Title

A Randomized Clinical Trial of Immediate Versus Delayed Glasses for Moderate Hyperopia in Children 3 to 5 Years of Age.

Authors

Holmes, Jonathan

Kulp, Marjean

Dean, Trevano

et al.

Publication Date

2019-12-01

DOI

10.1016/j.ajo.2019.06.021

Peer reviewed

Published in final edited form as:

Am J Ophthalmol. 2019 December ; 208: 145–159. doi:10.1016/j.ajo.2019.06.021.

A Randomized Clinical Trial of Immediate versus Delayed Glasses for Moderate Hyperopia in Children 3 to 5 Years of Age

Jonathan M. Holmes[1], **Marjean T. Kulp**[2], **Trevano W. Dean**[3], **Donny W. Suh**[4], **Raymond T. Kraker**[3], **David K. Wallace**[5], **David B. Petersen**[6], **Susan A. Cotter**[7], **Earl R. Crouch**[8], **Ingryd J. Lorenzana**[9], **Benjamin H. Ticho**[10], **Lisa C. Verderber**[11], **Katherine K. Weise**[12], **Pediatric Eye Disease Investigator Group**[*]

[1]Mayo Clinic, Rochester, Minnesota

[2]College of Optometry, The Ohio State University, Columbus, Ohio

[3]Jaeb Center for Health Research, Tampa, Florida

[4]University of Nebraska Medical Center, Omaha, Nebraska

[5]Indiana University, Indianapolis, Indiana

[6]Rocky Mountain Eye Care Associates, Salt Lake City, Utah

[7]Southern California College of Optometry at Marshall B. Ketchum University, Fullerton, California

[8]Virginia Pediatric Eye Center, Norfolk, Virginia

[9]Advanced Vision Center, Schaumburg, Illinois

[10]Ticho Eye Associates, Chicago Ridge, Illinois

[11]Pediatric Eye Associates, Wilmette, Illinois

[12]University of Alabama School of Optometry, Birmingham, Alabama

Abstract

Purpose: To compare VA and binocularity outcomes in moderately hyperopic children with normal VA and binocularity assigned to glasses versus observation.

Design: Prospective randomized clinical trial (RCT)

Methods: 119 3- to 5-year-olds with hyperopia between +3.00 diopters (D) and +6.00D spherical equivalent were randomly assigned to glasses versus observation (with glasses prescribed if deteriorated for subnormal distance VA or near stereoacuity, or manifest strabismus). Follow-up

Corresponding Author: Jonathan M. Holmes, BM, BCh, c/o Jaeb Center for Health Research, 15310 Amberly Drive Suite 350, Tampa, FL 33647; phone: (813) 975-8690, Fax (813) 975-8761, pedig@jaeb.org.

[*]A full list of participating study group members appears in the Acknowledgements section e-Supplement.

This article contains online-only material. Supplemental Material available at AJO.com The following should appear online-only: Tables 5A, 5B, 6.

occurred every 6 months. At 3 years, the treatment strategy was classified as “failed” if any of the following were met, both with and without correction: subnormal distance VA or stereoacuity; manifest strabismus; or strabismus surgery during follow-up.

Results: Of 84 (71%) completing the primary outcome examination, failure occurred in 5 (12%; 95% CI = 4% to 26%) of 41 assigned to glasses and 4 (9%; 95% CI = 3% to 22%) of 43 assigned to observation (difference = 3%; 95% CI = −12% to 18%; P = 0.72). Deterioration prior to 3 years (requiring glasses per protocol) occurred in 29% (95% CI = 19% to 43%) assigned to glasses and 27% (95% CI = 17% to 42%) assigned to observation.

Conclusion: In a RCT comparing glasses to observation for moderately hyperopic 3- to 5-year-olds with normal VA and binocularity, failure for VA or binocularity was not common. With insufficient enrollment and retention, our study was unable to determine whether immediate glasses prescription reduces failure rate, but low failure rates suggest immediate glasses prescription for these children may not be needed to prevent failure for VA and/or binocularity.

Introduction

It is not known whether it is beneficial to immediately prescribe glasses for moderate hyperopia among children 3 to 5 years of age without manifest strabismus and with age-normal visual acuity (VA) and stereoacuity, or whether it is reasonable to follow and prescribe glasses only if the child develops reduced VA, reduced stereoacuity, or manifest strabismus. We recently reported the results of a randomized clinical trial (RCT)[1] that compared VA outcomes and stereoacuity outcomes, and the rates of development of manifest strabismus, after a 3-year follow-up period, in children ages 1 to 2 years with moderate hyperopia [spherical equivalent (SE) +3.00D to +6.00D]. In that RCT, participants were randomized to 1) immediate glasses versus 2) observation without glasses unless reduced VA, reduced stereoacuity, or manifest strabismus was found at one of the 6-monthly visits. Our results[1] in 1- to 2-year-olds were inconclusive; the 95% confidence interval around the point estimate on the treatment group difference of proportions meeting failure criteria (31% favoring glasses to 4% favoring observation) was consistent with either a small to moderate benefit or no benefit of immediate glasses compared with careful observation (glasses only if deteriorated).

We simultaneously performed a parallel RCT to address whether immediate glasses improved VA and binocularity outcomes over observation (with glasses when needed) in 3- to 5-year-old children with moderate hyperopia, where children in the current RCT were old enough to, and required to, demonstrate age-normal VA and age-normal stereoacuity, in addition to no manifest strabismus. We compared VA, stereoacuity, strabismus outcomes, and changes in refractive error after 3 years of follow-up.

Methods

The study was supported through a cooperative agreement with the National Eye Institute of the National Institutes of Health and was conducted according to the tenets of the Declaration of Helsinki by the Pediatric Eye Disease Investigator Group at 41 academic-based and community-based clinical sites. The protocol and Health Insurance Portability and

Accountability Act-compliant informed consent forms were approved by institutional review boards, and a parent or guardian of each study participant gave written informed consent. An independent data and safety monitoring committee provided study oversight. The study is listed on www.clinicaltrials.gov (identifier, ; accessed October 31, 2018). The full study protocol is available on the Pediatric Eye Disease Investigator Group website (www.pedig.net; accessed October 31, 2018).

Eligibility Exam and Criteria

In parallel with our previous study,[1] children 3 to <6 years of age were eligible if they had moderate hyperopia of +3.00D to +6.00D SE in at least one eye, with astigmatism ≤1.50D in each eye and SE anisometropia ≤1.50D by cycloplegic refraction, and no manifest strabismus at distance (3m) and near (33cm) by cover-uncover test. In this older cohort, children were also required to have age-normal monocular distance VA in each eye (20/50 or better for age 3 years, 20/40 or better for age 4 years, and 20/32 or better for age 5 years) by the Amblyopia Treatment Study HOTV© VA testing protocol[2,3] and age-normal near stereoacuity [400 seconds of arc (arcsec) or better for age 3 years, 200 arcsec or better for ages 4 or 5 years] by Randot Preschool Stereotest (Stereo Optical Co., Inc., Chicago, IL).[4] Children with a history of manifest strabismus or prior hyperopic correction were excluded. Complete eligibility criteria are listed in Table 1. Information regarding any diagnosis and/or treatment for ADHD, and family history of amblyopia and/or strabismus was also collected.

Treatment

Identical to our previous parallel study,[1] participants were randomly assigned with equal probability, using a permuted block design stratified by clinical site, to either prescribed glasses or observation [with glasses prescribed only if pre-specified deterioration criteria were confirmed (Table 2)]. Those randomized to glasses were prescribed a partial hyperopic correction (i.e., partial plus; lenses with the sphere reduced symmetrically by 1.00D from the hyperopic cycloplegic refraction) and the full astigmatism (magnitude and axis) correction at enrollment to be worn full time for the duration of the study. A partial plus correction was prescribed because some providers cite evidence that partial correction of hyperopia does not impede emmetropization,[5–8] and most pediatric eye care professionals usually prescribe less than the full cycloplegic refraction for hyperopia in the absence of strabismus or amblyopia.[9,10] Participants were not prescribed any other treatment unless there was confirmation of one or more deterioration criteria (reduced distance VA, reduced stereoacuity, or manifest strabismus) (Table 2). Participants who met deterioration criteria continued to return for study follow-up visits but were released to best clinical care at investigator discretion, with the caveat that partial-plus glasses (as specified below) should be prescribed for those not already wearing glasses, and full plus correction for those who developed manifest esotropia.

Follow-up Testing Procedures and Data Collection

As described in our previous study,[1] participants assigned to glasses were contacted two weeks after the enrollment exam to ensure that the glasses were received and to encourage adherence to glasses wear. A short course of bilateral cycloplegia could be prescribed if a participant was not compliant with glasses wear and the investigator believed that the

participant needed assistance relaxing his/her accommodation to adapt to the glasses. Any prescribed bilateral cycloplegia was to be discontinued at least two weeks prior to any study visit.

Follow-up visits occurred every 6 months (±1 month) for 3 years, with the primary outcome examination at 3 years (±1 month). For those in glasses, the prescription was verified by lensometry and adherence to glasses wear was estimated based on a discussion with the parent [not at all (≤1%), poor (>1% to <26%), fair (26 to 50%), good (>50 to 75%), or excellent (>75 to 100%)] at each follow-up visit.

All testing was completed by a study-certified examiner (pediatric optometrist, pediatric ophthalmologist, or certified orthoptist). At non-primary outcome 6-month follow-up visits, each participant was initially assessed by an unmasked examiner. Near stereoacuity was assessed at 40cm using the Randot Preschool Stereotest (Stereo Optical Co., Inc., Chicago, IL). Distance (3m) and near (33cm) ocular alignment were assessed using the cover-uncover test, simultaneous prism and cover test (if tropia present), and the prism and alternate cover test. Monocular distance VA was assessed in each eye without cycloplegia using the Amblyopia Treatment Study HOTV© VA testing protocol.[2,3] All unmasked testing was performed in the participants' optical correction, defined as no refractive correction in the observation group (unless previously meeting deterioration criteria), and hyperopic correction (as defined above) in the glasses group. The participant's current glasses were worn for testing if lensometry confirmed the glasses contained the appropriate correction; otherwise, trial frames were used. The parent was also asked, "Do you have concerns with your child's vision or ability to see well close up?" If one or more deterioration criteria (Table 2) appeared to be met during unmasked testing (and the participant had not previously met deterioration criteria), or parental concern was reported, a masked exam was performed. The masked exam consisted of a retest of the components failed on unmasked testing, both with appropriate hyperopic correction in trial frames and with no correction, and was performed on the same day as, or within 2 weeks of, the unmasked testing, to determine if deterioration criteria were truly met. If parental concern was expressed that would warrant starting treatment, in the absence of suspected deterioration by unmasked examination, all components were assessed by the masked examiner. Deterioration was also declared if treatment was started. The primary definition of deterioration was meeting deterioration criteria when confirmed by masked examination, tested in the correction strategy assigned at randomization (with trial frames if assigned to glasses, without trial frames if assigned to observation, Table 2). Following deterioration, guidelines for glasses to be prescribed for participants meeting deterioration criteria were: hyperopia not undercorrected by more than +1.00D SE, full correction of anisometropia, and astigmatism correction within 0.50D of full correction. For those participants who developed a manifest esotropia, full cycloplegic hyperopic correction was provided.

At the 3-year primary outcome visit, distance VA, near stereoacuity, and ocular alignment were assessed by a masked examiner to determine if the participant met the study "failure" criteria (Table 3). Each test was performed first in trial frames containing the appropriate hyperopic correction (1.00D sphere less than cycloplegic refraction if not previously prescribed full plus, or full plus if previously prescribed full plus) and second without

refractive correction. If any failure criteria (Table 3) (other than prior strabismus surgery) were met, that component was retested after a 10-minute break to confirm or refute failure. For participants with manifest strabismus at near during testing with their hyperopic correction in trial frames, cover testing at near was repeated with +3.00D lenses over the distance correction, but failure was still declared based on testing without the +3.00. If any failure criterion was confirmed both with and without correction, the participant was classified as a failure, unless the cycloplegic refraction obtained at the end of the examination indicated a change from the most recent cycloplegic refraction 6 months prior to the 3-year visit (change of >0.75D sphere, >0.75D cylinder, >0.75D in SE anisometropia, or axis ≥6 degrees when cylinder was >+1.00D). In such cases, a new refractive correction was provided, and an additional masked examination was performed 4 weeks later, where any previously failed component was retested in trial frames with the new refractive correction. Such participants were only classified as failed if the original failed component was still failed with the new refractive correction.

It is important to emphasize that “deterioration” and “failure” were defined differently for the present study. Deterioration could be declared at any follow-up examination, and was assessed by a masked examiner, with deterioration declared only if criteria were met in their randomized treatment (glasses or no glasses). Once deterioration was declared, additional non-protocol treatment was allowed. In contrast, “failure” (of the randomized treatment strategy) was only assessed at the 3-year outcome examination, by a masked examiner, with failure declared only if criteria were met both with and without their refractive correction worn in trial frames.

Primary Outcome

The primary outcome was failure or non-failure at 3 years after randomization (Table 3). “Failure” was conceptually defined as doing harm to one or more of: distance VA, near stereoacuity, and ocular alignment; therefore, participants were assessed for potential failure both with and without correction of their hyperopia at the primary outcome visit. Failure was declared only if criteria were met and confirmed both with and without correction (Table 3). For example, if a participant appeared to fail the strabismus criterion without correction (manifest strabismus by cover test), but was not tropic while wearing the hyperopic correction in trial frames, the participant was not declared a failure because the tropia was not present with refractive correction.

Statistical Analysis

Parallel to our previous study,[1] the sample size of 286 was chosen to provide 90% power to detect a difference in failure proportions at 3 years given expected 3-year failure proportions of 10% and 25% in the glasses and the observation groups respectively, and a type I error rate of 5%.

The primary outcome analysis was a treatment group comparison of the proportion of participants meeting failure criteria 3 years after randomization using Barnard’s test.[11] The treatment group difference in failure proportions and the 95% confidence interval (CI) were calculated using the Farrington-Manning test. The primary analysis was limited to

participants who completed the 3-year visit within 3 months prior to the target visit date and up to 6 months after the target visit date. Participants were not considered a failure for the primary analysis if testing was incomplete (e.g., if some testing or required re-testing was not completed, such that failure was not confirmed). Alternative approaches to the primary analysis are specified in Table 8.

Secondary analyses included treatment group comparisons of the individual components of the failure outcome at 3 years (distance VA, stereoacuity, manifest strabismus), binocular near VA, and change in refractive error over the 3-year period. VA measurements were converted from Snellen equivalents to logMAR (logarithm of the minimum angle of resolution) lines for analysis. Stereoacuity was evaluated as a continuous outcome by converting seconds of arc to logarithm of seconds of arc (in parentheses) as follows: 40 (1.60), 60 (1.78), 100 (2.00), 200 (2.30), 400 (2.60), 800 (2.90); participants with no detectable (nil) stereoacuity were assigned a value of 1600 (3.20).

Primary and secondary analyses followed a modified intent-to-treat principle, with no imputation of data for participants who missed the 3-year visit. Participants were analyzed based on randomized treatment assignment. To partially control for inflation in type I error rate due to testing multiple hypotheses, statistical significance in secondary analyses was defined as $p<0.01$. Analyses were conducted using SAS software version 9.4 (Cary, NC).

Results

Baseline Characteristics

Between April 2012 and August 2014, 119 participants were randomly assigned to the glasses group (N=61) or to the observation group (N=58). After 29 months, recruitment was stopped due to slow enrollment; only 42% of the planned sample size had been enrolled. Baseline characteristics were similar in the two groups (Tables 4A, 4B). Two participants were subsequently found not to have met the eligibility criteria for stereoacuity; they were included in the primary analysis, and excluded in a sensitivity analysis (Table 8).

Visit Completion and Treatment Adherence

The primary outcome examination was completed by 41 (67%) participants in the glasses group and 43 (74%) in the observation group (Figure 1). Compared with the 84 participants who completed the 3-year visit, the 35 participants who did not return were more likely to be African-American (49% vs 11%), but appeared similar with regard to other characteristics collected at baseline (Tables 5A, 5B).

Parents of children in the glasses group reported that glasses were worn more than 50% of the time by 65% of participants at 6 months, 76% of participants at 12 months, 84% at 18 months, 85% at 24 months, 85% at 30 months, and 85% at 36 months (Table 6). We had somewhat incomplete data on the use of cycloplegic drops to enhance glasses compliance, but only one child in the glasses group was recorded as having been prescribed atropine drops for 3 days.

There were four treatment-related protocol deviations. One participant in the glasses group received non-protocol treatment in the absence of meeting deterioration criteria and one in the glasses group did not receive the protocol-specified glasses prescription after meeting deterioration criteria. Two participants in the observation group did not receive glasses upon meeting deterioration criteria.

Primary Outcome (Failure at 3 years)

At the 3-year primary outcome exam, 5 (12%; 95% CI = 4% to 26%) of 41 participants in the glasses group and 4 (9%; 95% CI = 3% to 22%) of 43 in the observation group met failure criteria (difference=3%; 95% CI = −12% to 18%; P = 0.72). Reasons for failure are listed in Table 7. One participant in the observation group and no participant in the glasses group failed due to manifest strabismus. When tested with +3.00D lenses over the distance correction, that participant still had manifest strabismus at near.

Alternative statistical approaches for the analysis of the primary outcome yielded similar results (Table 8). Results for subgroup analyses are reported in Table 9.

Deterioration Prior to 3 Years

The cumulative proportion of participants meeting deterioration criteria in their assigned treatment (Table 2) was 27% (95% CI = 17% to 42%) in the observation group (Figure 2) and 29% (95% CI = 19% to 43%) in the glasses group. We did not plan statistical comparison of deterioration between the groups (in contrast to comparison of failure), because we expected *a priori* that deterioration would occur more frequently in the observation group, due to development of accommodative esotropia, for example. Reasons for deterioration are listed in Table 10.

In the observation group, among those who completed the study, failure at 3 years occurred in 1 (8%) of 13 who met deterioration criteria prior to 3 years and 3 (10%) of 30 who did not. In the glasses group, failure at 3 years occurred in 2 (22%) of 9 who met deterioration criteria prior to 3 years and 3 (9%) of 32 who did not.

Secondary Analyses

Mean change in refractive error from baseline to 3 years was greater in the observation group, both in the more hyperopic eye at enrollment (difference=0.60D; 99% CI = 0.11D to 1.09D; P = 0.002; Figure 3A) and in the less hyperopic eye at enrollment (difference=0.58D; 99% CI = 0.10 to 1.06; P = 0.002; Figure 3B). While eyes of participants in the observation group became somewhat less hyperopic on average, little change in average refractive error was observed in eyes of participants in the glasses group (Table 11).

No statistically significant treatment group differences were observed for any of the following factors at 3 years: distance VA, binocular near VA, near stereoacuity, proportion of participants with amblyopia, or proportion of participants with manifest strabismus (Tables 12, 13).

The presence of esotropia without glasses (measured without trial frames) at the 3-year outcome examination could be considered a measure of the development of accommodative

esotropia. Zero (0%) of 41 (95% CI = 0% to 9%) in the glasses group and 1 (2%) of 43 in the observation group (95% CI = 0% to 12%) had such an esotropia, which was not statistically different between treatment groups (difference −2%, 95% CI = −24% to 19%).

Regarding the possible influence of baseline esophoria on outcome, only 11 participants had a measurable near esophoria at enrollment (by prism and alternate cover test), 4 in the observation group (range 2 to 10 pd) and 7 in the glasses group (range 2 to 6 pd). One of four in the observation group (with 4pd esophoria at enrollment) met failure criteria for stereoacuity. None of the seven in the glasses group met failure criteria, but 2 of these did not complete the primary outcome examination. In 11 of 119 participants, prism and alternate cover test was not recorded at enrollment. With such small numbers of participants having near esophoria, we cannot draw conclusions regarding the influence of baseline esophoria on failure.

Discussion

In our randomized clinical trial, we found no significant difference in failure proportions between 3- to 5-year-old children with moderate hyperopia (+3.00D to +6.00D SE) treated with immediate glasses versus treated with glasses only if deteriorated, when undergoing 6-monthly follow-up. “Failure” was conceptually defined as doing harm to one or more of: distance VA, near stereoacuity, and ocular alignment, and therefore failure was declared only if criteria were met and confirmed both with and without hyperopic correction at the primary outcome visit; failure did not include development of reduced VA, stereoacuity, or strabismus that could immediately be remediated with glasses. In contrast, “deterioration” prior to the 3-year primary outcome, requiring prescription or change of glasses, was defined as development of reduced VA, stereoacuity, or strabismus while in the randomized treatment. Our study was inconclusive regarding whether or not immediate prescription of glasses reduces failure for VA or binocularity, because we had poorer than planned enrollment and retention, resulting in wide 95% CIs and potentially biased estimates. Nevertheless, whether or not glasses were prescribed in moderately hyperopic children (+3.00 to +6.00D, presenting at 3 to 5 years, with age-normal VA, age-normal stereoacuity, and no manifest strabismus), failure at 3 years (for reduced VA, reduced near stereoacuity, or manifest strabismus) was not common.

There are no previous studies with which we can directly compare our findings. A number of previous studies that have addressed whether or not there is a benefit of prescribing immediate glasses for moderate hyperopia enrolled children during the first year of life.[5,12–14] Our parallel RCT[1] enrolled 1- and 2-year-old children and found higher failure rates than the present study at the 3-year outcome. Comparing studies of older and younger children may suggest that younger children with moderate hyperopia, and no manifest strabismus on presentation, are at higher risk for development of subsequent strabismus than older children. Nevertheless, in each previous study of younger children, it was not possible to test VA and stereoacuity at enrollment using standard clinical testing methods (due to participant age), so it is likely that a proportion of children in those studies differed from the children in the present study regarding normality of VA and stereoacuity at enrollment. It is entirely possible that the 1- to 2-year-old children of the parallel study, and the 3- to 5-year-

old children of the current study, differed in important baseline characteristics, making direct comparison fraught with potential bias. It is also possible that there are differences in the response of the hyperopic visual system to glasses between the 3- to 5-year-old children enrolled in the present study compared with the younger children in other studies.

Regarding which failure criteria components were met, all but two children met the failure criterion of reduced stereoacuity, rather than reduced VA or development of manifest strabismus (Table 7). It is possible that our estimates of failure are overestimates, because, despite incorporating re-testing of stereoacuity into our protocol, variability of testing,[15] regression to the mean, and/or poor cooperation create potential for misclassification, particularly when dichotomizing across a threshold and particularly if the mean of the study population is closer to the threshold than a normal population. On the other hand, failure classification required that the child test below age norms with and without trial frames on testing and retesting after a break. Despite the possibility of overestimating failure for stereoacuity, it has been previously reported that children with high hyperopia (≥+5.00) have worse average stereoacuity than children with lower levels of hyperopia,[16] and hyperopic children have worse average near stereoacuity than emmetropic children.[15,17] Therefore, monitoring for reduced stereoacuity may be warranted because treatment of reduced stereoacuity with glasses may be beneficial. We only have data on the specific treatment strategy studied in our protocol, monitoring those without glasses every 6 months and prescribing if deterioration criteria were met. The proportion of failures at 3 years might have been higher, lower, or the same, if glasses had not been prescribed on detecting deterioration at 6-monthly visits. Our study did not address the different question of whether or not outcomes are influenced by glasses treatment during follow-up for reduced stereoacuity.

In a planned secondary analysis, we found a small but statistically significant mean difference in emmetropization between the glasses and observation groups (about 1/5 of a diopter per year) in favor of observation. The proportion of children whose hyperopia reduced by 1.00D or more over the 3-year study period was numerically higher with observation than with glasses, but did not reach statistical significance at the pre-specified alpha of 0.01. While Ingram also reported in a retrospective study that partial correction of hyperopia impedes emmetropization,[18] Atkinson's prospective study concluded that partial correction does not impede emmetropization.[5,6] Furthermore, Yang et al[7], reported that the amount of hyperopic undercorrection was significantly associated with the degree of emmetropization and that only full hyperopic correction inhibited emmetropization. It is possible that our requirement to change the glasses only if there was a change of 0.75D SE in refractive error may have left some of these hyperopic children (wearing glasses) insufficiently undercorrected. The issue of whether partial correction of hyperopia impedes emmetropization remains unanswered.

It is noteworthy that in the glasses group the main reason for deterioration was reduced VA. Because no child in the glasses group failed at 3 years for reasons of VA (tested both with and with correction), cases of earlier deterioration may have occurred for one of a number of reasons: (1) not relaxing into partial hyperopic correction despite wearing glasses; or (2) non-adherence with glasses wear resulting in inability to relax into glasses when worn for

testing, or (3) change in refraction. Deterioration criteria were not reevaluated in new glasses when children deteriorated prior to 3 years but had a change in refraction, therefore the proportion of those who met deterioration criteria in glasses due to a change in refractive error is unknown. Most importantly, deterioration prior to 3 years required meeting criteria in the randomized treatment, whereas failure at 3 years required meeting criteria both with and without refractive correction.

The main limitations of our study were slow recruitment resulting in closure of enrollment before the planned sample size was reached, and greater than expected loss to follow-up, resulting in wide 95% CIs and potentially biased estimates. Informal discussions with investigators suggested that barriers to recruitment included the requirements to have no manifest strabismus and/or age-normal stereoacuity at enrollment in these children with moderate hyperopia. Our estimates of adherence to wearing glasses may have been biased by loss to follow-up because children wearing the glasses successfully may have been more likely to return. Our results are generalizable only to children meeting the eligibility criteria for the present study, specifically those 3 to 5 years of age with moderate hyperopia and normal distance VA, normal near stereoacuity, no measurable manifest strabismus, and followed according to our protocol of follow-up visits at 6-month intervals and treated with glasses when meeting pre-specified criteria for deterioration. In addition, we enrolled only 15 children with hyperopia between +5.00D to +6.00D range in the more hyperopic eye (Table 4B). Future studies might investigate issues that our study did not address, such as symptoms (e.g., asthenopia), accommodative amplitude and accuracy,[17] psychosocial effects,[19,20] and the effect of glasses correction on reading ability in these children.[21]

In summary, our study was inconclusive regarding whether or not immediate prescription of glasses reduces failure for VA or binocularity; our ability to determine whether there is a difference between these treatment approaches was limited by lower than anticipated enrollment and higher than anticipated loss to follow-up. Nevertheless, failure at 3 years (development of reduced VA, reduced near stereoacuity, or manifest strabismus) is not common whether or not glasses are prescribed for hyperopic children (+3.00 to +6.00D) presenting at 3- to 5-years, with age-normal VA, age-normal stereoacuity, and no manifest strabismus. The low failure rate in each group suggests that immediate prescription of glasses (for the prevention of decreased VA, decreased stereoacuity, and manifest strabismus in these children) may not be necessary. Based on the rates of apparent deterioration during 3 years of follow-up, semi-annual monitoring of VA and binocularity may be considered in such children.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgements

A) Funding/Support: Supported by National Eye Institute of National Institutes of Health, Department of Health and Human Services EY011751, EY023198, and EY018810. The funding organization had no role in the design or conduct of this research.

B) Financial Disclosures: No financial disclosures.

C) Other acknowledgements: A full list of participating members of the Pediatric Eye Disease Investigator Group may be found in the Supplemental Material available at AJO.com

References

1. Kulp MT, Holmes JM, Dean TW, et al. Immediate versus delayed spectacle treatment for moderate hyperopia in children 1 to <3 years of age. Ophthalmology. 2018;X(X):XX–XX.
2. Holmes JM, Beck RW, Repka MX, et al. The Amblyopia Treatment Study visual acuity testing protocol. Arch Ophthalmol. 2001;119(9):1345–1353. [PubMed: 11545641]
3. Moke PS, Turpin AH, Beck RW, et al. Computerized method of visual acuity testing: adaptation of the amblyopia treatment study visual acuity testing protocol. Am J Ophthalmol. 2001;132(6):903–909. [PubMed: 11730656]
4. Birch E, Williams C, Drover J, et al. Randot Preschool Stereoacuity Test: normative data and validity. J AAPOS. 2008;12(1):23–26. [PubMed: 17720573]
5. Atkinson J, Braddick O, Bobier B, et al. Two infant vision screening programmes: prediction and prevention of strabismus and amblyopia from photo- and videorefractive screening. Eye (Lond). 1996;10 (Pt 2):189–198. [PubMed: 8776448]
6. Atkinson J, Anker S, Bobier W, et al. Normal Emmetropization in infants with spectacle correction for hyperopia. Invest Ophthalmol Vis Sci. 2000;41(12):3726–3731. [PubMed: 11053269]
7. Yang HK, Choi JY, Kim DH, Hwang JM. Changes in refractive errors related to spectacle correction of hyperopia. PloS one. 2014;9(11):e110663. [PubMed: 25372594]
8. Somer D, Karabulut E, Cinar FG, Altiparmak UE, Unlu N. Emmetropization, visual acuity, and strabismus outcomes among hyperopic infants followed with partial hyperopic corrections given in accordance with dynamic retinoscopy. Eye (Lond). 2014;28(10):1165–1173. [PubMed: 25033902]
9. Wallace DK, Christiansen SP, Sprunger DT, et al. Esotropia and Exotropia Preferred Practice Pattern(R). Ophthalmology. 2018;125(1):P143–p183. [PubMed: 29108746]
10. Chuck RS, Jacobs DS, Lee JK, et al. Refractive Errors & Refractive Surgery Preferred Practice Pattern(R). Ophthalmology. 2018;125(1):P1–P104. [PubMed: 29108748]
11. Barnard GA. Significance tests for 2 × 2 tables. Biometrika. 1947;34(1–2):123–138. [PubMed: 20287826]
12. Ingram RM, Walker C, Wilson JM, Arnold PE, Lucas J, Dally S. A first attempt to prevent amblyopia and squint by spectacle correction of abnormal refractions from age 1 year. Br J Ophthalmol. 1985;69(11):851–853. [PubMed: 3904821]
13. Ingram RM, Arnold PE, Dally S, Lucas J. Results of a randomised trial of treating abnormal hypermetropia from the age of 6 months. Br J Ophthalmol. 1990;74(3):158–159. [PubMed: 2182103]
14. Anker S, Atkinson J, Braddick O, Nardini M, Ehrlich D. Non-cycloplegic refractive screening can identify infants whose visual outcome at 4 years is improved by spectacle correction. Strabismus. 2004;12(4):227–245. [PubMed: 15545141]
15. Adams WE, Leske DA, Hatt SR, Holmes JM. Defining real change in measures of stereoacuity. Ophthalmology. 2009;116(2):281–285. [PubMed: 19091410]
16. Kulp MT, Ying G-S, Huang J, et al. Associations between hyperopia and other vision and refractive error characteristics. Optom Vis Sci. 2014; 91(4):383–389. [PubMed: 24637486]
17. Ciner EB, Kulp MT, Maguire MG, et al. Visual function of moderately hyperopic 4-and 5-year-old children in the vision in preschoolers - hyperopia in preschoolers study. Am J Ophthalmol. 2016;170:143–152 [PubMed: 27477769]
18. Ingram RM, Gill LE, Lambert TW. Effect of spectacles on changes of spherical hypermetropia in infants who did, and did not, have strabismus. Br J Ophthalmol. 2000;84(3):324–326. [PubMed: 10684846]
19. Walline JJ, Sinnott L, Johnson ED, Ticak A, Jones SL, Jones LA. What do kids think about kids in eyeglasses? Ophthalmic Physiol Opt. 2008;28(3):218–224. [PubMed: 18426420]
20. Yamada T, Hatt SR, Leske DA, Holmes JM. Spectacle wear in children reduces parental health-related quality of life. Journal of AAPOS : the official publication of the American Association for

Pediatric Ophthalmology and Strabismus/American Association for Pediatric Ophthalmology and Strabismus. 2011;15(1):24–28.

21. VIP-HIP Study Group, Kulp MT, Ciner E, et al. Uncorrected Hyperopia and Preschool Early Literacy: Results of the Vision in Preschoolers-Hyperopia in Preschoolers (VIP-HIP) Study. Ophthalmology. 2016;123(4):681–689. [PubMed: 26826748]

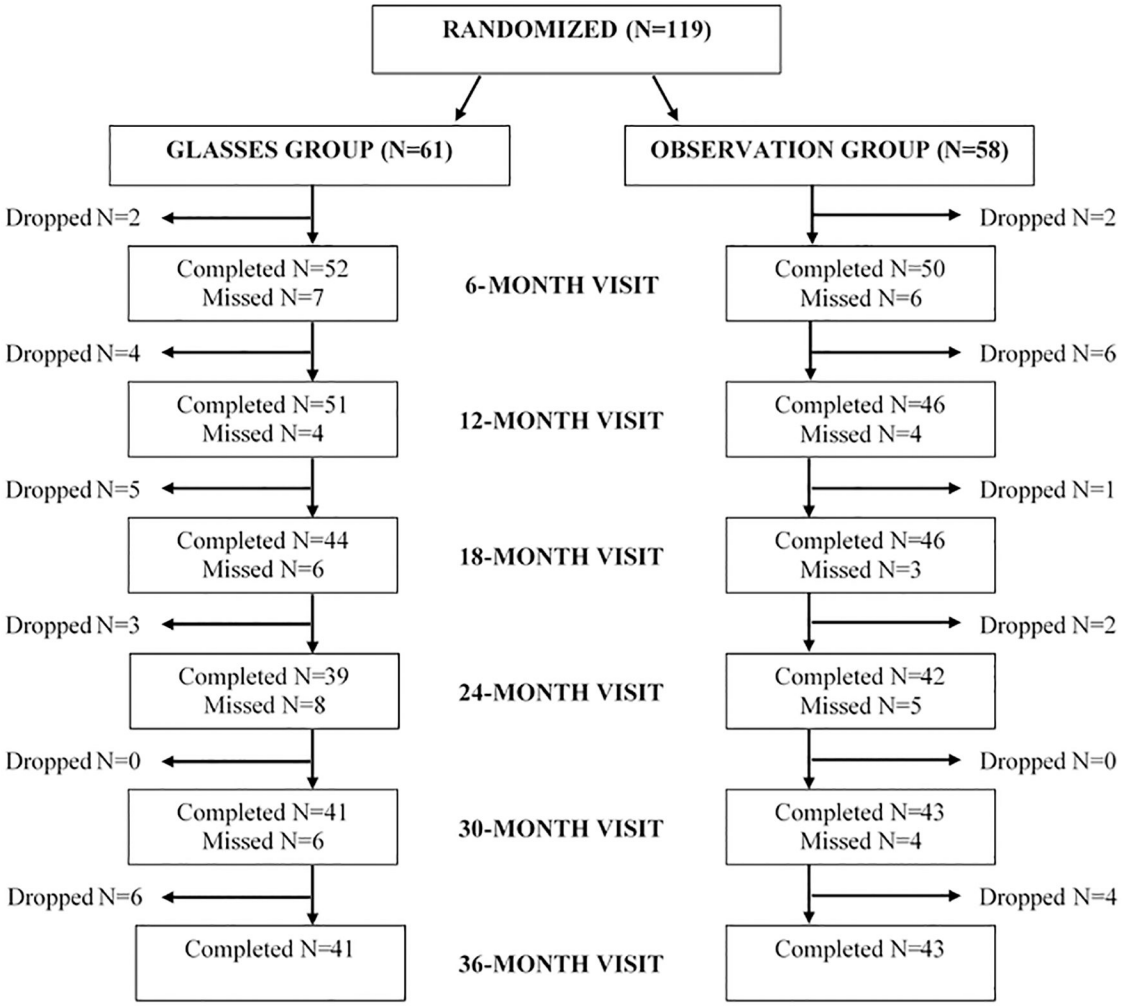

Figure 1.

Patient flow though randomized clinical trial of immediate versus delayed glasses for moderate hyperopia in children 3 to 5 years of age. One participant in the glasses group and one in the observation (delayed glasses) group completed the 36-month visit but did not complete the required additional follow-up visit to reassess failure after receiving a new glasses prescription. These participants are not reported as dropped in the figure.

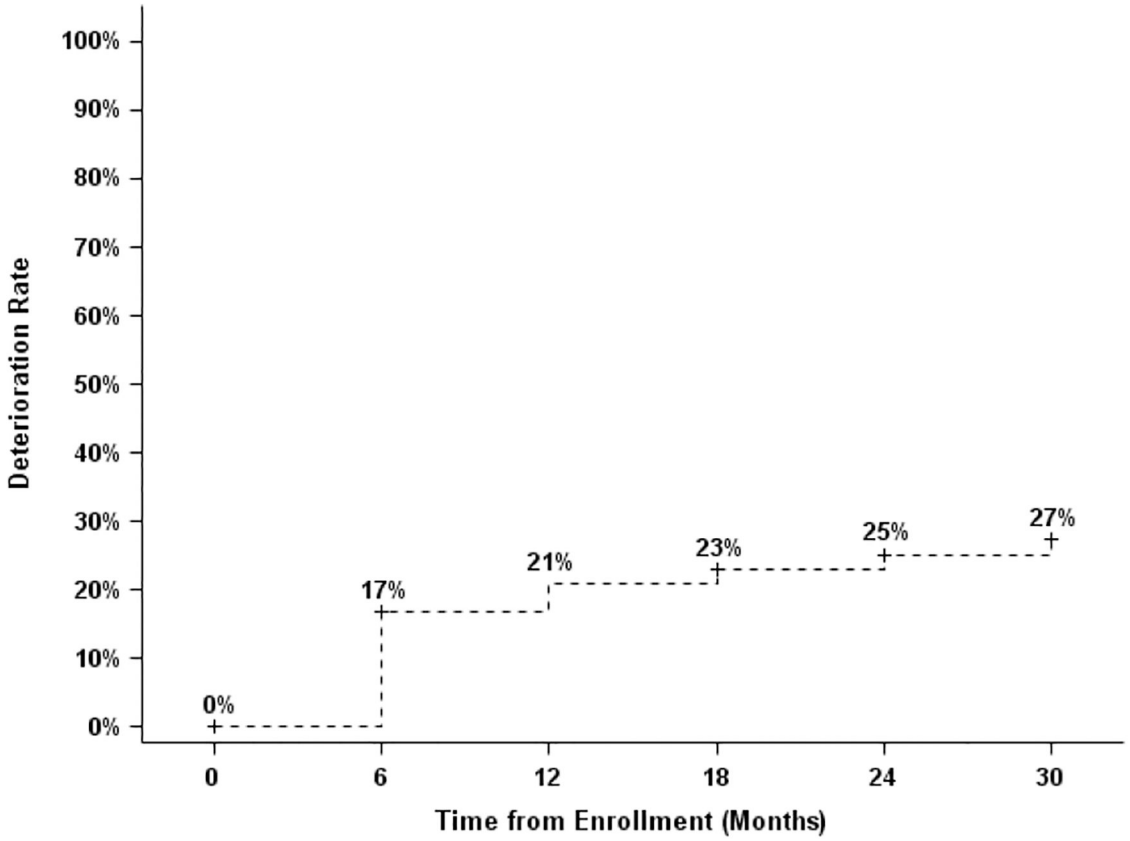

Figure 2.

Estimates of Deterioration Rate in Observation (delayed glasses) Group during a randomized clinical trial of immediate versus delayed glasses for moderate hyperopia in children 3 to 5 years of age

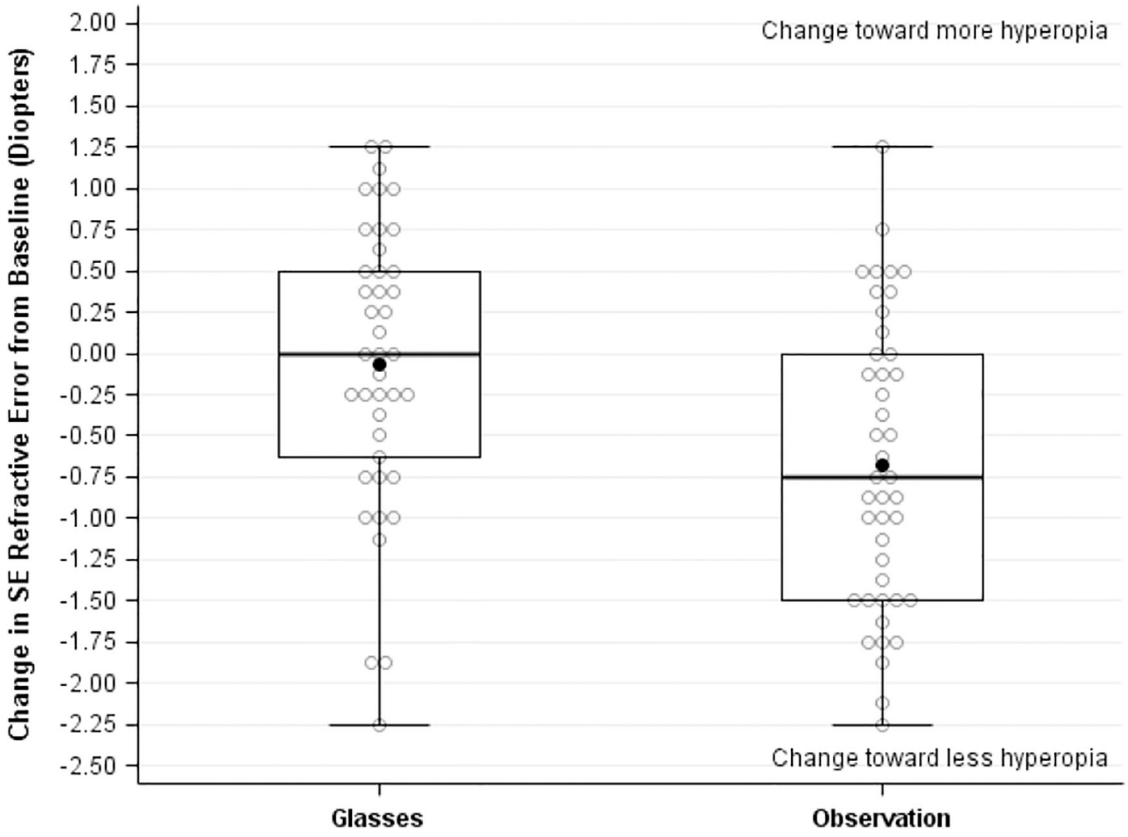

Figure 3A.

Change in Refractive Error from Baseline to 3 Years for Eye with Greater Hyperopia at Baseline in a randomized clinical trial of immediate versus delayed glasses for moderate hyperopia in children 3 to 5 years of age. The top and bottom of each box represents the 75th and 25th percentiles of the data, respectively. Group medians are represented by the bold horizontal lines in each box and group means by the filled circles. The bars extending above and below each box represent 1.5 times the interquartile range (difference between the 75th and 25th percentiles), or the maximum (or minimum) observed value within the range if not as extreme as the calculated value. Open circles represent reported refractive errors.

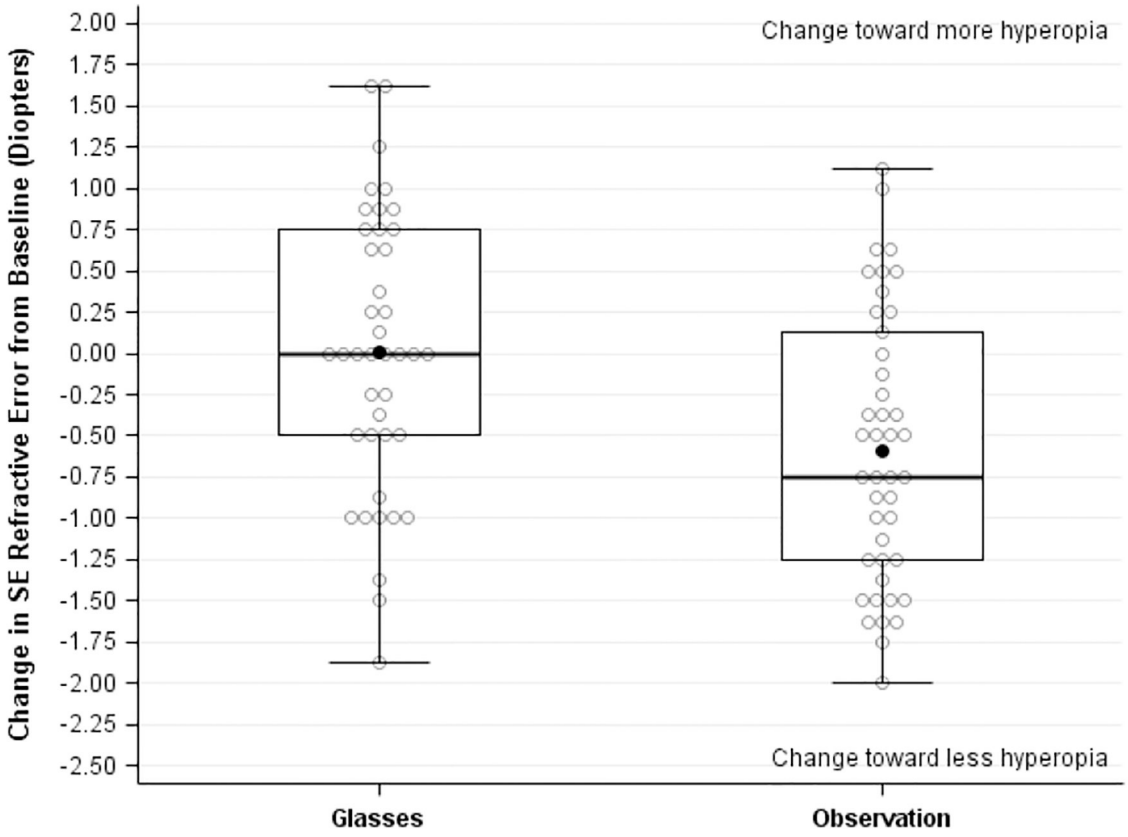

Figure 3B.

Change in Refractive Error from Baseline to 3 Years for Eye with Less Hyperopia at Baseline in a randomized clinical trial of immediate versus delayed glasses for moderate hyperopia in children 3 to 5 years of age. The top and bottom of each box represents the 75th and 25th percentiles of the data, respectively. Group medians are represented by the bold horizontal lines in each box and group means by the filled circles. The bars extending above and below each box represent 1.5 times the interquartile range (difference between the 75th and 25th percentiles), or the maximum (or minimum) observed value within the range if not as extreme as the calculated value. Open circles represent reported refractive errors.

Table 1:

Eligibility Criteria in a randomized clinical trial of immediate versus delayed glasses for moderate hyperopia in children 3 to 5 years of age.

The following criteria must be met for the patient to be enrolled in the study:	
1	Age 36 to <72 months
2	Spherical equivalent refractive error between +3.00D and +6.00D (by cycloplegic refractions) in either eye
3	Astigmatism ≤1.50D in both eyes
4	Spherical equivalent anisometropia ≤1.50D
5	Normal uncorrected monocular visual acuity for age (20/50 or better for age 3 years, 20/40 or better for age 4 years, and 20/32 or better for age 5 years) in each eye using the Amblyopia Treatment Study HOTV© visual acuity testing protocol without cycloplegia
6	Zero (0) or 1 logMAR line interocular difference in uncorrected visual acuity without cycloplegia using the Amblyopia Treatment Study HOTV© visual acuity testing protocol without cycloplegia
7	Normal near stereoacuity for age (400 arcsec or better for age 3 years, 200 arcsec or better for ages 4 or 5 years) using the Randot Preschool Stereoacuity test
8	Gestational age ≥32 weeks
9	Investigator is willing to prescribe glasses per protocol or observe hyperopia untreated for 3 years unless specific criteria for deterioration (Table 2) are confirmed
10	Parent understands the protocol and is willing to accept randomization to either glasses or no glasses initially, and is willing to wear glasses as prescribed or accept that glasses will not be prescribed by the investigator unless specific deterioration criteria (Table 2) are confirmed
11	Parent has phone (or access to phone) and is willing to be contacted by Jaeb Center staff
12	Relocation outside of area of an active PEDIG site for this study within the next 36 months is not anticipated.
13	No measurable manifest strabismus at distance (3 meters) or near (1/3 meter) by cover/uncover testing. Heterophoria is eligible.
14	No previously documented strabismus (parental report must be confirmed by investigator)
15	No clinical evidence of manifest or latent nystagmus
16	No prior treatment of refractive error with glasses or contact lenses unless duration of glasses or contact wear was one week or less and occurred more than 2 months prior to enrollment
17	No prior intraocular, refractive, or extraocular surgery
18	No prior treatment for amblyopia
19	No prior therapy for vergence/accommodation
20	No parental concerns over learning or development
21	No ocular co-morbidity that may reduce visual acuity
22	No symptoms of blur or asthenopia
23	No developmental delay, diagnosed by pediatrician or Individualized Education Program (IEP)
24	No known neurological anomalies (e.g. cerebral palsy, Down syndrome)

Table 2:

Deterioration Criteria (Prior to 3-Year Outcome; Assessed in Randomized Treatment) in a randomized clinical trial of immediate versus delayed glasses for moderate hyperopia in children 3 to 5 years of age.

Deterioration

The participant was considered to have met deterioration criteria if ANY of the following criteria were met while wearing randomized correction by an unmasked examiner at a protocol-specified or non-protocol mandated visit after randomization but prior to the 3-year outcome exam, and confirmed by a retest performed by a masked examiner.

1. Any measurable manifest strabismus detected by cover/uncover test in primary gaze at distance (3 meters) or at near (1/3 meter)

2. Distance VA below age norms in either eye (see below)

3. ≥2 logMAR lines of IOD if VA is 20/25 or worse in the better-seeing eye (applies to IOD in either with or without correction but not one eye with and the other without)

4. ≥3 logMAR lines of IOD if VA is 20/20 or better in the better-seeing eye (applies to IOD in either with or without correction but not one eye with and the other without)

5. Stereoacuity at near by Randot Preschool Stereoacuity test below age normal values (see below)

6. Non-protocol treatment is received in the absence of meeting deterioration criteria

Age Normal Values for Stereoacuity and VA		
Age range	***Stereoacuity Level Needed to Meet Deterioration Criteria (arcsec)[4]***	***VA Level Needed to Meet Deterioration Criteria***
36–47 months (3 years)	800 or worse	20/63 or worse
48–59 months (4 years)	400 or worse	20/50 or worse
60–71 months (5 years)	400 or worse	20/40 or worse
72–83 months (6 years)	200 or worse	20/40 or worse
≥84 months (≥7 years)	100 or worse	20/32 or worse

VA = visual acuity; logMAR = logarithm of minimum angle of resolution; IOD = interocular difference; arcsec = seconds of arc

Table 3:

Failure Criteria (At the 3-Year Outcome Visit, Assessed With and Without Hyperopic Correction in Trial Frames, Requiring Failure and Confirmation With and Without Correction) in a randomized clinical trial of immediate versus delayed glasses for moderate hyperopia in children 3 to 5 years of age.

Failure (primary outcome)

The participant was considered to have met failure criteria if ANY of the following criteria (with the exception of strabismus surgery prior to the 3-year outcome exam) were met during testing by a masked examiner at the 3-year examination both with and without trial frames (without prism or bifocal), and the criteria was confirmed by a retest, with and without trial frames.

1. Any measurable manifest strabismus in primary gaze at distance (3 meters) or at near (1/3 meter) not correctable with distance refractive correction alone

2. Strabismus surgery prior to the 36-month outcome exam

3. Distance VA below age norms in either eye

4. ≥2 logMAR lines of IOD if VA is 20/25 or worse in the better-seeing eye (applies to IOD in either with or without correction but not one eye with and the other without)

5. ≥3 logMAR lines of IOD if VA is 20/20 or better in the better-seeing eye (applies to IOD in either with or without correction but not one eye with and the other without)

6. Stereoacuity measured at near by Randot Preschool Stereoacuity test below age normal values

Age Normal Values for Stereoacuity and VA		
Age range	***Stereoacuity Level Needed to Meet Failure Criteria (arcsec)***	***VA Level Needed to Meet Failure Criteria***
36–47 months (3 years)	800 or worse	20/63 or worse
48–59 months (4 years)	400 or worse	20/50 or worse
60–71 months (5 years)	400 or worse	20/40 or worse
72–83 months (6 years)	200 or worse	20/40 or worse
≥84 months (≥7 years)	100 or worse	20/32 or worse

VA = visual acuity; logMAR = logarithm of minimum angle of resolution; IOD = interocular difference; arcsec = seconds of arc

Table 4A:

Baseline Characteristics of Enrolled Participants in a randomized clinical trial of immediate versus delayed glasses for moderate hyperopia in children 3 to 5 years of age.

	Glasses (N=61)		Observation (N=58)	
	N	**%**	**N**	**%**
Female	38	62%	32	55%
Race/Ethnicity				
Asian	2	3%	0	0%
Black/African American	12	20%	14	24%
Hispanic	13	21%	7	12%
White	34	56%	35	60%
More than one race	0	0%	1	2%
Unknown/not reported	0	0%	1	2%
Age at Enrollment				
3 years	19	31%	20	34%
4 years	31	51%	30	52%
5 years	11	18%	8	14%
Mean (SD), years	4.4 (0.7)		4.4 (0.7)	
Family History of Amblyopia[a]	16	26%	17	29%
Family History of Strabismus[b]	11	18%	16	28%
Diagnosis of ADHD	0	0%	0	0%

ADHD = Attention-Deficit/Hyperactivity Disorder; SD = standard deviation

[a]Family history of amblyopia was not available for 2 (3%) participants in glasses group and 3 (5%) in observation group.

[b]Family history of strabismus was not available for 2 (3%) participants in glasses group and 1 (2%) in the observation group.

Table 4B:

Ocular Characteristics at Baseline for Enrolled Participants in a randomized clinical trial of immediate versus delayed glasses for moderate hyperopia in children 3 to 5 years of age.

	Glasses (N=61)		Observation (N=58)	
	N	%	N	%
SE Refractive Error: More hyperopic eye				
+2.00D to <+3.00D	0	0%	0	0%
+3.00D to <+4.00D	37	61%	32	55%
+4.00D to <+5.00D	16	26%	19	33%
+5.00D to +6.00D	8	13%	7	12%
Mean (SD), diopters	3.93 (0.71)		3.94 (0.74)	
SE Refractive Error: Less hyperopic eye				
+2.00D to <+3.00D	10	16%	10	17%
+3.00D to <+4.00D	34	56%	30	52%
+4.00D to <+5.00D	12	20%	13	22%
+5.00D to +6.00D	5	8%	5	9%
Mean (SD), diopters	3.60 (0.78)		3.59 (0.81)	
Anisometropia				
0.00D to <+0.50D	42	69%	39	67%
+0.50D to <+1.00D	16	26%	14	24%
+1.00D to +1.50D	3	5%	5	9%
Mean (SD), diopters	0.33 (0.36)		0.34 (0.34)	
Astigmatism: More astigmatic eye				
0.00D to <+0.50D	29	48%	29	50%
+0.50D to <+1.00D	23	38%	18	31%
+1.00D to +1.50D	9	15%	11	19%
Mean (SD), diopters	0.45 (0.45)		0.44 (0.44)	
Astigmatism: Less astigmatic eye				
0.00D to <+0.50D	40	66%	41	71%
+0.50D to <+1.00D	14	23%	12	21%
+1.00D to +1.50D	7	11%	5	9%
Mean (SD), diopters	0.32 (0.42)		0.25 (0.36)	
Distance Visual Acuity: Better-seeing Eye				
20/16	5	8%	3	5%
20/20	16	26%	18	31%
20/25	25	41%	18	31%
20/32	9	15%	13	22%
20/40	6	10%	6	10%
20/50	0	0%	0	0%
Mean (SD), logMAR	0.09 (0.11)		0.10 (0.11)	
Distance Visual Acuity: Worse-seeing Eye				
20/16	2	3%	0	0%

	Glasses (N=61)		Observation (N=58)	
	N	**%**	**N**	**%**
20/20	7	11%	7	12%
20/25	26	43%	25	43%
20/32	15	25%	15	26%
20/40	8	13%	9	16%
20/50	3	5%	2	3%
Mean (SD), logMAR	0.15 (0.11)		0.16 (0.10)	
Stereoacuity at Near				
40	9	15%	7	12%
60	21	34%	12	21%
100	13	21%	15	26%
200	12	20%	16	28%
400	6	10%	6	10%
Nil	0	0%	1	2%
Failed pretest	0	0%	1	2%
Median, seconds of arc	100		100	

D = diopters; SD = standard deviation; SE = spherical equivalent; logMAR = logarithm of minimum angle of resolution

Table 5A:

Baseline Characteristics Among Completers and Non-completers in a randomized clinical trial of immediate versus delayed glasses for moderate hyperopia in children 3 to 5 years of age.

	Completed (N=84)		Not Completed (N=35)	
	N	**%**	**N**	**%**
Female	50	60%	20	57%
Race/Ethnicity				
Asian	1	1%	1	3%
Black/African American	9	11%	17	49%
Hispanic	13	15%	7	20%
White	60	71%	9	26%
More than one race	1	1%	0	0%
Unknown/not reported	0	0%	1	3%
Age at Enrollment				
3 years	33	39%	6	17%
4 years	36	43%	25	71%
5 years	15	18%	4	11%
Mean (SD), years	4.4 (0.7)		4.5 (0.6)	
Family History of Amblyopia[a]	24	29%	9	26%
Family History of Strabismus[b]	21	25%	6	17%
Diagnosis of ADHD	0	0%	0	0%

ADHD = Attention-Deficit/Hyperactivity Disorder; SD = standard deviation

[a]Family history of amblyopia was not available for 5 (6%) participants who completed the 3-year primary outcome visit and 0 (0%) participants who did not complete the 3-year primary outcome visit.

[b]Family history of strabismus was not available for 3 (4%) participants who completed the 3-year primary outcome visit and 0 (0%) participants who did not complete the 3-year primary outcome visit.

Table 5B:

Ocular Characteristics at Baseline for Completers and Non-completers in a randomized clinical trial of immediate versus delayed glasses for moderate hyperopia in children 3 to 5 years of age.

	Completed (N=84)		Not Completed (N=35)	
	N	%	N	%
SE Refractive Error: More hyperopic eye				
+2.00D to <+3.00D	0	0%	0	0%
+3.00D to <+4.00D	47	56%	22	63%
+4.00D to <+5.00D	24	29%	11	31%
+5.00D to +6.00D	13	15%	2	6%
Mean (SD), diopters	3.96 (0.78)		3.89 (0.58)	
SE Refractive Error: Less hyperopic eye				
+2.00D to <+3.00D	15	18%	5	14%
+3.00D to <+4.00D	45	54%	19	54%
+4.00D to <+5.00D	15	18%	10	29%
+5.00D to +6.00D	9	11%	1	3%
Mean (SD), diopters	3.61 (0.85)		3.58 (0.65)	
Anisometropia				
0.00D to <+0.50D	54	64%	27	77%
+0.50D to <+1.00D	23	27%	7	20%
+1.00D to +1.50D	7	8%	1	3%
Mean (SD), diopters	0.35 (0.37)		0.31 (0.29)	
Astigmatism: More astigmatic eye				
0.00D to <+0.50D	41	49%	17	49%
+0.50D to <+1.00D	29	35%	12	34%
+1.00D to +1.50D	14	17%	6	17%
Mean (SD), diopters	0.44 (0.44)		0.47 (0.44)	
Astigmatism: Less astigmatic eye				
0.00D to <+0.50D	58	69%	23	66%
+0.50D to <+1.00D	19	23%	7	20%
+1.00D to +1.50D	7	8%	5	14%
Mean (SD), diopters	0.27 (0.38)		0.32 (0.42)	
Distance Visual Acuity: Better-seeing Eye				
20/16	6	7%	2	6%
20/20	24	29%	10	29%
20/25	29	35%	14	40%
20/32	15	18%	7	20%
20/40	10	12%	2	6%
20/50	0	0%	0	0%
Mean (SD), logMAR	0.10 (0.11)		0.09 (0.10)	
Distance Visual Acuity: Worse-seeing Eye				
20/16	1	1%	1	3%

	Completed (N=84)		Not Completed (N=35)	
	N	**%**	**N**	**%**
20/20	12	14%	2	6%
20/25	33	39%	18	51%
20/32	23	27%	7	20%
20/40	10	12%	7	20%
20/50	5	6%	0	0%
Mean (SD), logMAR	0.15 (0.11)		0.15 (0.10)	
Stereoacuity at Near				
40	11	13%	5	14%
60	24	29%	9	26%
100	20	24%	8	23%
200	17	20%	11	31%
400	10	12%	2	6%
Nil	1	1%	0	0%
Failed pretest	1	1%	0	0%
Median, seconds of arc	100		100	

D = diopters; SD = standard deviation; SE = spherical equivalent; logMAR = logarithm of minimum angle of resolution

Table 6:

Glasses Wear Adherence in the Glasses Group by Visit in a randomized clinical trial of immediate versus delayed glasses for moderate hyperopia in children 3 to 5 years of age.

	6-month		12-month		18-month		24-month		30-month		36-month	
	N	%	N	%	N	%	N	%	N	%	N	%
Excellent (>75%)	19	37%	31	62%	29	66%	25	64%	30	73%	27	66%
Good (>50% to 75%)	14	27%	7	14%	8	18%	8	21%	5	12%	8	20%
Fair (26% to 50%)	14	27%	7	14%	4	9%	6	15%	2	5%	1	2%
Poor (>1% to <26%)	4	8%	3	6%	1	2%	0	0%	1	2%	2	5%
Not at all (≤1%)	0	0%	2	4%	2	5%	0	0%	3	7%	3	7%

Table 7:

Failure Criteria at 3 Years in a randomized clinical trial of immediate versus delayed glasses for moderate hyperopia in children 3 to 5 years of age.

	Glasses (N=41)		Observation (N=43)	
	N	**%**	**N**	**%**
3-Year Failure Status[a]				
Failure	5	12%	4	9%
Not failure	36	88%	39	91%
Difference in Proportions (glasses minus observation) with 95% Confidence Interval	3% (−12% to 18%)			
Barnard's Exact Test for Difference in Proportions	P = 0.72			
Reasons for Failure at 3-Year Exam[b]				
Stereoacuity	5	12%	3	7%
Strabismus	0	0%	1[c]	2%
Visual acuity	0	0%	1	2%

[a] Failure had to be met and confirmed with and without trial frames.

[b] Failure criteria may have been met for more than one reason. Denominator is the number of participants who completed the study.

[c] One participant had esotropia.

Table 8:

Primary Outcome and Alternative Statistical Approaches in a randomized clinical trial of immediate versus delayed glasses for moderate hyperopia in children 3 to 5 years of age.

Analysis Approach[a]	**Difference (Glasses – Observation Group)**	**95% CI**
Primary Analysis[b] **No imputation for missing data.**	**3%**	**–12% to 18%**
Excluding ineligible participants[b,c]	3%	–13% to 18%
Excluding 3-year exams completed outside the protocol window (36 ±2 months, N=10)[b]	4%	–11% to 20%
Failure based on meeting failure criteria on the first or single test (not including results of retest, and not excluding participants who did not have a retest).[b]	8%	–8% to 25%
Multiple imputation Three-year failure status imputed for 35 participants with incomplete data at 3 years	4%	–11% to 18%
Include age at the 36-month visit as an adjustment covariate in the model.[b,d]	4%	–10% to 17%

CI = confidence interval

[a] For analyses other than the primary analysis, the modification to the analysis is specified.

[b] Participants were included in analysis if at least one test of visual acuity, stereoacuity, or ocular alignment was obtained (one or more parameters). The outcome determination was based on all available data for visual acuity, stereoacuity, and ocular alignment, i.e. test and retest when available. If a required test or retest was not completed for a parameter, the participant was classified as not meeting failure criterion (or criteria) for that parameter.

[c] Two participants were enrolled despite not meeting eligibility criteria for stereoacuity; both were randomized to observation. Neither met failure criteria at 3 years.

[d] Barnard's exact test does not allow for the adjustment of covariates. Binomial regression was used to compare failure rates in treatment groups.

Table 9:

Failure at 3 Years by Treatment Group According to Subgroups of Baseline Factors in a randomized clinical trial of immediate versus delayed glasses for moderate hyperopia in children 3 to 5 years of age.

	Glasses			Observation		
	Failed N	Total N	% Failed	Failed N	Total N	% Failed
Race						
Non-white	2	12	17%	1	12	8%
White	3	29	10%	3	31	10%
Gender						
Female	4	26	15%	3	24	13%
Male	1	15	7%	1	19	5%
Family History of Amblyopia						
Yes	3	12	25%	0	12	0%
No	2	29	7%	4	31	13%
Family History of Strabismus						
Yes	3	9	33%	0	12	0%
No	2	32	6%	4	31	13%
SE Anisometropia						
0.00D to <+0.50D	3	27	11%	4	27	15%
+0.50D to <+1.00D	2	11	18%	0	12	0%
+1.00D to +1.50D	0	3	0%	0	4	0%
Mean Refractive Error at Enrollment (D)						
+2.50D to <+4.00D[a]	3	29	10%	2	29	7%
+4.00D to <+5.00D	1	7	14%	1	8	13%
+5.00D to +6.00D	1	5	20%	1	6	17%

D = diopters

[a]Participants were eligible if moderate hyperopia (+3.00D to +6.00D SE) was reported in at least one eye. Data are presented as the mean of the two eyes of each participant. Refractive error in the less hyperopic eye was less than +3.00D in 20 participants who completed the 3-year primary outcome visit, yielding a minimum mean of +2.50D.

Table 10:

Deterioration Criteria Met (Prior to 3 Years) in a randomized clinical trial of immediate versus delayed glasses for moderate hyperopia in children 3 to 5 years of age.

	Glasses (N=61)		Observation (N=58)	
	N	**%**	**N**	**%**
Actuarial Estimate of Cumulative Deterioration Rate	16	29%	14	27%
Reasons for Deterioration[a]				
Stereoacuity	4	7%	7	12%
Strabismus[b]	0	0%	2	3%
Visual Acuity	13	21%	5	9%
Treatment due to parental concern[c]	0	0%	3	5%
Treatment prescribed against protocol[d]	1	2%	0	0%

[a]Denominator is the number of enrolled participants.

[b]Esotropia was reported for both participants who met deterioration criteria due to strabismus.

[c]Three participants received glasses: one for burning eyes during near work, one for squinting, and one for struggles with near tasks.

[d]Participant prescribed patching for concerns of amblyopia.

Table 11:

Change in Refractive Error from Baseline to 3 Years in a randomized clinical trial of immediate versus delayed glasses for moderate hyperopia in children 3 to 5 years of age.

	More Hyperopic Eye		Less Hyperopic Eye	
	Glasses (N=41)	**Observation (N=43)**	**Glasses (N=41)**	**Observation (N=43)**
Mean change in SE refractive error from baseline to 3 years[a] (D)	−0.07	−0.67	0	−0.58
Difference in means (99% CI)	0.60 (0.11 to 1.09)		0.58 (0.10 to 1.06)	
Test for difference in means[b,c]	P = 0.002		P = 0.002	
Proportion where hyperopia reduced by 1.00D or more over 3 years	17%	42%	20%	37%
Difference in percentages (99% CI)	−25% (−49% to 1%)		−18% (−42% to 8%)	
Test for difference in percentages[c,d]	0.013		0.08	

SE = spherical equivalent; D = diopters; CI = confidence interval

[a] Negative values indicate a shift in the myopic direction.

[b] An analysis of covariance model adjusting for refractive error at enrollment was used to compare mean change in refractive error between treatment groups.

[c] Results are considered statistically significant if p<0.01.

[d] Barnard's exact test was used to compare proportions between treatment groups.

Table 12:

Visual Acuity at 3 Years in a randomized clinical trial of immediate versus delayed glasses for moderate hyperopia in children 3 to 5 years of age.

	Glasses (N=41)	Observation (N=43)
Mean distance VA in better-seeing eye (logMAR)[a,b]	–0.06	–0.07
Difference in means (99% CI)	0.01 (−0.02 to 0.04)	
Test for difference in means[c,f]	P = 0.22	
Mean distance VA in worse-seeing eye (logMAR)[a,b]	–0.03	–0.01
Difference in means (99% CI)	–0.02 (−0.06 to 0.03)	
Test for difference in means[c,f]	P = 0.41	
Proportion who failed to meet age-normal VA at distance[g]	0 (0%)	1 (2%)
Difference in percentages (99% CI)	–2% (−18% to 13%)	
Test of difference in percentages[f,h]	P = 0.51	
Proportion with amblyopia at distance[e]	0 (0%)	1 (2%)
Difference in percentages (99% CI)	–2% (−18% to 13%)	
Test of difference in percentages[f,h]	P = 0.51	
Mean Binocular near VA (logMAR)[b,i]	0.01	0.04
Difference in means (99% CI)	–0.04 (−0.12 to 0.05)	
Test for difference in means[d,f]	P = 0.21	

CI = confidence interval; logMAR = logarithm of minimum angle of resolution; VA = visual acuity

[a] Evaluated the best of the values reported with and without trial frames, during initial assessment and retest

[b] Converted Snellen equivalents to logMAR equivalents (in parentheses) as follows: 20/16 (−0.1), 20/20 (0), 20/25 (0.1), 20/32 (0.2), 20/40 (0.3)

[c] An analysis of covariance model, adjusting for age at the 3-year visit and visual acuity at baseline, was used to compare mean visual acuity between treatment groups.

[d] An analysis of covariance model, adjusting for age at the 3-year visit, was used to compare mean visual acuity between treatment groups.

[e] Participants were classified as having amblyopia if any of the following criteria were met: 1) the interocular difference was ≥2 logMAR lines of IOD if VA is 20/25 or worse in the better-seeing eye, or 2) the interocular differences was ≥3 logMAR lines of IOD if VA is 20/20 or better in the better-seeing eye. 3) VA less than age normal in each eye (presumed bilateral amblyopia)

[f] Results are considered statistically significant if p<0.01.

[g] Participants were classified as failing to meet age-normal visual acuity if, for either eye, distance visual acuity was below age-normal values both with and without trial frames, during initial assessment and re-test.

[h] Barnard's exact test was used to compare proportions between treatment groups.

[i] Assessment completed in randomized correction.

Table 13:

Manifest Strabismus and Stereoacuity at 3 Years in a randomized clinical trial of immediate versus delayed glasses for moderate hyperopia in children 3 to 5 years of age.

	Glasses (N=41)	Observation (N=43)
Proportion with manifest strabismus with and without correction	0 (0%)	1 (2%)
Difference in percentages (99% CI)	–2% (−18% to 13%)	
Test of difference in percentages[a,b]	P = 0.51	
Mean stereoacuity[c,d]	1.76	1.75
Difference in means (99% CI)	0.02 (−0.11 to 0.14)	
Test for difference in means[b,e]	P = 0.74	
Proportion who failed to meet age-normal stereoacuity[f]	5 (12%)	3 (7%)
Difference in percentages (99% CI)	5% (−14% to 26%)	
Test of difference in percentages[a,b]	P = 0.53	

CI = confidence interval

[a] Barnard's exact test used to compare proportions between treatment groups

[b] Results are considered statistically significant if p<0.01.

[c] Evaluated the best of the values reported with and without trial frames, during initial assessment and retest

[d] Converted seconds of arc to logarithm of seconds of arc (in parentheses) as follows: 40 (1.60), 60(1.78), 100 (2.00), 200 (2.30), 400 (2.60), 800 (2.90), Nil (3.20)

[e] An analysis of covariance model was used to compare mean change in stereoacuity between treatment groups. The analysis controlled for age at the 3-year visit, anisometropia at the most recent visit, and stereoacuity at enrollment.

[f] Participants were classified as failing to meet age-normal stereoacuity if near stereoacuity was below age-normal values both with and without trial frames, during initial assessment and re-test.