Review Article

Evaluating the Validity and Reliability of Telemedicine for Strabismus Detection: A Systematic Review and Meta-Analysis

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Abstract

Purpose: This study aimed to systematically review the validity and reliability of telemedicine methods in evaluating strabismus.
Materials and Methods: Electronic medical databases, including Medline (PubMed), Web of Science, Scopus, and Embase, were systematically reviewed up to April 2021. Two authors independently conducted study selection, data extraction, and quality assessment. Restricted Maximum Likelihood was used to calculate pooled sensitivity, specificity, and reliability. Heterogeneity of the studies was assessed by I-squared statistic (I^2) value, and a funnel plot was used to assess publication bias.
Results: A total of 1190 original studies were evaluated. Finally, 8 studies were selected for systematic review and meta-analysis. The pooled estimation of sensitivity was 0.80 (95 % CI: 0.69-0.88, I^2: 81.8 %, T^2: 0.01, P for heterogeneity < 0.001), the pooled estimation of specificity was 0.91 (95 % CI: 0.77-0.97, I^2: 96.9 %, T^2: 0.01, P for heterogeneity < 0.001), and the pooled estimation of reliability was 0.91 (95 % CI: 0.83-0.99, I^2: 0.00 %, T^2: 0.00, P for heterogeneity: 0.94). Additionally, the Diagnostic Odds Ratio (DOR) index for telemedicine strabismus detection was 43.3. In other words, the odds of a positive result in strabismic patients were 43 times higher than in non-strabismic patients.
Conclusion: The results of this review indicate that the sensitivity, specificity, and reliability of telemedicine in strabismus detection are acceptable. Telemedicine emerges as an easy, inexpensive, accurate, and reliable method for diagnosing strabismus.

Keywords: Telemedicine; Smartphone Application; Strabismus; Accuracy; Specificity.

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Introduction

Strabismus is one of the common ocular disorders affecting about 2-3 % of the population [1-3]. The manifestation of strabismus has negative effects on many aspects of the patient's life [4-5]. Additionally, patients in advanced stages of strabismus often require intensive treatments, including costly surgeries, which can strain both health systems and individuals [6,7]. Therefore, early detection of ocular abnormalities like strabismus is essential to prevent adverse prognoses and other disruptions in life [8]. Early detection may also improve the chances of effective treatment [9-12], thereby reducing the burden of strabismus through various screening programs and early detection approaches worldwide [13,14].

Some strabismic patients go undiagnosed or are diagnosed late due to limited access to health facilities and specialists, as well as shifts in health policies, particularly during the COVID-19 pandemic, such as quarantine measures and changes in health service priorities [15-18,19]. A modern approach to strabismus detection, such as smartphone-based screening applications, offers a home-screening method that reduces diagnosis costs. Currently, numerous mobile applications with various approaches are designed to detect strabismus online. However, one significant concern in diagnostic tests is the accuracy and reliability of the test. Previous studies have been conducted to determine the validity and reliability of this method for detecting strabismus [20-22]. However, there has not been a comprehensive comparison and calculation of the pooled sensitivity and specificity of telemedicine. Hence, this study was conducted to systematically review previous studies and calculate the pooled validity and reliability of telemedicine in strabismus detection.

Materials and Methods

The present study was conducted according to the guidelines of the preferred reporting items for systematic reviews and meta-analyses (PRISMA) statement [23,24]. The primary outcomes of interest in this study were the sensitivity, specificity, and reliability of telemedicine methods for detecting strabismus.

Search strategy

Electronic medical databases, including Medline (PubMed), Web of Science (WOS), Scopus, and Embase, were systematically reviewed. The search was conducted without language or time limitations up to April 2021. Search strategies included the following terms and Medical Subject Headings (MeSH) terms: "Sensitivity", "Specificity", "Feasibility", "Telemedicine", "Teleophthalmology", "Mobile Health", "mHealth", "Screening", "Strabismus", "Squint", "Eye Deviation", and "Ocular Deviation" in the title, abstract, and keywords of articles.

Study selection

In the first step, the title, abstract, and keywords of included articles were independently screened by two authors. Original articles conducted on humans, comparing telemedicine methods with a gold standard, and reporting sensitivity and specificity as outcomes were included in this review. Exclusions comprised case reports, book chapters, meta-analyses, systematic reviews, and studies utilizing duplicate data. Studies lacking pertinent information or using duplicate data were also excluded. Eligibility and any discrepancies were resolved through authors' consensus. Finally, full-text review and data extraction were conducted independently by the two authors.

Data extraction

Data extraction was conducted using a researcher-made checklist to collect article information, including authors, year of publication, country, study design, sample size, methods, and key outcomes (sensitivity, specificity, and reliability), by two researchers independently. Any discrepancies were resolved through consensus among the authors.

Quality assessment

Quality assessments of the included studies were performed by two researchers. In case of discrepancies in the quality score for each item, corresponding author's opinion was used. The quality assessment of diagnostic accuracy studies (QUADAS-2) checklist was used to assess the risk of bias or quality of included studies [25-27]. For this study, a low risk of bias was assumed if all the questions were answered "yes." If an answer was either "no" or "unclear," a moderate to high risk of bias was considered.

Statistical analysis

Studies were assessed using $\chi2$ analysis and inconsistency values [12]. An I-squared statistic (I^2) value greater than 75 % was considered indicative of high heterogeneity, and variables with $I^2 \geq 50$ % were subjected to sensitivity analysis. Additionally, meta-regression was used to detect the effect of independent variables on the validity of telemedicine. Publication bias was assessed using a funnel plot and Begg's test. Receiver operating characteristic (ROC) analysis, area under the curve (AUC), and the Moses-Littenberg meta-analytical method were conducted to describe the association between test sensitivity and specificity. All analyses were performed using Stata version 16, and a p-value ≤ 0.05 was considered statistically significant.

Results

In our systematic review and meta-analysis, a total of 1190 studies were included in the initial literature search. Two authors removed 1108 articles due to duplication and unrelated topics. Among the remaining 82 articles, 72 were excluded due to lack of data after title, abstract, and keyword screening. Finally, 8 articles were included in the final systematic review (Figure 1).

Of these 8 records, all studies were cross-sectional and of excellent to moderate quality [28-35]. Most studies were conducted in the USA (4 studies), following by China (2 studies), Canada (1 study), and Kenya (1 study). The newest study was published in 2021, and the oldest was published in 2015 (Tables 1 and 2).

Sensitivity

Among the eight studies used to estimate the pooled sensitivity of telemedicine in screening for strabismus, sensitivity ranged from 59 % to 99 %. Additionally, the pooled estimate of sensitivity was 0.80 (95 % CI: 0.69-0.88, I^2: 81.8 %, T^2: 0.01, P for heterogeneity < 0.001) (Figure 2).

Meta regression analysis

Based on the meta-regression results, the sample size used in different studies as well as study year did not have a significant effect on the final estimate value (P> 0.05). The distribution of the estimated sensitivity by sample sizes was shown in figure 2. Based on figure 2, the sensitivity value had decreasing

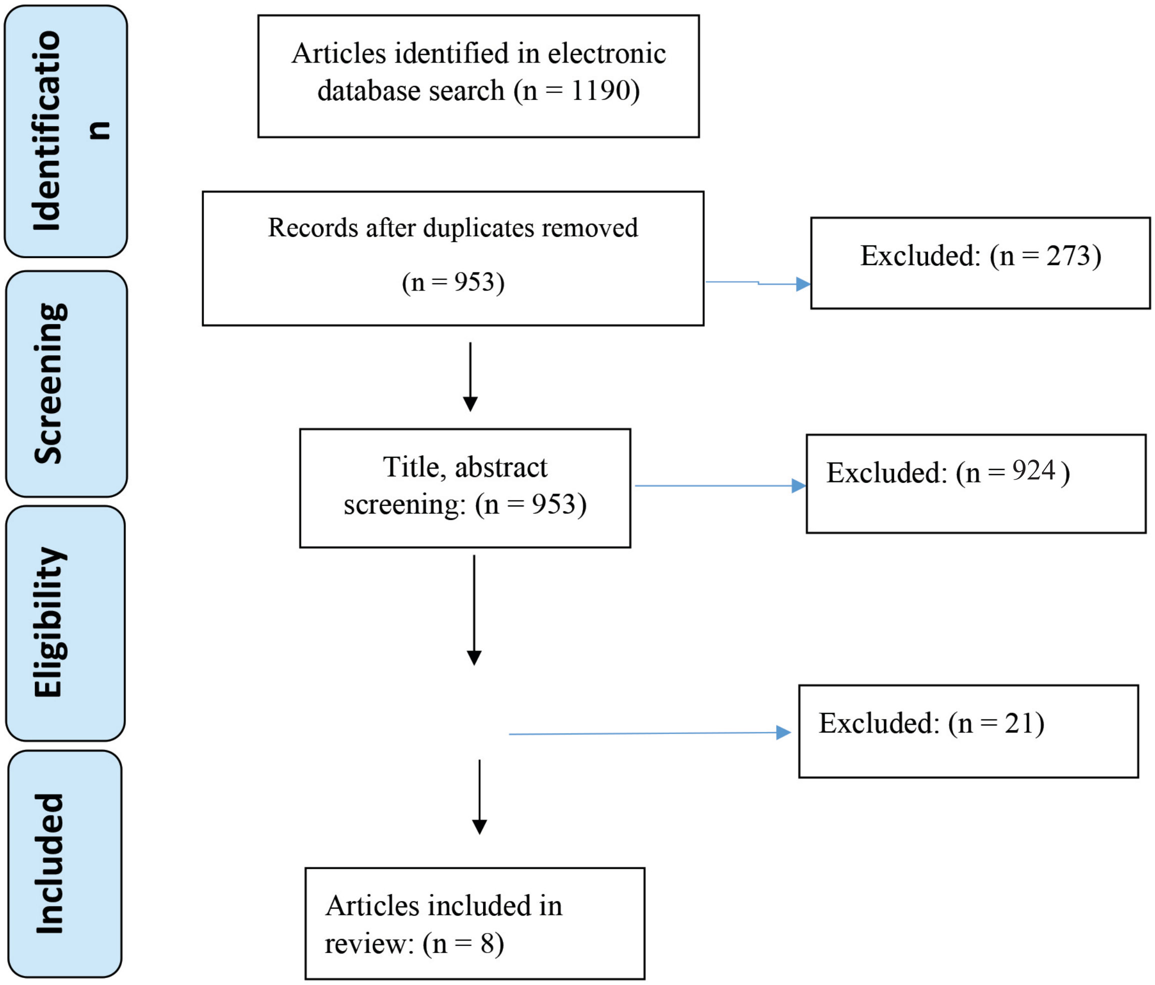

Figure 1: PRISMA flow diagram for the studies included in the current systematic review

trend according to sample size; however, that's not statistically significant (P=0.18).

Publication bias

The distribution of the funnel plot, and Begg's test showed there was no evidence of publication bias among the included articles that estimated the sensitivity of telemedicine in screening for strabismus (P = 0.6) (Figure 2).

Specificity

Among eight studies used to estimate the pooled specificity of telemedicine in screening for strabismus the reported specificity ranged 67 % to 0.99 %. Additionally, the pooled estimation of specificity was calculated as 0.91 (95 % CI: 0.77-0.97, I^2: 96.9 %, T^2: 0.01, P for heterogeneity < 0.001) (Figure 3).

Meta regression analysis

Based on the meta-regression results, the sample size used in different studies, as well as the study year, did not have a significant effect on the estimated specificity value (P > 0.05). The distribution of estimated specificity by sample sizes of articles is shown in figure 3. According to figure 3, the specificity value exhibited a decreasing trend with increasing sample size; however, this trend was not statistically significant (P = 0.12).

Table 1: study characteristics and sensitivity, specificity reports of included studies

Study	Author	Design	Country	Sample Size	Application	Age	Sensitivity % (95 % CI)	Specificity % (95 % CI)	Reliability % (95 % CI)
1	Cheng et al. 2021 (28)	cross-sectional	USA	133	EyeTurn	6-10 years	83.33 (35.88 - 89.25)	76.47 (58.83-89.25)	NR
2	Ma et al. 2020 (29)	cross-sectional	China	100	Smartphone Imaging	range = 8-10 year	80 (56.34-94.27)	97.5 (91.26-99.7)	NR
3	Ma et al. 2017 (30)	cross-sectional	China	101	NR	NR	98.6 (83.4-100)	100 (94.5-100)	91 (82.7 – 100)
4	Peterseim et al. 2018 (31)	cross-sectional	USA	206	GoCheck	3.84 year range = 0.5, 7 year	75.7 (64.3-84.9)	66.7 (57.1-75.3)	NR
5	Bastawrous et al. 2015 (32)	cross-sectional	Kenya	293	The Peek Acuity	mean age, 65 years; range, 55-97	84.6 (54.5-97.6)	97.7 (94.8-99.3)	NR
6	Sabri et al. 2021 (33)	cross-sectional	Canada	80	video-recorded screening	4.8 years	68 (55.5-77.5)	91.5 (82.5- 96)	92 (55-100)
7	Silbert et al. 2015 (34)	cross-sectional	USA	174	GoCheck Kids	1-6 years	59 (47.8-70.3)	74 (67.5-80.4)	NR
8	Arnold et al. 2018 (35)	cross-sectional	USA	287	GoCheck Kids	1-6 years, mean=3.62	76 (71-81)	85 (80-90)	NR

NR: Not Reported

Table 2: Quality assessment of included studies

Study	Patients Selection	Index Test	Reference Standard	Flow and Timing
Cheng et al. 2021 (28)				
Ma et al. 2020 (29)				
Ma et al. 2017 (30)				
Peterseim et al. 2018 (31)				
Bastawrous et al. 2015 (32)				
Sabri et al. 2021 (33)				
Silbert et al. 2015 (34)				
Arnold et al. 2018 (35)				

Green: Low or acceptable bias, Red: High bias, Yellow: unclear

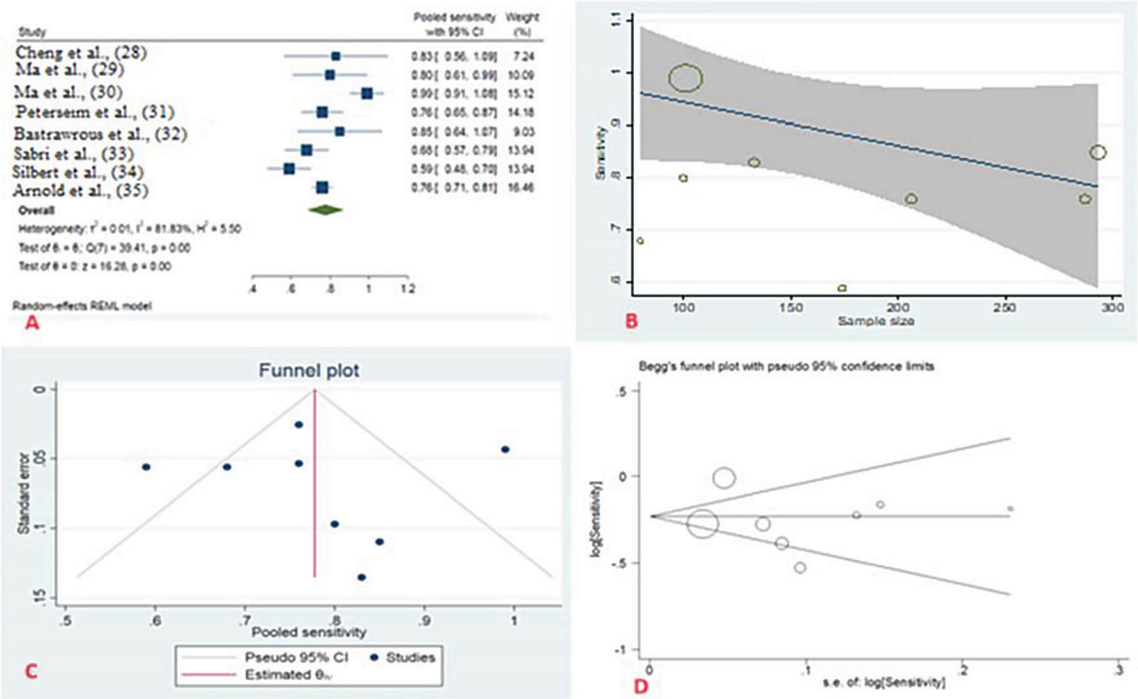

Figure 2: A: The forest plots of pooled sensitivity of telemedicine in the screening of strabismus, B: The distribution of estimated sensitivity according to different sample sizes, C: The funnel plot to assess publication bias in the estimation of sensitivity

Publication bias

The distribution of the funnel plot, and Begg's test showed there was no evidence of publication bias among the included articles that estimated the sensitivity of telemedicine in screening for strabismus (P = 0.6) (Figure 3).

Reliability

Two studies reported the reliability of telemedicine in strabismus screening. The study by MA et al., [30] reported the reliability of this test as 91 % (95 % CI: 0.83, 1.00), and the study by Sabri et al., [33] reported the reliability of this test as 92 % (95 % CI: 0.70, 1.00). Additionally, the hierarchical modeling is shown in table 3 and figure 5. The Diagnostic Odds Ratio (DOR) index for telemedicine strabismus detection was 43.3. In other words, the odds of being positive in strabismic patients were 43 times higher than in non-strabismic patients (Table 3).

Discussion

This study aimed to determine the pooled validity and reliability of telemedicine for detecting strabismus. To our knowledge, it is the first systematic review and meta-analysis conducted for this purpose.

Our results indicated that the sensitivity, specificity, and reliability of telemedicine in detecting strabismus were estimated at 0.80 (95 % CI: 0.69-0.88, I^2: 81.8 %, T^2: 0.01, P for heterogeneity < 0.001), 0.91 (95 % CI: 0.77-0.97, I^2: 96.9 %, T^2: 0.01, P for heterogeneity < 0.001), and 0.91 (95 % CI: 0.83-0.99, I^2: 0.00 %, T^2: 0.00, P for heterogeneity: 0.94), respectively.

Based on our results the specificity, reliability,

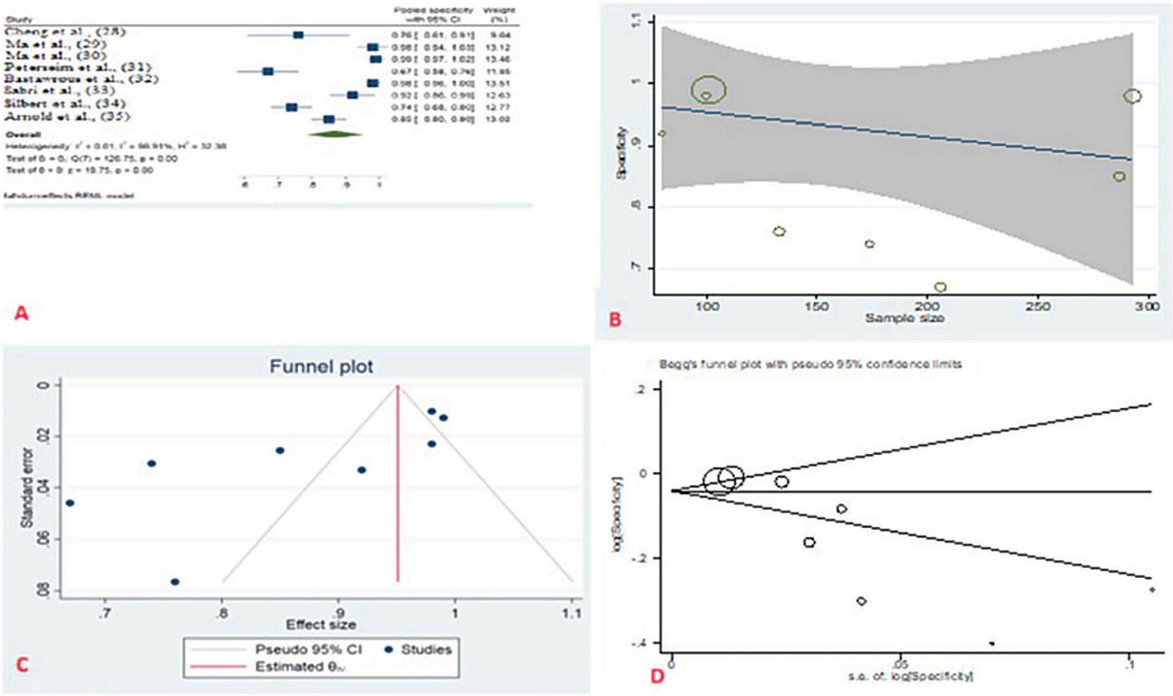

Figure 3: A: The forest plots of pooled specificity of telemedicine in the screening of strabismus, B: The distribution of estimated specificity according to different sample sizes, C: The funnel plot to assess publication bias in the estimation of specificity

and sensitivity of this method were excellent. This diagnostic tool can accurately identify 91 % of healthy individuals as healthy and diagnose 80 % of strabismus patients as unhealthy. Since the specificity of this test is high and the false-positive rate is very low, we can confidently refer participants with positive test results to clinics. However, the 80 % sensitivity may result in a 20 % false-negative rate, indicating individuals with strabismus may be incorrectly identified as healthy. Hence, we should be aware of the

Table 3: The performance evaluation of telemedicine in the detection of strabismus using meta-analysis with hierarchical modeling

Indices	Coefficient	SE	95 % CI	
Sensitivity	0.80	0.05	0.69	0.88
Specificity	0.91	0.05	0.77	0.97
Diagnostic Odds Ratio (DOR)	43.03	35.94	8.37	221.19
LR+	9.21	5.39	2.92	29.02
LR-	0.21	0.06	0.12	0.37
1/LR-	4.67	1.32	2.68	8.13

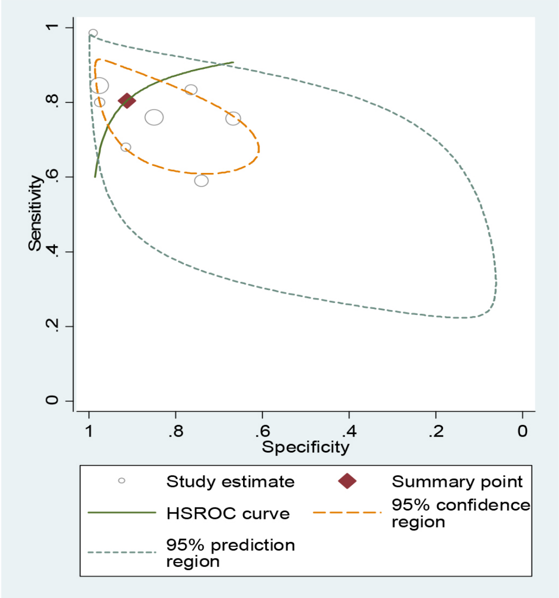

Figure 5: Hierarchical summary receiver operating characteristic curves in estimation of pooled sensitivity and specificity

error rate of this test.

The prevalence of strabismus and amblyopia is remarkable worldwide [36-38]. Detecting ocular disorders is a high priority in the population, particularly among children and young adults, as timely treatment in this age range is highly effective [9, 39]. However, if ocular abnormalities are not addressed promptly, they can lead to other conditions or complications, such as uncorrectable visual impairment, falls, disruptions in daily activities, reduced quality of life, and mental stress or anxiety [39-47].

An important consideration in recent years has been the global COVID-19 pandemic and its associated health policies [48,49]. Previous studies have reported a decrease in patient referrals to health centers due to COVID-19 quarantine measures, fear of contracting the virus in healthcare settings, and concerns about spreading it within families, among other factors [50, 51].

Another factor that has elevated the priority of telemedicine is the availability of these healthcare services, especially in countries with low or middle levels of healthcare access [52, 53].

While many countries have screening programs for detecting ocular abnormalities in children and students, such programs are often neglected in adults [54-58]. Additionally, factors such as time constraints distance to health centers, and the cost of examinations may contribute to deprivation in adults [39, 59].

Many of these challenges can be addressed with the emergence of telemedicine. Telemedicine applications have been designed to overcome barriers to healthcare by enabling patients or clinicians to conduct imaging protocols using smartphones [60-64]. Previous studies have shown that most families worldwide have access to the internet and cell phones [65]. Hence, the utilization of telemedicine for strabismus detection is widely accessible to most patients in various countries.

Strength and Limitations

Given that this study utilized a systematic review and meta-analysis methodology, we believe that the results are reliable, and valid.

However, our study has certain limitations. One limitation is that it evaluated the ability of the applications to measure eye alignment primarily in near fixation or only in one direction, such as the horizontal direction. Additionally, since most of these applications used flash to take pictures, participants were unable to wear glasses, which could have affected the results.

Another limitation reported in the included studies was the inability to mask or blind clinicians/readers to the source of the images and patients, potentially influencing the scoring and leading to information bias.

Conclusion

The results of this review indicate that the sensitivity, specificity, and reliability of telemedicine in strabismus detection are acceptable. Telemedicine emerges as an easy, inexpensive, accurate, and reliable method for diagnosing strabismus.

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Footnotes and Financial Disclosures

Conflict of interest:

The authors have no conflict of interest with the subject matter of the present manuscript.