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Impact of Vision Impairment and Ocular Morbidity and Their Treatment on Depression and Anxiety in Children

A Systematic Review

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Topic: This systematic review and meta-analysis summarizes existing evidence to establish whether vision impairment, ocular morbidity, and their treatment are associated with depression and anxiety in children.

Clinical Relevance: Understanding and quantifying these associations support early detection and management of mental health symptoms in children with vision impairment and ocular morbidity. Additionally, this review provides evidence in favor of insurance coverage for timely strabismus surgery.

Methods: We searched 9 electronic databases from inception through February 18, 2021, including observational and interventional studies assessing whether vision impairment, ocular morbidity, or both and their treatment are associated with depression, anxiety, or both in children. We used narrative synthesis and meta-analysis with the residual maximum likelihood method. A protocol was registered and published on The International Prospective Register of Systematic Reviews (identifier: CRD42021233323).

Results: Among 28 992 studies, 28 956 studies (99.9%) were excluded as duplicates or unrelated content. Among 36 remaining studies, 21 studies (58.3%) were observational studies concerning vision impairment, 8 studies (22.2%) were observational studies concerning strabismus, and 7 studies (19.4%) were interventional studies. Vision impaired children demonstrated significantly higher scores of depression (standard mean difference [SMD], 0.57; 95% confidence interval [CI], 0.26−0.89; 11 studies) and anxiety (SMD, 0.62; 95% CI, 0.40−0.83; 14 studies) than normally sighted children. In particular, children with myopia demonstrated higher scores of depression (SMD, 0.58; 95% CI, 0.36−0.81; 6 studies) than normally sighted children. Strabismus surgery significantly improved symptoms of depression (SMD, 0.59; 95% CI, 0.12−1.06; 3 studies) and anxiety (SMD, 0.69; 95% CI, 0.25−1.14; 4 studies) in children.

Conclusion: Among children, vision impairment is associated with greater symptoms of depression and anxiety. Surgical treatment of strabismus improved these symptoms. Further randomized controlled trials exploring the impact of public health measures for myopia correction on mental health in children are needed. Scaling up access to strabismus surgery could improve the mental health of affected children. *Ophthalmology 2022;129:1152-1170 © 2022 by the American Academy of Ophthalmology. This is an open access article under the CC BY license (http://creativecommons.org/licenses/by/4.0/).*

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Vision impairment (visual acuity, <6/12) or blindness (visual acuity, <3/60) affects at least 2.2 billion people worldwide, including an estimated 19 million children 0 to 14 years of age, among whom 1.4 million have irreversible blindness.[1,2] Children with vision impairment tend to participate in fewer physical activities,[3] to have lower academic achievement,[4] and to be more socially isolated.[5,6] For these reasons, vision impairment may adversely affect the mental health of children.[7] Depression and anxiety are 2 common psychiatric disorders associated with vision impairment.[8−11] An existing large body of work focuses on the impact of vision impairment on depression and anxiety in older adults. A recent systematic review found that the prevalence of depression among patients with vision impairment older than 65 years was 25%,[8] far higher than that among unaffected persons.[12] It is also estimated that 15.6% of older adults with vision impairment face subthreshold anxiety and that 7.5% receive a diagnosis of an anxiety disorder.[9]

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Although the prevalences of ocular morbidity, depression, and anxiety are lower among children than among adults, the total burden of these conditions is higher because of the length of time children are affected if the underlying disorders are not identified and corrected. Furthermore, adolescents experiencing subthreshold depressive symptoms have an increased risk of mental health problems developing later in life, such as depression, anxiety, substance dependence, and suicide[13–16]; however, studies investigating mental health in vision impaired children are relatively few, and their findings are inconsistent. A previous systematic review found that the overall association between vision impairment and mental health among children and young adults was inconsistent because of differences in research aims, study design, and definitions of visual impairment among the included studies.[7]

Beyond vision impairment, common chronic ocular morbidities such as strabismus[17] also may cause adverse cosmetic, functional, and psychological consequences among children,[18–20] eventually affecting their development and maturation. Although much research has been conducted on the impact of strabismus on the quality of life and mental health of adults, the effect of strabismus on children has not been studied extensively. A school-based study in China demonstrated that children with strabismus showed a significantly higher prevalence of indicators of depression and anxiety than the healthy control group.[20] Several interventional studies also have shown that strabismus surgery not only offers cosmetic benefits but also can improve the psychosocial health and quality of life of children.[21–24]

All of these findings suggest a need to understand the impact of vision impairment and ocular morbidity and their treatment on depression and anxiety in children, providing evidence to guide policies such as insurance coverage for strabismus surgery, which in some countries is excluded frequently as a cosmetic procedure. This systematic review analyzed published literature to establish whether vision impairment and ocular morbidity and their treatment are associated with depression and anxiety in children.

Methods

We followed the Preferred Reporting Items for Systematic Review and Meta-Analysis reporting guidelines[25] (Appendix 1, available at www.aaojournal.org). A protocol was registered and published on The International Prospective Register of Systematic Reviews (identifier: CRD42021233323).

Search Methods for Identifying Studies

We searched MEDLINE, Embase, Web of Science, PsycINFO, Cochrane Database of Systematic Reviews, the Cochrane Central Register of Controlled Trials in the Cochrane Library, CINAHL, and Chinese databases WANFANG MED ONLINE and China National Knowledge Infrastructure from inception through February 18, 2021, without language restriction. The search strategy was developed under guidance of an information specialist (R.F.). We tested the search strategy through an iterative process before finalizing our combinations of terms (Appendix 2, available at www.aaojournal.org). The reference lists of relevant articles were checked for potentially relevant articles.

Eligibility Criteria

According to these criteria, the following types of studies were considered eligible for inclusion:

1. Studies that enrolled children or young adults, as long as the mean age of participants was < 18 years. Studies focused on mental health in adults with vision impairment or ocular morbidity as children were also included in the narrative synthesis. Vision impairment was defined according to the International Classification of Diseases, 11th Revision[26]; distance vision impairment comprises 4 levels: mild (presenting visual acuity, < 6/12), moderate (presenting visual acuity, < 6/18), severe (presenting visual acuity, < 6/60), and blindness (presenting visual acuity, < 3/60). Thus, a participant falling into any of these categories (that is, with presenting visual acuity of < 6/12) would be classified as having vision impairment.
2. Observational and interventional studies, including randomized controlled trials (RCTs) and before-and-after studies with no control group. The intervention had to be ophthalmic.
3. Studies with a comparison group, such as normally sighted children.
4. Studies with outcome variables that included the prevalence, scores, or both for depression, anxiety, or both.
5. Any study setting was permitted.
6. Original studies published in peer-reviewed journals.

Study Selection, Data Collection, and Risk of Bias Assessment

Two reviewers (D.L. and H.N.) independently screened all titles and abstracts for eligibility. For potentially eligible studies, reviewers read the full-text articles to determine final inclusion or exclusion. Two reviewers (D.L. and S.O.) extracted data independently into an Excel file, version 2201 (Microsoft Corporation), whereas an additional 2 coauthors (N.W. and B.X.) reviewed data extraction forms for English and Chinese articles, respectively, to cross-check for accuracy and validity.

For observational studies, the extracted data consisted of the authors' names, publication year, study design, country, diagnosis, sample size, demographic characteristics of study participants (i.e., age, gender), the instruments used to measure depression and anxiety, and summary of findings. For interventional studies, beyond the characteristics listed above, we also recorded the type of intervention in each group and within- and between-group before-and-after changes. Any disagreement was resolved by discussion within the research team. If data regarding the major outcomes were not presented in the article, we contacted the corresponding authors to obtain the raw dataset. In cases where authors could not be contacted despite 3 attempts, we excluded the studies from the meta-analysis and described them narratively.

The risk of bias and quality of studies were assessed using the Joanna Briggs Institute critical appraisal checklist for observational studies and RCTs and the relevant National Institutes of Health (United States) quality assessment tool for other study designs. We identified 6 articles in languages other than English and Chinese (1 each in Greek, Korean, Spanish, and Serbian and 2 in Portuguese). After reviewing the abstracts, which were in English, we found that none of these studies included the outcome of interest and therefore were excluded.

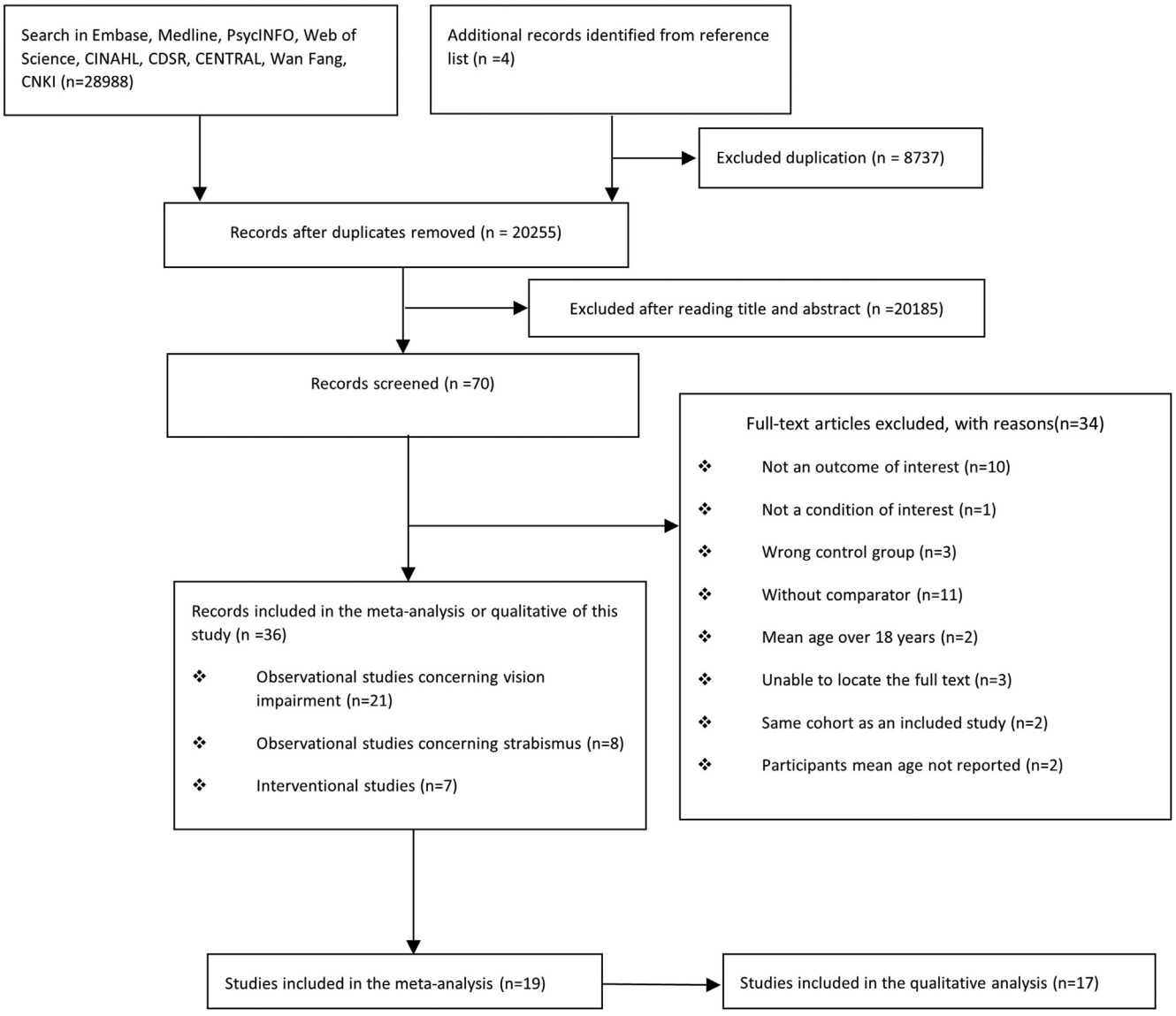

Figure 1. Flowchart showing the study selection process.

Data Synthesis and Analysis

Mental health associations with vision impairment and ocular morbidities (i.e., strabismus) were reported separately because strabismus, being an observable condition, could affect children's mental health differently than unobvious causes of vision loss (e.g., amblyopia). We also reported the results separately from observational and interventional studies. We first described the study characteristics and meta-analyzed the reported outcomes. Meta-analysis was conducted using the meta suite of commands in Stata statistical software, version 17.0 (Stata Corporation). Meta-analysis was carried out separately for studies reporting depression versus anxiety. A narrative synthesis was conducted for studies not eligible for meta-analysis.

Because various tools were used to measure depression and anxiety in different studies, standardized mean differences (SMDs) were used in the pooled analyses. Nine of the 15 studies covering vision impairment concerned myopia, and many did not specify the participants' visual acuity or the exact cause(s) of nonmyopic impaired vision. Thus, it was not possible to perform subgroup analysis by level or exact cause of vision impairment, and instead, this was achieved by stratifying by myopia versus other causes. A random-effects model was used because of heterogeneity between studies. A leave-one-out sensitivity analysis was carried out to evaluate the relative impact of studies on the meta-analytic outcomes. Data were displayed using Forest plots for depression and anxiety separately.

Results

During initial database searches, 28 988 articles were identified, whereas 4 studies were located using the reference lists of the identified studies. We excluded 8737 as duplicates. After abstract and title screening, 70 articles were eligible for full-text evaluation,

Table 1. Characteristics of Observational Studies Included in the Systematic Review (n = 29)

Author(s) (Year)	a) Country b) Study Design c) Setting d) Diagnosis	a) Sample Size b) Sex (%) c) Age (Yrs), Mean ± Standard Deviation (Range)	a) Definition of Exposure b) Ascertainment of Exposure c) Control Group	a) Outcome Indicator(s) b) Outcome Measurement Tool(s)	Summary of Findings
Hasselt et al (1986)[54]	a) United States b) Cross-sectional c) School d) Blindness	a) 52 b) 100% male c) Mean, 17.2 (SD not specified; 13–19)	a) The degree of corrected vision in the better eye was 20/200 or worse, or severe restriction was present in the visual field b) Not specified c) Normally sighted	a) Anxiety b) CBCL	Both residential and public school groups with visual impairment were significantly more anxious than the normally sighted control group by teacher proxy-reported CBCL ($P < 0.03$).
Chen (1992)[48]	a) China b) Cross-sectional c) School d) Myopia	a) 266 b) Not specified c) Primary school students	a) Not specified b) Health check record c) Normally sighted	a) Depression and anxiety b) SCL-90	Depression ($P < 0.005$) and anxiety ($P < 0.005$) scores were higher in children with myopia versus emmetropia.
Huurre et al (2000)[6]	a) Finland b) Cross-sectional c) School d) Vision impairment	a) 722 b) 48.6% male c) Not specified (12–17)	a) Not specified b) Medical record c) Normally sighted	a) Depression b) Modified 13-item BDI	Vision impaired girls showed a significantly higher prevalence of depression than their normally sighted counterparts ($P < 0.05$).
Koenes et al (2000)[50]	a) United States b) Cross-sectional c) School d) Blindness	a) 51 b) 49% male c) Blind group mean, 15 (12–18); sighted group mean, 16 (12–18)	a) The state standard for legal blindness (State of New Mexico, 1993) b) Measured c) Without myopia	a) Depression b) BDI	The incidence of depression among blind adolescents was significantly higher than that of normally sighted peers ($P < 0.005$).
Wang et al (2003)[46]	a) China b) Cross-sectional c) Hospital d) Amblyopia	a) 160 b) 58.8% male c) Not specified (6–16)	a) Expert consensus of Strabismus and Amblyopia Group, Pediatric Ophthalmology Society, Chinese Medical Association (1985) b) Measured c) Healthy children	a) Depression and anxiety b) SAS, SDS, CBCL	Depression ($P < 0.01$) and anxiety ($P < 0.01$) scores in children with amblyopia were significantly higher than those of the control group.
Hu et al (2007)[47]	a) China b) Cross-sectional c) School d) Amblyopia	a) 200 b) 47% male c) Study group, 5.62 ± 0.77 (4–6); control group, 5.68 ± 0.73 (not specified)	a) Expert consensus of Strabismus and Amblyopia Group, Pediatric Ophthalmology Society, Chinese Medical Association (1996) b) Measured c) Healthy children	a) Depression b) CBCL	The difference in depression scores between the 2 groups was not significant ($P = 0.051$).

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Table 1. (Continued.)

Author(s) (Year)	a) Country b) Study Design c) Setting d) Diagnosis	a) Sample Size b) Sex (%) c) Age (Yrs), Mean ± Standard Deviation (Range)	a) Definition of Exposure b) Ascertainment of Exposure c) Control Group	a) Outcome Indicator(s) b) Outcome Measurement Tool(s)	Summary of Findings
Garaigordobil et al (2009)[40]	a) Spain b) Cross-sectional c) School d) Vision impairment	a) 90 b) 54.4% male c) 14.99 ± 2.02 (12–17)	a) Not specified b) Medical record c) Normally sighted	a) Depression and anxiety b) Revised SCL-90	The difference in depression and anxiety subscales between vision impaired children and the control group was not significant.
Bolat et al (2010)[37]	a) Turkey b) Cross-sectional c) School d) Vision impairment	a) 80 b) 57.5% male c) 12.82 ± 1.17 (11–14)	a) Congenital complete visual impairment b) Not specified c) Normally sighted	a) Depression and anxiety b) The Piers–Harris Children's Self-Concept Scale, CDI	Score of depression among adolescents with visual impairment was similar to that of normally sighted peers ($P = 0.582$), whereas score of anxiety was higher among vision impaired adolescents than that of the control group ($P = 0.025$).
Wei et al (2011)[53]	a) China b) Cross-sectional c) Hospital d) Amblyopia	a) 158 b) 50.6% male c) Not specified (4–11)	a) Diagnostic criteria of Strabismus from Chinese Association for Pediatric Ophthalmology and Strabismus (1985) b) Measured c) Healthy children	a) Depression and anxiety b) CBCL	The difference in depression and anxiety scores between amblyopic children and the normally sighted group was not significant in either girls or boys.
Liu et al (2012)[41]	a) China b) Cross-sectional c) School d) Myopia	a) 286 b) 46.9% male c) Study group, 13.8 ± 2.4 (14–16); control group, 13.6 ± 2.5 (14–16)	a) Not specified b) Health check record c) Normally sighted	a) Depression and anxiety b) SCL-90	The scores of the depression ($P < 0.05$) and anxiety ($P < 0.05$) subscales of vision impaired children were significantly higher than those of control group.
Alimovic et al (2013)[55]	a) Croatia b) Cross-sectional c) School d) Vision impairment	a) 80 b) 51.3% male c) Vision impaired, 7.46 (4–11); control group, 7.13 (4–11)	a) Visual impairments were defined according to Croatian regulations on the composition and working methods of expert evaluation in social welfare realization process (Ministry of Labor and Social Welfare and Ministry of Health, 2002) b) Medical record c) Normally sighted	a) Depression and anxiety b) CBCL (4–18)	Anxiety and depression scores of vision impaired children were not significantly higher than those of normally sighted peers.

Table 1. (Continued.)

Author(s) (Year)	a) Country b) Study Design c) Setting d) Diagnosis	a) Sample Size b) Sex (%) c) Age (Yrs), Mean ± Standard Deviation (Range)	a) Definition of Exposure b) Ascertainment of Exposure c) Control Group	a) Outcome Indicator(s) b) Outcome Measurement Tool(s)	Summary of Findings
Guo et al (2015)[39]	a) China b) Cross-sectional c) School d) Myopia	a) 631 b) Not specified c) Not specified	a) Not specified b) Not specified c) Normally sighted	a) Depression and anxiety b) SCL-90	The scores of the depression ($P < 0.01$) and anxiety ($P < 0.01$) subscales were significantly higher in children with myopia than in peers with emmetropia.
Panday et al (2015)[44]	a) India b) Cross-sectional c) School d) Congenital visual impairment	a) 60 b) 0 male c) Study group, 14.93 ± 2.03; control group, 14.73 ± 1.79	a) Not specified b) Not specified c) Normally sighted	a) Depression and anxiety b) DASS	Scores of depression ($P = 0.01$) and anxiety ($P = 0.01$) were greater among adolescent girls with visual impairment than in normally sighted peers.
Ayaki et al (2016)[49]	a) Japan b) Cross-sectional c) Hospital d) Myopia	a) 278 b) 44% male c) 14.2 ± 2.6 (10−19)	a) High myopia (≤−6.00 D), mild myopia (−5.75 to −0.50 D), and no myopia (−0.25 to +2.75 D) b) Measured c) Without myopia	a) Depression and anxiety b) HADS	The differences in depression and anxiety scores among children with high myopia, mild myopia, and no myopia were not statistically significant.
Hamurcu et al (2016)[51]	a) Turkey b) Cross-sectional c) School d) Vision impairment	a) 74 b) 47.3% male c) Study group, 12.32 ± 3.38 (7−18); control group, 10.82 ± 2.18 (7−15)	a) Not specified b) Medical record c) Normally sighted	a) Anxiety b) STAI-C	A higher level of trait anxiety was found in vision impaired children and adolescents than in the normally sighted control participants ($P = 0.004$).
Łazarczyk et al (2016)[56]	a) Poland b) Cross-sectional c) School d) Myopia	a) 239 b) 33.1% male c) Not specified (13−17)	a) Not specified b) Medical record c) Emmetropia	a) Anxiety b) STAI-C	Girls with myopia showed a higher prevalence of trait anxiety than their peers with emmetropia and without vision defects.
Li et al (2016)[52]	a) China b) Cross-sectional c) School d) Myopia	a) 252 b) 41.3% male c) 16.21 ± 2.36 (15−18)	a) Not specified b) Health check record c) Normally sighted	a) Depression and anxiety b) SCL-90	Depression ($P < 0.01$) and anxiety ($P < 0.01$) scores in students with myopia were higher than those of students with emmetropia.

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Table 1. (Continued.)

Author(s) (Year)	a) Country b) Study Design c) Setting d) Diagnosis	a) Sample Size b) Sex (%) c) Age (Yrs), Mean ± Standard Deviation (Range)	a) Definition of Exposure b) Ascertainment of Exposure c) Control Group	a) Outcome Indicator(s) b) Outcome Measurement Tool(s)	Summary of Findings
Zhou (2019)[42]	a) China b) Cross-sectional c) School d) Myopia	a) 300 b) 50.3% male c) Normally sighted, 16.6 ± 0.16 (15–17); mild myopia, 16.71 ± 0.12 (15–16); moderate myopia, 16.72 ± 0.11 (15–16); severe myopia 16.79 ± 0.07 (15–16)	a) Using visual acuity as a surrogate measurement for refractive error b) Measured c) Normally sighted	a) Anxiety b) SAS	Anxiety score was greater with higher levels of myopia ($P < 0.05$).
Li et al (2020)[38]	a) China b) Cross-sectional c) School d) Myopia	a) 1103 b) 53.0% male c) 15.3 (14–17)	a) The mild myopia group (SE, < 3.00 D), the moderate myopia group (SE, 3.00–6.00 D), and the severe myopia group (SE, > 6.00 D) b) Measured c) Emmetropia	a) Depression and anxiety b) SAS, SDS	Depression ($P = 0.03$) and anxiety ($P = 0.018$) scores among students with myopia were significantly higher than those of students with emmetropia.
Cai et al (2020)[43]	a) China b) Cross-sectional c) School d) Myopia	a) 1407 b) 54.3% male c) Not specified	a) Myopia group (SE, <−0.5 D), moderate myopia group (SE, −0.5 to −3.00 D), and moderate and severe myopia group (SE, > 3.00 D) b) Measured c) Emmetropia	a) Anxiety b) SASC	Children with myopia showed worse measures of social anxiety than those with emmetropia ($P < 0.01$).
Xu et al (2020)[45]	a) China b) Cross-sectional c) Community d) Myopia	a) 766 b) 56.4% male c) 14.32 ± 2.64 (12–16)	a) Myopia defined as VA < 5.0 and SE <−0.5 D b) Measured c) Normally sighted	a) Depression and anxiety b) SAS, SDS	The prevalences of depression (25.4% vs. 8.65%; $P<0.001$) and anxiety (22.4% vs. 10.6%; $P = 0.006$) in myopic children were higher than in children with emmetropia.
Mohney et al (2008)[33]	a) United States b) Case-control c) Hospital d) Strabismus	a) 814 b) 50.4% male c) Not specified (< 19)	a) Not specified b) Medical record c) Without strabismus	a) Depression and anxiety b) DSM-4 codes	No significant difference was found in terms of depression and anxiety between strabismus and control groups.

Table 1. (Continued.)

Author(s) (Year)	a) Country b) Study Design c) Setting d) Diagnosis	a) Sample Size b) Sex (%) c) Age (Yrs), Mean ± Standard Deviation (Range)	a) Definition of Exposure b) Ascertainment of Exposure c) Control Group	a) Outcome Indicator(s) b) Outcome Measurement Tool(s)	Summary of Findings
McKenzie et al (2009)[31]	a) United States b) Case-control c) Hospital d) Strabismus	a) 366 b) 35.8% male c) Not specified (< 19)	a) Acquired, intermittent exodeviation of at least 10 PD b) Medical record c) Without strabismus	a) Depression and anxiety b) DSM-4 codes	Boys with intermittent exotropia were more likely to demonstrate major depression ($P = 0.02$). Girls with intermittent exotropia were more likely to demonstrate anxiety or phobia ($P = 0.04$).
Kilgore et al (2010)[36]	a) United States b) Retrospective observational case series c) Hospital d) Strabismus	a) 184 b) 35.9% male c) Not specified (< 19)	a) Acquired, intermittent exodeviation of at least 10 PD b) Strabismus surgery c) Young adults who had childhood intermittent exotropia and did not undergo surgery	a) Depression and anxiety b) DSM-4 codes	Strabismus surgery for children with intermittent exotropia, regardless of success or age at surgery, did not alter the development of mental illness, including depression, by early adulthood.
Olson et al (2011)[34]	a) United States b) Case-control c) Hospital d) Strabismus	a) 254 b) 52.0% male c) Not specified (< 19)	a) Congenital esotropia was defined as a nonaccommodative esotropia that developed by 6 mos of age in a neurologically intact child b) Medical record c) Without strabismus	a) Depression and anxiety b) DSM-4 codes	No significant difference was found in terms of depression or anxiety between the 2 groups.
Lin et al (2014)[20]	a) China b) Cross-sectional c) School d) Strabismus	a) 3903 b) 52.2% male c) Mean, 12.9 (SD not specified; 10–17)	a) If any tropia was present at distance or near, with or without spectacles b) Measured c) Without strabismus	a) Depression and anxiety b) Key screening questions recommended by health bodies in the United States and United Kingdom	Children with strabismus showed a significantly higher prevalence of depression and anxiety ($P < 0.01$ for all).
Ji et al (2017)[30]	a) China b) Cross-sectional c) Hospital d) Strabismus and amblyopia	a) 203 b) 52.2% male c) Study group, 8.83 ± 2.92 (6–14); control group, 8.52 ± 3.11 (5–14)	a) Expert consensus on amblyopia diagnosis, Pediatric Ophthalmology Society, Chinese Medical Association (2011) b) Measured c) Healthy children	a) Depression and anxiety b) SASC	Children with strabismus and amblyopia demonstrate worse psychological problems, including depression ($P < 0.05$) and anxiety ($P < 0.05$).

(*Continued*)

Table 1. (Continued.)

Author(s) (Year)	a) Country b) Study Design c) Setting d) Diagnosis	a) Sample Size b) Sex (%) c) Age (Yrs), Mean ± Standard Deviation (Range)	a) Definition of Exposure b) Ascertainment of Exposure c) Control Group	a) Outcome Indicator(s) b) Outcome Measurement Tool(s)	Summary of Findings
Merdler et al (2017)[32]	a) Israel b) Case-control c) Military preconscription assessment d) Strabismus	a) 662 641 b) 59% male c) 17.3 ± 0.59 (not specified)	a) Not specified b) Medical record c) Without strabismus	a) Anxiety b) Presence of corresponding FFS codes	Children with uncorrected strabismus were more likely to demonstrate anxiety (OR, 1.91; 95% CI, 1.02−3.57; $P = 0.047$).
Merdler et al (2017)[32]	a) Israel b) Case-control c) Military preconscription assessment d) Strabismus	a) 1598 b) Corrected strabismus, 55.7%; uncorrected strabismus, 55.2% c) Corrected strabismus, 17.25 ± 0.49; uncorrected strabismus, 17.45 ± 0.63	a) Not specified b) Strabismus correction c) Participants with uncorrected strabismus	a) Anxiety b) Presence of corresponding FFS codes	Anxiety was more common in those with uncorrected strabismus. Strabismus correction was not associated significantly with anxiety disorder (OR, 2.978; 95% CI, 1.013−8.754; $P = 0.06$).
Zhang et al (2019)[29]	a) China b) Cross-sectional c) Hospital d) Strabismus	a) 98 b) 48.0% male c) Not specified (7−13)	a) Not specified b) Measured c) Healthy children	a) Anxiety b) SASC	Strabismus worsens children's mental health, including anxiety ($P = 0.006$).

BDI = Beck Depression Inventory; CBCL = Child Behavior Checklist; CDI = Children's Depression Inventory; CI = confidence interval; D = diopter; DASS = Depression, Anxiety, and Stress Scale; DSM-4 = Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition; FFS = Fitness-For-Service; HADS = Hospital Anxiety and Depression Scale; OR = odds ratio; PD = prism diopter; SAS = Self-Rating Anxiety Scale; SASC = Social Anxiety Scale for Children; SCL-90 = Symptom Checklist-90; SD = standard deviation; SDS = Self-Rating Depression Scale; SE = spherical equivalent; STAI-C = State-Trait Anxiety Inventory for Children; VA = visual acuity.

Table 2. Characteristics of Intervention Studies Included in the Systematic Review (n = 7)

Author(s) (Year)	a) Country b) Study Design c) Setting d) Diagnosis	a) Sample Size Taken b) Sex (%) c) Age (Yrs), Mean ± Standard Deviation (Range)	a) Definition of Exposure b) Intervention of Study Group c) Intervention of Control Group	a) Outcome Indicator(s) b) Outcome Measurement Tool(s)	Summary of Findings
Archer et al (2005)[21]	a) United States b) Before-and-after studies with no control group c) Hospital d) Strabismus	a) 98 b) Not specified c) 4.5 ± 3.3 (< 15)	a) Not specified b) Strabismus surgery c) NA	a) Depression and anxiety b) Modified version of the RAND Health Insurance Study questionnaire	Statistically significant improvements were observed in the subscales of depression ($P < 0.01$) and anxiety ($P = 0.01$) after strabismus surgery.
Chai et al (2009)[22]	a) China b) Prospective interventional c) Hospital d) Strabismus	a) 60 b) 46.7% male c) Heterophoria, 8.3 ± 2.8 (not specified); heterotropia, 8.4 ± 2.6 (not specified)	a) Not specified b) Strabismus surgery c) NA	a) Depression and anxiety b) HADS	Compared with preoperative values, significant improvements were noted after surgery in anxiety ($P < 0.05$) and depression ($P < 0.05$) scores.
Jing (2009)[23]	a) China b) Before-and-after studies with no control group c) Hospital d) Strabismus	a) 168 b) Not specified c) Not specified (8–14)	a) Not specified b) Strabismus surgery c) NA	a) Anxiety b) SASC	Social anxiety can improve significantly after strabismus surgery ($P < 0.001$).
Ziaei et al (2016)[24]	a) Iran b) Before-and-after studies with no control group c) Hospital d) Strabismus	a) 87 b) 47.1% male c) 8.7 ± 4 (5–15)	a) Not specified b) Strabismus surgery c) NA	a) Depression and anxiety b) Modified RAND Health Insurance Study questionnaire	Depression ($P < 0.001$) and anxiety ($P < 0.001$) scores improved significantly after strabismus surgery.
Kim et al (2013)[27]	a) Korea b) Before-and-after studies with no control group c) Hospital d) Strabismus	a) 25 b) 60% male c) Mean, 4.7 (3–7)	a) Not specified b) Part-time occlusion c) NA	a) Depression and anxiety b) CBCL	No significant difference was found in terms of depression or anxiety after part-time occlusion.
Guan et al (2018)[28]	a) China b) Cluster-randomized controlled trial c) School d) Myopia	a) 19 934 b) 52.0% male c) 10.5 ± 1.10	a) Myopia ≤−0.5 D b) Providing free glasses c) Providing prescription	a) Learning Anxiety Physical Anxiety b) MHT	Providing free glasses had no effect on Learning Anxiety and the Mental Health Test scores and a small but significant reduction in physical anxiety.

(*Continued*)

Table 2. (Continued.)

Author(s) (Year)	a) Country b) Study Design c) Setting d) Diagnosis	a) Sample Size Taken b) Sex (%) c) Age (Yrs), Mean ± Standard Deviation (Range)	a) Definition of Exposure b) Intervention of Study Group c) Intervention of Control Group	a) Outcome Indicator(s) b) Outcome Measurement Tool(s)	Summary of Findings
Ozates et al (2019)[35]	a) Turkey b) Before-and-after studies with no control group c) Hospital d) Strabismus	a) 83 b) 49.4% male c) Latent deviation group, 16.6 ± 2.1 (14−21); manifest exotropia group, 17.5 ± 2.0 (14−21)	a) Not specified b) Strabismus surgery c) NA	a) Depression and anxiety b) HADS, STAI	Strabismus surgery improved the trait anxiety symptom in children with latent deviation ($P = 0.006$), whereas in the manifest exotropia group, both anxiety and depression symptoms improved ($P < 0.001$).

CBCL = Child Behavior Checklist; HADS = Hospital Anxiety and Depression Scale; MHT = Mental Health Test; NA = not applicable; RAND = Research And Development; SASC = Social Anxiety Scale for Children; STAI = State-Trait Anxiety Inventory.

after which a further 34 articles were excluded (Appendix 3, available at www.aaojournal.org). In total, 36 studies were included in the systematic review (Fig 1).[6,20−24,27−56]

Study Characteristics

Of the 36 included studies, 21 observational studies (58.3%) concerned vision impairment, 8 observational studies (22.2.%) concerned strabismus, and the remaining 7 studies (19.4%) were interventional. The 21 observational studies concerning vision impairment enrolled 7255 participants (mean sample size, 346 participants; standard deviation, 372 participants; range, 51−1407 participants) and were published between 1986 and 2020. According to the World Bank income level,[57] 14 of these studies were performed in low- or middle-income countries,[37−39,41−48,51−53] and 7 studies were performed in high-income countries.[6,40,49,50,54−56] These 21 studies were of cross-sectional design. Depression and anxiety were reported in 16 studies[6,37−41,44−50,52,53,55] and 17 studies,[37−44,46,48,49,51−56] respectively.

The 8 observational studies concerning strabismus enrolled 668 463 participants (median, 310 participants; interquartile range, 194-2359 participants) and were published between 2008 and 2019. Three of these studies were carried out in low- or middle-income countries, all in China.[20,29,30] Five were carried out in high-income countries: 1 in Israel[32] and 4 in the United States.[31,33,34,36] Of these, depression and anxiety were reported in 6 studies[20,30,31,33,34,36] and 8 studies,[20,29−34,36] respectively.

The 7 studies concerning the intervention enrolled 20 455 participants (median, 87 participants; interquartile range, 60−168 participants) and were published between 2005 and 2019. The study from China had the largest sample size of 19 934.[28] Five of these studies were carried out in low- or middle-income countries: 3 in China,[22,23,28] 1 in Iran,[24] and 1 in Turkey.[35] Two were carried out in high-income countries, 1 each in the United States[21] and Korea.[27] Characteristics of the included studies are summarized in Table 1 for observational studies and Table 2 for interventional studies.

Methodologic Quality of Included Studies

Of the 29 observational studies, 17 studies scored low using the Joanna Briggs Institute quality appraisal checklist. The most common problems were (1) failure to define inclusion criteria clearly[37,39−41,44,46,50,52,53,55,56]; (2) inability to measure the condition in a valid and reliable manner[6,37,39−42,44,48,51−56]; (3) lack of objective, standard criteria used for measurement of the condition[6,29,37,39,41,42,44,48,51−54,56]; and (4) inability to identify and address potential confounding factors.[32] The remaining 7 studies concerning the treatment scored well using the Joanna Briggs Institute or National Institutes of Health quality appraisal checklists. The most common problems were (1) absence of sample size justification,[21−24,27] (2) lack of description of the intervention,[21−24] (3) failure to enroll all eligible participants,[21] (4) loss to follow-up of eligible participants,[23] (5) using a convenience sample to recruit eligible participants,[21] (6) lack of description regarding whether patients and control participants matched appropriately,[32] and (7) lack of description of whether participants were analyzed in the groups to which they were randomized (Table 3).[28]

Quantitative Synthesis with Meta-analysis

The 11 studies (3928 participants, 54.6% who were vision impaired) that reported scores for depression were included in a meta-analysis (Appendix 4, available at www.aaojournal.org). Children with vision impairment showed higher depression

Table 3. Checklist Results for Assessing Methodologic Quality of the Selected Studies (n = 36)

Study Type	Question												
	1	*2*	*3*	*4*	*5*	*6*	*7*	*8*	*9*	*10*	*11*	*12*	*13*
Cross-sectional[a]													
Hasselt et al (1986)[54]	*	*	§	§	‡	‡	*	*					
Chen (1992)[48]	*	*	§	§	‡	‡	*	§					
Huurre et al (2000)[6]	*	*	†	†	‡	‡	*	*					
Koenes et al (2000)[50]	§	*	*	*	‡	‡	*	*					
Wang et al (2003)[46]	§	*	*	*	‡	‡	*	*					
Hu et al (2007)[47]	*	*	*	*	‡	‡	§	*					
Garaigordobil et al (2009)[40]	§	*	§	*	‡	‡	*	*					
Bolat et al (2010)[37]	§	*	§	§	‡	‡	*	*					
Wei et al (2011)[53]	§	*	§	§	‡	‡	*	*					
Alimovic et al (2012)[55]	§	*	§	*	‡	‡	*	*					
Liu et al (2012)[41]	†	*	§	§	‡	‡	*	*					
Lin et al (2014)[20]	*	*	*	*	*	*	*	*					
Guo et al (2015)[39]	†	*	†	†	‡	‡	*	*					
Panday et al (2015)[44]	†	*	†	†	‡	‡	*	*					
Ayaki et al (2016)[49]	*	*	*	*	*	*	*	*					
Łazarczyk et al (2016)[56]	†	*	†	†	‡	‡	*	*					
Li (2016)[52]	§	*	†	§	‡	‡	*	*					
Hamurcu et al (2016)[51]	*	*	§	§	‡	‡	*	*					
Ji et al (2017)[30]	*	*	*	*	‡	‡	*	*					
Zhou et al (2019)[42]	*	*	†	†	‡	‡	*	*					
Zhang et al (2019)[29]	*	*	§	§	‡	‡	*	*					
Cai et al (2020)[43]	*	*	*	*	‡	‡	*	*					
Li et al (2020)[38]	*	*	*	*	‡	‡	*	*					
Xu et al (2020)[45]	*	*	*	*	*	*	*	*					
Before-and-after studies with no control group[b]													
Archer et al (2005)[21]	*	*	*	†	‖	*	*	‡	*	*	‡	‡	
Chai et al (2009)[22]	*	*	*	*	‖	*	*	‡	*	*	‡	‡	
Jing (2009)[23]	*	*	*	*	‖	*	*	‡	†	*	‡	‡	
Ziaei et al (2016)[24]	*	*	*	*	‖	*	*	‡	*	*	‡	‡	
Ozates et al (2019)[35]	*	*	*	*	*	*	*	‡	*	*	‡	‡	
Kim et al (2012)[27]	*	*	*	*	‖	*	*	‡	*	*	‡	‡	
Randomized controlled trial[c]													
Guan et al (2018)[28]	*	*	*	*	*	‡	*	*	§	*	*	*	*
Case-control[d]													
Mohney et al (2008)[33]	*	*	*	*	*	*	*	*	‡	*			
McKenzie et al (2009)[31]	*	*	*	*	*	*	*	*	‡	*			
Olson et al (2012)[34]	*	*	*	*	*	*	*	*	‡	*			
Merdler et al (2017)[32]	§	§	*	*	*	†	†	*	‡	*			
Case series[e]													
Kilgore et al (2014)[36]	*	*	*	*	*	*	*	*	*	*			

Question Key: (A) Joanna Briggs Institute tool questions for cross-sectional study assessment. Question 1: Were the criteria for inclusion in the sample clearly defined? Question 2: Were the study subjects and the setting described in detail? Question 3: Was the exposure measured in a valid and reliable way? Question 4: Were objective, standard criteria used for measurement of the condition? Question 5: Were confounding factors identified? Question 6: Were strategies to deal with confounding factors stated? Question 7: Were the outcomes measured in a valid and reliable way? Question 8: Was appropriate statistical analysis used? (Joanna Briggs Institute, 2020).
(B) National Institutes of Health tool questions for before-and-after studies with no control group study assessment. Question 1: Was the study question or objective clearly stated? Question 2: Were eligibility/selection criteria for the study population prespecified and clearly described? Question 3: Were the participants in the study representative of those who would be eligible for the test/service/intervention in the general or clinical population of interest? Question 4: Were all eligible participants that met the prespecified entry criteria enrolled? Question 5: Was the sample size sufficiently large to provide confidence in the findings? Question 6: Was the test/service/intervention clearly described and delivered consistently across the study population? Question 7: Were the outcome measures prespecified, clearly defined, valid, reliable, and assessed consistently across all study participants? Question 8: Were the people assessing the outcomes blinded to the participants' exposures/interventions? Question 9: Was the loss to follow-up after baseline 20% or less? Were those lost to follow-up accounted for in the analysis? Question 10: Did the statistical methods examine changes in outcome measures from before to after the intervention? Were statistical tests performed that provided *P* values for the before-to-after changes? Question 11: Were outcome measures of interest taken multiple times before the intervention and multiple times after the intervention (i.e., did they use an interrupted time-series design)? Question 12: If the intervention was conducted at a group level (e.g., a whole hospital, a community, etc.), did the statistical analysis take into account the use of individual-level data to determine effects at the group level? (National Heart, Lung and Blood Institute, 2021).
(C) Joanna Briggs Institute tool questions for randomized controlled trials study assessment. Question 1: Was true randomization used for assignment of participants to treatment groups? Question 2: Was allocation to groups concealed? Question 3: Were treatment groups similar at the baseline? Question 4: Were participants blind to treatment assignment? Question 5: Were those delivering treatment blind to treatment assignment? Question 6: Were outcomes assessors blind to treatment assignment? Question 7: Were treatment groups treated identically other than the intervention of interest? Question 8: Was follow-up complete, and if not, were differences between groups in terms of their follow-up adequately described and analyzed? Question 9: Were participants

analyzed in the groups to which they were randomized? Question 10: Were outcomes measured in the same way for treatment groups? Question 11: Were outcomes measured in a reliable way? Question 12: Was appropriate statistical analysis used? Question 13: Was the trial design appropriate for the topic and were any deviations from the standard randomized controlled trial design accounted for in the conduct and analysis? (Joanna Briggs Institute, 2020).
(D) Joanna Briggs Institute tool questions for case-control study assessment. Question 1: Were the groups comparable other than the presence of disease in cases or the absence of disease in control participants? Question 2: Were patients and control participants matched appropriately? Question 3: Were the same criteria used for identification of patients and control participants? Question 4: Was exposure measured in a standard, valid, and reliable way? Question 5: Was exposure measured in the same way for patients and control participants? Question 6: Were confounding factors identified? Question 7: Were strategies to deal with confounding factors stated? Question 8: Were outcomes assessed in a standard, valid, and reliable way for patients and control participants? Question 9: Was the exposure period of interest long enough to be meaningful? Question 10: Was appropriate statistical analysis used? (Joanna Briggs Institute, 2020).
(E) Joanna Briggs Institute tool questions for case series assessment. Question 1: Were there clear criteria for inclusion in the case series? Question 2: Was the condition measured in a standard, reliable way for all participants included in the case series? Question 3: Were valid methods used for identification of the condition for all participants included in the case series? Question 4: Did the case series have consecutive inclusion of participants? Question 5: Did the case series have complete inclusion of participants? Question 6: Was there clear reporting of the demographics of the participants in the study? Question 7: Was there clear reporting of clinical information of the participants? Question 8: Were the outcomes or follow-up results of patients clearly reported? Question 9: Was there clear reporting of the presenting site(s)/clinic(s) demographic information? Question 10: Was statistical analysis appropriate? (Joanna Briggs Institute, 2020).
*Yes, the study satisfactorily met the respective quality criterion.
†No, the study did not meet the respective quality criterion.
‡Not applicable.
§Unclear whether the study has met the respective quality criterion.
‖Cannot determine.

scores than control participants (pooled SMD, 0.57; 95% confidence interval [CI], 0.26−0.89; $I^2 = 94.3\%$; Fig 2). Six studies in which myopia was the cause of vision impairment showed significantly higher depression scores than children with normal vision (SMD, 0.58; 95% CI, 0.36−0.81; $I^2 = 85.6\%$). Five studies with other causes of vision impairment found a similar point estimate compared with control participants, which was imprecise because of high heterogeneity and did not reach nominal statistical significance (SMD, 0.58; 95% CI, −0.08 to 1.25; $I^2 = 94.7\%$). Leave-one-out sensitivity analyses showed that, after removing the potential outlier studies, the pooled effect size still suggested higher depression scores in vision impaired children than in normally sighted children (Supplemental Figs 1 and 2, available at www.aaojournal.org).

Fourteen studies (5226 participants, 60.2% who were vision impaired) providing anxiety scores were included in a meta-analysis (Appendix 5, available at www.aaojournal.org). Vision impaired children showed higher anxiety scores (pooled SMD, 0.62; 95% CI, 0.40−0.83; $I^2 = 91.3\%$; Fig 3). Both children with myopia and those with other causes of vision impairment showed higher anxiety scores than normally sighted children. Effects did not differ between subgroups with myopic vision impairment (SMD, 0.49; 95% CI, 0.32−0.66; $I^2 = 84.3\%$) compared with those with other causes of vision impairment (SMD, 0.93; 95% CI, 0.34−1.53; $I^2 = 88.7\%$; $P = 0.16$). Leave-one-out sensitivity analyses showed that, after excluding the potential outlier studies, the pooled effect size suggested a higher anxiety score in vision impaired children than in normally sighted children (Supplemental Figs 3 and 4, available at www.aaojournal.org).

Three studies[21,24,35] and 4 studies[21,23,24,35] concerning strabismus surgery with complete data were included in the meta-analysis of depression and anxiety, respectively (Appendices 6 and 7, available at www.aaojournal.org). Strabismus surgery significantly improved the symptoms of depression (SMD, 0.59; 95% CI, 0.12−1.06; $I^2 = 85.3\%$; Fig 4) and anxiety (SMD, 0.69; 95% CI, 0.25−1.14; $I^2 = 86.4\%$; Fig 5).

Qualitative Synthesis

Overall, the 6 studies concerning vision impairment and depression and anxiety among children included in the qualitative synthesis indicated that the impact of vision impairment on depression and anxiety was mixed[45,47,50,53−55] (Table 1). Four studies (949 participants) found that vision impaired adolescents showed higher prevalence or scores of depression and anxiety than their normally sighted peers.[45,50,54,55] The other 2 studies (358 participants) found that vision impaired children did not show a significantly higher score in the subdomain of proxy-reported anxiety or depression than normally sighted children.[47,53]

The observational studies concerning strabismus also were described narratively because of the heterogeneity of the study design and the diverse outcomes reported. Five studies (666 401 participants) indicated a positive association between strabismus and depression, anxiety, or both in children.[20,29−32] Two retrospective studies (1068 participants) suggested that, although the children with strabismus were at increased risk for mental illness developing by early adulthood, the differences of prevalence in depression and anxiety were not statistically significant compared with children without strabismus.[33,34]

Of the 4 studies (1867 participants) assessing the impact of strabismus treatment on depression and anxiety not included in the meta-analysis,[22,27,32,36] 1 interventional study found that strabismus surgery statistically improved the symptoms of anxiety and depression both in patients with heterotropia and in patients with heterophoria.[22] Another interventional study indicated that the depression and anxiety subscale scores were unchanged after occlusion therapy in children with intermittent exotropia.[27] One case-control study found a borderline significant association between strabismus correction and anxiety (odds ratio, 2.98; 95% CI, 1.01−8.75; $P = 0.06$).[32] A retrospective observational case series study suggested that strabismus surgery for children with intermittent exotropia did not decrease or alter the development of mental illnesses, including major depression, by early adulthood, regardless of surgical success or age at surgery.[36] The only cluster RCT included 19 934 participants and found that providing free glasses to primary school children in China did not reduce students' fear of examinations or excessive concern about test scores (learning anxiety); however, a small, yet significant, reduction in students' excessive concerns about their bodies (physical anxiety) was found.[28]

Discussion

In this systematic review, we observed a significant positive association between vision impairment and scores of depression and anxiety in children and significant

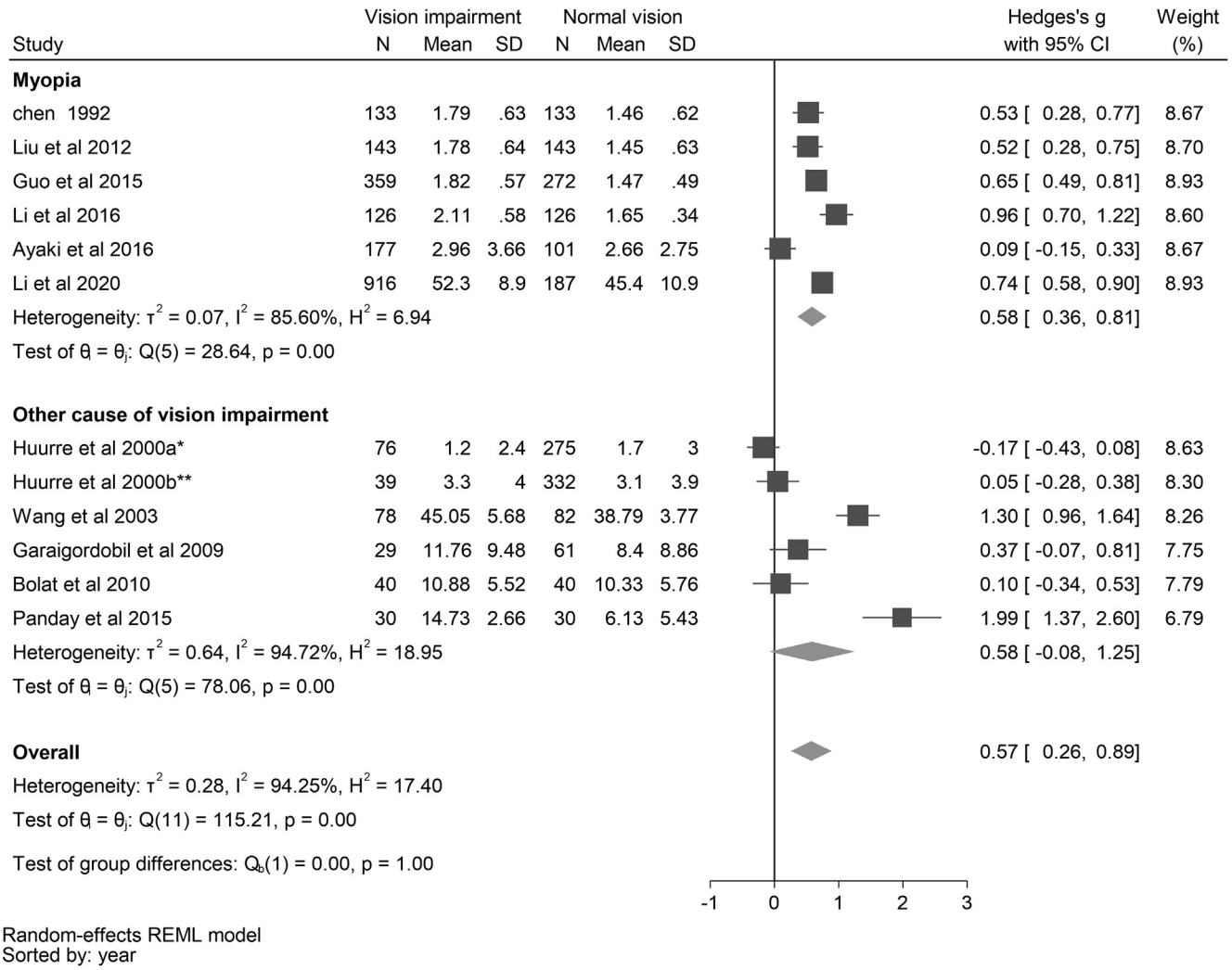

Figure 2. Forest plot showing the random-effects model for the association between depression and vision impairment in children. CI = confidence interval; SD = standard deviation; * = boy; ** = girl; REML = Restricted Maximum Likelihood.

improvement of depression and anxiety symptoms after strabismus surgery among children. The differences in anxiety scores between children with visual impairment resulting from either myopia or other causes compared with children with emmetropia or control children, respectively, were both significant, whereas the difference in depression scores was significant only among children with visual impairment resulting from myopia (but not resulting from other causes) compared with children with emmetropia or control children, respectively.

The quality of most included studies was low to moderate. Most studies did not clearly describe the sampling methods used, did not report the definition of vision impairment, and used various tools to measure depression and anxiety in children. These limitations made it challenging to interpret the results collectively and limited external validity.

Twenty-two of the 36 studies are from low- and middle-income countries, and 9 studies[28,38,39,41–43,45,48,52] concerning myopia were conducted in China with larger sample sizes (including 24 964 participants). The high proportion of studies from China and low- or middle-income countries in general likely reflects the high prevalence of myopia in the former[58] and the importance of unaddressed children's vision deficits in the latter, potentially reducing the generalizability of our conclusions. Uncorrected refractive error continues to be the leading cause of vision impairment worldwide,[59] and more than half of the children 6 to 18 years of age in China have myopia.[60] The inability to see clearly and the proven impact of poor vision on educational performance may be a source of anxiety and depression, especially in the highly pressurized Chinese educational environment.[4] Furthermore, only 15% of children needing glasses and living in China's underserved rural western areas have them.[4] This review identified only 1 RCT involving myopia correction and mental health, and although it found that providing free eyeglasses did not reduce learning anxiety, a small but statistically significant reduction was observed in physical anxiety.[28] More RCTs

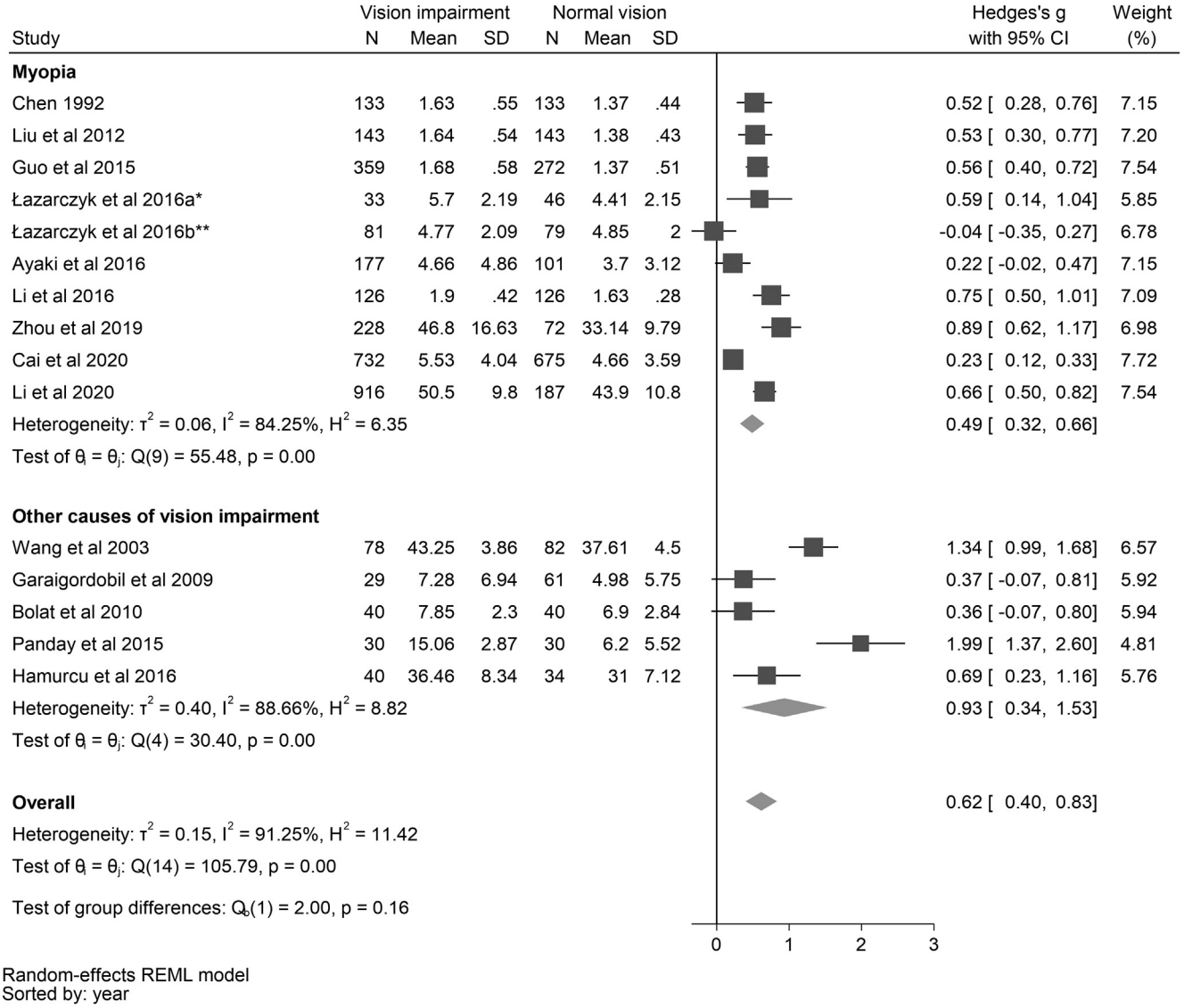

Figure 3. Forest plot showing the random-effects model for the association between anxiety and vision impairment in children. CI = confidence interval; SD = standard deviation; * = boy; ** = girl; REML = Restricted Maximum Likelihood.

are needed to explore the causal association between ophthalmic treatment and mental health among children, with special attention paid to myopia.

The difference in the burden of depression between control participants and those with vision impairment resulting from causes other than myopia was not significant. The predominant causes of vision impairment in these studies were congenital eye conditions. These children may have lived for a long time with vision impairment and may have adapted to the disability and resulting functional limitations. In addition, most children in these studies were recruited from schools or hospitals for the blind, which may be better equipped than conventional schools to provide the support system these children require.[7] Certainly, it is encouraging for program planners that the children whose vision impairment is linked most strongly with depression and anxiety, that is, those with myopia, have the most readily treatable ocular condition.

Interestingly, of the 6 studies concerning vision impairment and depression and anxiety among children included in the qualitative synthesis, 4 studies found that vision impaired adolescents showed higher prevalence or scores of depression and anxiety than their normally sighted peers.[45,50,54,55] However, 2 studies that used proxy-reported anxiety or depression found that vision impaired children (compared with normally sighted children) did not show significantly higher scores.[47,53] This may indicate difficulty for proxies (parent, guardian, or caretaker) to identify signs of anxiety or depression in children. Future studies to improve proxy identification of signs of anxiety and depression in children are needed.

Most observational studies concerning strabismus found a positive association between strabismus and depression, anxiety, or both, except for 2 studies in which the numbers of patients with strabismus were small (n = 127 and n = 407).[33,34] A recent, large study in South Korea (n = 654 152) found that children with strabismus did not show higher depression and

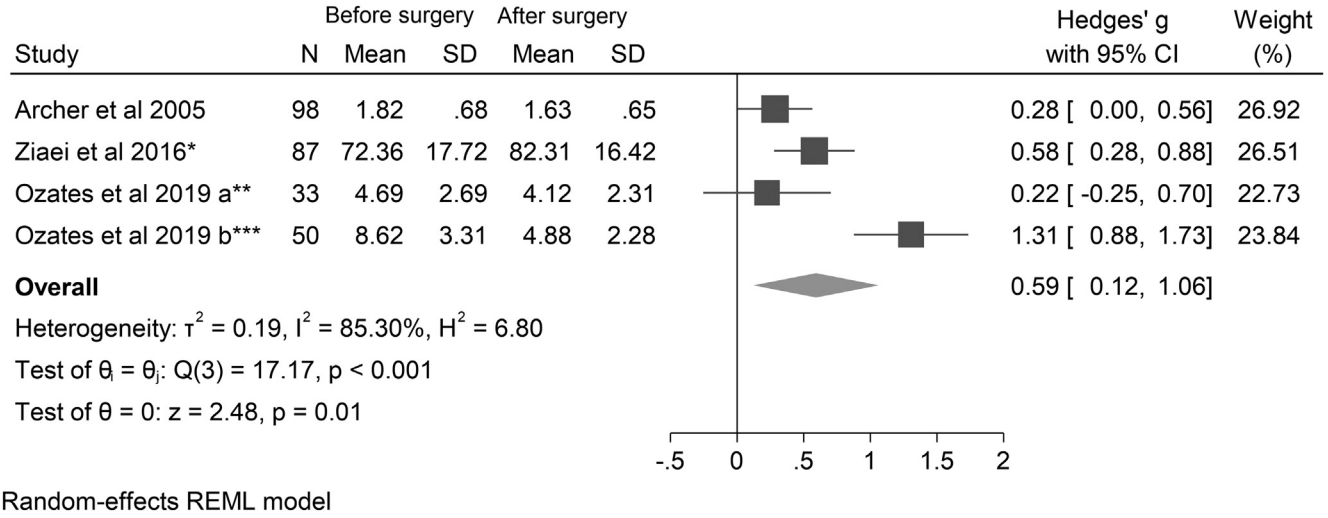

Figure 4. Forest plot showing the random-effects model of the impact of strabismus surgery on depression in children. CI = confidence interval; SD = standard deviation; * = higher score represents better function (the original standardized mean difference was −0.58; we changed the sign of the standardized mean difference); ** = latent deviation group; *** = manifest exotropia group; REML = Restricted Maximum Likelihood.

anxiety prevalence than children with conjunctivitis after adjusting for age, preterm birth, or cerebral palsy and mental retardation.[61] However, this study used administrative data from health insurance records, which might have underdiagnosed strabismus-related depression and anxiety. Another study reported that children with allergic conjunctivitis experienced reduced quality of life.[62] Additionally, 1 recent study using commercial insurance claims data including 12 005 189 participants found that children younger than 18 years with strabismus have higher odds of mental illnesses, including anxiety and depression, than children without strabismus. However, 64.5% and 46.0% in the strabismus and control group, respectively, also harbored at least 1 systemic comorbid condition, such as cancer of the brain and nervous system or leukemia, which was adjusted for in the multivariate analysis.[63] Interestingly, a study from 2003 suggested that an association between strabismus and mental illness has a genetic basis: a transcription factor gene named *PMX2B* was associated with both schizophrenia and constant exotropia.[64]

Interventional studies showed that treating strabismus could improve mental health, including depression and anxiety. The worldwide estimated prevalence of strabismus is as high as 1.93%,[17] and the present review indicates that early detection and treatment may impact children's mental health profoundly. Negative attitudes toward strabismus

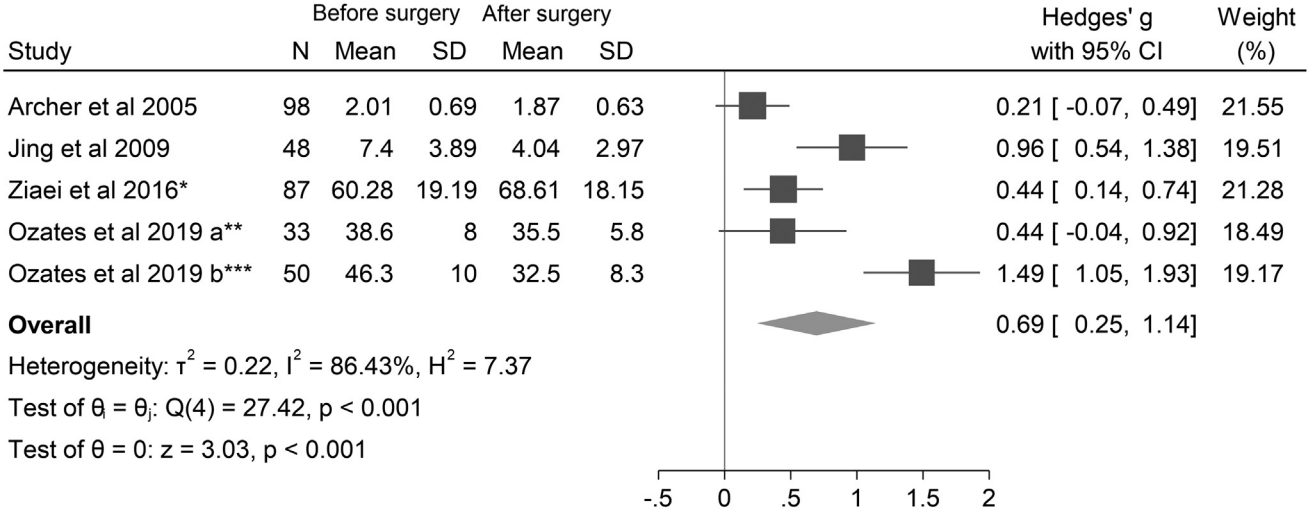

Figure 5. Forest plot showing the random-effects model of the impact of strabismus surgery on anxiety in children. CI = confidence interval; SD = standard deviation; * = higher score represents better function (the original standardized mean difference was −0.44; we changed the sign of the standardized mean difference); ** = latent deviation group; *** = manifest exotropia group; REML = Restricted Maximum Likelihood.

seem to emerge as early as 6 years of age and increase with age.[65] However, in developing countries, including China, India, and Vietnam, strabismus surgery often is considered cosmetic and may not be covered by medical insurance.[66–68] The average costs of strabismus surgery in China and Vietnam are US $700[67] and US $154,[68] respectively. Eight in 10 patients in China paid out of pocket for the surgery,[67] which could deter patients of low socioeconomic status from seeking treatment. The current review provides evidence in favor of insurance coverage for strabismus surgery.

Strengths of this review include the broad and comprehensive nature of the search strategy and the inclusion of studies from low-, middle-, and high-income countries. However, only 1 included study was conducted in a lower-to middle-income country.[44] Thus, extrapolation of these results to such settings must be carried out with care.

The main limitation of this systematic review is that high heterogeneity was found among the included studies. All observational studies concerning vision impairment included in the meta-analysis were cross-sectional, most of the interventional studies followed before-and-after designs without a control group, and only 1 RCT for myopia was included. This precluded a clearer understanding of any mechanism of causality. In addition, the average ages of the participants in studies concerning vision impairment and strabismus included in the meta-analysis were 14.9 and 9.78 years, respectively, which may limit generalizing our results to children of all ages.

Despite these limitations, our findings have importance for health care planners designing interventions and prioritizing resource allocation. We suggest that further RCTs on myopia correction and its impact on mental health are needed to identify strategies to improve the mental health of children with myopia. This review also underscored the importance and potential impact of early detection and treatment of strabismus in children and provides evidence in favor of insurance coverage for timely strabismus surgery to help improve children's overall health and, in turn, decrease costs for future mental health disorders.

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HUMAN SUBJECTS: No human subjects were included in this study. This is a systematic review using published de-identified data. Informed consent was not obtained.

No animal subjects were included in this study.

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Analysis and interpretation: Li, Chan, Virgili, Piyasena, Negash, Whitestone, O'Connor, Xiao, Clarke, Cherwek, Singh, She, Wang, Boswell, Prakalapakorn, Patnaik, Congdon

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Overall responsibility: Li, Chan, Virgili, Piyasena, Negash, Whitestone, O'Connor, Xiao, Clarke, Cherwek, Singh, She, Wang, Boswell, Prakalapakorn, Patnaik, Congdon

Abbreviations and Acronyms:
CI = confidence interval; **RCT** = randomized controlled trial; **SMD** = standardized mean difference.

Keywords:
Anxiety, Depression, Childhood vision impairment, Myopia, Strabismus.

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