

A Meta-Analysis of Association Between Strabismus in Children/Adolescents and Risk of Mental Health Disorders

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Background: Strabismus, or eye misalignment, is a common condition in children and adolescents. This meta-analysis examined the association between strabismus and mental health disorders including attention deficit hyperactivity disorder (ADHD), anxiety, depression. The strength and consistency of the relationships between strabismus and the risk of mental health disorders and how the associations vary according to characteristics including study size, temporal trends, and type of strabismus type were assessed.

Methods: We conducted a meta-analysis with nine observational studies published between 2008 and 2024, involving 683,942 participants. The effect sizes were calculated as odds ratios (ORs) with 95% confidence intervals (CIs), and heterogeneity was assessed using the I^2 statistic to determine the associations between strabismus and mental health disorders.

Results: The analyses revealed a significant positive association between strabismus and mental health disorders, with a weighted average OR of 1.92 (95% CI: 1.38–2.66; $I^2 = 99.7\%$). Temporal trends suggested that earlier studies reported larger effect sizes, whereas more recent studies showed modest although significant associations. The strongest associations were observed in studies of exotropia; the ORs ranged from 1.44 to 2.70. The study sizes and precisions varied; larger studies provided more reliable estimates and smaller studies showed wider CIs.

Conclusion: Strabismus was significantly associated with an increased risk of ADHD, anxiety, and depression. This association was consistent across different strabismus types and study designs. These findings underscore the importance of mental health screening in children and adolescents with strabismus, particularly those with exotropia. Further research should explore the mechanisms underlying this relationship and the effects of early intervention programs.

Keywords: exotropia, esotropia, attention deficit hyperactivity disorder, anxiety, depression

Introduction

Strabismus, characterized by eye misalignment, is a common ocular condition that affects 2–7% of children globally. Beyond its impact on visual function, such as impaired binocular vision and amblyopia, strabismus has also been associated with psychosocial challenges, including stigma, low self-esteem, and difficulties in social interactions. These psychosocial stressors may associate with mental health conditions—such as anxiety, depression, and attention deficit hyperactivity disorder (ADHD)—among children with strabismus.^{1–4}

The American Academy of Neurology emphasizes the need to address the psychosocial effects of neurological and neurodevelopmental conditions in pediatric populations. This underscores the importance of early detection and intervention to improve long-term outcomes in affected individuals. Children with strabismus face unique psychological burdens, further reinforcing the necessity for holistic care strategies.

Studying the association between strabismus and mental health disorders is essential for several reasons. First, understanding these relationships can help identify high-risk populations, enabling early psychological screening and intervention. Second, addressing the mental health issues in children with strabismus can significantly improve their

quality of life, academic performance, and social integration. Finally, robust evidence for this association can inform healthcare policies and promote integrated care models.⁵

However, previous studies exploring the relationship between strabismus and mental health outcomes have reported inconsistent findings. These discrepancies may stem from methodological limitations such as small sample sizes, cross-sectional designs, lack of standardized diagnostic criteria, and failure to control for potential confounding variables. Additionally, most studies have focused on specific mental health outcomes or strabismus subtypes, limiting the generalizability of their findings. These limitations highlight the need for a comprehensive synthesis of the available evidence.

This meta-analysis systematically evaluated the associations between strabismus and mental health disorders in children and adolescents. Anxiety, depression, and ADHD were the mental health disorders reviewed. By integrating data from observational studies, this review aimed to provide evidence to guide clinical care and inform strategies for comprehensive ophthalmological and psychological management.

Materials and Methods

Study Protocol and Registration

We used the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) criteria to comprehensively evaluate our review and meta-analysis ([Supplementary Material 1](#)).⁶ Our protocol has been registered in the International Prospective Register of Systematic Reviews (PROSPERO) (CRD42024591511). This research followed the guidelines of the Declaration of Helsinki. No new data or patient information was collected during this study. The studies used in this meta-analysis were conducted under the ethical approval of IRB for each study.

Search Strategy

A comprehensive literature search was conducted using electronic databases, including PubMed, Scopus, and the Cochrane Library, from 2000 to 2024. Search terms comprised combinations of keywords and MeSH terms such as “strabismus”, “mental health”, “psychiatric disorders”, “child”, and “adolescents”. In addition, the reference lists of included studies were manually identify of additional relevant articles. No language restrictions were applied ([Supplementary Material 2](#)).

Study Selection

Observational studies that evaluated the association between strabismus and mental health disorders in children and adolescents were systematically reviewed and analyzed. Studies were included if they met all of the following criteria: observational design (case-control, cohort, or cross-sectional), reported an association between strabismus and mental health disorders (anxiety, depression, and ADHD), included participants aged 0–18 years, and provided effect sizes (odds ratios [ORs], hazard ratios [HRs], or relative risks [RRs]) with 95% confidence intervals (CIs).

Exclusion Criteria

Studies were excluded if they lacked sufficient data to calculate effect sizes; focused on adult populations; or were reviews, case reports, or editorials.

Data Extraction

Two independent reviewers extracted the data using a standardized form. Discrepancies were resolved by consensus or consultation with a third reviewer. The extracted data included study characteristics (author, year, design, location), participant characteristics (age, sample size, strabismus type), mental health outcomes (anxiety, depression, ADHD), and effect sizes and 95% CIs.

Quality Assessment

The Newcastle-Ottawa Scale (NOS) was used to assess the quality of the included studies.⁷ Studies that scored ≥ 7 points were considered high quality ([Supplementary Material 3](#)).

Statistical Analyses

Pooled effect sizes (ORs) with 95% CIs were calculated using a random effects model to account for inter-study heterogeneity. Heterogeneity was assessed using the I^2 statistic, with values $>50\%$ indicating substantial heterogeneity. Subgroup analyses were performed based on strabismus type (esotropia, exotropia). Sensitivity analyses were conducted to examine the robustness of the results by excluding low-quality studies and those with extreme effect sizes. Statistical significance was set at $p < 0.05$. All statistical analyses were performed using R (version 4.4.1) with the metafor and meta-packages.⁸ Publication bias was assessed using funnel plots; however, Egger's test was not performed because the number of studies included was < 10 .

Results

Study Selection

The initial search yielded 32,189 articles. After removing duplicates, 9211 unique studies remained. Following title and abstract screening, 8521 studies were excluded because they did not meet the inclusion criteria. A full-text review of 207 studies resulted in the inclusion of 9 observational studies in the final meta-analysis. ([Supplementary Material 4](#)).^{9–17} A PRISMA flow diagram summarizing the study selection process is displayed in [Figure 1](#).

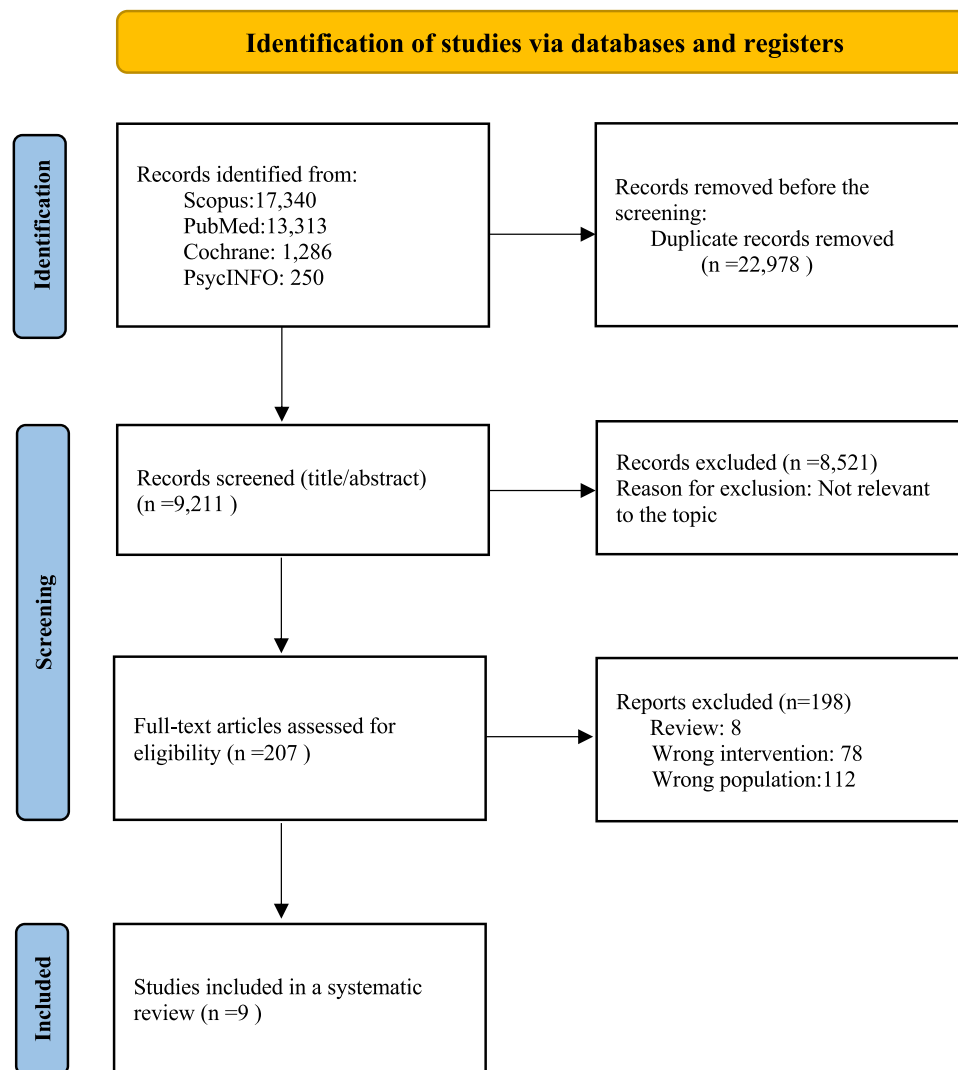


Figure 1 PRISMA flow diagram.

Table 1 Characteristics of Included Studies

| Study | Design | Region | Strabismus Type | Mental Health Outcomes | Sample Size (Cases/Controls) |
|-------------------------------------|-----------------|-------------|-----------------|---------------------------|------------------------------|
| Mohney et al (2008) ⁹ | Cohort | USA | Esotropia | Depression, Anxiety | 168/125 |
| McKenzie et al (2009) ¹⁰ | Case-Control | USA | Exotropia | Anxiety, ADHD | 183/183 |
| Cumurcu et al (2011) ¹¹ | Cross-Sectional | Turkey | Combined | Social Phobia, Depression | 42/47 |
| Olson et al (2012) ¹² | Cohort | USA | Esotropia | ADHD, Anxiety | 127/127 |
| Kilgore et al (2014) ¹³ | Cohort | USA | Exotropia | Mood Disorders, Anxiety | 63/121 |
| Merdler et al (2017) ¹⁴ | Case-Control | Israel | Combined | ADHD, Anxiety | 1598/661,043 |
| Tsai et al (2021) ¹⁵ | Cohort | Taiwan | Esotropia | ADHD | 2049/8196 |
| Choi et al (2021) ¹⁶ | Cohort | South Korea | Combined | Anxiety, Mood Disorders | 327,076/327,076 |
| Lee et al (2022) ¹⁷ | Cohort | USA | Exotropia | Anxiety, Depression | 352,636/11,652,553 |

Abbreviations: USA, United State of America; ADHD, attention deficit hyperactivity disorder.

Study Characteristics

The included studies comprised 9 observational studies published between 2008 and 2024, with a total of 683,942 participants. These studies originated from diverse geographical locations including North America, Asia, and Europe. The study designs included 5 cohort studies, 3 case-control studies, and 1 cross-sectional study. The key characteristics of these included studies are summarized in Table 1.

Pooled Effect Size

This meta-analysis revealed a significant association between strabismus and the risk of mental health disorders in children and adolescents. The pooled OR was 1.92 (95% CI: 1.38–2.66; $I^2 = 99.7\%$), indicating that children with strabismus are approximately twice as likely to have mental health disorders compared to those without strabismus (Figure 2).

Heterogeneity

Substantial heterogeneity was observed among the included studies ($I^2 = 99.7\%$, $p = 0.000$).

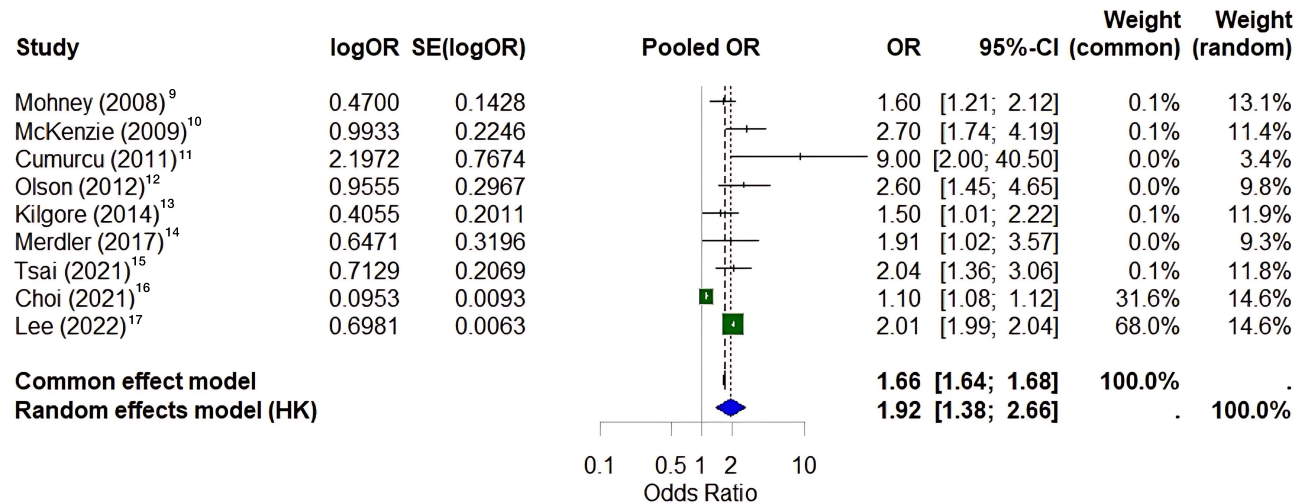


Figure 2 Effect sizes of mental health outcomes in the included studies. [Heterogeneity $I^2 = 99.7\%$, $\tau^2 = 0.1796$, $p = 0$].

Abbreviations: OR, odds ratio; SE, standard error; CI, confidence interval; HK, Hartung-Knapp; I^2 , I-square heterogeneity statistic; τ^2 , tau-square statistic; p, p-value.

Subgroup Analyses

The overall analyses showed that all strabismus types were associated (increased OR > 1). The overall common effects model had an OR = 4.27 [95% CI: 4.20–4.33] and random effects model had an OR = 5.24 [95% CI: 3.45–7.94]. There was very high heterogeneity overall ($I^2 = 99.7\%$, $\tau^2 = 0.2667$, $p < 0.0001$), which indicated substantial variation among studies.

For the unspecified type subgroup analysis, the combined data from the studies by Cumurcu et al,¹¹ Merdler,¹⁴ and Choi¹⁶ had a common effects model, OR = 3.01 [95% CI: 2.95–3.07], random effects model OR = 4.18 [95% CI: 1.94–9.02]), and moderate heterogeneity ($I^2 = 36.8\%$, $\tau^2 = 0.2284$, $p = 0.2057$).

For the esotropia subgroup analysis, the combined data from the studies by Mohny et al,⁹ Olson et al,¹² and Tsai et al,¹⁵ common effects model OR = 4.14 [95% CI: 3.27–5.25], random effects model OR = 5.60 [95% CI: 2.84–11.03], and substantial heterogeneity ($I^2 = 54.6\%$, $\tau^2 = 0.1979$, $p = 0.1102$).

For the exotropia subgroup analysis combined data from the studies by McKenzie et al,¹⁰ Kilgore et al¹³ and Lee et al¹⁷ had a common effects model OR = 7.26 [95% CI: 7.09–7.45], random effects model OR = 5.96 [95% CI: 2.38–14.90], and substantial heterogeneity ($I^2 = 58.8\%$, $\tau^2 = 0.5673$, $p < 0.0001$).

The test results for subgroup differences using common effects were $\chi^2 = 2070.20$, $df = 2$ ($p = 0.000$). The test for subgroup differences using random effects were $\chi^2 = 0.44$, $df = 2$ ($p = 0.8040$) (Figure 3).

Publication Bias

Visual inspection of the funnel plot showed slight asymmetry, which suggested potential publication bias (Figure 4).

Discussion

Principal Findings

This meta-analysis demonstrated a significant association between strabismus and an increased risk of mental health disorders in children and adolescents. The pooled OR (1.92, 95% CI: 1.38–2.66) suggests that individuals with strabismus were twice as likely to experience mental health conditions compared to their peers without strabismus. The subgroup analyses revealed that exotropia exhibited the strongest association, followed by esotropia and unspecified strabismus types.

Comparisons with Previous Research

This meta-analysis is consistent with earlier research¹⁸ demonstrating an association between strabismus and mental health conditions. Similarly, studies by Mohny et al⁹ and McKenzie et al¹⁰ reported increased odds of developing mental health disorders in individuals with strabismus. These findings align with a broader body of evidence indicating that children and adolescents with are at greater risk of psychological challenges, including anxiety, depression, and ADHD.

Although earlier studies tended to report higher ORs (Cumurcu et al¹¹ reported an OR as high as 9.0), more recent and larger-scale studies, such as those by Lee et al¹⁷ and Choi et al,¹⁶ have shown more moderate effect sizes (ORs approximately 1.1–2.0). This discrepancy may reflect the improved methodological rigor of recent studies such as larger sample sizes, population-based designs, and improved control of confounding factors.

This meta-analysis advances the field with 2 unique contributions. First, by including data from 9 studies across diverse populations and settings, the results provide a comprehensive estimate of an association between strabismus and mental health conditions in children and adolescents. Second unlike earlier reviews, we stratified the results by strabismus subtypes. This revealed a stronger association between mental health outcomes and exotropia than with esotropia.

We evaluated the potential for publication bias using a funnel plot, which had not been systematically addressed in previous studies.

The association between strabismus and mental health disorders remained robust across multiple studies and populations. However, this study suggests that the magnitude of the effect may be less dramatic than that previously

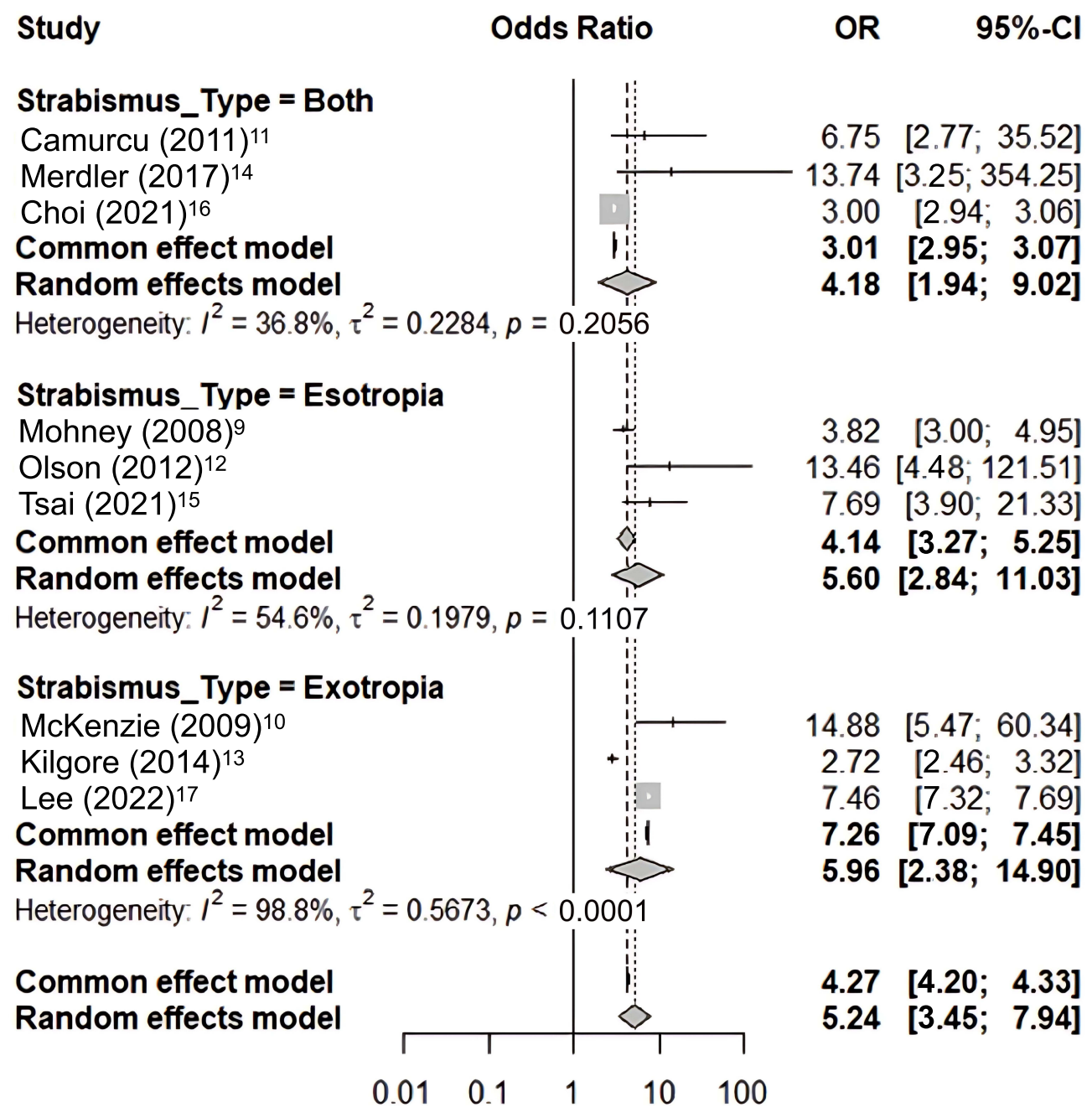


Figure 3 Forest plot of mental health outcomes by strabismus types. [Heterogeneity $I^2 = 99.7\%$, $\tau^2 = 0.2567$, $p = 0$; Test for subgroup differences (common effect): $X^2 = 2970.20$, $df = 2$, $p = 0$; Test for subgroup differences (random effect): $X^2 = 0.44$, $df = 2$, $p = 0.8040$].
Abbreviations: OR, odds ratio; CI, confidence interval; I^2 , I-square heterogeneity statistic; τ^2 , tau-square statistic; p, p-value; X^2 , chi-square statistic; df, degree of freedom.

reported in smaller or less-rigorous studies. This finding underscores the importance of continued research with high methodological quality and larger sample sizes.

Potential Mechanisms

The observed associations can be attributed to several potential mechanisms. Children with visible ocular misalignment may face stigmatization, bullying, or reduced self-esteem, contributing to anxiety and depression.^{19,20} Shared neural pathways between the visual and cognitive systems may predispose individuals with strabismus to neurobehavioral

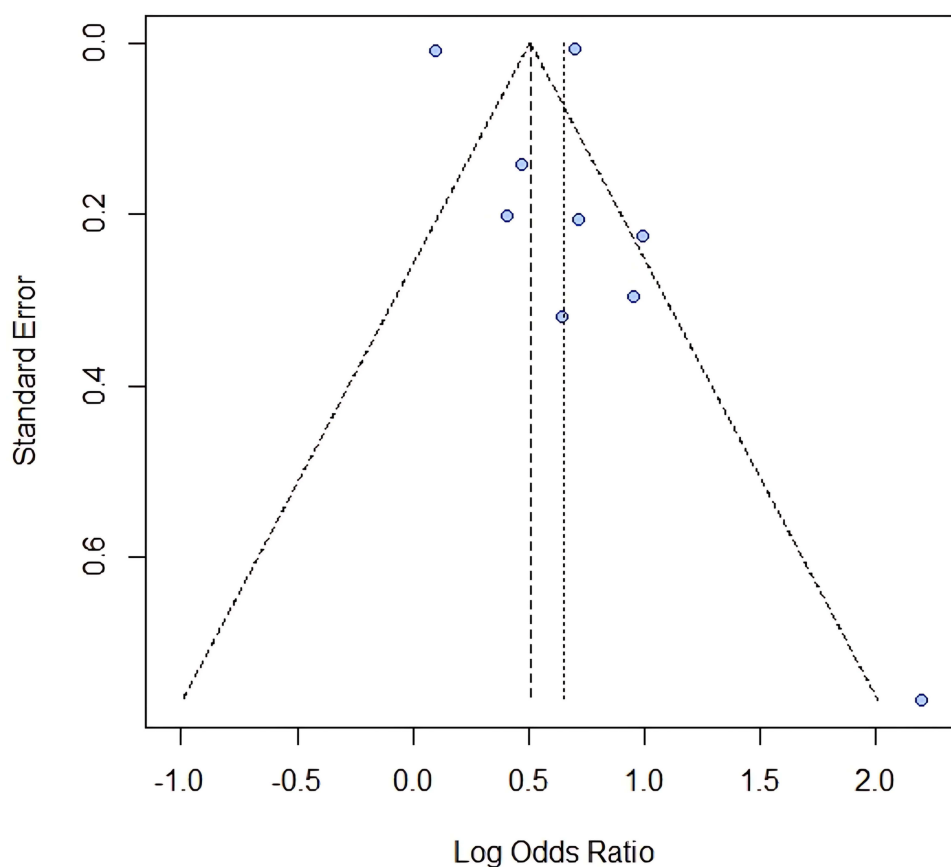


Figure 4 Funnel plot assessing publication bias in the meta-analysis, with each point representing an individual study's effect size (log odds ratio) plotted against its standard error.

disorders, such as ADHD.^{21,22} Strabismus is often associated with other developmental or neurological conditions, which may independently increase the risk of mental health disorders.^{9,23,24}

Healthcare Disparities and Mental Health Outcomes

Healthcare disparities may influence both the recognition and management of mental health conditions among children with strabismus. Socioeconomic status, access to specialized ophthalmologic and psychiatric care, cultural attitudes toward mental illness, and disparities in healthcare infrastructure can all contribute to differential outcomes. Children from underserved or marginalized communities may experience delayed diagnoses or reduced access to mental health support, amplifying the psychological burden of strabismus. These disparities may also lead to underreporting of mental health disorders in certain populations, which could partly explain the observed heterogeneity across studies. Future research should account for these contextual variables and explore how health systems and policies can be optimized to ensure equitable care for all children with strabismus.

Clinical Implications

1. Comprehensive mental health screening: Mental health assessments should be integrated into the routine care of children and adolescents diagnosed with strabismus. Special focus should be given to conditions such as ADHD and anxiety, which had the strongest associations in the analyses. Screening tools should be age-appropriate and consider potential comorbidities commonly observed in children with strabismus.
2. Tailored interventions by strabismus type: Exotropia: Given its strong association with anxiety and ADHD, patients with exotropia may benefit from targeted psychological interventions such as cognitive-behavioral therapy for anxiety and behavior management strategies for ADHD. Esotropia: Interventions for children with esotropia may

focus on bolstering self-esteem and addressing mood-related challenges through counseling or peer support programs. Other Strabismus: A more generalized approach combining psychological and social interventions may be suitable for this group.

3. Multidisciplinary care teams: Healthcare systems should develop multidisciplinary care pathways involving ophthalmologists, pediatricians, psychologists, and social workers to ensure holistic management of children with strabismus. These teams could facilitate early diagnosis and intervention and help prevent the progression of mental health challenges.
4. Parental education and support: Parents should be educated about the increased risk of mental health disorders in children with strabismus, including signs to monitor and seek help. Family centered approaches such as counseling or parent support groups could alleviate caregiver stress and improve the children's psychosocial environments.
5. School and community interventions: Collaborating with schools to reduce the stigma associated with strabismus could improve the social experiences of affected children. Peer education programs and anti-bullying campaigns could foster a more inclusive environment and reduce the psychosocial burden of strabismus.
6. Early surgical or non-surgical interventions: Prompt correction of strabismus using surgical or orthoptic methods may reduce psychosocial challenges and improve quality of life. Posttreatment follow-up should include assessments of both visual and mental health outcomes.
7. Cultural considerations in care: In societies where physical appearances heavily influence social interactions, the psychosocial impact of strabismus may be amplified. Therefore, culturally sensitive care plans should address these issues.
8. Digital and telehealth solutions: Telehealth platforms provide accessible mental health support, particularly to families in rural or underserved areas. Digital tools, such as mobile applications for anxiety management or attention-training programs, could complement traditional interventions.
9. Policy implications: Health policies should prioritize funding for integrated care programs that combine strabismus treatment with mental health services. Advocacy efforts should emphasize the long-term cost savings associated with early interventions that address both ophthalmological and psychological needs.

Strengths

The comprehensive inclusion of recent and diverse studies increased the generalizability of the findings. The subgroup and sensitivity analyses enhanced the robustness of the results. The examination of various mental health outcomes provided a nuanced understanding of these associations.

Limitations

The high heterogeneity ($I^2 = 99.7\%$) reflected variability in the included study designs, populations, and outcome definitions. The cross-sectional design of several studies limited causal inferences.

A potential publication bias, as studies that found no association between strabismus and mental health disorders may have been underreported or unpublished, leading to their underrepresentation in the analysis, while smaller studies with positive findings may have been overrepresented. The unspecified subgroups in some studies may not have revealed the true effect sizes of exotropia and esotropia on mental health disorders.

Future Research Directions

1. Longitudinal studies: Prospective studies are needed to establish causal pathways between strabismus and mental health disorders.
2. Mechanistic insights: Research exploring the biological and psychosocial mechanisms underlying this association could guide targeted interventions.
3. Effects of interventions: Studies evaluating the impact of early strabismus correction on mental health outcomes would provide valuable clinical insights.
4. Subgroup analyses: Future studies should explore the differences in mental health outcomes according to age, sex, chronicity, etiology, and strabismus severity.

Conclusion

This meta-analysis underscores the significant association between strabismus and mental health disorders in children and adolescents. These findings highlight the importance of integrating mental health considerations into strabismus management, particularly for high-risk subgroups. Early identification and intervention could improve the overall well-being of affected individuals. Holistic and multidisciplinary care approaches are warranted for these children and adolescents. However, owing to the potential for publication bias, the results should be interpreted judiciously.

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Disclosure

The authors report no conflicts of interest in this work.

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