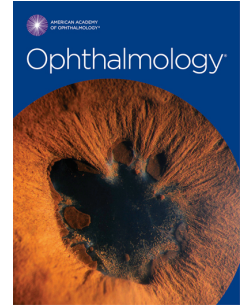


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Impact of vision impairment and ocular morbidity and their treatment on depression and anxiety in children: A systematic review

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1 **TITLE - Impact of vision impairment and ocular morbidity and their treatment on**
 2 **depression and anxiety in children: A systematic review**

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51 **Running head:** Vision impairment, Ocular morbidity, on children's mental health

52 **Abbreviations and acronyms:** CI (confidence interval), IQR (Interquartile Range), JBI (Joanna
53 Briggs Institute), NIH (National Institutes of Health), OR (odds ratio), PRISMA (Preferred Reporting
54 Items for Systematic Review and Meta-Analysis), QoL (Quality of Life), RCT (randomized
55 controlled trial), SD (standard deviation), SMD (standardised mean difference), USA (United States
56 of America).

57 **Keywords:** Vision impairment; ocular morbidity; treatment; depression; anxiety; mental health;
58 children

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63 ABSTRACT**64 Topic:**

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

68 Clinical Relevance:

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

72 Methods:

73 We searched nine electronic databases from inception to February 18, 2021, including observational
74 and interventional studies assessing whether vision impairment and/or ocular morbidity and their
75 treatment are associated with depression and/or anxiety in children. We used narrative synthesis and
76 meta-analysis with the residual maximum likelihood method. A protocol was registered and published
77 on The International Prospective Register of Systematic Reviews (PROSPERO, CRD42021233323).

78 Results:

79 Among 28,992 studies, 28,956 (99.9%) were excluded as duplicates or unrelated content. Among 36
80 remaining studies, 21 (58.3%) were observational studies concerning vision impairment, eight
81 (22.2%) were observational studies concerning strabismus, and seven (19.4%) were interventional
82 studies. Vision-impaired children experienced significantly higher scores of depression (Standard
83 Mean Difference [SMD] 0.57, 95% Confidence Interval (CI) 0.26-0.89, 11 studies) and anxiety (SMD
84 0.61, 95% CI 0.40-0.821, 14 studies) than normally-sighted children. In particular, myopic children
85 experienced higher scores of depression (SMD 0.59, 95% CI 0.36-0.81, six studies) than normally-
86 sighted children. Strabismus surgery significantly improved symptoms of depression (SMD: 0.59 95%
87 CI 0.12-1.06, three studies) and anxiety (SMD: 0.69 95% CI 0.24-1.14, four studies) in children.

88 Discussion:

89 Among children, vision impairment is associated with greater symptoms of depression and anxiety.
90 Surgical treatment of strabismus improved these symptoms. Further randomized controlled trials
91 exploring the impact of public health measures for myopia correction on mental health in children are
92 needed. Scaling up access to strabismus surgery could improve the mental health of affected children.

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94

95 Introduction

96 Vision impairment (< 6/12) or blindness (< 3/60) affects at least 2.2 billion people worldwide,
97 including an estimated 19 million children aged 0-14 years, among whom 1.4 million have
98 irreversible blindness.^{1,2} Children with vision impairment tend to participate in fewer physical
99 activities,³ have lower academic achievement,⁴ and are more socially isolated.^{5,6} Due to these reasons,
100 vision impairment may adversely affect the mental health of children.⁷ Depression and anxiety are
101 two common psychiatric disorders associated with vision impairment.⁸⁻¹¹ An existing large body of
102 work focuses on the impact of vision impairment on depression and anxiety in older adults. A recent
103 systematic review found that the prevalence of depression among patients with vision impairment
104 aged older than 65 years was 25%,⁸ far higher than that among unaffected persons.¹² It is also
105 estimated that 15.6% of older adults with vision impairment face sub-threshold anxiety, and 7.5% are
106 diagnosed with anxiety disorders.⁹

107 While the prevalence of ocular morbidity, depression, and anxiety are lower among children
108 compared to adults, the total burden of these conditions is higher due to the length of time children are
109 affected if the underlying disorders are not identified and corrected. Furthermore, adolescents
110 experiencing sub-threshold depressive symptoms have an increased risk of developing mental health
111 problems, such as depression, anxiety, substance dependence, and suicide later in life.¹³⁻¹⁶ However,
112 studies investigating mental health in vision-impaired children are relatively few, and their findings
113 are inconsistent. A previous systematic review found that the overall association between vision
114 impairment and mental health among children and young adults was inconsistent due to differences in
115 research aims, study design, and definitions of visual impairment between the included studies.⁷

116 Beyond vision impairment, common chronic ocular morbidities such as strabismus¹⁷ may also cause
117 adverse cosmetic, functional, and psychological consequences among children,¹⁸⁻²⁰ eventually
118 affecting their development and maturation. Although much research has been conducted on the
119 impact of strabismus on the quality of life (QoL) and mental health of adults, the effect of strabismus
120 on children has not been extensively studied. A school-based study in China demonstrated that
121 children with strabismus had a significantly higher prevalence of indicators of depression and anxiety
122 than the healthy control group.²⁰ Several interventional studies have also shown that strabismus
123 surgery offers not only cosmetic benefits, but also can improve the psychosocial health and QoL of
124 children.²¹⁻²⁴

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

129 impairment, ocular morbidity and their treatment are associated with depression and anxiety in
130 children.

131 **Methods**

132 We followed the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA)
133 reporting guidelines²⁵ (PRISMA checklist-Supplementary File 1). A protocol was registered and
134 published on The International Prospective Register of Systematic Reviews (PROSPERO,
135 CRD42021233323).

136 **Search Methods for Identifying Studies**

137 We searched MEDLINE, Embase, Web of Science, PsycINFO, Cochrane Database of Systematic
138 Reviews, and the Cochrane Central Register of Controlled Trials in the Cochrane Library, CINAHL
139 and Chinese databases WANFANG MED ONLINE and China National Knowledge Infrastructure
140 (CNKI) from inception to February 18, 2021, without language restriction. The search strategy was
141 developed under guidance of an information specialist (RF). We tested the search strategy through an
142 iterative process before finalising our combinations of terms (Supplementary File 2). The reference
143 lists of relevant papers were checked for potentially relevant articles.

144 **Eligibility Criteria**

145 According to these criteria, the following types of studies were considered eligible for inclusion: (1)
146 Studies that enrolled children or young adults, as long as the mean age of participants was <18 years.
147 Studies focused on mental health in adults who had vision impairment (defined according to the
148 International Classification of Diseases 11 (2018)²⁶, distance vision impairment comprises four levels:
149 mild (presenting visual acuity < 6/12), moderate (presenting visual acuity <6/18), severe (presenting
150 visual acuity <6/60) and blindness (presenting visual acuity <3/60). Thus, a participant falling into
151 any of these categories (that is, with presenting visual acuity < 6/12) would be classified as having
152 vision impairment) or ocular morbidity as children were also included in the narrative synthesis; (2)
153 Observational and interventional studies, including randomized controlled trials (RCTs) and before-
154 after studies with no control group. The intervention had to be ophthalmic; (3) Studies with a
155 comparison group, such as normally sighted children; (4) Studies with outcome variables that
156 included the prevalence and/or scores for depression and/or anxiety; (5) Any study setting was
157 permitted. (6) Original studies published in peer-reviewed journals.

158 **Study Selection, Data Collection, and Risk of Bias Assessment**

159 Two reviewers (DL and HN) independently screened all titles and abstracts for eligibility. For
160 potentially eligible studies, reviewers read the full-text articles to determine final inclusion or
161 exclusion. Two reviewers (DL and SO) extracted data independently into an Excel file (version 2201,

162 Microsoft Corporation, Redmond, WA), while an additional two co-authors (NW and BX) reviewed
163 data extraction forms for English and Chinese articles, respectively, to cross-check for accuracy and
164 validity.

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

174 The risk of bias and quality of studies were assessed using the Joanna Briggs Institute (JBI) critical
175 appraisal checklist for observational studies and RCTs and the relevant National Institutes of Health
176 (NIH) (USA) quality assessment tool for other study designs. We identified six articles in languages
177 other than English and Chinese (one each in Greek, Korean, Spanish, and Serbian; and two in
178 Portuguese). After reviewing the abstracts, which were in English, we found that none of these studies
179 included the outcome of interest and were therefore excluded.

180 **Data Synthesis and Analysis**

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

189 Since various tools were used to measure depression and anxiety in different studies, standardised
190 mean differences (SMD) were used in the pooled analyses. Nine out of the 15 studies covering vision
191 impairment concerned myopia, and many did not specify the participants' visual acuity or the exact
192 cause(s) of non-myopic impaired vision. It was thus not possible to perform subgroup analysis by
193 level or exact cause of vision impairment, and instead, this was done stratifying by myopia versus
194 other causes. A random-effects model was used due to heterogeneity between studies. A 'leave-one-
195 out' sensitivity analysis was carried out to evaluate the relative impact of studies on the meta-analytic
196 outcomes. Data were displayed using Forest plots for depression and anxiety separately.

197 **Results**

198 During initial database searches, 28988 articles were identified, while four studies were located using
 199 the reference lists of the identified studies. We excluded 8737 as duplicates. After abstract/title
 200 screening, 70 articles were eligible for full-text evaluation, after which a further 34 articles were
 201 excluded. In total, 36 studies were included in the systematic review (Figure 1).^{6,20-24,27-56}

202 *Insert Figure 1 here*

203 **Study Characteristics**

204 Of the 36 included studies, 21 (58.3%) observational studies concerned vision impairment, eight
 205 observational studies (22.2%) concerned strabismus, and the remaining seven (19.4%) were
 206 interventional studies. The 21 observational studies concerning vision impairment enrolled 7,064
 207 participants (mean sample size n=346, standard deviation (SD)=363, range: 52–1407) and were
 208 published between 1986 and 2020. According to the World Bank income level,⁵⁷ 14 of these studies
 209 were performed in low- or middle-income countries^{37-39,41-48,51-53} and seven in high-income
 210 countries.^{40,6,49,50,54-56} These 21 studies were of cross-sectional design. Depression and anxiety were
 211 reported in 16^{6,37-41,44-50,52,53,55} and 17^{37-44,46,48,49,51-56} studies, respectively.

212 The eight observational studies concerning strabismus enrolled 668,463 participants (median=310,
 213 interquartile range (IQR), 1388) and were published between 2008 and 2019. Three of these studies
 214 were carried out in low- or middle-income countries, all in China^{20,29,30} Five were carried out in high-
 215 income countries: one in Israel,³² and four in the United States of America (USA).^{31,33,34,36} Depression
 216 and anxiety were reported in six^{20,30,31,33,34,36} and eight of these studies,^{20,29-34,36} respectively.

217 The seven studies concerning the intervention enrolled 20930 participants (median=98, IQR, 59) and
 218 were published between 2005 and 2019. The study from China had the largest sample size of
 219 19,934.²⁸ Five of these studies were carried out in low- or middle-income countries: three in
 220 China,^{22,23,28} one in Iran²⁴ and one in Turkey.³⁵ Two were carried out in high-income countries, one
 221 each in the USA²¹ and Korea.²⁷ Characteristics of the included studies are summarised in Table 1 for
 222 observational studies and Table 2 for interventional studies.

223 *Insert Table 1 and 2 here*

224 **Methodological quality of included studies**

225 Of the 29 observational studies, 17 studies scored low using the JBI quality appraisal checklist. The
 226 most common problems were: (1) failure to define inclusion criteria clearly,^{37,39-41,44,46,50,52,53,55,56} (2)
 227 inability to measure the condition in a valid and reliable manner,^{6,37,39-42,44,48,51-56} (3) lack of objective,
 228 standard criteria used for measurement of the condition,^{6,29,37,39,41,42,44,48,51-54,56} and (4) inability to
 229 identify and deal with potential confounding factors.³² The remaining seven studies concerning the

230 treatment scored well using the JBI or NIH quality appraisal checklists. The most common problems
231 were (1) absence of sample size justification,^{21-24,27} (2) lack of description of the intervention,²¹⁻²⁴ (3)
232 failure to enroll all eligible participants,²¹ (4) loss to follow-up of eligible participants,²³ (5) using a
233 convenience sample to recruit eligible participants,²¹ (6) lack of description whether cases and
234 controls matched appropriately,³² and (7) lack of description of whether participants were analysed in
235 the groups to which they were randomised²⁸ (Table 3).

236 *Insert Table 3 here*

237 **Quantitative synthesis with meta-analysis**

238 The 11 studies (3,926 participants, 54.3% vision-impaired) that reported scores for depression were
239 included in a meta-analysis. Children with vision impairment had higher depression scores than
240 controls (pooled SMD: 0.57, 95% CI: 0.26-0.89; $I^2=94.3%$; Figure 2). Six studies in which myopia
241 was the cause of vision impairment, showed significantly higher depression scores compared to
242 children with normal vision (SMD: 0.59, 95% CI: 0.36-0.81; $I^2=85.4%$). Five studies with other
243 causes of vision impairment found a similar point estimate compared to controls, which was imprecise
244 due to high heterogeneity and did not reach nominal statistical significance (SMD 0.58, 95% CI -0.08-
245 1.25; $I^2=94.7%$).

246 *Insert Figure 2 here*

247 Leave-one-out sensitivity analyses showed that after removing the potential outlier studies, the pooled
248 effect size still suggested higher depression scores in visually impaired children compared to normally
249 sighted children. (Supplementary Figures 1 and 2).

250 Fourteen studies (5245 participants, 60.1% vision-impaired) providing anxiety scores were included
251 in a meta-analysis. Visually impaired children had higher anxiety scores (pooled SMD: 0.61, 95% CI:
252 0.40-0.82; $I^2=91.1%$; Figure 3). Both children with myopia, and those with other causes of vision
253 impairment, had higher anxiety scores than normally sighted children. Effects did not differ between
254 sub-groups with myopic vision impairment (SMD: 0.48, 95% CI: 0.32-0.64, $I^2=82.9%$) compared to
255 those with other causes of vision impairment (SMD: 0.93, 95% CI: 0.34-1.53, $I^2=88.7%$, $p=0.15$).

256 *Insert Figure 3 here*

257 Leave-one-out sensitivity analyses showed that, after excluding the potential outlier studies, the
258 pooled effect size suggests a higher anxiety score in visually impaired children compared to normally
259 sighted children. (Supplementary Figures 3 and 4).

260 Three^{21,24,35} and four^{21,23,24,35} studies concerning strabismus surgery with complete data were included
261 in the meta-analysis of depression and anxiety, respectively. Strabismus surgery significantly

262 improved the symptoms of depression (SMD: 0.59, 95% CI: 0.12-1.06; $I^2=85.3\%$; Figure 4) and
263 anxiety (SMD: 0.69, 95% CI: 0.25- 1.14; $I^2=86.4\%$; Figure 5).

264 *Insert Figure 4 and 5 here*

265

266 **Qualitative synthesis**

267 Overall, the six studies concerning vision impairment and depression and anxiety among children
268 included in the qualitative synthesis indicated that the impact of vision impairment on depression and
269 anxiety was mixed^{45,47,50,53-55} (Table 1). Four studies (949 participants) found that vision-impaired
270 adolescents had higher prevalence or scores of depression and anxiety than their normally sighted
271 peers.^{45,50,54,55} The other two studies (358 participants) found that vision-impaired children did not
272 have a significantly higher score in the subdomain of proxy-reported anxiety/depression than
273 normally sighted children.^{47,53}

274 The observational studies concerning strabismus were also described narratively due to the
275 heterogeneity of the study design and the diverse outcomes reported. Five studies (667,211
276 participants) indicated a positive association of strabismus and depression and/or anxiety in
277 children.^{20,29-32} Two retrospective studies (1,068 participants) suggested that although the children
278 with strabismus were at increased risk for developing mental illness by early adulthood, the
279 differences of prevalence in depression and anxiety were not statistically significant compared to
280 children without strabismus.^{33,34}

281 Of the four studies (1,927 participants) assessing the impact of strabismus treatment on depression
282 and anxiety not included in the meta-analysis,^{22,27,32,36} one interventional study found strabismus
283 surgery statistically improved the symptoms of anxiety and depression in both heterotropia and
284 heterophoria patients.²² Another interventional study indicated that the depression/anxiety subscale
285 scores were unchanged after occlusion therapy in children with intermittent exotropia.²⁷ One case-
286 control study found a borderline significant association between strabismus correction and anxiety
287 (Odds Ratio [OR]=2.98; 95% CI, 1.01-8.75; P=0.06).³² A retrospective observational case series study
288 suggested that strabismus surgery for children with intermittent exotropia did not decrease or alter the
289 development of mental illnesses including major depression by early adulthood, regardless of surgical
290 success or age at surgery.³⁶ The only cluster-RCT included 19934 participants and found that
291 providing free glasses to primary school children in China did not reduce students' fear of
292 examinations or excessive concern about test scores (learning anxiety); however, there was a small,
293 yet significant, reduction in students' excessive concerns about their bodies (physical anxiety).²⁸

294 **DISCUSSION**

295 In this systematic review, we observed a significant positive association between vision impairment
296 and scores of depression and anxiety in children and significant improvement of depression and
297 anxiety symptoms after strabismus surgery among children. The difference in anxiety scores between
298 children with visual impairment due to either myopia or other causes compared to emmetropic or
299 control children, respectively, were both significant, while the difference in depression scores was
300 only significant among children with visual impairment due to myopia (but not due to other causes)
301 compared to emmetropic or control children, respectively.

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

306 Twenty-two out of the 36 studies are from low- and middle-income countries, and nine
307 studies^{28,38,39,41-43,45,48,52} concerning myopia were conducted in China with larger sample sizes
308 (including 24964 participants). The high proportion of studies from China and LMICs in general,
309 likely reflects the high prevalence of myopia in the former⁵⁸ and the importance of unaddressed
310 children's vision deficits in the latter, potentially reducing the generalizability of our conclusions.
311 Uncorrected refractive error continues to be the leading cause of vision impairment worldwide,⁵⁹ and
312 over half of the children aged 6-18 years in China are myopic.⁶⁰ The inability to see clearly and the
313 proven impact of poor vision on educational performance might be a source of anxiety and
314 depression, especially in the highly-pressurized Chinese educational environment.⁴ Further, only 15%
315 of children needing glasses and living in China's underserved rural western areas have them.⁴ This
316 review identified only one RCT involving myopia correction and mental health, and although it found
317 providing free eyeglasses did not reduce learning anxiety, a small but statistically significant
318 reduction was observed in physical anxiety.²⁸ More RCTs are needed to explore the causal association
319 between ophthalmic treatment and mental health among children, with special attention to myopia.

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

329 Interestingly, of the six studies concerning vision impairment and depression and anxiety among
330 children included in the qualitative synthesis, four studies found that vision-impaired adolescents had
331 higher prevalence or scores of depression and anxiety than their normally sighted peers.^{45,50,54,55} In
332 comparison, two studies which used proxy-reported anxiety/depression found that vision-impaired
333 children (compared to normally sighted children) did not have significantly higher scores.^{47,53} This
334 may indicate difficulty for proxies (parent/guardian/caretaker) to identify signs of anxiety/depression
335 in children. Future studies to improve proxy identification of signs of anxiety/depression in children
336 are needed.

337 Most observational studies concerning strabismus found a positive association between strabismus
338 and depression and/or anxiety, except for two studies in which the numbers of strabismus patients
339 were small (n=127 and 407).^{33,34} A recent large study in South Korea (n=654152) found that children
340 with strabismus did not have higher depression and anxiety prevalence than children with
341 conjunctivitis after adjusting for age, preterm birth, or cerebral palsy and mental retardation.⁶¹
342 However, this study used administrative data from health insurance records, which might have
343 underdiagnosed strabismus-related depression and anxiety. Another study has reported that children
344 with allergic conjunctivitis had reduced QoL.⁶² Additionally, one recent study using commercial
345 insurance claims data including 12,005,189 participants found that children younger than 18 years
346 with strabismus have higher odds of mental illnesses including anxiety and depression than children
347 without strabismus. However, 64.5% and 46.0% in the strabismus and control group, respectively,
348 also had at least one systemic comorbid condition such as cancer of the brain and nervous system or
349 Leukaemia, which was adjusted for in the multivariable analysis.⁶³ Interestingly, a study from 2003
350 suggests that an association between strabismus and mental illness has a genetic basis: a transcription
351 factor gene named *PMX2B* was associated with both schizophrenia and constant exotropia.⁶⁴

352
353 Interventional studies showed that treating strabismus could improve mental health, including
354 depression and anxiety. The worldwide estimated prevalence of strabismus is as high as 1.93%,¹⁷ and
355 the present review indicates that early detection and treatment might profoundly impact children's
356 mental health. Negative attitudes towards strabismus appear to emerge as early as six years and
357 increase with age.⁶⁵ However, in developing countries, including China, India and Vietnam,
358 strabismus surgery is often considered cosmetic and may not be covered by medical insurance.⁶⁶⁻⁶⁸
359 The average costs of strabismus surgery in China and Vietnam are USD 700⁶⁷ and USD 154,⁶⁸
360 respectively. Eight in ten patients in China paid out-of-pocket for the surgery,⁶⁷ which could deter
361 patients of low socioeconomic status from seeking treatment. The current review provides evidence in
362 favour of insurance coverage for strabismus surgery.

363 Strengths of this review include the broad and comprehensive nature of the search strategy and the
364 inclusion of studies from low-middle- and high-income countries. However, only one included study

365 was conducted in a lower-middle-income country.⁴⁴ Thus, extrapolation of these results to such
366 settings must be done with care.

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

374

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

382

383 Additional Information

384

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391 synthesis as co-reviewers. DL prepared the first draft, and VFC, NC and GV provided revisions,
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395

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402

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561 **FIGURE 1.** Flow chart of the study selection process

562

563 **FIGURE 2.** Forest plot of the random-effects model for the association between depression and
564 vision impairment in children

565 [Figure. 2 footnotes] *: boys; **: girl.

566

567 **FIGURE 3.** Forest plot of the random-effects model for the association between anxiety and vision
568 impairment in children

569 [Figure 3 footnotes] *: boys; **: girl.

570

571 **FIGURE 4.** Forest plot of the random-effects model of the impact of strabismus surgery on
572 depression in children

573 [Figure 4 footnotes] *Higher score represents better function, the original SMD is -0.58, we change
574 the sign of the SMD.

575 **: Latent deviation group, ***: Manifest exotropia group.

576

577 **FIGURE 5.** Forest plot of the random-effects model of the impact of strabismus surgery on anxiety in
578 children

579 [Figure 5 footnotes] *Higher score represents better function, the original SMD is -0.58, we change
580 the sign of the SMD

581 **a: Latent deviation group, ***b: Manifest exotropia group.

582

TABLE 1. Characteristics of observational studies included in the systematic review (N=29)

Author (Year)	a) Country b) Study design c) Setting d) Diagnosis	a) Sample size b) Sex (%) c) Age, years Mean \pmSD (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 age:17.2 SD: not specified Range (13-19)	a) The degree of corrected vision in the better eye was 20/200 or worse, or there was severe restriction in the visual field b) Not specified c) Normally sighted	a) Anxiety b) Child Behavior Checklist (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) Not specified	a) Not specified b) Health check record c) Normally sighted	a) Depression and anxiety b) Symptom Checklist (SCL-90)	Depression ($P < 0.005$) and anxiety ($P < 0.005$) scores were higher in children with myopia versus emmetropia.
Huurte 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) Not specified c) Normally sighted	a) Depression b) Modified 13-item Beck's Depression Inventory (RS-BDI)	Vision impaired girls had significantly higher depression score than their normally sighted counterpart ($P < 0.05$).

Koenes et al, (2000) ⁵⁰	<ul style="list-style-type: none"> a) United States b) Cross-sectional c) School d) Blindness 	<ul style="list-style-type: none"> a) 51 b) 49% male c) Blind group mean age 15, Sighted group 16 d) rang (12-18) 	<ul style="list-style-type: none"> a) The state standard for legal blindness (State of New Mexico, 1993) b) Measured c) Without myopia 	<ul style="list-style-type: none"> a) Depression b) The Beck Depression Inventory 	The incidence of depression among blind adolescents was significantly higher than that of normally sighted peers (P<0.005)
Wang et al, (2003) ⁴⁶	<ul style="list-style-type: none"> a) China b) Cross-sectional c) Hospital d) Amblyopia 	<ul style="list-style-type: none"> a) 160 b) 58.8% male c) Not specified (6-16) 	<ul style="list-style-type: none"> a) Consensus of Strabismus and amblyopia Group, Pediatric Ophthalmology Society, Chinese Medical Association (1985) b) Measured c) Healthy children 	<ul style="list-style-type: none"> a) Depression and anxiety b) Self-Rating Anxiety Scale (SAS), Self-Rating Depression Scale (SDS), Child Behavior Checklist (CBCL) 	Depression (P<0.01) and anxiety (P<0.01) scores in children with amblyopia were significantly higher than that of the control group.
Hu et al, (2007) ⁴⁷	<ul style="list-style-type: none"> a) China b) Cross-sectional c) School d) Amblyopia 	<ul style="list-style-type: none"> a) 200 b) 47% male c) Study group 5.62±0.77 (4-6) Control group 5.68±0.73 (Not specified) 	<ul style="list-style-type: none"> a) Consensus of Strabismus and amblyopia Group, Pediatric Ophthalmology Society, Chinese Medical Association (1996) b) Measured c) Healthy children 	<ul style="list-style-type: none"> a) Depression b) Child Behaviour Checklist (CBCL) 	The difference in depression scores between the two groups was not significant (P =0.051).

Garaigordobil et al, (2009) ⁴⁰	<ul style="list-style-type: none"> a) Spain b) Cross-sectional c) School d) Vision impairment 	<ul style="list-style-type: none"> a) 90 b) 54.4% male c) 14.99±2.02 (12–17) 	<ul style="list-style-type: none"> a) Not specified b) Medical record c) Normally sighted 	<ul style="list-style-type: none"> a) Depression and anxiety b) The Revised Symptom Checklist (SCL-90-R) 	The difference in depression and anxiety subscales between vision-impaired children and the control group is not significant.
Bolat et al, (2010) ³⁷	<ul style="list-style-type: none"> a) Turkey b) Cross-sectional c) School d) Vision impairment 	<ul style="list-style-type: none"> a) 80 b) 57.5% male c) 12.82±1.17 (11-14) 	<ul style="list-style-type: none"> a) Congenital complete visual impairment b) Not specified c) Normally sighted 	<ul style="list-style-type: none"> a) Depression and anxiety b) The Piers-Harris Children's Self-Concept Scale, Children's Depression Inventory (CDI) 	Prevalence of depression among adolescents with visual impairment is similar to that of normally sighted peers (P=0.582), whereas anxiety was more common among impaired adolescents (P=0.025).
Wei et al, (2011) ⁵³	<ul style="list-style-type: none"> a) China b) Cross-sectional c) Hospital d) Amblyopia 	<ul style="list-style-type: none"> a) 158 b) 50.6% male c) Not specified (4-11) 	<ul style="list-style-type: none"> a) Diagnostic criteria of Strabismus from Chinese Association for Pediatric Ophthalmology and Strabismus (1985) b) Measured c) Healthy children 	<ul style="list-style-type: none"> a) Depression and anxiety b) Child Behavior Checklist (CBCL) 	The difference in depression and anxiety scores between amblyopic children and the normally sighted group were not significant, in either girls or boys.
Liu et al, (2012) ⁴¹	<ul style="list-style-type: none"> a) China b) Cross-sectional c) School d) Myopia 	<ul style="list-style-type: none"> a) 286 b) 46.9% male c) Study group 13.8±2.4(14-16) Control group 	<ul style="list-style-type: none"> a) Not specified b) Health check record c) Normally sighted 	<ul style="list-style-type: none"> a) Depression and anxiety b) Symptom Checklist (SCL-90) 	The depression (P<0.05) and anxiety (P<0.05) subscales of vision-impaired children were significantly higher than that of control group.

13.6±2.5(14-16)

Alimovic et al,
(2013)⁵⁵

- a) Croatia
- b) Cross-sectional
- c) School
- d) Vision impairment

- a) 80
- b) 51.3% male
- c) Not specified (4-11)

- a) Visual impairments were defined according to Croatian regulations on the composition and working methods of expert evaluation in social welfare realisation process (Ministry of Labor and Social Welfare and Ministry of Health 2002).
- b) Medical record
- c) Normally sighted

- a) Depression and anxiety
- b) Child Behavior Check List/4–18(CBCL/4–18)

Anxiety and depression scores of vision-impaired children were not significantly higher than that of normally sighted peers.

Guo et al, (2015)³⁹

- a) China
- b) Cross-sectional
- c) School
- d) Myopia

- a) 650
- b) Not specified
- c) Not specified

- a) Not specified
- b) Not specified
- c) Normally sighted

- a) Depression and anxiety
- b) Symptom Checklist (SCL-90)

The depression ($P<0.01$) and anxiety ($P<0.01$) subscales were significantly higher in myopic children than in emmetropic peers.

Panday et al, (2015) ⁴⁴	<ul style="list-style-type: none"> a) India b) Cross-sectional c) School d) Congenital visual impairment 	<ul style="list-style-type: none"> a) 60 b) 0 male c) Study group 14.93±2.03 Control group 14.73±1.79 	<ul style="list-style-type: none"> a) Not specified b) Not specified c) Normally sighted 	<ul style="list-style-type: none"> a) Depression and anxiety b) Depression, Anxiety and Stress Scale (DASS) 	Depression (P=0.01) and anxiety (P=0.01) were greater among adolescent girls with visual impairment in comparison to normally sighted peers.
Ayaki et al, (2016) ⁴⁹	<ul style="list-style-type: none"> a) Japan b) Cross-sectional c) Hospital d) Myopia 	<ul style="list-style-type: none"> a) 278 b) 44% male c) 14.2 ± 2.6 (10-19) 	<ul style="list-style-type: none"> a) High myopia ($\leq -6.00D$), mild myopia ($-5.75D$ to $-0.50D$), and no myopia ($-0.25D$ to $+2.75D$) b) Measured c) Without myopia 	<ul style="list-style-type: none"> a) Depression and anxiety b) The Hospital Anxiety and Depression Scale (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	<ul style="list-style-type: none"> a) Turkey b) Cross-sectional c) School d) Vision impairment 	<ul style="list-style-type: none"> a) 74 b) 47.3% male c) Study group 12.32 ± 3.38 (7-18) Control group 10.82 ± 2.18 (7-15) 	<ul style="list-style-type: none"> a) Not specified b) Medical record c) Normally sighted 	<ul style="list-style-type: none"> a) Anxiety b) The State-Trait Anxiety Inventory for Children (STAI-C) 	A higher level of anxiety was found in visually impaired children and adolescents compare to the normally sighted control (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) State-Trait Anxiety Inventory (STAIC)	Girls with myopia had a higher prevalence of trait anxiety as compared to their emmetropic peers 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) Symptom Checklist (SCL-90)	Depression (P< 0.01) and anxiety (P< 0.01) scores in myopic students were higher than that of emmetropes.
Zhou, (2019) ⁴²	a) China b) Cross-sectional c) School d) Myopia	a) 300 b) 50.3% male c) Not specified	a) Using visual acuity as a surrogate measurement for refractive error b) Measured c) Normally sighted	a) Anxiety b) Self-Rating Anxiety Scale	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 (spherical equivalent (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	a) Depression and anxiety b) Self-Rating Anxiety Scale (SAS), Self-Rating Depression Scale (SDS)	Depression (P=0.03) and anxiety scores (0.018) among students with myopia were significantly higher than that of emmetropic students.

c) Emmetropia

Cai et al, (2020) ⁴³	<ul style="list-style-type: none"> a) China b) Cross-sectional c) School d) Myopia 	<ul style="list-style-type: none"> a) 1407 b) 54.3% male c) Not specified 	<ul style="list-style-type: none"> a) The myopia group (SE < -0.5 D), the moderate myopia group (-0.5 D -3.00 D), and the moderate and severe myopia group (SE > 3.00 D). b) Measured c) Emmetropia 	<ul style="list-style-type: none"> a) Anxiety b) Social Anxiety Scale for Children (SASC) 	Children with myopia had worse measures of social anxiety) than those with emmetropia (P <0.01).
Xu et al, (2020) ⁴⁵	<ul style="list-style-type: none"> a) China b) Cross-sectional c) Community d) Myopia 	<ul style="list-style-type: none"> a) 766 b) 56.4% male c) 14.32±2.64 (12-16) 	<ul style="list-style-type: none"> a) Myopia is defined as VA<5.0 and SE<-0.5D. b) Measured c) Normally sighted 	<ul style="list-style-type: none"> a) Depression and anxiety b) Self-Rating Anxiety Scale (SAS), Self-Rating Depression Scale (SDS) 	The prevalence 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 emmetropic children.
Mohney et al, (2008) ³³	<ul style="list-style-type: none"> a) United States b) Case-control c) Hospital d) Strabismus 	<ul style="list-style-type: none"> a) 814 b) 50.4% male c) Not specified (< 19) 	<ul style="list-style-type: none"> a) Not specified b) Medical record c) Without strabismus 	<ul style="list-style-type: none"> a) Depression and anxiety b) Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition codes (DSM-4) 	There was no significant difference in terms of depression and anxiety between the strabismus group and the control group.

McKenzie et al, (2009) ³¹	<ul style="list-style-type: none"> a) United States b) Case-control c) Hospital d) Strabismus 	<ul style="list-style-type: none"> a) 366 b) 35.8% male c) Not specified (< 19) 	<ul style="list-style-type: none"> a) Acquired, intermittent exodeviation of at least 10 prism diopters (PD) b) Medical record c) Without strabismus 	<ul style="list-style-type: none"> a) Depression and anxiety b) Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition codes (DSM-4) 	<p>Boys with intermittent exotropia were more likely to develop major depression (P=0.02).</p> <p>Girls with intermittent exotropia were more likely to develop anxiety or phobia (P=0.04).</p>
Kilgore et al, (2010) ³⁶	<ul style="list-style-type: none"> a) United States b) Retrospective observational case series c) Hospital d) Strabismus 	<ul style="list-style-type: none"> a) 184 b) 35.9% male c) Not specified (<19) 	<ul style="list-style-type: none"> a) Acquired, intermittent exodeviation of at least 10 PD b) Strabismus surgery c) Young adults who had childhood Intermittent Exotropia and did not had surgery 	<ul style="list-style-type: none"> a) Depression and anxiety b) Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition codes (DSM-4) 	<p>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</p>
Olson et al, (2011) ³⁴	<ul style="list-style-type: none"> a) United States b) Case-control c) Hospital d) Strabismus 	<ul style="list-style-type: none"> a) 254 b) 52.0% male c) Not specified (<19) 	<ul style="list-style-type: none"> a) Congenital esotropia was defined as a nonaccommodative esotropia that developed by 6 months of age in a neurologically intact child. 	<ul style="list-style-type: none"> a) Depression and anxiety b) Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition codes (DSM-4) 	<p>There was no significant difference in terms of depression and anxiety between the two groups.</p>

			b) Medical record c) Without strabismus		
Lin et al, (2014) ²⁰	a) China b) Cross-sectional c) School d) Strabismus	a) 3903 b) 52.2% male c) Mean age:12.9 SD: Not specified Rang: (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 had 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) Children's social anxiety scale	Children with strabismus and amblyopia have worse psychological problems, including depression (P < 0.05) and anxiety(P < 0.05).
Merdler et al, (2017) ³²	a) Israel b) Case-control c) Military Pre-conscription assessment d) Strabismus	a) 662641 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 fitness-for-service (FFS) codes	Children with uncorrected strabismus were more likely to develop 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 pre-prescription 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 fitness-for-service (FFS) codes	Anxiety was more common in those with uncorrected strabismus. Strabismus correction was not significantly associated with anxiety disorder was observed (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) Children's social anxiety scale	Strabismus worsens children's mental health including anxiety (P=0.006).

SD: Standard Deviation

TABLE 2. Characteristics of intervention studies included in the systematic review(N=7)

Author (Year)	a) Country b) Study design c) Setting d) Diagnosis	a) Sample size taken b) Sex (%) c) Age, years Mean \pmSD (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-after studies with no control group c) Hospital d) Strabismus	a) 98 b) Not specified c) 4.5 \pm 3.3(Not specified)	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 subscale of depression (<0.01) and anxiety (0.01) after strabismus surgery.
Chai et al (2009) ²²	a) China b) Prospective interventional c) Hospital	a) 120 b) 46.7% male c) Heterophoria	a) Not specified b) Strabismus surgery	a) Depression and anxiety b) The Hospital Anxiety and	Compared with pre-operative values, significant improvements were noted after

	d) Strabismus	8.3 ± 2.8 (Not specified) Heterotropia 8.4 ± 2.6 (Not specified)	c) NA	Depression Scale (HADS)	surgery in anxiety (P<0.05) and depression scores (P<0.05).
Jing (2009) ²³	a) China b) Before-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) Children's social anxiety scale	Social anxiety can be significantly improved after strabismus surgery (P<0.001).
Ziaei et al (2016) ²⁴	a) Iran b) Before-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	<ul style="list-style-type: none"> a) Korea b) Before-after studies with no control group c) Hospital d) Strabismus 	<ul style="list-style-type: none"> a) 25 b) 60% male c) Mean age 4.7 years (3-7) 	<ul style="list-style-type: none"> a) Not specified b) Part-time occlusion c) NA 	<ul style="list-style-type: none"> a) Depression and anxiety b) The Child Behavior Checklist (CBCL) 	There was no significant difference in terms of depression /anxiety after part-time occlusion.
Guan et al (2018) ²⁸	<ul style="list-style-type: none"> a) China b) Cluster-Randomized Controlled Trial c) School d) Myopia 	<ul style="list-style-type: none"> a) 19934 b) 52.0% male c) 10.5±1.10 	<ul style="list-style-type: none"> a) Myopia is ≤ -0.5 diopters b) Providing free glasses c) Providing Prescription 	<ul style="list-style-type: none"> a) Learning Anxiety Physical Anxiety b) Mental Health Test (MHT). 	Treatment has no effect on Learning Anxiety and the Mental Health Test, and a small but significant reduction in Physical Anxiety
Ozates et al, (2019) ³⁵	<ul style="list-style-type: none"> a) Turkey b) Before-after studies with no control group 	<ul style="list-style-type: none"> a) 83 b) 49.4% male 	<ul style="list-style-type: none"> a) Not specified b) Strabismus surgery 	<ul style="list-style-type: none"> a) Depression and anxiety 	Strabismus surgery improved the trait anxiety symptom in children with Latent deviation(P=0.006), while in Manifest exotropia group,

c) Hospital d) Strabismus	c) Latent deviation group 16.6±2.1(14-21) Manifest exotropia group 17.5±2.0(14-21)	c) Before-after design, without control group	b) Depression subscale Hospital Anxiety and Depression Scale (HAD-D), State-Trait Anxiety Inventory (STAI)	both anxiety and depression symptoms were improved (P<0.001).
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SD: Standard Deviation; NA: Not applicable

TABLE 3. The checklist results for assessing the methodological quality of the selected studies (N=36)

CROSS-SECTIONAL STUDY	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8
Hasselt et al (1986) ⁵⁴	✓	✓	±	±	◆	◆	✓	✓
Chen et al (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 ⁽⁹⁾ (2011) ⁵³	±	☑	±	±	◆	◆	☑	☑
Alimovic et al (2012) ⁵⁵	±	☑	±	☑	◆	◆	☑	☑
Liu et al (2012) ⁴¹	☒	☑	±	±	◆	◆	☑	☑

Lin et al (2014) ²⁰	✓	✓	✓	✓	✓	✓	✓	✓
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Guo et al (2015) ³⁹	✗	✓	✗	✗	◆	◆	✓	✓
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Panday et al (2015) ⁴⁴	✗	✓	✗	✗	◆	◆	✓	✓
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Ayaki et al (2016) ⁴⁹	✓	✓	✓	✓	✓	✓	✓	✓
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Łazarczyk et al	✗	✓	✗	✗	◆	◆	✓	✓
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(2016)⁵⁶

Li (2016) ⁵²	±	✓	✗	±	◆	◆	✓	✓
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BEFORE-AFTER STUDIES WITH NO CONTROL GROUP	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11	Q12
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	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11	Q12	Q13
Guan et al (2018) ²⁸	✓	✓	✓	✓	◆	◆	✓	✓	±	✓	✓	✓	✓
CASE-CONTROL	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10			
Mohney et al (2008) ³³	✓	✓	✓	✓	✓	✓	✓	✓	◆	✓			
McKenzie et al (2009) ³¹	✓	✓	✓	✓	✓	✓	✓	✓	◆	✓			

Olson et al (2012) ³⁴	✓	✓	✓	✓	✓	✓	✓	✓	◆	✓
Merdler et al (2017) ³²	±	±	✓	✓	✓	✗	✗	✓	◆	✓
CASE SERIES	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10
Kilgore et al (2014) ³⁶	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓

Question key: *JBI tool questions for cross-sectional study assessment*: Q1 = "Were the criteria for inclusion in the sample clearly defined?", Q2 = 2 Were the study subjects and the setting described in detail?", Q3 = "Was the exposure measured in a valid and reliable way?", Q4 = "Were

objective, standard criteria used for measurement of the condition?", Q5 = "Were confounding factors identified?", Q6 = "Were strategies to deal with confounding factors stated?", Q7 = "Were the outcomes measured in a valid and reliable way?", Q8 = "Was appropriate statistical analysis used?" (Joanna Briggs Institute, 2020).

NIH tool questions for before-after studies with no control group study assessment: Q1 = " Was the study question or objective clearly stated?", Q2 = "Were eligibility/selection criteria for the study population prespecified and clearly described?", Q3 = " 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?", Q4 = " Were all eligible participants that met the prespecified entry criteria enrolled?", Q5 = " Was the sample size sufficiently large to provide confidence in the findings?", Q6 = " Was the test/service/intervention clearly described and delivered consistently across the study population?", Q7 = " Were the outcome measures prespecified, clearly defined, valid, reliable, and assessed consistently across all study participants?", Q8 = " Were the people assessing the outcomes blinded to the participants' exposures/interventions?", Q9 = "Was the loss to follow-up after baseline 20% or less? Were those lost to follow-up accounted for in the analysis?", Q10 = "Did the statistical methods examine changes in outcome measures from before to after the intervention? Were statistical tests done that provided p values for the pre-to-post changes?", Q11 = "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)?", Q12 = "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)

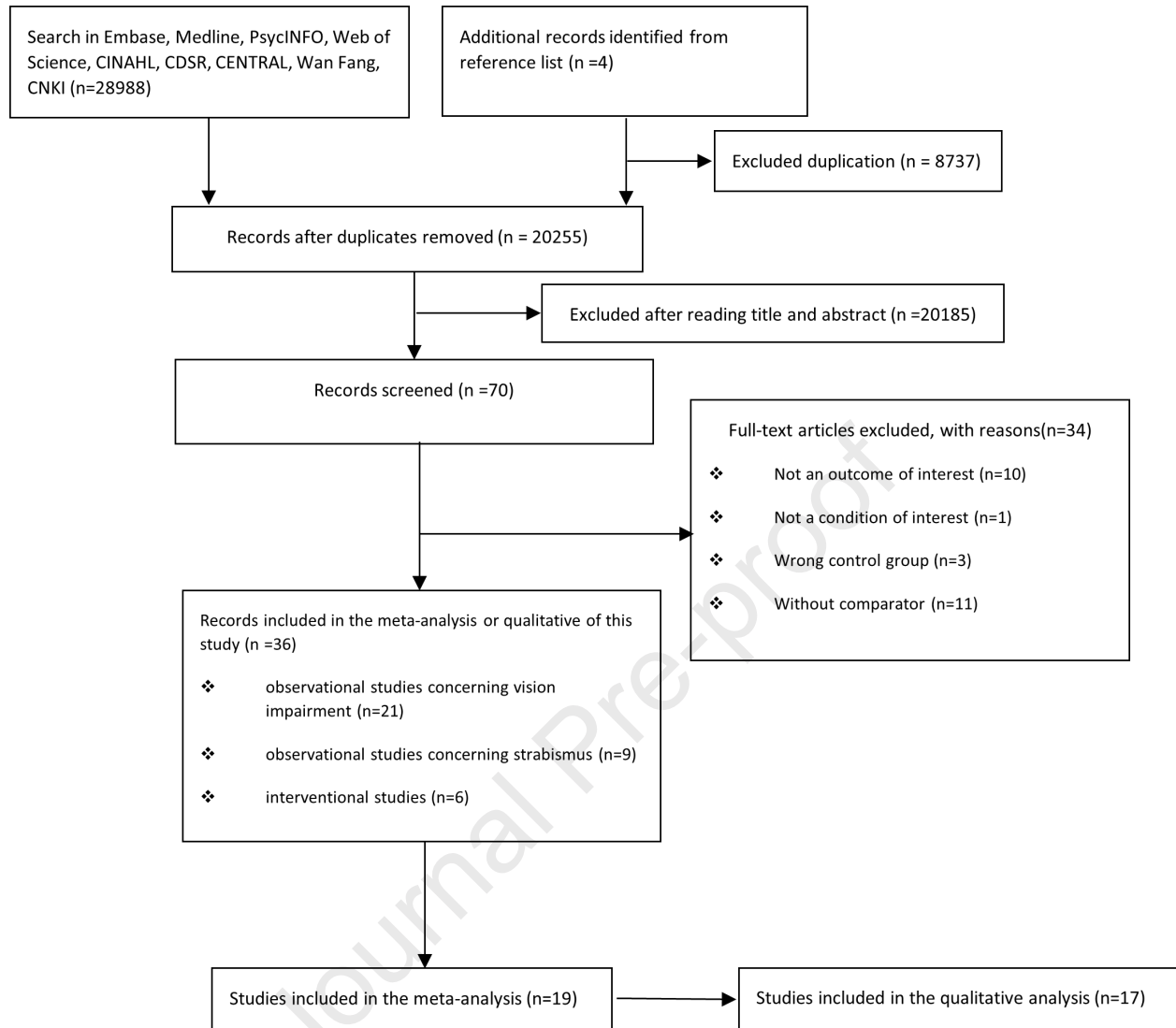
JBI tool questions for randomized controlled trials study assessment: Q1 = "Was true randomization used for assignment of participants to treatment groups?", Q2 = "Was allocation to groups concealed?", Q3 = "Were treatment groups similar at the baseline?", Q4 = "Were participants blind to treatment assignment?", Q5 = "Were those delivering treatment blind to treatment assignment?", Q6 = "Were outcomes assessors blind to treatment assignment?", Q7 = "Were treatment groups treated identically other than the intervention of interest?", Q8 = "Was follow up complete and if not, were differences between groups in terms of their follow up adequately described and analyzed?", Q9 = "Were participants analyzed in the groups to which they were randomized?", Q10 = "Were outcomes measured in the same way for treatment groups?", Q11 = "Were outcomes measured in a reliable way?", Q12 = "Was appropriate statistical analysis used?", Q13 = "Was the trial design appropriate for the topic, and any deviations from the standard RCT design accounted for in the conduct and analysis?" (Joanna Briggs Institute, 2020).

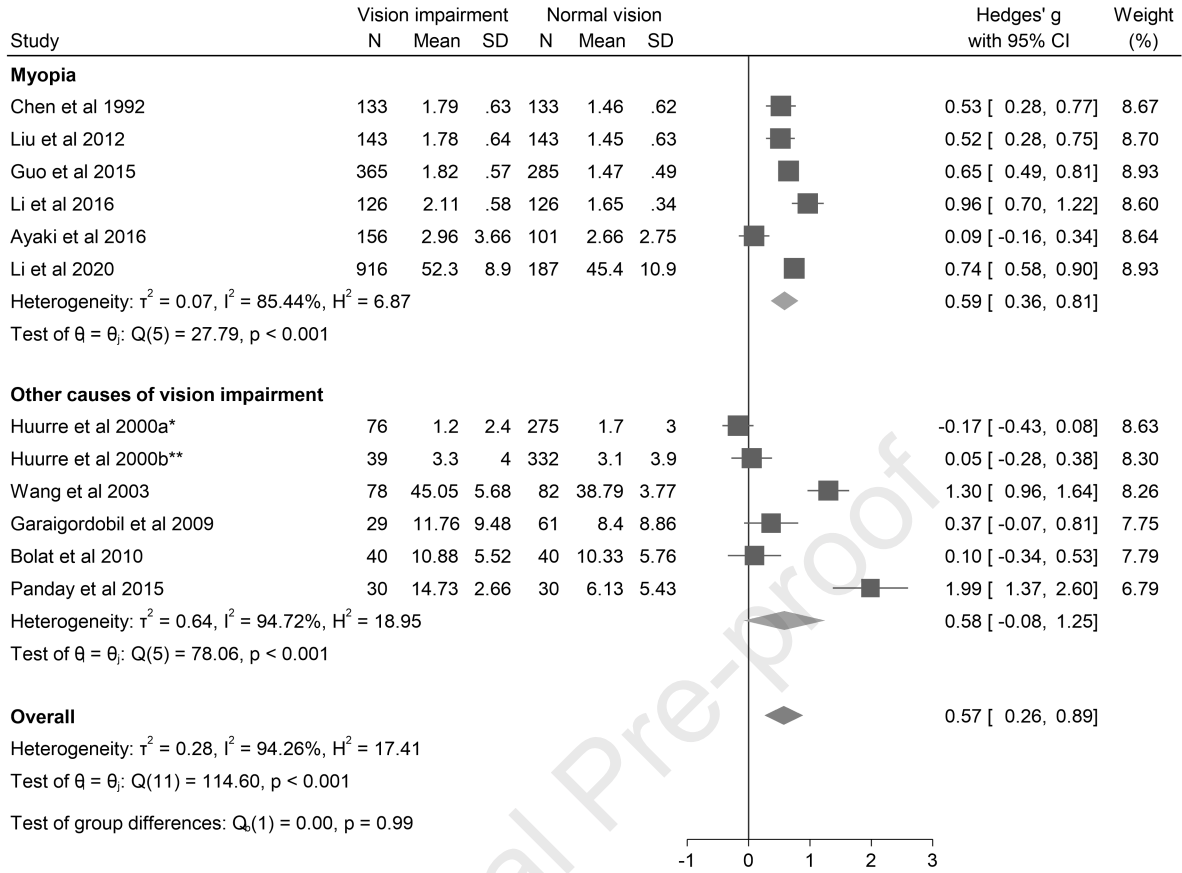
JBI tool questions for case-control study assessment: Q1 = "Were the groups comparable other than the presence of disease in cases or the absence of disease in controls?", Q2 = "Were cases and controls matched appropriately?", Q3 = "Were the same criteria used for identification of cases and controls?", Q4 = "Was exposure measured in a standard, valid and reliable way?", Q5 = "Was exposure measured in the same way for cases and controls?", Q6 = "Were confounding factors identified?", Q7 = "Were strategies to deal with confounding factors stated?", Q8 = "Were outcomes assessed in a standard, valid and reliable way for cases and controls?", Q9 = "Was the exposure period of interest long enough to be meaningful?", Q10 = "Was appropriate statistical analysis used?" (Joanna Briggs Institute, 2020).

JBI tool questions for case series assessment: Q1 = "Were there clear criteria for inclusion in the case series?", Q2 = "Was the condition measured in a standard, reliable way for all participants included in the case series?", Q3 = "Were valid methods used for identification of the condition for all participants included in the case series?", Q4 = "Did the case series have consecutive inclusion of participants?", Q5 = "Did the case series have complete inclusion of participants?", Q6 = "Was there clear reporting of the demographics of the participants in the study?", Q7 = "Was there clear reporting of clinical information of the participants?", Q8 = "Were the outcomes or follow-up results of cases clearly reported?", Q9 = "Was there clear reporting of the presenting site(s)/clinic(s) demographic information?", Q10 = "Was statistical analysis appropriate?" (Joanna Briggs Institute, 2020).

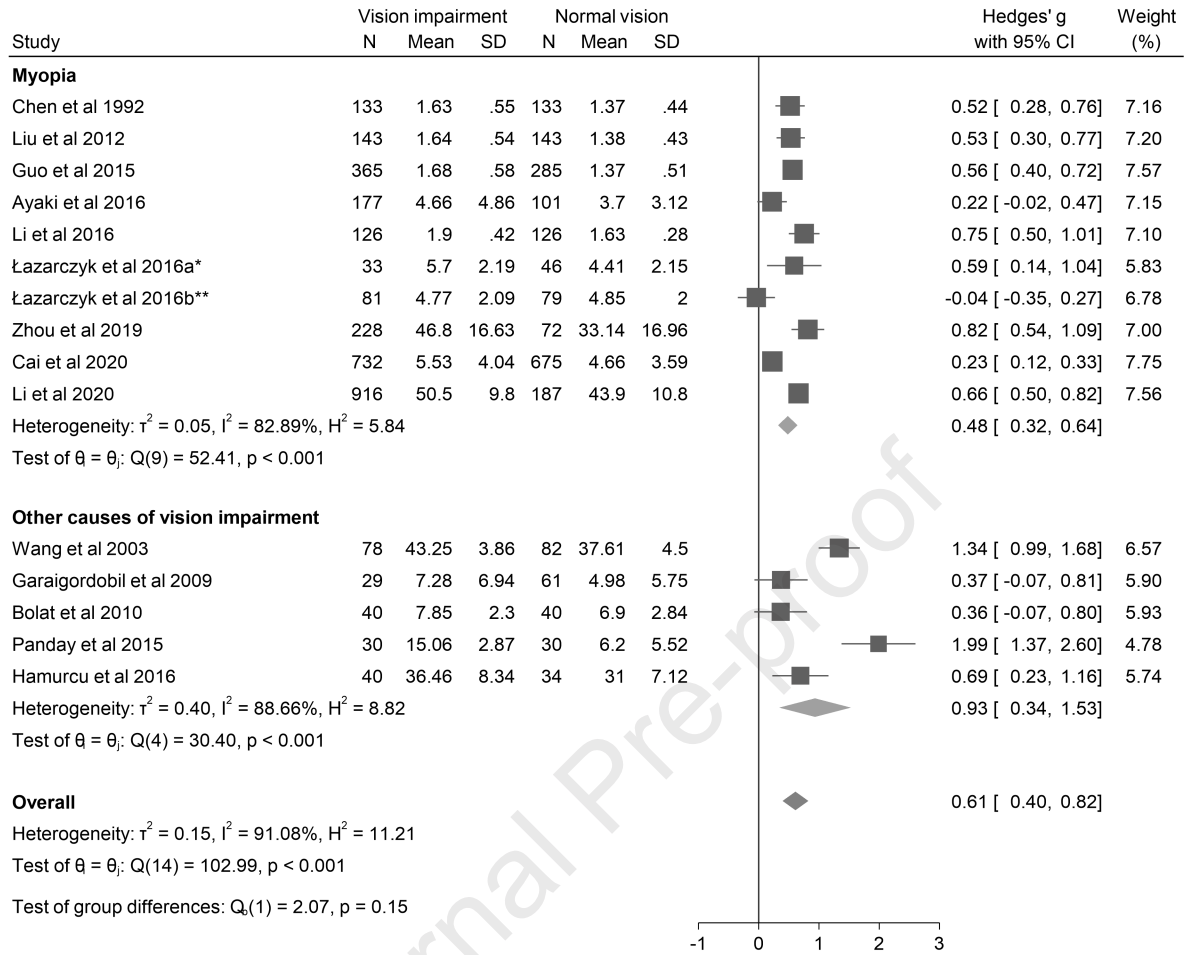
Answers legend: = yes the study satisfactorily met the respective quality criterion; = no the study did not meet the respective quality criterion; = not applicable; and \pm = unclear whether the study has met the respective quality criterion; $*$ = cannot determine.

Journal Pre-proof

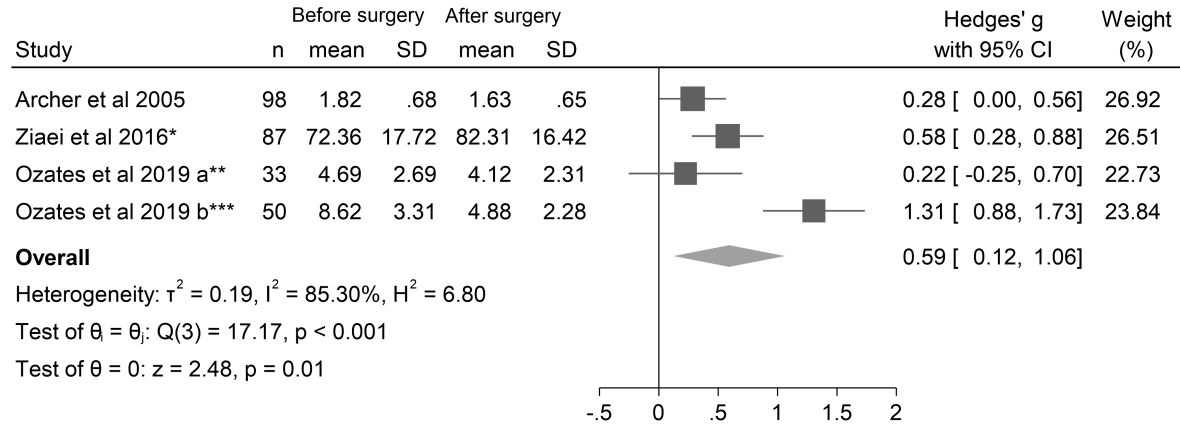




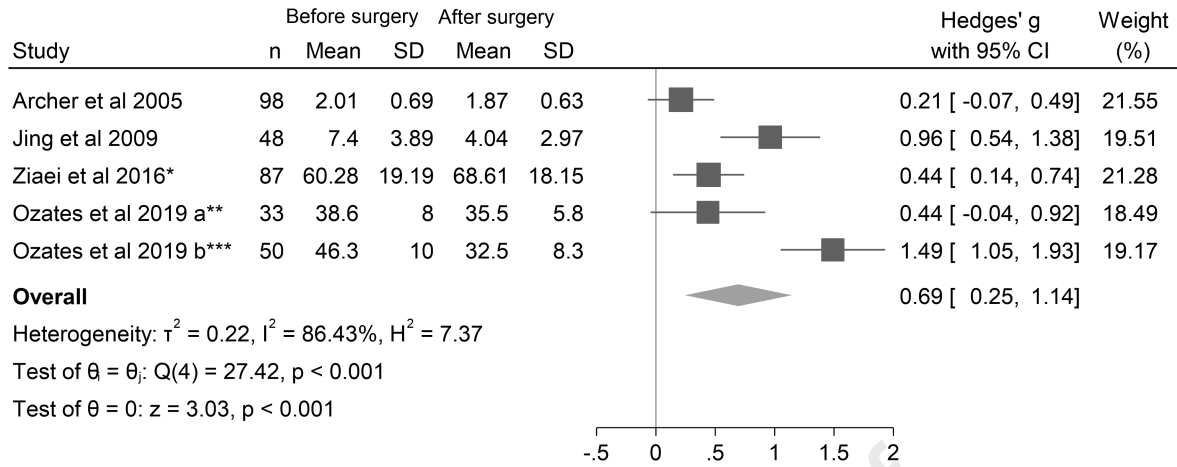
Random-effects REML model
Sorted by: year



Random-effects REML model
Sorted by: year



Random-effects REML model



Random-effects REML model

Précis

We systematically reviewed the existing evidence for the association between eye condition and mental health in children. Meta-analysis revealed vision impairment is associated with greater symptoms of depression and anxiety in children.

Journal Pre-proof