Screening Algorithms to Reduce Burden of Pediatric HIV Testing

A Systematic Review and Meta-analysis

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Background: The accuracy of symptom screening to identify children eligible for further HIV testing in generalized epidemics has been examined in several studies. We performed a systematic review and meta-analysis of these studies.

Methods: We screened 5 databases and abstracts from 4 HIV/AIDS conferences. Studies were included if they were performed in clinical settings, included children of 0–15 years old, and used a signs/symptoms screen to determine eligibility for HIV testing. The primary outcomes were sensitivity and specificity of the screening tools. A meta-analysis was performed to evaluate the utility of a screening tool in the outpatient setting.

Results: Our search returned 5529 database results and approximately 6700 conference abstracts, of which 36 articles were reviewed and 7 met criteria for inclusion. All were prospective or cross-sectional studies that developed and/or validated a screening tool to identify children at higher risk for being HIV infected. Sensitivity of the screening tools ranged from 71% to 96%, whereas specificity ranged from 25% to 99%. Meta-analysis of studies evaluating outpatient screening tools revealed a sensitivity of 81.4%, with a specificity of 69.4% for detecting HIV infection.

Conclusions: Few studies have evaluated the use of screening tools for HIV diagnosis in children. Screening tools that exist showed only moderate sensitivity and specificity and missed a substantial number of HIV-infected children in high-prevalence areas. In outpatient settings, the use of a screening tool may help reduce the number of HIV tests needed to identify an HIV-infected child, but at the cost of missed diagnoses. Further studies are needed to determine whether this represents a resource-saving mechanism.

Key Words: HIV, screening algorithm, decision support technique

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Advances in the implementation of prevention of mother-to-child transmission (PMTCT) and early infant diagnosis have led to decreased incidence in pediatric HIV and improved rapid identification of cases. Despite downtrending incidence rates, the prevalence of pediatric HIV remains high in Southern Africa where up to 1 in 36 children is HIV infected (Eswatini, prevalence of 2.8%), although the prevalence of pediatric HIV in other Sub-Saharan African countries is closer to ≤1%.[1] Unfortunately, diagnosis and treatment of HIV-infected children still lag behind that of adults. Children accounted for 10% of new HIV infections globally in 2018, yet only 54% of children living with HIV were on antiretroviral therapy compared with 62% of adults and 82% of pregnant women.[2] The situation is worse in West and Central Africa, where only 26% of HIV-infected children of 0–14 years old received antiretroviral therapy.[3] Worldwide, adolescents are one of few populations in which HIV-related deaths are still increasing.[4] Time has nearly run out to meet the ambitious 90–90–90 goals for children, and case finding among children and adolescents needs to be a priority.

Early identification of HIV infection in children is essential to provide linkage to care and facilitate antiretroviral therapy initiation. Although many HIV-infected children develop severe HIV-related signs and symptoms in the first year of life and present to care, others may remain without symptoms or have only mild symptoms, and therefore go undetected for years.[5] The World Health Organization (WHO) currently has clear recommendations for provider-initiated testing and counseling (PITC) of certain high-risk groups, such as infants of HIV-infected mothers, children presenting to inpatient wards, children attending tuberculosis or malnutrition clinics, and adolescents seeking antenatal or sexual and reproductive health services, but recommends context-dependent strategies for children outside of these groups.[6,7] New guidelines from the President's Emergency plan for AIDS Relief have focused on similar high-risk populations and index testing (testing the family of infected adults or children) and recommended against universal testing due to declining positivity rates and resource limitations.[8] This leads to highly variable application of PITC, which also faces numerous barriers, including resource limitations (human, financial, and structural) as well as social and legal constraints. For example, testing children for HIV comes with unique ethical challenges surrounding consent and disclosure of results, which are exacerbated in the orphan and vulnerable youth and children population.[9,10] It is also complicated by the implications of a positive result, in particular, the guilt and stigma that can be associated with vertical transmission.[9–11] Furthermore, due to misconceptions regarding pediatric HIV, health care workers (HCWs) underestimate the importance of screening for late-presenting vertical transmission.[9–11] With rates of pediatric HIV declining overall, it is unclear when and how to move toward more targeted approaches to testing.

In an era of flat to decreasing external funding, especially as adult case finding targets are reached, stakeholders are looking for efficiencies in HIV programming. One potential efficiency is to reduce the number of HIV tests performed by stratifying patients based on risk. Several countries are implementing the use of a screening questionnaire or diagnostic algorithm to risk stratify patients. These consist of a series of questions asked by a HCW and answered by a guardian or older child about signs or symptoms associated with HIV infection and/or demographic characteristics. An ideal screening test for pediatric HIV would identify infection early and maximize sensitivity, while also reducing the number of

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tests performed to minimize costs. Several studies have examined the accuracy of symptom screening to identify children eligible for further HIV testing in generalized epidemics. To our knowledge, a systematic review and meta-analysis of these studies have not yet been done. To review the evidence and provide consolidated data to inform programmatic decision-making, we performed a systematic review and meta-analysis to review the accuracy of symptom screens to identify children living with HIV in generalized epidemic settings.

MATERIALS AND METHODS

Search Strategy

We included case-control, cross-sectional cohort or randomized controlled trials that identified or evaluated a screening tool for HIV infection in children of 0–15 years old of unknown HIV status (no documented HIV test results). We included studies in healthcare settings in countries with a generalized HIV epidemic defined as HIV prevalence >1% among pregnant women. We excluded any trials that limited testing to high-risk populations (eg, infants of HIV-infected mothers who are presenting for early infant diagnosis testing as part of routine PMTCT or children referred to a clinic due to suspicion of HIV infection). No limitations were placed on date or publication status. Only studies in English were considered.

The following databases were searched: Embase, PubMed, Cochrane, Scopus, and the Web of Science with a final search date of December 10, 2018. All databases were screened using the appropriate medical subject headings, keywords, and Boolean operators. Duplicate citations in EMBASE and PubMed were excluded based on PubMed ID numbers in search results. All titles and abstracts were reviewed by 2 authors (S.L.C., K.D.M.) for applicability, and any potential articles identified by either author underwent a full-text review. Finally, references of included studies were reviewed for additional references. Any discrepancies were resolved by discussion between the review authors, or if they are unable to resolve, by decision of a third review author (J.E.C.).

All abstracts presented as oral or poster presentations at the following conferences from 2015 to June 2019 were reviewed: International AIDS Conference; International AIDS Society Conference on HIV Pathogenesis, Treatment and Prevention; Conference on Retroviruses and Opportunity Infections; and International Conference on AIDS and sexually transmitted infections in Africa. No search criteria were used to limit results.

Evaluation of Bias

We appraised the quality of included studies with the Quality Assessment of Diagnostic Accuracy Studies (QUADAS-2) tool.[12] QUADAS-2 consists of 4 domains: patient selection, index test, reference standard, and flow and timing. Risk of bias is judged as "low," "high," or "unclear." If the answers to all signaling questions for a domain are "yes," then risk of bias can be judged low.

Data Extraction

Data extraction was performed independently by both reviewers using a standardized form. Principal summary measures were sensitivity, specificity, true positives, false positives, false negatives, and true negatives for each screen, as well as the percent of children who screened positive. When these numbers were not specifically reported, they were calculated from reported sensitivity, specificity, and study size.

Meta-analysis

Meta-analysis was performed using OpenMetaAnalyst for 4 outpatient studies. Pooled sensitivity and specificity estimates were calculated using the diagnostic random effects model. When articles included multiple potential screens, the most sensitive screen was selected for inclusion given the current high priority in capturing HIV-infected individuals and initiating treatment.

RESULTS

The database search produced 5529 results and over 6700 conference titles/abstracts, which were screened to identify 36 articles for full-text review, of which 7 met criteria for inclusion in this systematic review (Fig. 1).[13–19] No conference abstracts from the specified dates met our inclusion criteria. The most common reason for exclusion after full article review (n = 17) was that these studies exclusively used screening tools applied to HIV-exposed infants presenting for PMTCT care.

Description of Studies

Included studies were conducted from 2003 to 2018 and involved 21,044 pediatric patients. All were prospective or cross-sectional studies that developed and/or validated a screening tool

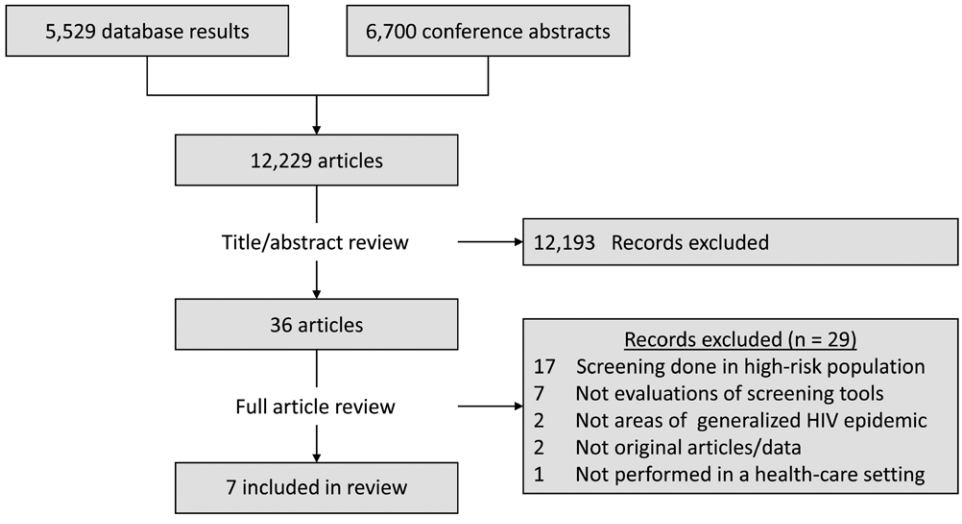

FIGURE 1. Flow chart of literature search for studies evaluating pediatric HIV screening tools.

TABLE 1. Characteristics of Studies Included in the Systematic Review

Title (Journal)	Author (year)	Country	Clinical Setting	No. Study Population	HIV Prevalence (%)	Age Range	Screening Tool (No. Considered Positive)	Sensitivity (%)	Specificity (%)	Population Screening Positive (%)
Development of a clinical algorithm to prioritise HIV testing of hospitalized pediatric patients in a low resource moderate prevalence setting (*Archives of Disease in Childhood*)	Allison et al (2011)[17]	Papua New Guinea	Inpatient ward	487	11.3	1 mo to 11 y	4 questions. 2 historic, 2 examination findings. (≥1)	96.3	25.0	77.4
Validation of a screening tool to identify older children living with HIV in primary care facilities in high HIV prevalence settings (*AIDS*)*	Bandason et al (2016)[15]	Zimbabwe	Outpatient clinic	9568	4.7	6–15 y	4 questions. All historic. (≥1)	80.4	66.3	35.9
Clinicoepidemiologic scoring system for early diagnosis of pediatric HIV (*Indian Pediatrics*)	Bandyopadhyay et al (2009)[18]	India	Outpatient clinic	378	24.3	18 mo to 14 y	17 weighted questions. 12 historic, 5 examination findings. (score >9)	95.7	98.6	24.3
A primary care level algorithm for identifying HIV-infected adolescents in populations at high risk through mother-to-child transmission (*Tropical Medicine and International Health*)*	Ferrand et al (2011)[16]	Zimbabwe	Outpatient clinic	255	17.0	10–18 y	5 questions. All historic. (≥2)	74.0	80.0	29.0
Diagnosis of pediatric HIV infection in a primary health care setting with a clinical algorithm (*Bulletin of the World Health Organization*)*	Horwood et al (2003)[14]	South Africa	Outpatient clinic	690	28.7	2 mo to 5 y	4 questions. All historic. (≥1)	92.4	31.5	75.4
Pediatric HIV management at primary care level: an evaluation of the integrated management of childhood illness (IMCI) guidelines for HIV (*BMC Pediatrics*)*	Horwood et al (2009)[13]	South Africa	Outpatient clinic	1064	7.1	0–5 y	8 questions. 5 historic, 3 examination findings. (≥3)	71.1	88.1	16.1
Simple screening tool to help identify high-risk children for targeted HIV testing in Malawian inpatient wards (*Journal of Acquired Immune Deficiency Syndromes*)	Moucheraud et al (2018)[19]	Malawi	Inpatient ward	8602	1.1	1–15 y	6 questions. All historic. (≥1)	84.4	39.6	60.7

*This study was included in the meta-analysis.

to identify children at higher risk for being HIV infected. The studies included 5 from Sub-Saharan Africa, 1 from India, and 1 from Papua New Guinea (Table 1).[13–19] The regional setting was variable and included some urban settings, rural settings, or both. Five studies were conducted at outpatient clinics and 2 at inpatient wards. One study focused exclusively on adolescents, whereas the remainder included a mix of infants, children, and some younger adolescents. HIV prevalence in the study population ranged from 1.1% to 28.7% and generally was lower in more recent studies. Risk of bias was judged to be low based on QUADAS-2 evaluation standards. The reference standard was an HIV antibody test in all cases.

Three studies (2 from Zimbabwe and 1 from Malawi) used the same base screening tool with small modifications. Ferrand et al[16] developed the original screening tool for outpatient adolescents using the test/train method in which they developed an algorithm on half of the study population and tested it on the other half. In this review, we present data from the "test" population only. Bandason et al[15] validated the screening tool developed by Ferrand et al[16] prospectively in outpatient older children in Zimbabwe. In an inpatient study in Malawi, Moucheraud et al[19] based their screening tool on the one developed by the Zimbabwe group and tested it prospectively.

Two studies from South Africa (both Horwood et al[13,14]) used tools that were based on the WHO Integrated Management of Childhood Illness (IMCI) algorithm for pediatric HIV infection. In 2003, Horwood et al[14] developed an algorithm to identify symptomatic HIV infection in their study population using 4 preliminary screening questions to qualify for further screening and compared it to a serologic test. Here, we present data for those 4 screening questions without the full algorithm due to the higher sensitivity of the simpler tool. In 2009, Horwood et al prospectively evaluated the full algorithm previously developed to identify suspected symptomatic HIV infection as applied by IMCI-trained health workers compared with IMCI experts. They classified some children as "HIV exposed" and some as "suspected symptomatic HIV infection" and compared classification to HIV test results. Here we include data for "suspected symptomatic HIV infection" only.

Bandyopadhyay et al[18] performed a single-center study in Kolkata, India, in which they developed a screening tool that was specific to the local context and risk factors for acquiring HIV and prospectively evaluated it on their study population. The screen consists of 17 questions, of which 5 were specific to the father's location, job, and health, with a weighted scoring system of 38 points.

Finally, Allison et al[17] developed their screening tool using multivariate regression analysis to ascertain independent predictors of HIV infection in their inpatient population in Papua New Guinea and then retrospectively applied the tool to the same study population.

Description of Screening Tools

Most common signs/symptoms or medical history were growth characteristics (4/7), overall poor health or functional status (3/7), recurring skin problems (3/7), ear discharge (3/7), or ever being admitted to a hospital (3/7) (Table 2). The most common physical examination questions were lymphadenopathy (3/7) and oral candidiasis (3/7). The only common demographic characteristic was having a deceased parent (3/7). One screen (Bandyopadhyay et al[18]) included several questions relevant to perceived local risk factors, such as father's location and occupation. Most screens were 4–6 questions long, and all were administered by HCW. Most screens (6/7) used a simple scoring system of one point for each answer with the exception of Bandyopadhyay et al[18] (Table 2).

TABLE 2. Summary of Screening Tools

Study	Criteria 1	Criteria 2	Criteria 3	Criteria 4	Criteria 5	Criteria 6	Criteria 7	Criteria 8	Criteria 9	Criteria 10	Criteria 11	Criteria 12–17	Definition of Positive Screen
Allison et al[17]	Low weight for age	Lymphadenopathy (≥2 locations)	Oral candidiasis	Persistent fever (≥1 mo)	—	—	—	—	—	—	—	—	≥1
Bandyopadhyay et al[18]	Failure to thrive	Chronic diarrhea >1 mo	Generalized lymphadenopathy	Extensive seborrheic dermatitis	Extensive molluscum contagiosum	Persistent oral candidiasis >2 mo	Recurrent pneumonia/TB	Persistent fever >1 mo	Bilateral nontender parotitis	Hepatomegaly	History of blood transfusion in child	Parental factors*	≥9†
Bandason et al[15]	Poor health in last 3 mo	Recurrent skin problems	Deceased parent	Ever admitted to the hospital	—	—	—	—	—	—	—	—	≥1
Ferrand et al[16]	Poor health in past 3 mo	Recurrent skin problems	Deceased parent	Ever admitted to the hospital	Signs or symptoms of STI	—	—	—	—	—	—	—	≥2
Horwood et al[14]	Weight loss	Persistent diarrhea in last 3 mo	Pneumonia currently	Ear discharge ever	—	—	—	—	—	—	—	—	≥1
Horwood et al[13]	Poor weight gain or weight loss	Persistent diarrhea in last 3 mo	Pneumonia currently	Ear discharge ever	Low weight for age	Lymphadenopathy (≥2 locations)	Oral candidiasis	Parotid gland enlargement	—	—	—	—	≥3
Moucheraud et al[19]	Sicker more often than other children in last 3 mo	Recurrent skin problems	Deceased parent	Frequent ear discharge	Ever admitted to the hospital	Shorter or smaller than other children	—	—	—	—	—	—	≥1

*Parental factors included: (1) father is a truck driver/migrant laborer/transport worker; (2) father's place of work is in Mumbai/Chennai/Hyderabad/Bangalore; (3) father suffers from all or any of 2 of the following (wasting/chronic diarrhea/TB); (4) father suffers from only one of the following, but not 2/3 of the following (wasting/chronic diarrhea/TB); and (5) history of sudden death in either parent without any definite cause.

†Questions were weighted for a maximum score of 38.

STI indicates sexually transmitted infection; TB, tuberculosis.

Sensitivity and Specificity

Sensitivity of the screening tools to detect pediatric HIV infection ranged from 71% to 96%, whereas specificity ranged from 25% to 99% (Table 1). The study by Bandyopadhyay et al[18] was the only study with both a sensitivity and a specificity >80%.

Meta-analysis

A meta-analysis of 4 outpatient studies which used a similar screening tool showed a sensitivity of 81.4% (confidence interval, 70.5–88.9; I^2 = 85.47%; P < 0.001) and a specificity of 69.4% (confidence interval, 46.7–85.5; I^2 = 99.29%; P < 0.001) (Fig. 2). One outpatient study (Bandyopadhyay et al[18]) was excluded from the meta-analysis because of lack of generalizability of the screening test.

DISCUSSION

Inpatient Studies

Previous systematic reviews have suggested that universal testing is optimal in some health care settings, particularly pediatric inpatient wards and nutrition centers, due to the very high prevalence of HIV in these populations.[20] In our review, we identified 2 studies that evaluated the utility of a screening tool on pediatric inpatient wards. Allison et al[17] evaluated a high-prevalence (11%) inpatient population, and the screening had a high sensitivity of 96%, but given the low specificity and high prevalence of the population, would require 78% of the hospitalized patients to be tested for HIV. Moucheraud et al[19] evaluated their screening tool in a low-prevalence inpatient population (1.1%) and found a modest sensitivity of 84.4%, with a negative predictive value of 99.6%.

Using data from these studies, we can compare the relative usefulness of a screen in high- and low-prevalence inpatient settings. In a theoretical inpatient population with a high HIV prevalence (10%), using data from the study by Allison et al,[17] for every 270 children screened, 61 children (23% of those screened) would be spared serologic tests and one HIV diagnosis would be missed (Table 3). In a low-prevalence setting (1%), using data from the study by Moucheraud et al,[19] for every 641 children screened, 252 would be spared serologic tests (39% of those screened) and one HIV diagnosis would be missed. Taken together, these studies suggest that if test kits are not available to administer to all inpatients, a screening tool may increase the yield of HIV testing in this population but carries a significant risk of missed diagnoses, especially in high-prevalence areas. In moderate- or low-prevalence settings with limited resources, a screening tool may be an effective case finding method and have an acceptable number of missed diagnoses. However, this must be balanced against the costs in terms of training and human resource time required to implement the screening tool. Additionally, the specificity of the screening tools in the studies by Allison et al[17] and Moucheraud et al[19] was low (25% and 40%, respectively). This is likely explained by the presence of co-endemic conditions, such as malnutrition and tuberculosis, that cause similar symptom profiles, especially in the high-risk pediatric inpatient population. This means that the majority of pediatric inpatients will screen positive (77% and 61% in these studies, respectively), and therefore, require a serologic or virologic test. Thus, further studies are required to determine whether the use of a screening tool would actually be cost-effective or reduce burden to the health system as opposed to universal testing on the inpatient population.

Outpatient Studies and Meta-analysis

HIV prevalence in pediatric outpatient centers is lower than inpatient centers (2.7% vs 21.1% in a previous systematic review of similar contexts)[20] due to the frequency of HIV-related illness or infection requiring hospitalization. Outpatient centers may, therefore, be a more ideal location for targeted screening to reduce burden to the health care system. Five of the included studies were performed in outpatient settings, all with a mix of well and sick visits with the exception of the study by Horwood et al[13] that only included sick visits. Despite different locations and age ranges, the screening questions were similar, with all screens including at least one question on constitutional symptoms (weight loss, failure to thrive, or health status affecting daily life) and recurrent infections (either skin, pulmonary, or ear infections). There was significant variability in the sensitivity and specificity of each screen (77.1%–96.3% and 31.5%–98.7%, respectively). The very high sensitivity detected in the study by Bandyopadhyay et al[18] was probably a result of the extensive nature of the questionnaire which takes into account local risk factors for HIV acquisition. Although not generalizable to other populations, this study suggests that screening tools could be improved by the addition of questions relevant to local risk factors for HIV transmission. However, this was unlikely to be pertinent for international guidelines on pediatric testing and thus was not included in the meta-analysis.

Compared with the inpatient studies, the pooled results of the outpatient studies had lower sensitivity (81.6%), which is consistent with the expectation that more HIV-infected children presenting to an outpatient setting will be asymptomatic and thus not screen positive. Similarly, the outpatient screens had higher specificity, which is likely due to lower prevalence of confounding diseases seen in outpatients compared with those admitted to the hospital. Using these data, in a theoretical population with high outpatient prevalence of 5%, screening would result in one missed HIV diagnosis for every 108 patients screened. In a population with moderate prevalence (1%), screening would lead to one missed HIV diagnosis per 538 patients screened (Table 3). Using a weighted average for the studies included in the meta-analysis, 36.3% of the population would require HIV testing.

This systematic review has several limitations. Only 2 studies among inpatients were identified, limiting our ability to perform a meta-analysis for this context. All studies included in the outpatient meta-analysis were conducted in sub-Saharan Africa and may not be generalizable to other regions. In addition, we were unable to perform secondary analysis by age group, sex, or country pediatric HIV prevalence due to lack of availability of these data in

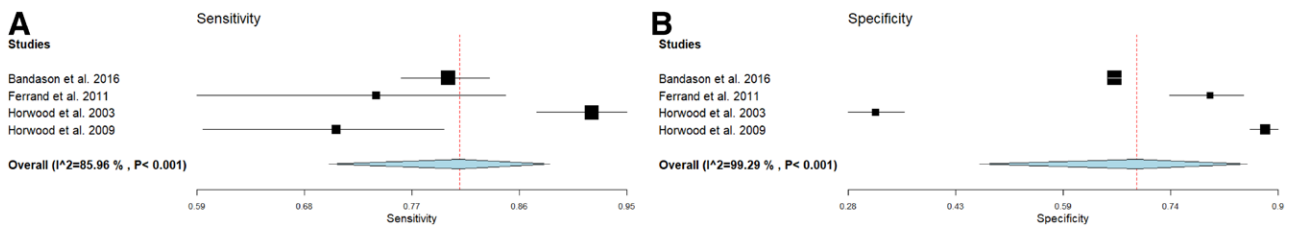

FIGURE 2. Forrest plot of sensitivity (A) and specificity (B) for outpatient screening tools to detect pediatric HIV infection.

TABLE 3. Number Needed to Test/Screen for Theoretic Populations

	Study Characteristics		Low Prevalence (1%)					High Prevalence (10%)				
Inpatient Studies	Sensitivity	Specificity	NNT Test to Identify 1 HIV-infected Patient With Universal Screening	NNT Test to Identify 1 HIV-infected Patient With Tool	Percent of Population Requiring HIV Test	NNT Screen for Each HIV Diagnosis Missed	No. HIV Diagnosis Missed per 10,000 People	NNT Test to Identify 1 HIV-infected Patient With Universal Screening	NNT Test to Identify 1 HIV-Infected Patient With Tool	Percent of Population Requiring HIV Test	NNT Screen for Each HIV Diagnosis Missed	No. HIV Diagnosis Missed per 10,000 People
Allison et al[17]	96.3	25	100	78	75	2703	4	10	8	77	270	37
Moucheraud et al[19]	84.4	39.6	100	72	61	641	16	10	7	63	64	156
	Study characteristics		Low prevalence (1%)					High prevalence (5%)				
Outpatient studies	Sensitivity	Specificity	NNT Test to Identify 1 HIV-infected Patient With Universal Screening	NNT Test to Identify 1 HIV-infected Patient With Tool	Percent of Population Requiring HIV Test	NNT Screen for Each HIV Diagnosis Missed	No. HIV Diagnosis Missed per 10,000 People	NNT Test to Identify 1 HIV-infected Patient With Universal Screening	NNT Test to Identify 1 HIV-infected Patient With Tool	Percent of Population Requiring HIV Test	NNT Screen for Each HIV Diagnosis Missed	No. HIV Diagnosis Missed per 10,000 People
Bandason et al[15]	80.4	66.3	100	42	34	510	20	20	9	36	102	98
Bandyopadhyay et al[18]	95.7	98.6	100	2	2	2326	4	20	1	6	465	22
Ferrand et al[16]	74	80	100	28	21	385	26	20	6	23	77	130
Horwood et al[14]	92.4	31.5	100	74	69	1316	8	20	15	70	263	38
Horwood et al[13]	71.1	88.1	100	18	12	346	29	20	4	15	69	145
Meta-analysis	81.4	69.4	100	38	31	538	19	20	8	33	108	93

the studies, which was probably due to small sample size in most studies.

Overall, with decreasing HIV prevalence, HIV risk screens will have higher negative predictive value. However, at current HIV prevalences in pediatric populations seeking medical care, there will still be significant number of diagnoses missed. Further studies are needed to validate these screening tools in different clinical and nonclinical contexts and to develop better screening tools. More ideal screening tools would include nonsymptom risk factors for HIV exposure to identify HIV-infected children before their infection becomes symptomatic and thus provide early access to treatment. The addition of risk factors pertinent to the local epidemic, as in the study by Bandyopadhyay et al,[18] would likely improve the sensitivity of the screen, but would be difficult to implement as an international policy recommendation, and could be resource intensive to develop.

Finally, further analysis is needed to evaluate the cost-effectiveness, acceptability, and overall resource burden (including training, implementation, and financial) of using the screening tools compared with WHO guidelines and universal screening for children with unknown HIV status. This must take into account the economic and health impact of delayed diagnosis. Although the trials included here are compared with universal screening, a recent study showed that a comprehensive intervention that increased testing in adolescents utilizing an HIV screening tool still increased identification of HIV-infected children from 198 to 534 over a 3-month period, with relatively minimal impact on percent of tests resulting positive (0.8% → 0.7%; $P < 0.001$).[21] This suggests that current PITC and screens are not optimal for the detection of HIV in children, and further expansion of testing is needed. Finally, the small number of studies identified by this systematic review strongly highlights the need for further exploration in this area. Caution should be taken when making large policy and implementation decisions based on such limited evidence.

CONCLUSIONS

With improved PMTCT and decreased HIV incidence in children, HIV testing yields are decreasing and efforts are being directed toward making HIV testing more efficient. This review shows that few studies have been done to develop and evaluate pediatric screening tools. Current screening algorithms that risk stratify patients to determine need for HIV testing showed only moderate sensitivity and specificity and missed a substantial number of HIV-infected children, especially in high-prevalence contexts (inpatient wards). In outpatient settings, use of a screening tool may increase the yield of HIV testing, but still comes at the risk of some diagnoses being missed. In both inpatient and outpatient contexts, further studies are needed to fully document the resources required to implement risk screening and determine whether this is a cost-effective approach to HIV case finding in children presenting to health care settings in generalized HIV epidemics.

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