisis, lamellar macula hole and/or foveal retinal detachment (FRD) in eyes with high myopic attributable to traction forces arising from adherent vitreous cortex, epiretinal membrane, internal limiting membrane, retinal vessels, and posterior staphyloma.
Myopia-associated glaucoma-like optic neuropathy	Optic neuropathy characterized by a loss of neuroretinal rim and enlargement of the optic cup, occurring in eyes with high myopia eyes with a secondary macrodisc or peripapillary delta zone at a normal IOP.

> A refractive error in which rays of light entering the eye parallel to the optic axis are brought to a focus in front of the retina when accommodation (accommodation, ocular) is relaxed. This results from an overly curved cornea or from the eyeball being too long from front to back. It also is called nearsightedness.

The recently released ICD-11 for Mortality and Morbidity Statistics (2018) includes the same definition (under code 9D00.0). The first sentence of this definition encapsulates the basic optics of myopia. The second sentence attempts to define the source of the refractive error, but fails to include the possible contribution of the lens. It also implies a strict divide between myopia associated with axial elongation (often referred to as axial myopia) and myopia associated with increased optical power of an eye (often referred to as refractive myopia). To address both issues, the definition would be made more accurate by omitting the second sentence or rephrasing as follows:

> Myopia: a refractive error in which rays of light entering the eye parallel to the optic axis are brought to a focus in front of the retina when ocular accommodation is relaxed. This usually results from the eyeball being too long from front to back, but can be caused by an overly curved cornea and/or a lens with increased optical power. It also is called nearsightedness.

This proposed definition has been submitted for consideration by the WHO.

3. Useful Qualifying Terms for Myopia

The above definition includes all forms and degrees of myopia, which is appropriate for a general definition of myopia as a subcategory of refractive disorders (i.e., category 9D00 within ICD-11 for Mortality and Morbidity Statistics [2018]). However, this definition encompasses a heterogeneous group of refractive errors. For research purposes, additional qualification is required to ensure that homogenous groups of myopes can be selected for trials or genetic studies. As indicated above, myopia can be differentiated into refractive myopia, in which the optical power of the cornea and/or lens is abnormally high in eyes with a normal optical axis length, and/or the more common axial myopia, in which the optical axis is too long in relation to the refractive power of the cornea and lens. Axial and refractive myopia often are defined as distinct entities:

> axial myopia—a myopic refractive state that can be attributed to excessive axial elongation

> refractive myopia—a myopic refractive state that can be attributed to changes in the structure or location of the image forming structures of the eye; that is, the cornea and/or lens.

While this distinction is useful in certain contexts (such as in keratoconus or eyes with very long axial lengths), the refraction of an eye depends on how well matched an eye's axial length is to its optical power, and so both factors are relevant in many eyes. When myopia is progressing, the distinction between axial and refractive myopia is easier to make as the axial length and optical power can be monitored

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with biometric techniques (see accompanying paper, IMI – Clinical Myopia Control Trials and Instrumentation Report).[10] Clinical trials and work with animal models of myopia have provided ample evidence that axial elongation is the primary factor driving myopic progression; when comparing intervention to reduce myopic progression, there is a clear relationship between the impact of an intervention on refraction and axial length.[3] Therefore, the inclusion and exclusion criteria of trials investigating treatments designed to reduce myopic progression should aim to primarily recruit axial myopes and exclude subjects with refractive myopia. To that end, many trials now include evidence of progression as an inclusion criterion, but additional age-specific normative data of ocular dimensions and growth patterns would enhance the ability of researchers to separate these two categories and ensure more homogeneous study populations. In animal studies, myopia arising from anterior segment changes (cornea or lens) often is differentiated from that resulting from increased posterior eye growth by measuring vitreous chamber depth. In clinical studies axial length is used almost universally. Introducing measurement of vitreous chamber depth into clinical studies may be a useful method of identifying myopic progression primarily associated with axial elongation.

As noted above, for the majority of myopia we cannot define a precise etiology and, hence, etiologic classifications currently are premature, but for certain rare forms of myopia a direct cause can be identified. The concept of primary compared to secondary myopia[11] is lacking in refractive studies. In comparison, a division into primary and secondary etiologies is well established in other fields, such as glaucoma. As is the case for glaucoma, many secondary forms of myopia exist, including syndromic forms of myopia associated with known Mendelian gene defects,[12,13] myopia arising from structural abnormalities of the cornea (e.g., keratoconus) or lens (e.g., microspherophakia), and drug-induced myopia. Such secondary forms of myopia can be axial and/or refractive. The term secondary myopia certainly has value, but the use of the term primary myopia is less obvious. In primary glaucoma no cause can be identified, whereas in the forms of myopia that may be considered primary there is a wide range of possible risk factors though no definite single cause. This means that secondary myopia is best reserved for situations where a single causative factor can be identified that is not a known population risk factor for myopia development. Therefore, the following definition for secondary myopia is proposed:

> Secondary Myopia: a myopic refractive state for which a single, specific cause (e.g., drug, corneal disease, or systemic clinical syndrome) can be identified that is not a recognized population risk factor for myopia development.

4. Quantitative Thresholds for Myopia

As well as defining myopia in descriptive terms, specific dioptric thresholds are required for many research purposes. This approach has the advantages of being quantitative and objective. While it may appear to be the simplest and least controversial means of classification, it is one where a great amount of inconsistency exists, reflecting the inherent difficulties in converting a continuous trait into a category of disease severity. There are wide variations between studies in choice of threshold, technique for measuring refractive error (automated refraction versus retinoscopy), use of cycloplegia, choice of cycloplegic, protocol for administration of cycloplegia, choice of refractive parameter to use, and how astigmatism is handled (e.g., spherical equivalent or least myopic meridian). As questions of technique and instrumentation for refraction are being addressed by other studies in this series (see accompanying study IMI – Clinical Myopia Control Trials and Instrumentation Report),[10] we will concentrate on the selection of the most appropriate thresholds.

When considering quantitative thresholds and descriptions of myopia, one issue that warrants standardization is the use of mathematical comparison symbols (e.g., $<$, $>$, $\leq$, and $\geq$) and nonmathematical words indicating a greater or lesser value. Myopic refractions are best expressed as negative values of Diopters. This creates potential ambiguities when comparing degrees of myopia. For example, does "$<$ –6.00 D" mean a refractive error more myopic than –6.00 D or a refractive error less myopic than –6.00 D? Both interpretations are in widespread use. Optics is a highly mathematical science and any quantitative descriptors must be mathematically valid. The most logically consistent approach is always to treat myopic refractive errors as negative values and use mathematical terms in their strict mathematical sense, so $<$ –6.00 D of myopia means refractive errors with values more minus, and, hence, more myopic than –6.00 D.

If a description is made in words and mathematical terms (such as being less than a negative number of diopters), then a refraction of "less than –6 D" should be described as "more myopic." If myopia is described as a positive dioptric value then the consistent mathematical approach indicates that "more than 6 D of myopia" represents refractions more myopic than –6 D. Similarly, phrases such as "higher degrees of myopia" should be interpreted as meaning more myopic prescriptions.

> Recommendation: In quantitative contexts, myopia always should be treated as a negative value and mathematical comparison symbols should be used in their strict mathematical sense.

4.1 Myopia, Low Myopia, and High Myopia

We propose that three quantitative categories, at a minimum, are required to describe the degree of myopia: myopia, low myopia, and high myopia. These terms are broadly accepted within this field, but they have no standardized definitions. A recent report of the WHO[14] noted that "there is currently no internationally agreed threshold for myopia or for high myopia." That publication proposed the following definitions, primarily with the requirements of Rapid Assessment of Avoidable Blindness in mind:

> Myopia is "a condition in which the spherical equivalent objective refractive error is $\leq$ –0.50 D in either eye."

> High Myopia is "a condition in which the spherical equivalent objective refractive error is $\leq$ –5.00 D in either eye."

The choice of spherical equivalent as a primary measure is widely accepted, but by referring to "either eye," these definitions are not suitable to studies in which individual eyes are analyzed. Where both eyes are used in a study, the use of "either eye" to define myopia means that some hyperopic eyes may be included in a study population of myopes. Furthermore, the term "objective refractive error" introduces a methodologic aspect into a definition that ideally should be independent of technique. The choice of thresholds for myopia and high myopia also is an issue where there is significant variation within the myopic literature. To ensure that the definitions of myopia and high myopia have the greatest acceptability and the most scientific use, the thresholds should be evidence-based, statistically appropriate, and clinically relevant. In the following section we provide an evidence-

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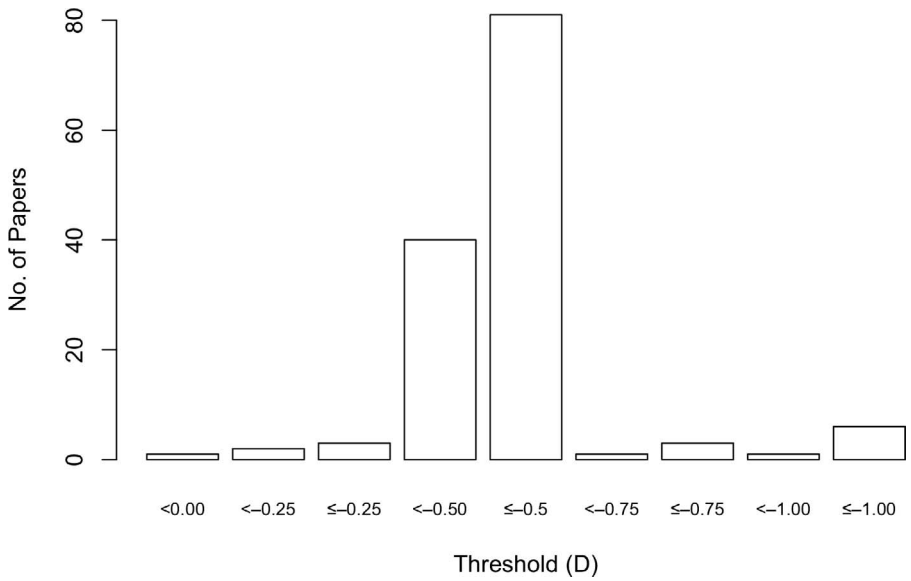

FIGURE 1. Variation in the choice of diagnostic thresholds for myopia in terms of spherical equivalent within epidemiologic studies included in meta-analysis ($n = 138$ studies).

based analysis of the thresholds for myopia and high myopia. Definition of these two thresholds—one for the diagnosis of myopia and a second for the diagnosis of high myopia—allow low myopia to be defined as myopia that does not meet the threshold for high myopia.

4.2 Choice of Diagnostic Threshold for Myopia

To determine the degree of consensus surrounding the choice of ≤ -0.50 D, we analyzed the thresholds used in epidemiologic surveys of refractive error and randomized controlled treatment trials of interventions for reducing myopia progression. The studies chosen for analysis met the criteria for inclusion in two recent meta-analyses covering these two aspects of myopia research and, therefore, have been prevalidated in terms of study quality.[2,3] A full list of these studies and their references are included in online Appendix 1.

Of the 138 epidemiologic/survey studies identified, 87.7% used < -0.50 D or ≤ -0.50 D as the threshold for myopia, with a clear preference for the inclusive threshold of ≤ -0.50 D (see Fig. 1). From network meta-analysis of intervention trials, 27 studies provided a threshold for myopia (one trial specifically targeted high myopes so reported no threshold for myopia). There was greater variation within these 27 studies as shown in Figure 2. The modal group was still ≤ -0.50 D, but many studies used higher degrees of myopia as an inclusion criterion. The majority of these studies were conducted and published before the publication of the WHO report.

For myopia, the evidence points to a preference for using a refractive threshold of ≤ -0.50 D. Although this represents an existing, informal standard within myopia research, it should be recognized that, from a statistical perspective, it is a flawed one. Other thresholds may be more appropriate according to the research question being addressed by a particular study. A recent analysis of the impact of different myopic thresholds in epidemiologic studies showed that even differences as small as 0.25 D could create false-positive and -negative associations for specific risk factors.[15] This occurs because the choice of threshold determines the composition of both eyes classified as myopic and non-myopic with respect to the distribution of putative risk factors. Choice of a low threshold, such as ≤ -0.50 D, may make intervention trials that use myopia onset a primary outcome variable appear more effective, but with a threshold change to just ≤ -0.75 D, the effect may be far smaller. This was apparent in a recent intervention study of the effect of increased time outdoors on myopia prevention.[16,17] Intervention trials for myopia often include evidence of myopic progression as an inclusion criterion. This provision may necessitate a more myopic inclusion threshold. As shown in Figure 2, for intervention trials there is a second peak in the distribution at -1.00 to -1.25 D. Finally, the method of refraction has a bearing on the choice of diagnostic threshold for myopia. Measurement error must be considered when selecting a threshold to avoid misclassification. With a more myopic threshold, such as -0.75 or -1.00 D, the probability that only "true" myopes are included is increased. Lack of cycloplegia also introduces a bias toward more myopic refraction results with a similar risk of misclassification. Therefore, studies that use noncycloplegic refraction techniques and include younger subjects should consider more myopic thresholds.

In summary, a refraction of ≤ -0.50 D merits selection as the evidence-based, consensus threshold for the diagnosis of myopia, but this threshold may not be appropriate for certain research questions. Where a different threshold is chosen for a study, investigators should clearly indicate the methodologic and statistical reasons for their choice. In such cases, a sensitivity analysis should be performed for the primary outcomes using the standard ≤ -0.50 D threshold cases to facilitate comparison with other studies whenever possible. Conversely, if a plausible risk of classification bias exists in a study, then a sensitivity analysis should be performed at more myopic thresholds (e.g., ≤ -0.75 or ≤ -1.00 D) whenever possible. This reporting standard ensures the maximal comparability of different studies, while minimizing the risk of false-positive and -negative findings due to classification bias.

4.3 Diagnostic Threshold for High Myopia

There is no clear biological basis in terms of axial length, refraction or other ocular biometric parameter to differentiate high from lower degrees of myopia. Nevertheless, high myopia is a widely used concept and must be defined as coherently as possible. Currently, there is no agreed quantitative threshold

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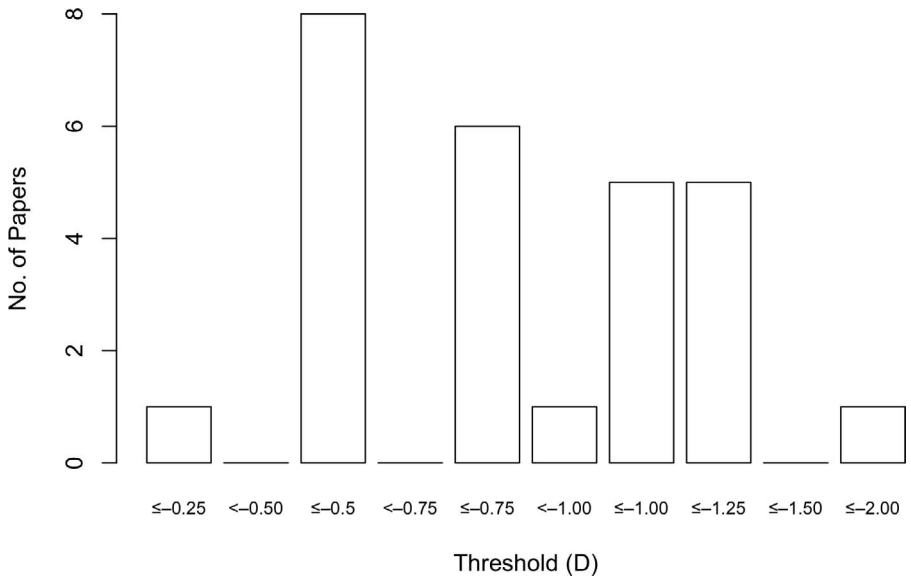

FIGURE 2. Variation in the choice of the inclusion thresholds for myopia in terms of spherical equivalent within intervention studies ($n = 27$ studies).

for high myopia. The WHO report[14] indicates that the threshold for high myopia of ≤ -5.00 D was chosen because -5.00 D of uncorrected myopia gives an estimated distance visual acuity of 6/172, a level that meets the threshold for blindness (<3/60 in the better eye). This approach emphasizes the impact of uncorrected refractive errors in populations with poor access to glasses.

Among 59 epidemiologic studies reviewed that reported on prevalence of high myopia 35.6% used < -5.00 or ≤ -5.00 D and 61% used < -6.00 or ≤ -6.00 D as the threshold for high myopia (Fig. 3). For the 25 intervention studies that included a threshold for high myopia, the most frequent upper inclusion threshold was ≥ -6.00 D (i.e., highly myopic eyes were excluded; $n = 8$, 32%) (Fig. 4). As this represents the upper end of the inclusion range, high myopia from the perspective of these trials was < -6.00 D. The second most common upper threshold for inclusion in the intervention trials was ≥ -4.0 D.

Overall the evidence-based consensus points to a threshold of -6.00 D for high myopia. It is less clear-cut whether this should be an inclusive threshold (i.e., ≤ -6.00 D) or an exclusive one (< -6.00 D). For consistency with the lower threshold for myopia, we propose that high myopia be defined as a refractive error ≤ -6.00 D.

However, as noted for the diagnostic threshold for myopia, the choice of threshold should be appropriate to the research question. If the impact of uncorrected refractive errors is a primary outcome measure of a study, then the ≤ -5.0 D threshold is well justified based on the impact of 5.0 D of uncorrected myopia on visual acuity. In such cases, astigmatism also should be considered, as less myopic spherical equivalents with significant astigmatism may have a greater impact on unaided visual acuity. However, high myopia is well known to be associated with increased risks of visual loss, and, to be clinically relevant, the threshold for high myopia should

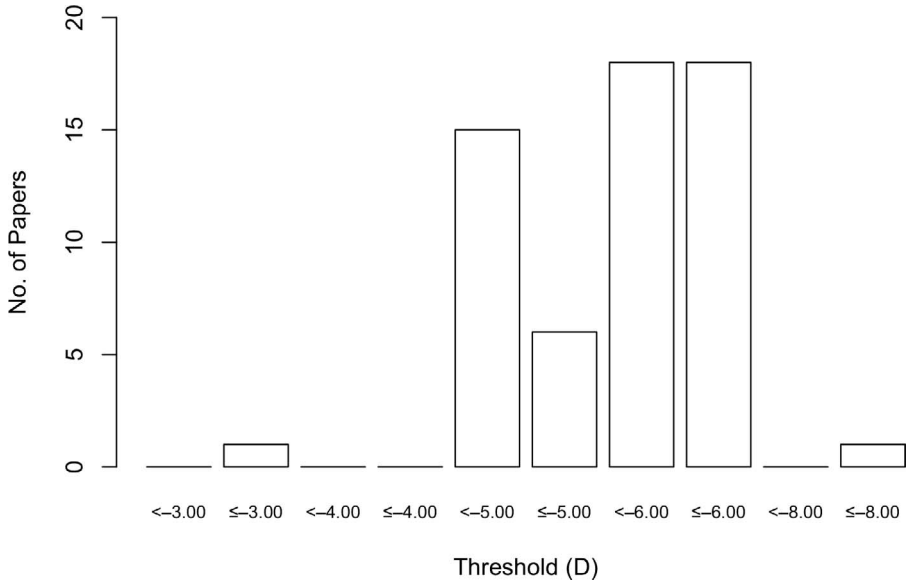

FIGURE 3. Variation in the choice of thresholds for high myopia within epidemiologic studies ($n = 59$ studies).

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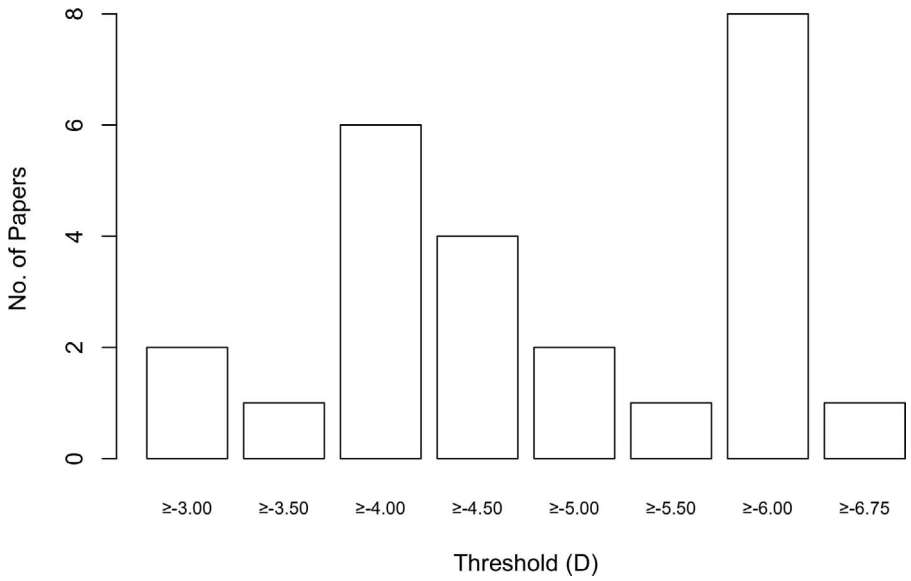

FIGURE 4. Variation in the choice of high myopia inclusion thresholds within intervention studies ($n = 25$ studies).

reflect this risk. In terms of risk of uncorrectable visual impairment, eyes more myopic than –6.00 D showed considerably greater individual risk of visual loss than lower degrees of myopia.[18,19] However, a threshold of –6.00 D does not consider that the incidence of a range of ocular diseases is increased at much lower degrees of myopia.[9] As proposed for the definition of myopia, in cases where a different threshold for high myopia is chosen for a study, investigators should clearly indicate the methodologic and statistical reasons for their choice. If there is a plausible risk of bias within a study design due to the choice of threshold, a sensitivity analysis should be done to quantify such potential biases. Results should be reported using the standard threshold of ≤ -6 D, as well as the chosen threshold to facilitate comparison of studies and meta-analysis.

4.4 Proposed Definitions

Based on this analysis, the following quantitative definitions are proposed. These definitions avoid the requirement for objective refraction so as to be independent of technique, but by making reference to relaxation of accommodation are compatible with cycloplegic and standard clinical subjective techniques. The definitions also relate to a single eye. An eye-specific definition is required to allow different approaches to analyzing data (e.g. by patient, eye, or an average of the two eyes) and avoiding classification errors within study populations. All stated refractive error thresholds relate to the spectacle-plane refraction.

> Myopia: a condition in which the spherical equivalent refractive error of an eye is $\leq$ –0.5 D when ocular accommodation is relaxed.
>
> High Myopia: a condition in which the spherical equivalent refractive error of an eye is $\leq$ –6.00 D when ocular accommodation is relaxed.

These definitions reflect common use within the field, but as noted above their appropriateness is study-dependent. Alternative thresholds are supported where appropriate, and sensitivity analysis of the primary outcomes to alternative thresholds are strongly recommended.

Refractions $\leq$ –0.5 and $>$ –6.00 D may be appropriately termed low myopia:

> Low Myopia: a condition in which the spherical equivalent refractive error of an eye is $\leq$ –0.5 and $>$ –6.00 D when ocular accommodation is relaxed.

Further subdivisions, such as intermediate or moderate myopia, often are used, but with little consistency. Where such terms are used in research studies, results also should be reported at the standard thresholds to facilitate comparison with other studies and facilitate meta-analysis.

5. The Concept of Pre-Myopia

The above definitions all consider myopia as a static variable, whereas most forms of myopia progress from onset for a variable period. Currently, reducing the rate of progression is a central goal of myopia research, but preventing the onset of myopia is an even more valuable target. Such interventions will require treatment of eyes before they become myopic. This logically requires a definition of "pre-myopia" (i.e., a non-myopic refraction in which a combination of risk factors and the observed pattern of eye growth indicate a high risk of progression to myopia). Longitudinal observational studies, such as the Collaborative Longitudinal Evaluation of Ethnicity and Refractive Error (CLEERE) study, have demonstrated that eyes destined to become myopic show an accelerated pattern of axial elongation several years before the onset of myopia.[20] In the CLEERE Study, a refraction close to emmetropia in North American children (7–13 years old) also has been shown to be the best single predictor of future myopia.[21] The exact threshold varying with age from $< +0.75$ D at age 6, $\leq +0.50$ D at ages 7 to 8, $\leq +0.25$ D at ages 9 to 10, and ≤ 0 D at age 11 years. The predictive accuracy of baseline refraction alone is likely to be insufficient to justify therapeutic interventions. In another predictive model, Zhang et al.[22] used baseline visual acuity and biometric data to predict onset of myopia over a 3-year period in 236 children from Xiamen in China (as a learning set) and 1979 predominantly Chinese children in Singapore (as a test set). They found that sex, visual acuity, height, anterior chamber depth, lens thickness, vitreous chamber depth, corneal curvature, and an interaction term

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between anterior chamber depth, lens thickness, and vitreous chamber depth could be used to predict myopia onset. In the future, it is expected that improved multifactorial risk scores will be developed that provide sufficient predictive accuracy to guide preventative therapies. Additional known risk factors that may contribute to such risk scores include the number of myopic parents, parental education, and identifiable environmental risk factors, such as time spent indoors/outdoors, activities and education, rate of change of axial length, rate of change of refraction, and genomic risk scores.[20,23–26] Even in the absence highly predictive risk models, pre-myopia is a useful concept at this stage and one that may promote further research.

Proposed definition of Pre-myopia:

> Pre-myopia – a refractive state of an eye of $\leq$ 0.75 D and $>$ 0.50 D in children where a combination of baseline refraction, age, and other quantifiable risk factors provide a sufficient likelihood of the future development of myopia to merit preventative interventions.

The above terms and definitions are summarized in Table 2.

6. The Structural Complications of Myopia

Higher degrees of myopia are associated with a range of structural changes within the retina, RPE, Bruch's membrane, choroid, optic nerve head, peripapillary area, optic nerve, and sclera. Of all the terms included in Table 1 that relate to these anatomical complications, "pathologic myopia" is the one that already has gained a degree of international consensus. This is the preferred term of the Meta-Analysis for Pathologic Myopia (META-PM) Study Group who have recently published a detailed photographic classification for myopic maculopathy.[27] In addition, the term "degenerative high myopia" implies that "degeneration" is the only mechanism behind these changes, whereas "pathologic myopia" appropriately avoids this confusion.

The current version of the ICD (ICD11 for Mortality and Morbidity Statistics, 2018) is notably out of step with this growing consensus. There is no reference to "pathologic myopia" within ICD-11 for Mortality and Morbidity Statistics (2018). The term "degenerative myopia," as used in ICD-10, is changed within ICD-11 to "degenerative high myopia" (code 9B76) with the following list of synonyms: degenerative myopia, progressive high degenerative myopia. Based on the existing international consensus generated by the META-PM consortium, this committee has proposed to the WHO that the term "pathologic myopia" should replace the current "degenerative high myopia" in future amendments of ICD-11.

> Pathologic Myopia: excessive axial elongation associated with myopia that leads to structural changes in the posterior segment of the eye (including posterior staphyloma, myopic maculopathy, and high myopia-associated optic neuropathy) and that can lead to loss of best corrected visual acuity.

It is important to note that this definition refers only to the structural changes in the posterior segment and their visual consequences. Pathologic myopia is sometimes equated with high myopia, and descriptions may include a refractive (e.g., –6.00, –5.00, or even –4.00 D in children) or axial length threshold (e.g., $>$ 25.5 or 26.5 mm).[28] There are many reasons why including refractive error or axial length is unhelpful. Many studies have demonstrated that myopic maculopathy extends to eyes of lower than –5.00 or –6.00 D, albeit at much lower prevalence.[29] A recent study from Taiwan shows posterior staphyloma can be found in eyes with $<$26.5 mm axial length.[30] Inclusion of refraction within a concept, such as pathologic myopia, also creates problems in relation to highly myopic eyes that have had refractive procedures (e.g., corneal, phakic intraocular lenses, clear lens, or cataract extraction). In these cases, the refraction of the eye may be normal, but the risk of pathologic myopia remains. Longitudinal studies also have demonstrated that for a given refractive error, the prevalence of pathologic myopia is age-dependent.[8,31] Therefore, a refractive definition for pathologic myopia would mean that outcome or intervention studies could not be compared reliably unless they were accurately age-matched.

6.1 Subdivisions of Pathologic Myopia

The complications of pathologic myopia affect a range of structures and present clinically as distinct diagnostic entities. Therefore, a series of definitions is required for all those conditions that come under the umbrella of pathologic myopia. As with other aspects of myopia, there is considerable variation in terminology and definitions for such conditions. The Clinical Modification of the existing ICD-10 system (ICD-10-CM) includes five conditions that were classified as subdivisions of "degenerative myopia:" choroidal neovascularization (CNV), macular hole formation, retinal detachment, foveoschisis, and other maculopathy. Other terms that commonly in use are: myopic macular degeneration, myopic maculopathy, myopic retinopathy, myopic chorioretinal atrophy, and myopic CNV.

The recent WHO publication on myopia included the term "myopic macular degeneration," which includes several of the ICD categories, and defined it as:

> Myopic Macular Degeneration: a vision-threatening condition occurring in people with myopia, usually high myopia that comprises diffuse, patchy macular atrophy with or without lacquer cracks, CNV, and Fuchs' spot.

The META-PM Study Group favors "myopic maculopathy" and provided a graded classification:

> Myopic Maculopathy, Category 0: no myopic retinal degenerative lesion.
>
> Myopic Maculopathy, Category 1: tessellated fundus.
>
> Myopic Maculopathy, Category 2: diffuse chorioretinal atrophy.
>
> Myopic Maculopathy, Category 3: patchy chorioretinal atrophy.
>
> Myopic Maculopathy, Category 4: macular atrophy.

These categories were defined with the aid of reference photographs.[27] The META-PM classification also provided for three additional "plus" features: lacquer cracks, myopic CNV, and Fuchs spot.

Myopic macular degeneration and myopic maculopathy are in widespread use. As terms, they often are used interchangeably, but clear differences of opinion exist on the use of the definitions. The WHO report stated that the META-PM classification system of myopic maculopathy was too complex for the purposes of data collection in population-based surveys. The report went on to propose that for Rapid Assessment of Avoidable Blindness (RAAB) surveys, which typically are performed with simple instrumentation, a simpler definition was required:

> The definition of Myopic Macular Degeneration for the purposes of RAAB surveys: A person who has vision impairment and vision acuity that is not improved by pinhole, which cannot be attributed to other causes, and (1) the direct ophthalmoscopy records a supplementary

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lens < −5.00 D and shows changes such as "patchy atrophy" in the retina or (2) the direct ophthalmoscopy records a supplementary lens < −10.00 D.

The META-PM classification is a much more clinically orientated schema that is ideally suited for natural history and intervention studies. However, it is primarily a photographic classification that does not provide a full description of all aspects of pathologic myopia. The impact on visual function may involve visual acuity, microperimetry, and electrophysiologic assessments. The morphologic changes in the retina and choroid can be defined in more detail by ocular coherence tomography (OCT), retinal auto fluorescence (AF), fluorescein angiography (FA), and indocyanine green angiography (ICG). Changes in the sclera, such as staphyloma, are best defined by a range of tools, including wide-field OCT,[32] magnetic resonance imaging (MRI),[33] and wide-field fundus imaging.[34] Detailed studies of the pathophysiology and etiology of pathologic myopia would likely involve such additional investigative tools.

It is clear that a single definition for the structural complications of pathologic myopia will not fit all potential applications. In relation to the choice of myopic macular degeneration (MMD) or myopic maculopathy (MM), neither term is currently referenced within ICD-11 for Mortality and Morbidity Statistics (2018). Achieving a consensus for one term over the other is a challenging issue. The META-PM definition of myopic maculopathy is a clinically oriented, diagnostic classification, whereas the WHO report's definition of myopic macular degeneration is a more general description. Therefore, we propose that MMD be used as the preferred categorical term for the macular complications of pathologic myopia. This general category then can usefully include specific sets of diagnostic criteria, such as the META-PM classification and a definition of MMD suitable for RAAB surveys. To cover the full range of research applications we suggest that three such subcategories are required:

1. A RAAB-appropriate survey definition that uses the limited data available from such study designs.
2. A standardized photographic classification for simple natural history, cohort, or intervention studies.
3. A detailed structural and functional classification, including a comprehensive range of clinical assessment and imaging. This would be appropriate for studies addressing pathophysiology, etiology, intervention, and detailed cohort studies.

The existing WHO and META-PM definitions satisfactorily cover the first two tiers. This requires a descriptive term for the RAAB-appropriate definition of MMD to differentiate it from MMD as defined above. We propose that the term "presumed myopic macular degeneration" would be appropriate. Within this scheme, "myopic maculopathy" should be used as specifically relating to the current META-PM photographic classification scheme and its future iterations. In relation to the third category, a range of more specific clinical terms is required. Three specific clinical terms associated with macular abnormalities are included in ICD-11 for Mortality and Morbidity Statistics (2018) covering CNV in high myopia, macular hole in high myopia, and foveoschisis in high myopia. These terms by no means cover the full range of macula complications seen within pathologic myopia. Therefore, it is anticipated that as our understanding of the pathophysiology of myopia develops, additional terms may be included within this final category over time.

CNV, as a leading cause of visual loss in pathologic myopia, certainly merits more detailed classification. The WHO definition of MMD and the META-PM classification refer to CNV and Fuchs' spots, though these can be considered different phases of the same process. Myopic CNV has three phases: active, scar, and atrophic phases (also known as CNV-related macular atrophy). A Fuchs' spot represents the scar phase of myopic CNV. The ICD-11 for Mortality and Morbidity Statistics (2018) category refers to high myopia, inherently introducing a refractive threshold. The phrase "CNV in pathologic myopia" is recommended, since CNV occurring in any degree of myopia may include idiopathic CNV and punctate inner choroidopathy (PIC)-associated CNV. It is hoped that a group, such as the META-PM Study Group, will address this issue in the future to create a comprehensive classification and grading for myopia-associated CNV.

Macular holes and retinoschisis at the posterior pole can occur in various conditions, but are seen commonly in eyes with other features of pathologic myopia. Therefore, they are an appropriate part of the pathologic myopia spectrum. As neither is specifically covered by the WHO definition of MMD, nor the META-PM classification, a specific diagnostic category is warranted. Within ICD-10-CM, the term "degenerative myopia with foveoschisis" is used. This term is potentially misleading as schisis seen in pathologic myopia often is extrafoveal. Furthermore, OCT studies of pathologic myopia have demonstrated that macular holes, lamellar macular holes, and retinoschisis can coexist within a clinical spectrum that also includes localized posterior retinal detachments.[35] The unifying factor in these complications is the existence of vitreoretinal or intraretinal traction. Myopic traction maculopathy (MTM) is an alternative term that is growing in popularity and more accurately encompasses the etiology of this set of conditions.[36]

6.1.1 Myopic Traction Maculopathy. A combination of macular retinoschisis, lamellar macula hole, and/or foveal RD (FRD) in highly myopic eyes attributable to anterior tractional forces arising from adherent vitreous cortex, epiretinal membrane, internal limiting membrane, or retinal vessels, and to posterior traction arising from a posterior staphyloma.

Macular Bruch's membrane defects can develop in the parafoveal and intrafoveal regions as part of the spectrum of pathologic myopia. They are characterized by the lack of Bruch's membrane, RPE, and choriocapillaris, and show a reduced or missing layer of retinal photoreceptors and of Sattler's layer in the choroid. A Bruch's membrane defect may arise de novo or in association with a widening lacquer crack, and result in a localized absolute scotoma.

6.1.2 Nonmacular Structural Complications of Pathologic Myopia. Two nonmacular complications are seen commonly in pathologic myopia: characteristic changes in the optic nerve and retinal detachments. Neither fall within the scope of the term MMD or the other terms discussed above.

The excessive axial elongation seen in most highly myopic eyes creates a range of changes in the optic nerve and peripapillary region. These include peripapillary atrophy, tilted optic discs,[37] and acquired megalodiscs,[38] Such changes, in particular an enlargement of the optic disc and development and enlargement of a peripapillary delta zone, have been linked to the increased rate of glaucomatous or glaucoma-like optic nerve damage observed in myopic eyes, or glaucoma-like optic nerve damage observed in highly myopic eyes. A recent study has shown that in eyes with myopia, but axial lengths ≤ 27.4 mm, glaucomatous optic neuropathy is associated with elevated IOP. In more highly myopic eyes, with axial lengths ≥ 27.5 mm, IOP was not associated with glaucomatous optic neuropathy.[39] Therefore, it has been proposed that the optic nerve damage observed in highly myopic eyes is not truly glaucomatous. The phrase "myopia-associated glaucoma-like optic neuropathy" has been used to describe this newly

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recognized condition. We propose that along with MTM, this condition be considered as part of the spectrum of pathologic myopia, with the following definition:

> Myopia-associated glaucoma-like optic neuropathy: optic neuropathy characterized by a loss of neuroretinal rim and enlargement of the optic cup, occurring in highly myopic eyes with a secondary macro disc or peripapillary delta zone at a normal IOP.

Retinal detachments are more common in high myopia and occur in younger ages in myopic than nonmyopic eyes. There is a clear monotonic relationship between the incidence of retinal detachment and refractive error extending to the low myopia range.[9] This increased risk is believed to relate to changes in the peripheral retina, such as lattice degeneration, as well as alterations in the composition and structure of the vitreous. Although lattice degeneration has been reported to be present in 60% of retinal detachments in eyes with high myopia, it also is present in 20% of nonmyopic retinal detachments.[40] Furthermore, despite a much greater lifetime risk of retinal detachment in eyes with myopia, and a younger age at onset, the majority of retinal detachments occur in eyes without myopia in most populations.[41] As such, we propose that retinal detachment, though a recognized and important complication of myopia, should not be considered as part of the spectrum of pathologic myopia.

The proposed definitions and terminology for the structural complications of myopia are listed in Table 3.

7. Discussion

Considering the variety of classifications, terminology and thresholds in use in the field of myopia research, achieving internationally accepted definitions is a challenging task. We hope the definitions listed in Tables 2 and 3 will be acceptable to a broad range of interests or, at the very least, start a process that may lead to a meaningful consensus. In developing these proposals, we have adopted a consensus and evidence-led approach. We also have included the following considerations that we regard as important criteria when adopting a clinical definition:

- Relevance to nature of the research question.
- Relevance to the underlying biology of myopia.
- Acceptability to researchers in the field.
- Use for developing health policy.

In addition to the definitions and thresholds presented above, we believe that it is important for future research that a set of reporting standards be adopted within the myopia research community. Acknowledging that some investigators may not adopt these definitions, we strongly urge that, where nonstandard qualifying terms are used to describe myopia, such terms be clearly defined within any publications. In addition, if the research question merits use of a refractive error threshold that differs from the standard proposed thresholds of –0.50 and –6.00 D, the results should be presented for the chosen and standard thresholds to facilitate comparison with other studies and meta-analysis, whenever possible. If a plausible risk of classification bias exists in a study, then a sensitivity analysis should be performed at more myopic thresholds (e.g., ≤ -0.75 or ≤ -1.0 D), whenever possible.

This report has not considered techniques for measuring refraction or for ensuring relaxation of accommodation, which is essential for accurate measurement of refraction. Other reports in this issue will review this in more detail, but cycloplegia should be considered the "gold standard" for any study of refraction including children.[10] Where studies with and without cycloplegia are compared, then an appropriate analysis of potential bias should be included as part of any publication.

The proposed thresholds in this report, as is standard in myopia research, relate to spherical equivalent spectacle-plane refraction on-axis. For most studies, this is adequate, though again this relates to the research question. If retinal defocus is an issue relevant to the study design (e.g., a study examining the impact of defocus on choroidal thickness or an intervention designed to influence eye growth through retinal defocus), then the potential impact of astigmatism and off-axis refraction must be considered. At a spherical equivalent diagnostic threshold of –0.50 D modest amounts of astigmatism can create hyperopic defocus along one meridian, thereby reversing the sign of retinal defocus. Similarly, small degrees of relative peripheral hyperopia may reverse the sign of retinal defocus off-axis in low myopia. In such cases myopia must be defined in relation to each astigmatic meridian and by retinal location.

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