

## SYSTEMATIC REVIEW

Role of un-correction, under-correction and over-correction of myopia as a strategy for slowing myopic progression

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Running Title: Role of correction in myopia progression

Keywords: un-correction; under-correction; myopia control; myopia progression; over-correction

**Background:** Myopia is linked to retinal pathology, so this systematic review investigates the association between un-, under-, and over-correction of myopic refractive error and myopia progression in children and adolescents (up to 18 years of age).

**Methods:** The literature search included 3 databases (PubMed, Web of Science, and Cochrane Central Register of Controlled Trials [CENTRAL]), and reference lists of retrieved studies in any language.

**Results:** Eight prospective cohort studies and one retrospective analysis of clinical data provided comparison data on un- and under-correction of myopia versus full-correction of myopia however the quality of studies and length of follow-up times varied. A forest plot showed no beneficial effect of under-correction with some studies finding an increase in myopia progression. While one study suggested that myopia progression is slower in an un-corrected cohort compared to those who are fully corrected, another study suggests the opposite. One study utilised anisomyopes to allow comparison of under-correction of one eye with full-correction of the fellow eye indicating that under-correction in one eye appears to slow the rate of myopia progression in that eye, while another study on full-correction only in one eye found that progression was faster in the un-corrected eye. No benefits of over-correction of myopia was found.

**Conclusions:** The overall findings are equivocal with under-correction suggesting a faster rate of myopia progression. There is no strong evidence of benefits from un-correction, monovision or over-correction. Hence, current clinical advice advocates for the full-correction of myopia. Further studies are warranted to determine the level of myopia that can be left uncorrected without impacting on myopia progression and how this changes with time.

Given the increase in prevalence of myopia worldwide and the associated risks of ocular pathology there is a growing need for strategies to slow myopia progression and ultimately to stop myopia onset <sup>1,2</sup>. As the eye responds by altering its growth rate to both the sign and amount of optical defocus it is hypothesised that by altering the amount of blur the eye receives it is possible to modulate eye growth and hence potentially slow myopia progression. As myopia typically develops in childhood, the easiest and most accessible form of correction is by a spectacle lens. Therefore, it would follow that having a spectacle intervention to slow myopia progression would be an easily accepted option. One way in which the amount of blur could be manipulated is via under-correction of the myopic spectacle correction. This strategy has been discussed in the literature from around the 1850s and appears to be a long-standing method used by some eye care practitioners in an attempt to avoid excessive accommodation. In a recent survey of 940 ophthalmologists worldwide 8.2% used under-correction of full myopia prescription as a strategy for myopia control <sup>3</sup> and a broader survey of 971 eye care practitioners identified 27.3% used under-correction 'sometimes' or 'always' when prescribing for young progressing myopes <sup>4</sup>. The rationale for prescribing under-correction for myopia is to bring the image shell in front of the retina to present a retarding blur stimulus based on findings from animal studies <sup>5</sup>; it is also considered to be an attempt to reduce the accommodative stimulus and demand at near and thus reduce the blur that drives accommodation <sup>1</sup>. Un-correction has a similar premise for low levels of myopia, although the functional benefits of prescribing make it unethical to not correct higher levels of myopia. Alternatively over-refraction could be considered so that when myopia progresses, the child is always fully corrected and that hyperopic blur is compensated by accommodation (although this could impact on visual fatigue).

In this report the current literature relating to different amounts of correction of myopia through spectacle lens use is reviewed.

### **Systematic review**

The two independent reviewers were not blinded to the investigator names or the sources of publication as many of the publications were already known to them. The eligibility of the studies was assessed first on literature review search of identified titles

and abstracts. Full manuscripts were retrieved for all studies identified as relevant and a decision for final inclusion was made after full examination of the papers.

## **Eligibility criteria**

### *Participants*

The inclusion criteria were children and adolescents,  $\leq 18$  years of age at baseline, with myopia defined as spherical equivalent refraction  $\leq -0.25$  dioptres, with or without astigmatism, without any ocular comorbidities including strabismus and amblyopia. Animals, adult population, subjects who did not have myopia, or subjects with myopia in combination with strabismus/amblyopia were excluded. Studies related to surgical interventions for myopia correction such as refractive surgery were not considered.

### *Interventions and comparators*

Studies in which any under-correction of the full refractive error for myopia control, over-correction of the full refractive error or no correction of the myopia was compared to full correction of myopia using single vision spectacles or placebo were included. No restriction on duration and amount of un-, under-, or over-correction was imposed.

### *Primary outcomes*

The primary outcomes regarded myopia progression and axial elongation as efficacy criteria. Myopia progression was assessed as the mean change in mean spherical equivalent refractive error, measured in dioptres. Mean change in axial length, measured in millimetres, was also evaluated. Outcomes reporting change in a 12-month or 24-month period were accepted and described. Reported adverse events were regarded as safety criteria.

## METHODS

### Search Strategy and Inclusion Criteria

The research question was, “What is the association between un-, under- and over-correction of full myopic refractive error and myopia progression in children and adolescents aged up to 18 years?” Un-correction was defined as not wearing an optical correction for any level of myopia  $\leq -0.25D$ . Under-correction was defined as a reduction in level of myopia corrected with an optical appliance. Over-correction was defined as an increase in level of myopia corrected with an optical appliance.

The authors separately and systematically conducted a search of 3 databases (Pubmed, Web of Science, and the Cochrane Central Register of Controlled Clinical Trials [CENTRAL] from their inception until June 2019). The following search strategy was performed in Pubmed and CENTRAL: myopi\* OR “myopia”[MeSH Terms] OR “short-sight” OR “short-sighted” OR “short-sightedness” OR “short sight” OR “short sighted” OR “short sightedness” OR “near-sight” OR “near-sighted” OR “near-sightedness” OR “near sight” OR “near sighted” OR “near sightedness” OR “refractive errors”[MeSH Terms] OR refract\*) AND (“under-correct”[MeSH Terms] OR un-correction\*). The same search was performed in Web of Science, but MeSH terms were not used.

Assessment of identified titles and abstracts commenced with a comparison against the research question. If considered potentially suitable, or if there was uncertainty regarding suitability after reading the title and abstract, full-text articles were subsequently retrieved. Reference lists from all identified studies were also examined. From the full-length articles, the studies were reviewed with respect to the following criteria. (1) reported un- or under- or over-correction of myopia, (2) reported myopia progression as the outcome measure, (3) reported a measure of the association either as an effect estimate with 95% confidence interval (CI) or standard error (SE) or data to calculate these, (4) were limited to children and adolescents (aged up to 18 years), and (5) myopia defined as spherical equivalent refraction  $\leq -0.25$  dioptres (as accepted by global consensus<sup>6</sup>; with or without astigmatism, without any ocular comorbidities including strabismus and amblyopia. We excluded studies without a precise definition of myopia, animal studies, and studies related to surgical interventions for myopia correction such as refractive surgery. When multiple publications from the same study population were available for the same study design

we included the publication that best addressed our research question. Studies were not limited according to study design, thus having the potential to include interventional as well as observational studies.

### **Data Extraction and Assessment of Study Quality**

To appropriately report the systematic review the authors were guided by the PRISMA checklist <sup>7</sup>. In addition for each study, the following characteristics were extracted: (1) last name of first author, (2) year of publication, (3) study design, (4) area of the study population, (5) number of subjects in the study, (6) age range of study subjects, (7) definition of myopia, (8) definition of un-, under- and over-correction of myopia , (9) 95% CI or SE, (10) adjustment for any confounding factors.

Study quality was assessed; the variables assessed for quality included the methods for selecting study participants, methods for determining myopia, study design (RCT, observational), methods for controlling confounding factors, statistical methods and conflict of interest.

## RESULTS

The Prisma Flow Diagram is shown in Figure 1.

The majority of evidence is reported for changes in myopia progression as spherical equivalent refraction. Some studies also report on change in axial length, and where they do, the change in axial length correlates with myopia progression.

### Un-corrected myopia

In a case controlled study on the effect of un-correction of myopia on myopia progression in a cohort of 12 year old Chinese children (N= 121), Sun and colleagues<sup>8</sup> found that the progression of myopia in the first year of the study was significantly less in children with no refractive correction ( $-0.39 \pm 0.48$  D) compared with children wearing full-correction ( $-0.57 \pm 0.36$  D,  $P = 0.03$ ), and the difference remained significant after adjusting for baseline SER, age, sex, age at myopia onset, height, number of myopic parents, and time spent in near work and outdoors ( $-0.39 \pm 0.06$  D vs.  $-0.58 \pm 0.06$  D,  $P < 0.01$ ).

In China, Hu and Guo recruited 90 participants and allocated them to be uncorrected, monocularly corrected or binocularly corrected<sup>9</sup>. Limitations are that the selection procedure was not specified, the groups were not well matched in terms of refractive error and key aspects such as age are not reported. Un-corrected participants had faster progression over a year's follow-up than those fully corrected ( $-0.95 \pm 0.12$  D versus  $-0.50 \pm 0.15$  D), but no statistics are reported<sup>9</sup>.

### Under-correction of myopia

There is minimal support in the literature for under-correction as a means of slowing progression.

Tokoro and Kabe (1965)<sup>10</sup> reported differences in myopia progression among a population of myopes aged 7 to 15 years based on wearing patterns from the following data: (1) full-correction of myopia and full-time wear (myopia progression of  $-0.75$  D  $\pm$  0.27, N=13), (2) under-correction ( $-0.54$  D  $\pm$  0.39, N=10), or (3) full-correction with part-time wear ( $-0.62$  D  $\pm$  0.32, N=10). The study design (small study sample, limited

statistical analysis, concurrent use of pharmacological intervention for myopia control) is such that the study findings have been subsequently criticised in the literature.

Adler and Millodot conducted a prospective randomised controlled trial to assess the effect of under-correction of myopia on the rate of myopia progression<sup>11</sup>. They randomly assigned 48 myopic children, aged six to 15 years to either a fully corrected group (n = 23) or to an under-corrected group (n = 25). The subjects in the latter group were undercorrected by +0.50 D. The study duration was 18 months. Optometric examinations were carried out at the beginning of the study, then at 6-month, 12-month and 18-month follow-up. The 12-month data are included in this report (see figure 2). Under-correction produced a slight, but not statistically significant, increase in myopic progression over the 18-month period equal to 0.17 D, compared to full-correction.

In a paired subject design, Chung and colleagues randomly assigned 94 children aged 9-14 years with myopia to an under-corrected group or a fully corrected control group for a two year prospective study<sup>12</sup>. The 47 children in the under-correction group were blurred by approximately 0.75 D (blurring visual acuity to 6/12), while the control group were fully corrected. Under-correction produced more rapid myopia progression (-1.00D vs -0.77D, 30%; ANOVA,  $F(1;374)=14.32, P<0.01$ ) and axial elongation (0.58 vs 0.65mm depicted graphically, 12%; ANOVA,  $F(1;374)=4.13, P=0.04$ ).

Li and colleagues in a prospective study, assessed myopia progression in 12-year old Chinese children<sup>13</sup>. 120 children (47.4 %) were under-corrected (the range of under-correction was -4.63D to -0.50D) and 133 children were fully corrected. They found no significant differences in myopia progression ( $P=0.46$ ) and axial elongation ( $P=0.96$ ) at 1 year between the two groups of children. Regression analysis showed a very weak, but statistically significant association in refractive error, but not axial length. This indicates that myopia progression significantly decreased with increasing amount of under-correction in all children ( $r^2=0.02, P=0.02$ ). Interpreting this finding means that an under-correction of more than 2D would be needed to slow progression by 0.25D.

Koomson and colleagues (2016) <sup>14</sup> conducted a 2-year single masked randomised control trial on 150 Ghanaian myopic children aged 10 to 15 years with mean baseline myopia of -1.98 to -0.50D. The children were randomly assigned to wear either a full-correction (n = 75) or +0.50D under-correction (n = 75) single vision spectacle lenses. An open-field autorefractor was used to obtain refraction data and ocular biometry results were determined using A-Scan ultrasonography. At 2 years, the mean amount that myopia progressed by in children in the full-correction group ( $-0.54 \pm 0.26\text{D}$ ) was not significantly different from that of the children in the under-correction group ( $-0.5 \pm 0.22\text{D}$ ) ( $P = 0.31$ ).

Chen (2014) <sup>15</sup> recruited age, sex and refractive error matched groups of 77 fully corrected and 55 under-corrected (by -0.25 to -0.50D) children with myopia and followed them for 1 year. Randomisation and masking are not reported. While at 6 months, no significant differences were observed, by 12 months the under-corrected group had statistically significant greater myopic progression than those fully corrected (-0.60D versus -0.52D; no SD, SE or CIs are reported).

Vasudevan and co-workers <sup>16</sup> retrospectively examined clinical practice records in the USA for rate of myopia progression and level of under-correction of myopia versus full-correction of myopia. They found a significant positive correlation between the under-correction of refractive error and the myopia progression ( $r = 0.301$ ,  $P < 0.01$ ), such that the greater the amount of under-correction, the greater the myopia progression. In addition, there was a significant positive correlation between myopia progression and the subjective refraction ( $r = 0.166$ ,  $P = 0.006$ ); that is, for a given amount of under-correction, the greater the myopic refraction, the greater the degree of myopia progression.

#### *MonoVisionCorrection*

Phillips studied the effect of monovision spectacle wear on myopia progression in 18 children aged 11 years and recorded slower progression of myopia in eyes of subjects that were under-corrected for distance vision <sup>17</sup>. Dominant eyes were fully corrected for distance vision and fellow eyes were un-corrected or corrected to keep the refractive

imbalance  $\leq 2.00$  D. Importantly all subjects accommodated to read with the fully corrected eye. The inter-eye difference in refraction was 0.36 D/year (95% CI: 0.54 to 0.19,  $P=0.0015$ ,  $n=13$ ); difference in vitreous chamber elongation was 0.13 mm/year (95% CI: 0.18 to 0.08,  $P=0.0003$ ,  $n=13$ ). It could be speculated from the results of this study that, by periodically alternating which eye is under-corrected, it may be possible to achieve myopia control; however, further clinical trial evidence would be needed to support this premise.

In the study by Hu and Guo reported above for un-correction compared to full-correction, 30 monocularly corrected participants showed faster progression over a year's follow-up than fully corrected individuals ( $-0.67 \pm 0.22$ D versus  $-0.50 \pm 0.15$ D), but no statistics are reported <sup>9</sup>.

### **Other Studies of Note**

#### *Over-correction of myopia*

There is one report on the use of over-correction of myopia as an intervention strategy in myopia control. In a case control study thirty-six children aged 7 to 15 years were given an over-correction of 0.75 D over the power required to correct their myopia <sup>18</sup>. These 36 experimental subjects were matched by control subjects selected at random from the files of a university optometry clinic. The criteria used in matching were sex, age of myopia onset, refractive error at onset, and duration of time covered by the record. The mean rate of change of refractive error for the experimental group was -0.49 D/year (range, +0.37 to -1.95 D/year) on retinoscopy and -0.52 D/year (range, +0.21 to -1.32 D/year) on subjective refraction. The mean rate of change for the control group was -0.47 D/year (range, +0.06 to -2.03 D/year) based on retinoscopy and -0.47 D/year (range, +0.28 to -1.72 D/year) determined by subjective refraction. Myopia progression rates for the experimental and control groups were not significantly different. The findings, as reported in an abstract, from a large (4,596 children) retrospective study in China found over-minusing among Grade 1 children was not associated with increase in myopia over 12 months ( $P=0.79$ ) perhaps due to small numbers in this category, whereas for Grade 7 children it was (0.15 D of additional myopic change for every dioptre of over-minusing at baseline,  $P<0.001$ ) <sup>19</sup>.

### *Part-time wear of single vision spectacles*

Parssinen and colleagues randomly assigned two hundred and forty mildly myopic school-children aged 9-11 years to three treatment groups and the progression of myopia was followed-up for three years. The treatment groups were: (1) minus lenses with full-correction for continuous use (the reference group), (2) minus lenses with full-correction to be used for distant vision only, and (3) bifocal lenses with +1.75 D addition. 237 children completed the three year data read. Interestingly the difference in the increase in spherical equivalents was not statistically significant in the right eye, but in the left eye the change in the distant use group was significantly higher (-1.87 D) than in the continuous use group (-1.46 D) ( $P = 0.02$ , Student's t test). No other differences between groups was found. The authors concluded that myopia progression cannot be slowed by reducing accommodation with bifocals or by reading without spectacles <sup>13</sup>.

Similarly Ong and co-workers on a cohort of 43 children with myopia from a longitudinal study of refraction assessed their myopia progression with regard to their lens wear patterns over a period of 3 years <sup>14</sup>. Refractions were obtained in a research setting by noncycloplegic retinoscopy performed by one experienced optometrist at regular intervals. Information regarding the subjects' prescription lens-wearing history was obtained from the participants and their eye care providers. Based on their wearing patterns, subjects were divided into four categories: (1) full-time wearers; (2) myopes who switched from distance to full-time wear; (3) distance wearers; and (4) nonwearers. The authors did not find a significant difference in myopia progression among the four groups.

### *Retrospective studies*

There are a number of retrospective studies in the academic literature which all suggest myopia is greater and/or has progressed quicker in children who were found to be under corrected than in those that were fully corrected <sup>22-24</sup>.

## DISCUSSION

It is understandable based on the animal study data that has been widely presented, that under-correction has been adopted by many clinicians in the past<sup>5</sup>. This has led to a series of clinical trials to provide an evidence-basis of this approach in humans; these studies have failed to detect a reduction in the progression in myopia and instead, at least half have shown that myopia progression is accelerated (Figure 2). So why might this occur? Animal correction is usually achieved by attaching lenses that fully encompass all visual angles worn on a full time basis. The visual environment is usually relatively close to the animal and does not vary widely in optical defocus range. In contrast, optical correction in human clinical trials only encompass visual angles dictated by the frame and vertex distance and can be removed during waking hours. Likewise, the human environment has a wide range of optical defocus and the retina is often receiving light from varying focal demands simultaneously. Hence under-correction amounts will vary with principal viewing distance and across the visual field. Therefore, controlled studies showing under-correction reduces accommodative effort and accommodative lag<sup>25, 26</sup> are of limited relevance in the natural world environment. There appears to be no relationship between the lag of accommodation and myopia progression<sup>14, 27</sup>.

It is not clear why under-correction would accelerate myopic progression, but study findings suggest that any malfunction of the sign detection mechanism in emmetropization can cause eye growth<sup>12</sup>. Progressing myopes have large accommodative lags, micro fluctuations and an increased depth of focus compared to non-myopes, but similar blur detection thresholds; hence they seem to be less sensitive to retinal defocus, but this is compensated by some form of an adjustment in the higher visual processes to preserve the subjective percept even when receiving poor retinal image quality<sup>28</sup>. Therefore this cortical processing seems to override retinal defocus in those for whom the emmetropization process has been compromised by a mismatch between the optical power of the eye and its axial length.

The premise for un-correction of refractive error to slow myopia progression is the same as that for under-correction, unless the peripheral optics of spectacle lenses create additional peripheral blur. Fewer studies have examined the impact of un-correction, but whether it is unilateral or bilateral, there is no strong evidence for its benefit. As visual impairment due to uncorrected refractive error is known to impact an individuals

education, productivity and independence <sup>29</sup>, such strategies cannot be ethically recommended.

A key question relating to the refractive correction of progressing myopes remains. At what level and period of under-correction does it accelerate eye growth and how do these factors interact? This knowledge is much needed to inform the frequency of eye examination follow-up and future prescribing practice.

## **CONCLUSIONS**

The evidence is equivocal in terms of full, un- or under-correction of myopia as a strategy for myopia control. Un-correction of myopia needs to be balanced ethically with correction of myopia for function. Some studies show no difference in myopia progression with under-correction whereas most show an increase in myopia progression compared with full-correction of myopia. There is also limited data to support part-time wear of spectacles for slowing myopia progression. Hence, current clinical advice advocates for the full-correction of myopia. Further studies are warranted to determine the level of myopia that can be left uncorrected without impacting on myopia progression and how this changes with time.

## **ACKNOWLEDGEMENT**

The authors are grateful to Björn Drobe and Daniel Spiegel for their insightful comments on the manuscript and to Essilor for funding the review.

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## FIGURE LEGENDS

**Figure 1.** Prisma Flow Diagram

**Figure 2.** Forest plot of mean difference in myopia progression (and 95% CIs) for mono-, un- and under-correction of myopia versus full-correction.

Under-correction \*under-correction of 0.50D, †under-correction of 0.25D, #confidence interval data not reported.