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ARTICLE

Models of myopia: the effect of accommodation, lenses and atropine

Antonio Medina[1] ✉

BACKGROUND: Two quantitative models for myopia have been proposed and used for myopic intervention, one derived from feedback theory, and the other from physiological and mechanical considerations. This paper shows that they both predict the same results indicating that they are valid and reliable. These models are the only ones that can make predictions about the effect of atropine and lenses on myopia, explain multiple observations heretofore unexplained and offer possible interventions.
OBJECTIVE: Using their predictive power we test the models by calculating and comparing the effect of accommodation, lenses or atropine. The models offer a rationale that makes atropine equivalent to a positive lens for purposes of refractive development.
METHODS: This report includes thought experiments, actual experiments and trials, as well as an analysis of clinical data and integrates and tests results from all of them for far-reaching conclusions.
RESULTS: Both models accurately predict the same myopia progression caused by near work. These models are simple but powerful enough to suggest what treatments are indicated. Interventions for prevention and control of myopia are evaluated analytically, in particular atropine and optical treatments, such as positive lenses and under correction.
CONCLUSION: Optical treatments have enormous potential; atropine is of questionable value since there are ways to get the same or superior effect with lenses of power calculated as described here.

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INTRODUCTION

The foundation for myopia control using positive lenses and atropine

Atropine and positive lenses have been used for a long time for the control of myopia with varied results based mainly on the hypothesis that associates accommodation with myopia development and progression.

There are two quantitative models for myopia, one derived from feedback theory or homeostasis [1], and the other from physiological and mechanical considerations [2]. They are very different in nature; however, they are not alternate, but complementary models. While one model explains what happens; the other explains why. Both can predict myopia development and progression numerically and for any individual. They can be used to predict the effect of accommodation, atropine, and positive lenses.

Feedback theory demonstrates that atropine used at a high dose not only halts but in some cases can reverse myopia progression and can predict its effect accurately. Feedback theory treats atropine as a positive lens because it cancels the near demand in full or in part. In theory, the same effect as that of atropine can be obtained with the use of positive lenses.

The equivalence of positive lenses and atropine has been described before [3], as well as the equivalence of negative lenses and near work [4]. Furthermore, it has been demonstrated that near work or negative lenses, in general, are the cause of myopia [3].

A positive lens cancels or reduces the negative power of the near demand. Near demand, in dioptres, is simply the time average accommodation [5]. A positive lens reduces myopia progression according to feedback theory because it cancels the equivalent negative lens that produces myopia. This effect was demonstrated in a 30-month study evidencing a lower myopia progression rate of 0.25D in that time [6] and a 3-year trial [7]. A significant reduction in myopia progression occurs while wearing a bifocal contact lens [8]. These lenses reduce accommodation [9]. Alternative hypothesis attributes their effectiveness to "peripheral refraction" effects, which have been discredited by some [10]. A recent study suggests that the effect of the positive addition in contact lenses is based on the defocus they impose on central, rather than peripheral vision [11].

We test here the predictions of the physiological model to evaluate whether it provides the same result as the feedback theory model.

METHODS

Analysis of the effect of accommodation, atropine and positive lenses based on the feedback theory myopia model

Figure 1 presents the refractive development of a hypothetical eye under several alternative interventions. It shows what happens theoretically to a young corrected myope when he is treated with a plus lens for near work. The figure also shows other interventions such as atropine and what actually happens, from clinical data. Atropine is equivalent to the application of a positive lens [3]. The power of that lens is equal to the near demand R_n, meaning that atropine disables accommodation completely as it probably occurs for a concentration of 1%. Lower

[1]Massachusetts Institute of Technology, EE Research Laboratory, 77 Massachusetts Ave, Cambridge, MA 02139, USA. ✉email: puerta@alum.mit.edu

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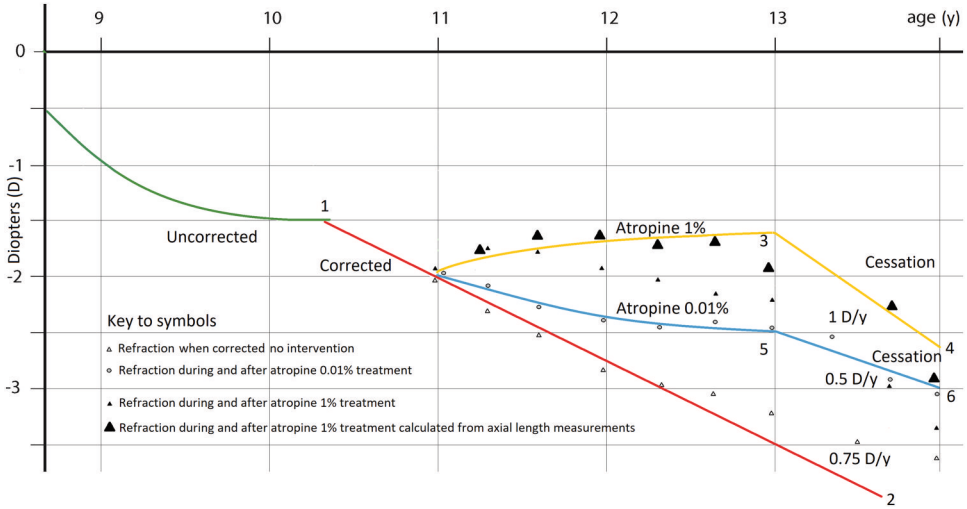

Fig. 1 Calculated effect of atropine treatment or a plus lens after myopia develops when the set point is not zero (curves) and corresponding clinical data (symbols). Refraction curves are calculated by feedback theory for a hypothetical child's eye with the following average constants. The time constant k = 2 years and near demand R_n = -2D, the set point is R_0 = +0.5D and the natural myopia is R = -1.5D, since $R = R_0 + R_n$. The green trace 1 is uncorrected refraction, showing that the child develops myopia before age 9 that stabilizes at -1.5D at age 10 without intervention. After age 10 predictions are plotted for the following alternative interventions: **a** (red trace). Full correction updated frequently results in a linear progression at a rate of R/k = -0.75D/y (section 2); **b** (orange trace). At age 11 with refraction -2D, additional lens correction of +2D, or equivalently, atropine 1% treatment from age 11 to 13 cancelling the -2D near demand (curved section 3) results in myopia reduction of almost 0.5D. Stopping atropine treatment at age 13 and maintaining correction used during treatment (straight section 4) results in a linear decline of -1D/y calculated as (R-u)/k where u = 0.5D; and **c** (blue trace). Partial cancelation of only 1D of the near demand by means of a lens of +1D or atropine 0.01% for 2 years (curved section 5). The resulting refraction at the end of this treatment is -2.5D. The myopia progression after cessation of this treatment (straight line 6) is -0.5D/y calculated as (R-u)/k where u = -0.5D. The rate of progression in intervention b after 1% atropine treatment is twice the one in c since we assume that the child wears the same glasses as at the beginning of the treatment and he is therefore over corrected in intervention b and under corrected in **c**. The horizontal axis could represent arbitrary years instead of age, used as an example. Symbols and data used are the same as in [13] for the same interventions. Large-filled triangles depict our calculated refractions from data axial lengths for atropine 1% treatment. Curves are based on general population average values for k and R_0. No attempt was made to fit the data to the curves, which would provide a better fit and the average values for this particular population.

concentrations of atropine that partially paralyze accommodation would simply reduce the power of that equivalent lens. We compare the theoretical results to actual refractive progressions.

We assumed the following values that are near known averages, for illustration. The time constant k = 2 years [1], near demand R_n = -2D (a representative number), the emmetropization set point is R_0 = +0.5D (near the population mean) and the natural myopia, defined as the end myopia that would develop without correction, is $R = R_0 + R_n$ = -1.5D [3].

The green trace is uncorrected refraction, showing that the child develops myopia before age 9 that stabilizes at his R = -1.5D about age 10 without intervention. Notice that he develops myopia of R = -1.5D, despite his set point being +0.5 because of his -2D near demand. Since starting at age 10 he is fully corrected for his myopia, his myopia follows the red straight line of slope m = R/k = -1.5/2 = -0.75D/y [12].

We start the plus lens (or atropine) intervention when the child is 11 years old at -2D. Starting at that time the equivalent plus lens of power A = +2D cancels the near demand R_n = -2D. The refraction of that eye, according to feedback theory, will seek to stabilize at the set point R_0 = +0.5D plus the power of the correcting lens -2D, or -1.5D. The orange trace shows the refractive time course under this intervention.

It can be calculated that at age 13 the eye has almost reached the asymptotic maximum benefit of the plus lens (a reduction in myopia of nearly 0.5D). We then stop the treatment but continue the correction with the same lens worn during treatment. Since the refraction of this eye is now about -1.5D it is overcorrected 0.5D. Feedback theory can tell us what will happen to this overcorrected eye. The equation for the myopic progression rate (m) for an eye that is under or over corrected is: m = (R-u)/k [1] where R is the natural myopia, u is the under/over correction and k is the time constant. In this eye R = -1.5D, u = 0.5D and k = 2 so m = -2/2 = -1D/y. After the atropine treatment, the progression of myopia is faster if we do not change the corrective lens used before treatment.

If we look at actual data from a clinical trial [13, 14], although the children treated with 1% atropine had an average increase in their myopia after 2 years the standard deviation also shows that a good number of them had a decrease in their myopia and were therefore overcorrected causing the observed "rebound."

We compare now the above theoretical results to data of actual refractive progressions in children. These results explain the myopia reversal reported in [13]. Such a phenomenon occurred when children were treated with 1% atropine and it is documented in Fig. 2 of that report. Notice that feedback theory predicts that this reversal and the after-cessation faster progression rate will only happen for a high enough concentration of atropine capable of cancelling the near demand significantly or completely. It also predicts that the "rebound" after treatment would be proportional to the concentration of atropine used. This is exactly what Chia et al. found. Their increased rate of progression after cessation of treatment with high concentration atropine was therefore probably an artifact as explained here. The same explanation applies to lower concentrations when the progression rate is less. Most of the children who had atropine 1% were overcorrected at the end of the treatment since their myopia was reduced, while the children having low concentration were under corrected because their myopia increased. The authors in [13–15] are silent about any change in the correction of the children. There is no indication that the children were prescribed new lenses at the end of the atropine treatment. The authors report "No intervention was administered" which indicates that correction was not changed [15]. So, we can validly assume that they were in fact overcorrected or under corrected by some amount depending on the concentration used [13, 14].

Feedback theory's overall prediction of the effect of atropine 1%, is a myopia reduction of value R_0 after intervention and an eventual return to the original progression R/k on cessation. Available data confirm this prediction [16, 17].

Analysis of the effect of accommodation, based on the physiological myopia model

Medina proposed a simple physiological mechanism that explains myopia as the result of frequent accommodation, caused by near work [2]. The

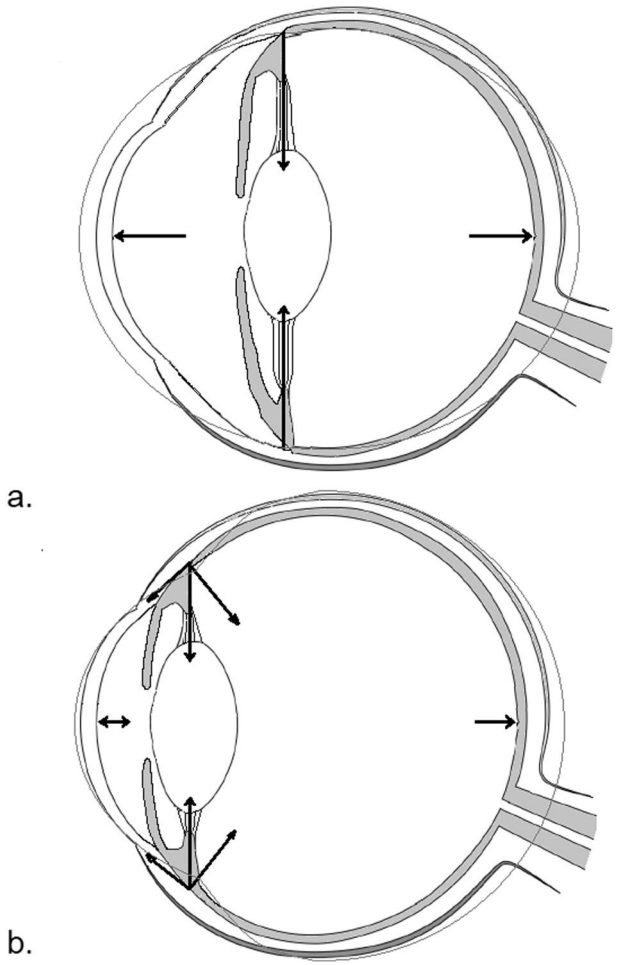

Fig. 2 The accommodated eye. a Generic mammal eye cross section showing the forces created by the ciliary muscle contraction. These forces are predominantly constricting the equator (vertical arrows) and are hydrostatically transmitted to the anteroposterior poles (horizontal arrows). An eye with ciliary muscle near the equator is depicted to visualize the transmission of equatorial forces to the poles as outward forces. **b** Human eye, showing the decomposition of ciliary muscle vertical forces in tangential and central orthogonal forces. There is an outward force at the posterior pole created by the compressing forces pointing to the centre of the eye. All forces are shown in a cross-section of the eye and have revolution symmetry around the polar axis. The globe deformation resulting from these forces is depicted exaggerated as the thin line of greatest polar distance in Fig. 2, showing elongation at the poles and constriction at the ciliary body.

hypothesis was that contraction of the ciliary muscle while accommodating applies a constricting force on the sclera that is transmitted by the vitreous humour to the posterior pole. The frequent and continued strain at the pole becomes permanent as shown in [18], resulting in axial myopia. Since correcting myopia with lenses removes the feedback and maintains the amount of accommodation, corrective lenses increase myopia. This model predicts that the posterior pole will strain and elongate by an amount that can be measured and it can calculate the resulting myopic progression with axial length increase data and existing equations.

Accommodation lengthens the eye at the posterior pole based on the myopia model

We can see how accommodation increases the axial length at the posterior pole with the help of Fig. 2. If the anterior segment of the eye takes almost half of the eye, that is the *corpus ciliare* and crystalline lens are placed near the plane of the equator of the ocular globe, as in the mouse eye, it is easy to see that contraction of the circular fibres of the ciliary muscle when accommodating will constrict the equator where they proximally attach. This constriction will reduce the length of the equator, increasing the humours pressure which will distance the poles of the eyes, where there is no constriction. Figure 2a. In essence, the constriction forces at the equator are hydrostatically transmitted to the poles, which distend since the volume of the eye is maintained because the aqueous and vitreous humours are incompressible. We can then move the position of the *corpus ciliare* forward, as in the human eye, to realize that the contraction of the ciliary muscle also constricts the sclera since it is attached to it through the scleral spur. Therefore, the vitreous pressure is also increased during accommodation but to a lesser degree (Fig. 2b). There is evidence that this constriction and increased pressure occur during accommodation in primates [19, 20] and that the shape of the myopic eye is as depicted in the outer thin trace in Fig. 2b [21]. The main difference when the ciliary lens and muscle are placed distant from the equator is that the pressures in the posterior and the anterior chamber may be different during accommodation. The reason is that during accommodation the vertical forces in Fig. 2b applied to the sclera by the contracted muscle can be decomposed into two orthogonal components, a component towards the centre of the eye which will increase its pressure, and a longitudinal component tangential to the sclera that will move the cornea forward, tend to increase the volume of the anterior chamber and therefore decrease its pressure. The vitreous pressure increase is partially transmitted to the anterior chamber because the chambers' interface, consisting of the anterior hyaloid membrane, zonule, ciliary lens and muscle is a viscous semi-rigid membrane. See Fig. 2b. Because there are opposing forces in the anterior chamber during accommodation, one tending to reduce its volume and another tending to increase it, its pressure (IOP) may increase or decrease during accommodation depending on which is greater, determined by the anatomy of a particular eye. This variability with subjects and with myopia has been reported [22–25]. The result is always elongation at the posterior pole, regardless of IOP. The accommodative increase in vitreous pressure and axial length has been hypothesized for quite some time as the cause of myopia in primates [20, 26]. It was not, however, until 2020 when it was shown that applying a stressing pressure on the cornea of living human eyes would permanently strain it, and the equation to calculate the strain was provided [18]. The collagen fibres in the anterior pole stretch permanently under constant stress and that stretch is proportional to the duration of the stress [18, 27]. If the anterior pole can stretch under pressure, the posterior pole should too.

RESULTS

Myopia progression calculated by the physiological myopia model

The axial length of the emmetropic eye increases while accommodating [25, 28, 29]. This elongation has been reported to be, on average, about 8μm for 3 dioptres of accommodation and higher for greater accommodation [25, 29].

Calculation of myopia progression from any sustained axial elongation is straightforward using general equations [18]. It will be calculated here for the 8μm corresponding to 3 dioptres of accommodation.

We can calculate the stress σ at the sclera from the axial elongation using the Laplace equation, $\sigma = P\Delta R/2\,h$ [18]. Where P is the vitreous pressure, approximately equal to the IOP, ΔR is the increment in the radius of curvature at the posterior pole, and h is the thickness of the sclera. The axial length elongation (ΔL) during 3D accommodation for emmetropic children of age matched to those in Fig. 1 is 8μm [25]. Substituting $\Delta R = \Delta L/2 = 8/2 = 4\mu m = 0.0004$ cm and average values for $P = IOP = 16$ mmHg $= 0.021$ kg/cm^2 and $h = 600\mu m = 0.06$ cm we obtain $\sigma = 0.021 \times 0.0004/0.12 = 0.00007$ kg/cm^2. The value used for the thickness of the sclera, 600μm, is the average value for non-elongated globes at the midpoint between the posterior pole and the equator [30].

The strain created at the posterior sclera is $\varepsilon = \sigma\, t/\eta$, where t is the time the stress σ is applied and η is a viscosity constant of the collagen in the eye [18]. In one year $\varepsilon = 0.00007 \times 60 \times 24 \times 365/1150 = 0.032$ or 3.2%/year, or 0.38 mm/year for an eye of radius

12 mm. We used the viscosity value $\eta = 1150$ kg min/cm^2 determined by Medina & Green [18] from six human corneas in vivo since it is not available for the sclera. Sclera and cornea have very similar collagen composition and it is known that they are very similar anatomically and mechanically [31–33], so the value used is justified. The reported values for the increment in axial length corresponding to 1D defocus range from 0.32 mm for 12 to 13-year-old children [34], to 0.35-0.40 mm for young adults [35]. Since we are studying emmetropic children at an age when they become myopic, we use the factor 0.32 mm/D for 12 to 13-year-olds from [34]. Using this conversion factor the elongation of 0.38 mm/year corresponds to 1.19D/year of myopia progression.

Myopia progression calculated by the feedback theory model

Feedback theory can also tell us the effect of -3D near demand (the result of a permanent 3D accommodation) on myopia progression in an individual with average eye parameters.

Calculation of myopia progression can be done using the equation $m = R/k$. See [1, 12] for alternative independent derivations of this equation. The myopia progression for a near demand $R_n = -3$D, using average values for time constant $k = 2$, set point $R_0 = +0.5$D, $R = R_0 + R_n = -2.5$D, is $m = R/k = -2.5/2 = -1.25$D/year.

This value is very close to the -1.19D/year progression calculated with the physiological model.

DISCUSSION

Prevailing models of myopia

The predictions of the physiological myopia model and feedback theory myopia are in substantial agreement.

In the past, it has been difficult to quantify the effect of near work and lenses on myopia because no quantitative models existed that could provide the expected effect. For this reason, the reported effect of lenses was inconsistent, variable and unreliable. Optical interventions such as under correction or bifocals for the control of myopia were done without any quantitative design or expectation. Not surprisingly the results were contradictory and inconclusive. Studies failed to find a significant link between positive lenses and myopia progression with exceptions that although statistically significant were not considered clinically significant [36]. A review of multifocal lens use found that their effect is variable and not sustained over time [37].

The models presented here are the only ones that can make quantitative predictions about the atropine effect on myopia and explain other observations heretofore unexplained. Feedback theory and its model of myopia do not rely on or depend on any particular physiological model while the accommodation model relies on biomechanics and supporting data. The theoretical model of myopia relies on one assumption and mathematic analysis, so it can only be disproved if the assumption is shown to be incorrect.

Both models produce the same results from the same stimulus or input although the assumptions and foundation for each model are very different. For the theoretical model, the only assumption is that emmetropization is based on feedback or homeostasis [1] while for the physiological model, the only assumption is that accommodation produces elongation of the ocular globe. Both assumptions are justified and supported by compelling evidence.

The physiological model for myopia also explains why hyperopia tends to diminish since accommodation must be used continuously to focus the retinal image. That model is self-contained in the eye and it does not depend on biochemical or nervous system mediation, other than accommodation. Several animal experiments suggest that emmetropization is independent of the central nervous system.

The theoretical model predicts that refractive error, and myopia in particular, is a reversible condition. It has been confirmed so for a very young age. For school-age we know that atropine can reverse somewhat myopia as the model predicts, but no experiments have been done in humans placing a strong positive lens or stopping correcting a myope to find a myopia reduction as it was done in animals [38]. Reversing more than about 5 dioptres of myopia is probably impossible due to the anatomical constraints of the orbit. Many believe that eye elongation is not reversible; however, this conclusion is based on the observation that corrected myopia maintains the elongation. No experiment has been conducted to explore what happens when correction or near work is removed. The questions of whether myopia is reversible or emmetropization is bi-directional, and how much and how important age is a factor are unanswered.

Prevalence of uncorrected myopia

Both models predict that if myopia is not corrected, it will not progress as indicated by the green trace in Fig. 1. Although we do not have uncorrected patients' data, we have studies that show the incidence of myopia in uncorrected children is low. This observation was noticed in populations as different as Asian (Singapore) and African (Ghana) which had similar prevalence [39, 40]. The models described here predict that myopia prevalence should be similar among any uncorrected population. The Singaporean population in general has a higher prevalence of myopia because low myopia is more likely to be corrected than in Africa, and consequently progresses to the point of being clinical myopia and counted for purposes of prevalence calculation. For the same reason, its average myopia is higher. The models also predict that the prevalence of uncorrected myopia should not change with age. The prevalence of uncorrected adult myopes in Nigeria has a value of 10% [41], similar to the uncorrected children.

CONCLUSIONS

The benefit of a physiological model for myopia

Myopia can be produced in primates [42, 43] and it can be reversed too [38]. Models for myopia tell us why, how and how much. The values for myopia progression obtained from the near demand using two completely independent methods: the myopia model and feedback theory are in remarkable agreement. The physiological model for myopia is therefore validated. Both models further agree that the progression of corrected myopia is linear [12] and they can predict it from the near demand alone, indicating that near work is causative of myopia since no other variable or factor needs to be considered.

Feedback theory is a black box with a transfer function; we can only change its output by changing its input. The benefit of having a physiological model for myopia versus a high-level theory like feedback theory is that a physiological model can pierce into the black box, we can change the output by changing the model itself. For example, we can change accommodation, or any other related variable, to change myopia prevalence, progression, reduction, or whatever the model allows.

Feedback theory establishes a causal link between near work and myopia based on the principle of equivalence of near work and negative lenses. The model described here shows causation based on a physiological scheme that produces the same result with the same amount of near work. Both models show near work results in myopic progression. The inescapable conclusion is that near work/negative lenses cause myopia and positive lenses, including equivalent atropine, can be used to neutralize negative lenses and the development and progression of myopia. The power of this view is that it is backed by the mathematics of feedback theory of emmetropization which can make detailed predictions amenable to testing and verification. The theory can in turn give us valuable insights into the use of atropine and optical interventions.

Optical intervention

Optical treatments have enormous potential. The myopia models can provide a comparative efficacy of optical intervention versus atropine and predict that low dose atropine, has a modest effect, reducing the progression of myopia by less than 1/2D over 2 or 3 years as it has been evinced in clinical trials [13, 14, 44]. The models can tell us what interventions, and what optical power must be used to achieve a desired result, how much a given under correction will reduce the myopia progression or what positive lens power will stop the progression. Knowing the expected results we can then make a well-informed decision on how to intervene. For example, a modest under correction may produce minimal results in a myope of several dioptres while using plus addition for near work, which in some cases can be achieved by removing the distance correction glasses, may produce a substantial reduction or stabilization of myopia progression. Positive lenses used for near or distance in a hyperopic eye can prevent myopia [45], and the models can tell us the power of those lenses. The intervention design needed for myopia control with positive lenses is relatively simple so it can provide an important reduction in the forecasted myopia prevalence [3, 46] and progression in the absence of intervention.

SUMMARY

What was known before

- Myopic interventions, such as atropine and under correction were of variable success. The critical variables were only conjectures and the available models were qualitative only.

What this study adds

- This paper identifies and describes the quantitative models of myopia and how to use them for the clinical treatment of myopia. This paper also addresses the current interest in atropine treatment for myopia analysing its indication The review goes deep into the physiological and theoretical rationale for these interventions to permit far-reaching conclusions.

DATA AVAILABILITY

All data supporting the findings of this study are available within the paper and the references cited.

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COMPETING INTERESTS

The author declares no competing interests.

ETHICAL APPROVAL

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards or were exempt because only retrospective analysis of data was involved.

INFORMED CONSENT

Informed consent was obtained from all individual participants included in the study or their parents when minors were involved.

ADDITIONAL INFORMATION

Correspondence and requests for materials should be addressed to Antonio Medina.