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ORIGINAL ARTICLE

Assessment of the detection accuracy of SARS-CoV-2 rapid antigen test in children and adolescents: An updated meta-analysis

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Abstract

Background: Real-time and appropriate antigen tests play a pivotal role in preventing severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) infection. However, a previous meta-analysis reported that the antigen test had lower sensitivity for the detection of SARS-CoV-2 in children. To provide a comprehensive evaluation of diagnostic efficiency, we performed an updated meta-analysis to assess the detection accuracy of SARS-CoV-2 antigen tests stratified by days after symptom onset and specimen type in children and adolescents.

Methods: We comprehensively searched for appropriate studies in the PubMed, Embase, and Cochrane Library databases. Studies on the diagnostic accuracy of antigen tests for SARS-CoV-2 in children and adolescents were included. The relevant data of the included studies were extracted to construct a 2×2 table on a per-patient basis. The overall sensitivity and specificity of the SARS-CoV-2 antigen tests were estimated using a bivariate random-effects model.

Results: Seventeen studies enrolling 10 912 patients were included in the present meta-analysis. For the detection accuracy of SARS-CoV-2 antigen tests, the meta-analysis generated a pooled sensitivity of 77.9% (95% confidence interval [CI]: 67.3%-85.8%) and a pooled specificity of 99.6% (95% CI: 98.9%-99.8%). The subgroup analysis of studies that examined antigen tests in symptomatic participants ≦7 days after symptom onset generated a pooled sensitivity of 79.4% (95% CI: 47.6%-94.2%) and a pooled specificity of 99.4% (95% CI: 98.2%-99.8%). Another subgroup analysis of studies that evaluated nasal swab specimens demonstrated a pooled sensitivity of 80.1% (95% CI: 65.0%-89.7%) and a pooled specificity of 98.5% (95% CI: 97.3%-9.2%).

Conclusion: Our findings demonstrated that the antigen test performed using nasal swab specimens exhibited high sensitivity for the detection of SARS-CoV-2 within 7 days after symptom onset. Therefore, antigen testing using nasal swabs may be effective in blocking SARS-CoV-2 transmission in children.

Keywords: Antigen test; COVID-19; Meta-analysis; Pediatrics; SARS-CoV-2

1. INTRODUCTION

The severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) has caused the global coronavirus disease 2019 (COVID-19) pandemic. Approximately 50% of patients with COVID-19 contract SARS-CoV-2 from asymptomatic patients.[1] Asymptomatic patients may still be able to transmit SARS-CoV-2. The pediatric population represents 1% of total hospitalized cases of COVID-19 and deaths. The most common symptoms at disease onset are fever and mild cough. Other clinical manifestations include sneezing, sore throat, rhinorrhea, myalgia, fatigue, vomiting, and diarrhea. Children may experience more upper airway symptoms than lower respiratory discomfort and begin to recover within 1 to 2 weeks.[2] Symptoms of SARS-CoV-2

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infected children are indistinguishable from other respiratory illnesses based on clinical symptoms.[3] Hence, accurate rapid tests become critical, valuable, and should be employed to differentiate SARS-CoV-2 infection from other common acute respiratory infections in children between the ages of birth and 2.[4]

SARS-CoV-2 diagnostic testing is an effective tool to contain COVID-19.[5] The present reference standard for COVID-19 diagnosis is reverse transcription-polymerase chain reaction (RT-PCR) using nasopharyngeal swab (NPS) specimens.[6] However, RT-PCR poses challenges, such as limited testing sites, laboratory expertise dependency, longer turnaround time, and higher costs. In contrast, the benefits of SARS-CoV-2 antigen tests include lower price, prompt turnaround, and rapid identification of COVID-19 patients.[7] Moreover, antigen tests have high sensitivity for the detection of SARS-CoV-2 within 7 days post symptom onset and are thought to be effective in screening for community-acquired infections.[8,9] The high sensitivity of the SARS-CoV-2 antigen test in symptomatic individuals demonstrates its utility for public health screening.[10]

Globally, public health initiatives such as immunization programs are being conducted to prevent COVID-19 and reduce the SARS-CoV-2 transmission in children. One dose of the vaccine reduced the risk of SARS-CoV-2 infection for at least 90 days in patients aged 12–17 years. Vaccination protection was enhanced by exposure to SARS-CoV-2 before vaccination. The severity of COVID-19 after vaccination was generally mild, while unvaccinated children were also generally mild.[11] Therefore, testing remains critical for COVID-19 diagnosis in vaccinated children.

A previous meta-analysis reported that antigen testing is sensitive for the SARS-CoV-2 detection in symptomatic children.[12] To provide more comprehensive knowledge of the accuracy of antigen testing, we evaluated the diagnostic performance of such tests stratified by specimen type and days after symptom onset. Therefore, this updated study aims to evaluate the diagnostic accuracy of SARS-CoV-2 antigen tests in children by systematically reviewing recently published articles.

2. METHODS

2.1. Literature search strategy

The meta-analysis was reported in accordance with the Preferred Reporting Items for Systematic Review and Meta-Analysis of Diagnostic Test Accuracy Studies: The PRISMA-DTA Statement.[13]

A literature search was conducted in the PubMed, Cochrane Library, and Embase databases. We searched for relevant studies using the following search strings: (COVID-19 OR severe acute respiratory syndrome coronavirus-2 OR SARS-CoV-2) AND (Antigen-Antibody Reactions OR antigen test or antigen testing OR SARS-CoV-2 antigen test) AND (Adolescent OR Child OR Pediatrics OR Infant, Newborn). We applied a combination of free text and Medical Subject Headings terms to identify potentially relevant studies. During the literature search procedure, there were no language restrictions. The Supplementary Material, http://links.lww.com/JCMA/A205 presents the detailed search strategy.

2.2. Inclusion and exclusion criteria

Studies that assessed the diagnostic accuracy of SARS-CoV-2 antigen tests with reference standards in children with suspected COVID-19 were included. Respiratory specimens, including nasopharyngeal swabs, nasopharyngeal aspirates, anterior nasal swabs, and nasal swabs, were obtained from symptomatic or asymptomatic patients. Studies using RT-PCR as a reference standard were included. Studies that provided sufficient data to construct a 2×2 table on a per-patient basis were included. Review articles, preprint articles, proposals, protocols, case reports, case series, conference abstracts, and conference papers were excluded. The last literature search was conducted on August 30, 2022. One reviewer initially screened the titles and abstracts of potentially eligible studies. After excluding irrelevant studies, two authors independently appraised these full-text articles to obtain studies that met our inclusion criteria. Disagreements were resolved through discussions.

2.3. Quality assessment

Quality Assessment of Diagnostic Accuracy Studies-2 (QUADAS-2) was used to evaluate the quality of included studies.[14] SARS-CoV-2 antigen testing in children is the index test and RT-PCR for SARS-CoV-2 is the reference standard, based on QUADAS-2. The QUADAS-2 comprises four domains. They are patient selection, index test, reference standard, and flow and timing. Each domain has criteria for assessing the risk of bias. The quality of a diagnostic test is assessed based on the risk of bias and the applicability of the study. QUADAS-2 also evaluated the applicability of this study to the research question. A study was considered high quality if each domain in the study displayed a low risk of bias.

2.4. Statistical analysis

We extracted values for true positives, true negatives, false positives, and false negatives from each included article to perform data synthesis to generate the summary sensitivity and summary specificity. We searched for further information in the Supplementary Materials, http://links.lww.com/JCMA/A205, if there was no sufficient data extracted in the main text. A diagnostic test's sensitivity is defined as the percentage of people with a target disorder who were correctly classified as having the condition, whereas a test's specificity is the percentage of individuals without a disorder who were classified correctly as not having the target disorder.[15]

We performed a meta-analysis using a bivariate random-effects model to produce summary sensitivity and specificity on a per-patient basis. We plotted a summary receiver operating characteristic (SROC) curve to calculate the overall diagnostic accuracy of the antigen test. An ideal test should have an area under the curve (AUC) of 0.97 or greater. An AUC of 0.93-0.96 is regarded as highly satisfactory, whereas an AUC of 0.75-0.92 is regarded as satisfactory.[16] Potential sources of heterogeneity among the included studies were explored by performing prespecified subgroup analyses including the presence of symptoms, specimen type, manufacturers of the index test, cycle threshold (Ct) cutoff value, and testing site. Summary sensitivity and specificity of the antigen test were calculated with 95% confidence intervals (CIs). In addition, we calculated the Spearman correlation coefficient between the logit of sensitivity and the logit of 1 – specificity to explore the threshold effect.[16] A positive correlation indicated the threshold effect. All analyses were performed using MetaDiSc version 1.4, MetaDTA, and RevMan 5.4 software.[17,18] A p value < 0.05 is considered statistically significant.

3. RESULTS

3.1. Meta-analysis

Seventeen studies with 10 912 patients were included in the meta-analysis.[19–35] Fig. 1 presents the literature search process, and Table 1 depicts the detailed characteristics of the included studies. Fourteen studies used a prospective study design. Eight studies enrolled participants from community testing sites and five studies enrolled participants from the emergency departments of hospitals. Twelve studies provided sufficient data for the antigen test performance in symptomatic patients, and four evaluated

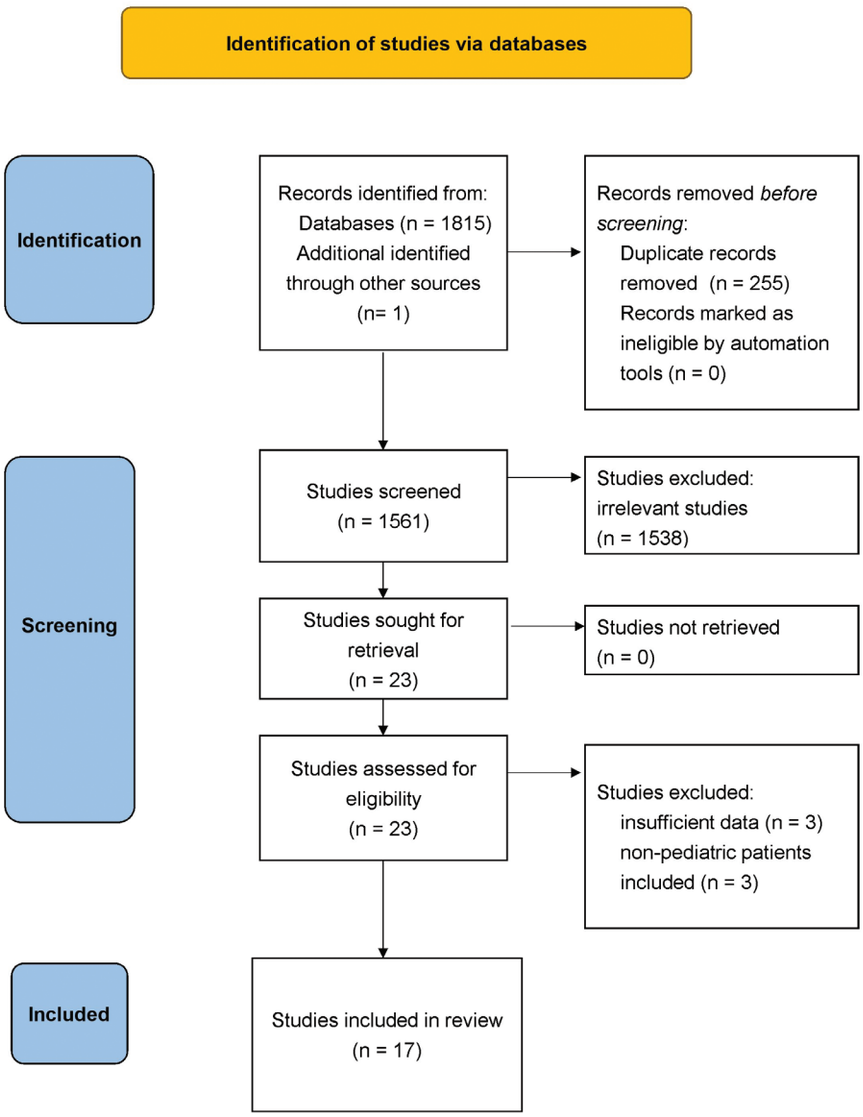

Fig. 1 Flow diagram of literature search.

the diagnostic performance of antigen testing in patients within 7 days of symptom onset. Eleven studies examined antigen tests using nasal swab samples, and five studies used NPS. Six studies assessed the Panbio COVID-19 Ag rapid test device and seven studies examined the performance of the BinaxNOW COVID-19 Ag card. Two studies have recorded SARS-CoV-2 variants. Seven studies reported the Ct values of positive RT-PCR tests, and eight studies revealed the cutoff value of Ct. The updated meta-analysis generated a summary sensitivity of 77.9% (95% CI: 67.3%-85.8%) and a summary specificity of 99.6% (95% CI: 98.9%-99.8%; Fig. 2). In addition, the AUC of the SROC for antigen tests was 0.99, indicating that antigen tests may be reliable for diagnosing COVID-19 in children and adolescents. Fig. 3 presents the sensitivity and specificity of the antigen tests for SARS-CoV-2 from the included studies.

3.2. Quality assessment

We applied QUADAS-2 to assess the quality of the studies in the updated meta-analysis. Regarding patient selection, seven studies enrolled patients randomly or consecutively; none of the studies used a case–control study design. For the patient selection domain, seven studies were judged to have a low risk of bias. All studies reported that index tests were interpreted without knowledge of the results of the reference standards. Therefore, all the studies in the updated meta-analysis were judged to have a low risk of bias in the index test domain. Regarding the reference standard domain, 16 studies reported that the reference standard was capable of correctly classifying the target disease. Regarding the flow and timing, 15 studies reported that all participants received a reference standard. All studies reported a reasonable interval between the index test and the reference standard. Twelve studies indicated that all participants were involved in the analysis. Eleven had a low risk of bias in the domains of flow and timing. Regarding applicability, the patient selection, index tests, and reference standards of the studies included in the study matched the SARS-CoV-2 antigen testing used in routine clinical practice. Fig. 4 illustrates the risk of bias in the studies, and Fig. 5 presents the overall quality of the studies in the updated meta-analysis.

Table 1

Characteristics of studies

Study	Study design	Testing site	Patient population	Prevalence (%)	Participants (total/data extraction)	Age median(range)	Days post symptom onset	Specimen type	Index test	SARS-CoV-2 variant	Threshold value (Ct)
Pepe et al[19]	Retrospective	Emergency department	Asymptomatic and symptomatic	NA	(1904/1890)	89 mos (0–14)	NA	Nasopharyngeal swab	Panbio COVID-19 Ag Rapid Test Device	NA	NA
Sun et al[20]	Prospective	High-throughput community testing site	Asymptomatic and symptomatic	5.2	(1054/1054)	8.9 (mean)	NA	Nasal swab	BinaxNOW COVID-19 Ag card	Delta	NA
Freeman et al[21]	Prospective	Hospital and Community Pediatrics	Asymptomatic and symptomatic	17.4 (symptomatic)	(411/387)	5.8 (mean, symptomatic) (0–16)	2.6 (mean)	Nasal swab	Sofia SARS-CoV-2 antigen assay	NA	NA
Schrom et al[22]	Cross-sectional prospective	Community testing site	Asymptomatic and symptomatic	40	(118/118)	≦12	≦7	nasal swab	BinaxNOW COVID-19 Ag card	Omicron	30
Sicilia et al[23]	Prospective	Outpatient screening center	Asymptomatic and symptomatic	20.2	(39/39)	<18	NA	Nasal swab	Panbio COVID-19 Ag Rapid Test Device	NA	38
Ollereet al[24]	Prospective	Pediatric emergency department	Asymptomatic and symptomatic	NA	(1011/990)	1.7 (0.4–5.2, ±IQR)	2.9 (mean)	Nasopharyngeal aspirate	COVID19Speed-Antigen Test	NA	NA
Denina et al[25]	Retrospective	Pediatric emergency department	Asymptomatic and symptomatic	5–12	(191/191)	5.8 (1.1–10.8, ±IQR) antigen test (+)	1 (median)	nasal swab	LumiraDx Sars-CoV-2 Antigen Test	NA	NA
Ford et al[7,26]	Prospective	Community testing site	Asymptomatic and symptomatic	NA	(225/217)	>5, ≦18	NA	Nasal swab	BinaxNOW COVID-19 Ag card	NA	37
L'Huillier et al[27]	Prospective	Pediatric testing center	Asymptomatic and symptomatic	583/100,000/ wk (peak incidence)	(885/822) symptomatic: 533 asymptomatic: 289	11.8 (9.0–14.3, ±IQR)	2 (median)	Nasopharyngeal swab	Panbio COVID-19 Ag Rapid Test Device	NA	NA
Eleftheriou et al[28]	Prospective	A hospital	Hospitalized children	6.86	(744/744)	7.7 (1.4–13.2)	2 (median)	nasopharyngeal swab	Panbio COVID-19 Ag Rapid Test Device	NA	NA
Sood et al[29]	Prospective	Walk-up testing site	Asymptomatic and symptomatic	NA	(783/774) symptomatic: 182 asymptomatic: 592	5–17	NA	Anterior nasal swab	BinaxNOW COVID-19 Ag card	NA	40
González-Donapetry et al[30]	Prospective	Pediatric emergency department	Symptomatic	4.1	(440/440)	3 (1–7, ±IQR)	1 (median)	Nasopharyngeal swab	Panbio COVID-19 Ag Rapid Test Device	NA	40 (nucleocapsid and envelope genes)
Villaverde et al[31]	Retrospective	Emergency departments of 7 centers	Symptomatic	5	(1620/1620)	0–16	≦5	Nasopharyngeal swab	Panbio COVID-19 Ag Rapid Test Device	NA	NA
Pollock et al[32,33]	Prospective	Drive-through testing site	Asymptomatic and symptomatic	18.2	(253/253)	NA	Children: 3 (median)	Anterior nasal swab	Access Bio CareStart COVID-19 Antigen test	NA	≤25, ≤30, ≤35
Pollock et al[32,33]	Prospective	Drive-through testing site	Asymptomatic and symptomatic	14.5	(928/928)	≦18	2 (median)	Anterior nasal swab	BinaxNOW COVID-19 Ag card	NA	40
Prince-Guerra et al[34]	Prospective	Two community-based testing sites	Asymptomatic and symptomatic	NA	(236/236)	10–17	NA	Anterior nasal swab	BinaxNOW COVID-19 Ag card	NA	NA
Pilarowski et al[35]	Prospective	At a plaza	Participants in an urban commercial transport hub	14.5 (13 to 18 y of age) 19.4 (<13 y of age)	(209/209)	<13, 13–18	NA	Nasal swab	BinaxNOW COVID-19 Ag Card	NA	35

COVID-19 = coronavirus disease 2019; CT = cycle threshold; IQR = interquartile range; NA = not available; SARS-CoV-2 = severe acute respiratory syndrome coronavirus-2.

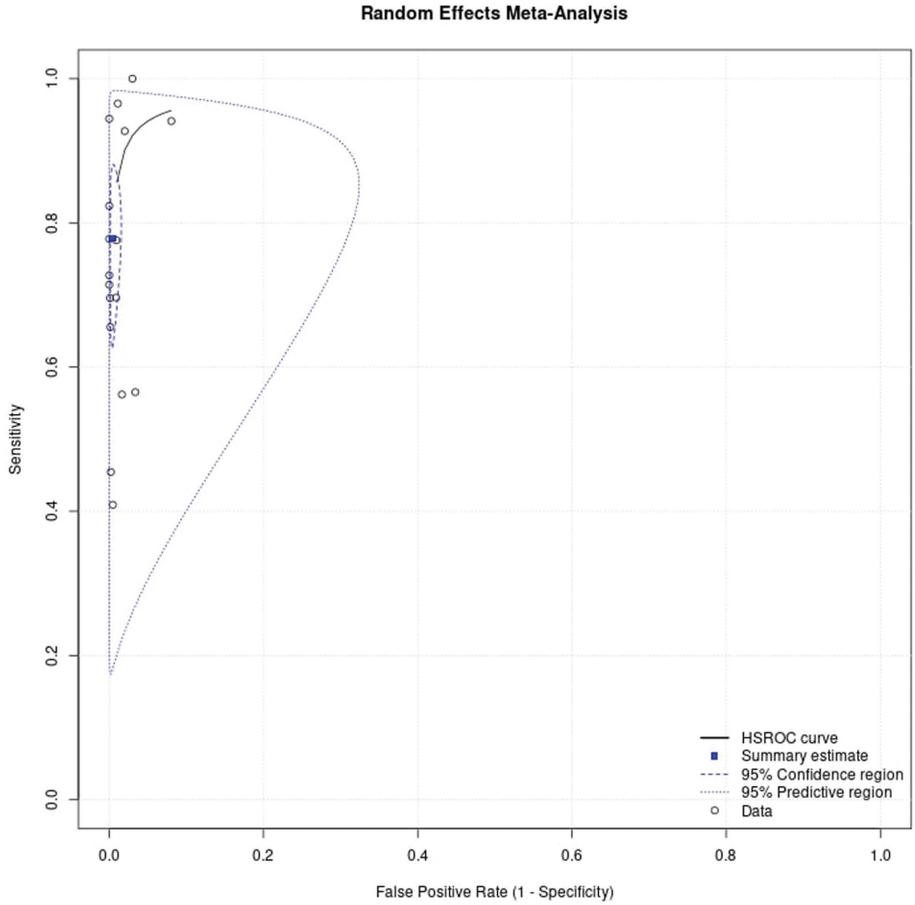

Fig. 2 Summary estimate (blue square) of the HSROC curve indicates a pooled sensitivity of 77.9% (95% CI: 67.3%-85.8%) and pooled specificity of 99.6% (95% CI: 98.9%-99.8%) for antigen tests. CI = confidence interval; HSROC = hierarchical summary receiver operating characteristic.

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Denina M 2021	16	14	1	160	0.94 [0.71, 1.00]	0.92 [0.87, 0.96]
Eleftheriou I 2021	42	0	9	693	0.82 [0.69, 0.92]	1.00 [0.99, 1.00]
Ford L 2021	25	0	10	182	0.71 [0.54, 0.85]	1.00 [0.98, 1.00]
Freeman MC 2022	45	3	13	326	0.78 [0.65, 0.87]	0.99 [0.97, 1.00]
Gonzalez-Donapetry P 2021	14	0	4	422	0.78 [0.52, 0.94]	1.00 [0.99, 1.00]
L'Huillier AG 2021	78	1	41	702	0.66 [0.56, 0.74]	1.00 [0.99, 1.00]
Pepe A 2022	51	0	3	1836	0.94 [0.85, 0.99]	1.00 [1.00, 1.00]
Pilarowski G 2020	28	2	1	178	0.97 [0.82, 1.00]	0.99 [0.96, 1.00]
Pollock NR 2021a	26	7	20	200	0.57 [0.41, 0.71]	0.97 [0.93, 0.99]
Pollock NR 2021b	94	7	41	786	0.70 [0.61, 0.77]	0.99 [0.98, 1.00]
Prince-Guerra JL 2021	9	1	13	213	0.41 [0.21, 0.64]	1.00 [0.97, 1.00]
Quentin O 2022	32	1	14	943	0.70 [0.54, 0.82]	1.00 [0.99, 1.00]
Schrom J 2022	18	3	0	97	1.00 [0.81, 1.00]	0.97 [0.91, 0.99]
Sicilia P 2022	8	0	3	28	0.73 [0.39, 0.94]	1.00 [0.88, 1.00]
Sood N 2021	127	9	99	539	0.56 [0.49, 0.63]	0.98 [0.97, 0.99]
Sun KJ 2022	51	20	4	979	0.93 [0.82, 0.98]	0.98 [0.97, 0.99]
Villaverde S 2021	35	3	42	1540	0.45 [0.34, 0.57]	1.00 [0.99, 1.00]

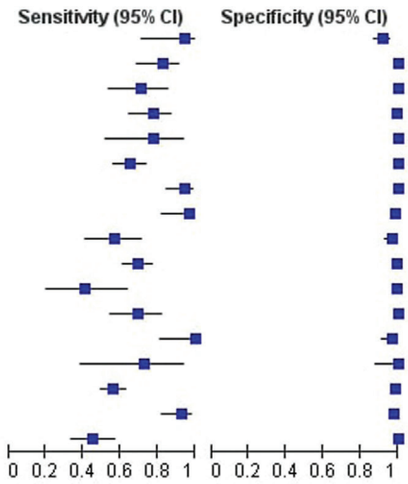

Fig. 3 Forest plot showing the sensitivity and specificity with 95% CIs of SARS-CoV-2 antigen tests of the included studies. CI = confidence interval; FN = false negative; FP = false positive; TN = true negative; TP = true positive.

3.3. Subgroup analysis

We conducted subgroup analyses according to the presence of symptoms, manufacturers of the index tests, specimen types, Ct threshold of RT-PCR, and antigen testing site. Twelve studies including 4,088 participants reported the accuracy of antigen tests for symptomatic patients. The meta-analysis generated a summary sensitivity of 77.3% (95% CI: 67.8%-84.7%) and a summary specificity of 99.4% (95% CI: 98.0%-99.8%). Four

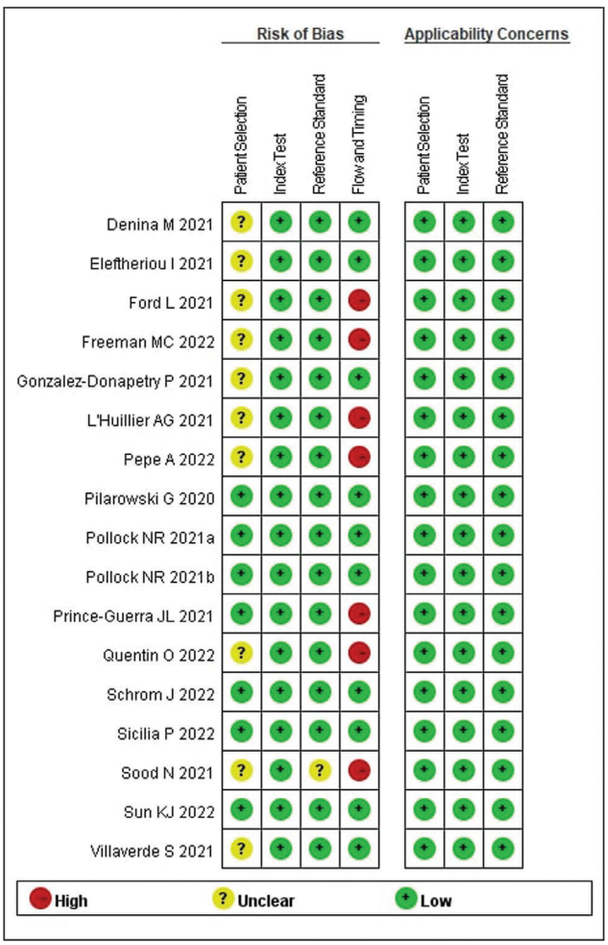

Fig. 4 Risk of bias of included studies.

studies performed antigen tests in 2565 participants ≦7 days after symptom onset. This subgroup analysis produced a pooled sensitivity of 79.4% (95% CI: 47.6%-94.2%) and a pooled specificity of 99.4% (95% CI: 98.2%-99.8%). Nine studies performed antigen tests in 3455 asymptomatic participants. The subgroup analysis generated a pooled sensitivity of 58.7% (95% CI: 44.3%-71.8%) and a pooled specificity of 99.2% (95% CI: 98.7%-99.6%). Based on the specimen type, we conducted a subgroup analysis of five studies that performed antigen tests using NPS in 5516 patients. This analysis generated a pooled sensitivity of 76.6% (95% CI: 57.2%-88.9%) and a pooled specificity of 100% (95% CI: 99.7%-100%). The subgroup analysis of the 11 articles that used nasal swabs demonstrated a summary sensitivity of 80.1% (95% CI: 65.0%-89.7%) and a summary specificity of 98.5% (95% CI: 97.3%-99.2%), respectively. This finding indicated that antigen tests using nasal swabs might exhibit high sensitivity for the detection of COVID-19. Seven studies, including 3536 patients, reported the accuracy of the BinaxNOW COVID-19 Ag card. The analysis generated a pooled sensitivity of 81.9% (95% CI: 59.3%-93.4%) and a pooled specificity of 98.6% (95% CI: 98.0%-99.1%). Four studies with 583 participants reported the accuracy of the antigen test, with a Ct value of 38 applied as the threshold value in RT-PCR. The analysis produced a pooled sensitivity of 90.9% (95% CI: 66.4%-98.0%) and a pooled specificity of 99.4% (95% CI: 96.3%-99.9%). Five studies including 5131 participants reported that antigen tests were performed in pediatric emergency departments. The subgroup analysis produced a pooled sensitivity of 80.5% (95% CI: 58.2%-92.4%) and a pooled specificity of 99.9% (95% CI: 98.0%-100%). Table 2 lists the pooled estimates of the subgroup analyses.

3.4. Evaluation of the threshold effect

To explore the potential source of heterogeneity, we conducted threshold analysis to explore the threshold effect. The Spearman's correlation coefficient was 0.2 (p = 0.4), indicating that there might not be a threshold effect between these studies.

4. DISCUSSION

The findings of this updated meta-analysis indicate that antigen tests exhibit increased sensitivity and specificity for the detection of SARS-CoV-2 in children, compared to that of a previous meta-analysis.[12] A pediatrician could nearly rule in the disease if a diagnostic test is highly specific and produces a positive result.[36] Antigen tests exhibit excellent specificity, which has a high positive predictive value. Therefore, during periods of high COVID-19 prevalence, children with positive antigen test results can be identified as having SARS-CoV-2 infection.[37] To our knowledge, this is the first updated meta-analysis examining the diagnostic accuracy of the antigen test for SARS-CoV-2 in children and adolescents. The results of our study indicated the practical clinical use of antigen testing for SARS-CoV-2. Higher viral load from the highly prevalent delta variant, ambient conditions for kit storage and use, quality of the test kit,

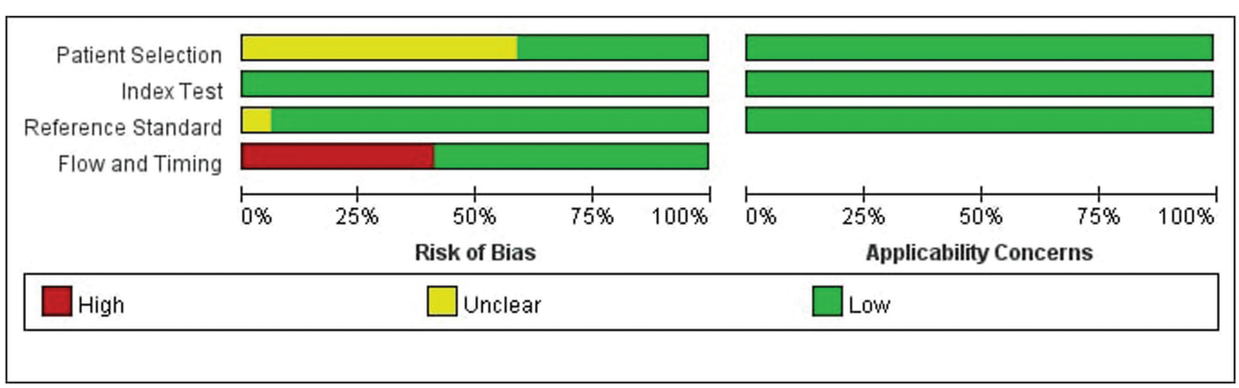

Fig. 5 Overall quality of studies in the meta-analysis.

Table 2

Subgroup analyses of the diagnostic accuracy of antigen tests

Subgroup	Number of studies	Number of patients	Sensitivity (%) (95% CI)	Specificity (%) (95% CI)
Symptomatic patients	12	4088	77.3 (67.8%-84.7%)	99.4 (98.0%-99.8%)
Symptomatic patients (≦7 d postsymptom onset)	4	2565	79.4 (47.6%-94.2%)	99.4 (98.2%-99.8%)
Asymptomatic patients	9	3455	58.7 (44.3%-71.8%)	99.2 (98.7%-99.6%)
Sample type: nasopharyngeal swab	5	5516	76.6 (57.2%-88.9%)	100 (99.7%-100%)
Sample type: nasal swab	11	4406	80.1 (65.0%-89.7%)	98.5 (97.3%-99.2%)
Index test (Panbio COVID-19 Ag Rapid Test Device)	6	5555	76.1 (59.4%-87.4%)	100 (99.7%-100%)
Index test (BinaxNOW COVID-19 Ag card)	7	3536	81.9 (59.3%-93.4%)	98.6 (98.0%-99.1%)
Threshold value (Ct = 38)	4	583	90.9 (66.4%-98.0%)	99.4 (96.3%-99.9%)
Testing site (pediatric emergency department)	5	5131	80.5 (58.2%-92.4%)	99.9 (98.0%-100%)
Testing site (community testing site)	8	3789	79.0 (58.4%-90.9%)	98.6 (97.8%-99.1%)

CI = confidence interval; Ct = cycle threshold.

and experienced healthcare testers may have contributed to the increased sensitivity of the SARS-CoV-2 antigen test in our study.[20]

Testing remains important during vaccine rollout as individuals hesitate or refuse to vaccinate, and more contagious SARS-CoV-2 variants emerge. Furthermore, frequent antigen testing might reduce SARS-CoV-2 infection and mortality.[38] In addition to ambulatory setting, antigen testing is an effective tool for SARS-CoV-2 detection in symptomatic patients for community transmission screening.[9]

The results of the subgroup analysis in the study revealed that antigen tests performed in pediatric patients within 7 days after symptom onset exhibited higher sensitivity. Antigen tests have lower sensitivity in asymptomatic pediatric participants according to the result of another subgroup analysis. Therefore, serial testing is crucial since a single test might not be sufficient to detect SARS-CoV-2 in asymptomatic children when they are prone to have a high pretest probability of COVID-19. Serial testing may help identify infected children since they develop higher viral loads subsequently.[29] The BinaxNOW COVID-19 Ag card may have higher sensitivity to detect SARS-CoV-2 than the overall estimate according to the subgroup analysis of studies that examined the commercial test kit. A study reported that COVID-19 antigen testing had a sensitivity of 81.1% to detect SARS-CoV-2 in vaccinated individuals who had Ct ≤ 30, and that antigen testing remains a reliable tool for detecting breakthrough infections in patients with high viral load.[39] Hence, SARS-CoV-2 antigen tests remain necessary in detecting post-vaccination infection.

Children with COVID-19 may have less severe symptoms when infected with SARS-CoV-2 than with other respiratory viruses.[40] In comparison to the adult population, children have a lower average viral load. The sensitivity of antigen tests in children can be reduced by a low viral load. Consequently, antigen tests in the pediatric population may become less sensitive.[41] Performing NPS in children is stressful and painful owing to poor cooperation, which might result in a lower sensitivity of antigen tests in children. Thus, saliva might be a suitable specimen type for antigen tests for COVID-19 diagnosis in the pediatric population.[42] Antigen tests with an anterior nasal swab specimen had a sensitivity of 100% within 6 days of disease onset and its use had the potential to reduce the burden on medical staff.[43] Moreover, antigen test performance revealed a significant correlation between self-collected nasal swabs in children and healthcare staff-collected swabs.[44] According to our meta-analysis, nasal swab antigen testing demonstrated a high sensitivity for SARS-CoV-2. Therefore, we suggest that antigen testing using nasal swab specimens may be accurate for the SARS-CoV-2 detection in children. In addition, deploying antigen testing resulted in a significant reduction of missed school days compared to optionally masked areas not employing this strategy.[45] Multisystem inflammatory syndrome in children (MIS-C) tends to be diagnosed 3 to 6 weeks after the peak of SARS-CoV-2 transmission. Although MIS-C has overlapping features with Kawasaki disease, clinical information in children with MIS-C is available, including present or recent SARS-CoV-2 infection validated by RT-PCR, antigen testing, or serology, or exposure to a suspected or confirmed COVID-19 patient up to 4 weeks before symptom onset.[46] Therefore, the SARS-CoV-2 antigen test might be used to differentiate MIS-C from Kawasaki disease in patients with evidence of prior SARS-CoV-2 exposure.

Although the outcomes of our updated meta-analysis indicated that the antigen test performed in patients within 7 days after symptom onset exhibited high sensitivity for the detection of SARS-CoV-2, this study has some limitations. The Ct threshold values for positive RT-PCR results reported in the included studies and the Ct values of COVID-19 patients were limited. Studies that enrolled participants consecutively or randomly were limited. Only two studies in the updated meta-analysis offered information on SARS-CoV-2 variants and no study provided information on the vaccination status of the participants. In addition, no study had evaluated the accuracy of the saliva antigen test for the diagnosis of COVID-19 in children in our updated meta-analysis.

In conclusion, our major findings indicate that SARS-CoV-2 antigen tests performed in children with COVID-19 within 7 days of symptom onset exhibit high sensitivity. Antigen tests using nasal swab specimens have yielded high sensitivity for the detection of SARS-CoV-2 in the pediatric population. Therefore, antigen tests may be an accurate tool to inhibit SARS-CoV-2 transmission in children. Further studies should assess the accuracy of antigen tests stratified by SARS-CoV-2 variants and examine the pediatric population using saliva specimens to ameliorate the applicability of antigen tests for COVID-19 diagnosis in children and adolescents.

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APPENDIX A. SUPPLEMENTARY DATA

Supplementary data related to this article can be found at http://links.lww.com/JCMA/A205.

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