EClinicalMedicine 37 (2021) 100961

Contents lists available at ScienceDirect

EClinicalMedicine

journal homepage: https://www.journals.elsevier.com/eclinicalmedicine

Research Paper

Performance of point-of-care tests for the detection of chlamydia trachomatis infections: A systematic review and meta-analysis

Ying Zhou[a,b,1], Ting-Ting Jiang[a,c,1], Jing Li[a,c], Yue-Ping Yin[a,c], Xiang-Sheng Chen[a,c,d,*]

[a] Institute of Dermatology, Chinese Academy of Medical Sciences & Peking Union Medical College, 12 Jiangwangmiao Street, Nanjing 210042, China
[b] Department of Dermatology, Affiliated Hospital of Guangdong Medical University, Zhanjiang, Guangdong, China
[c] National Center for STD Control, Chinese Center for Disease Control and Prevention, Nanjing, China
[d] Institute for Global Health and Sexually Transmitted Diseases, Southern Medical University, Guangzhou, China

ARTICLE INFO

Article History:
Received 20 January 2021
Revised 13 May 2021
Accepted 28 May 2021
Available online xxx

Keywords:
Chlamydia trachomatis
Diagnostics
Point-of-care
Meta-analysis

ABSTRACT

Background: Chlamydia trachomatis (CT) is one of the most prevalent bacterial sexually transmitted infections (STIs) globally but has been inadequately detected for intervention. Introduction of point-of-care tests (POCTs) for CT is critical for filling the intervention gaps. We conducted a systematical review and meta-analysis on diagnostic performance of POCTs for CT to assist in guiding the application of these assays in CT screening and detection.

Methods: We searched PubMed/Medline and Embase databases, from January 2004 to May 2021, for studies reporting the performance of POCTs for identifying CT using specimens collected from urethral, vaginal, cervical, anorectal, or pharyngeal site or of urine. Two investigators independently screened and extracted data for controlling the quality of data extraction. Any discrepancies in study selection and data extraction were resolved through consensus. We only included studies with sufficient data to estimate sensitivity and specificity, and used laboratory-based nucleic acid amplification test (NAAT) as the reference standard. The main outcomes were pooled sensitivity, specificity, and diagnostic odds ratio (DOR) and their corresponding 95% confidence intervals (CIs). Summary estimates were calculated using a random-effects model and summary receiver operator curves (SROCs) were generated using the Moses-Littenberg method. STATA 14.0 and Meta-DiSc 1.4 were used for statistical analysis. The study protocol is registered with PROSPERO, number CRD42019140544.

Findings: Of 3,038 records identified, 39 studies (42,336 specimens) were included in the study, including 14 studies on evaluation of antigen detection (AD)-based and 25 on NAAT-based POCTs. The overall pooled sensitivity, specificity and DOR were 56% (95% CI 45%–67%), 99% (95% CI 98%–99%) and 86 (95% CI 46–163), respectively, for AD-based POCTs and corresponding values for NAAT-based POCTs were 94% (95% CI 91%–96%), 99% (95% CI 99%–99%) and 1,933(95% CI 1,018–3,669), respectively. The pooled sensitivity of AD-based POCTs varied across the types of specimens, indicating 46% for cervical swabs (95% CI 37%–56%; range 22.7%–71.4%), 52% for vaginal swabs (95% CI 34%–70%; range 17.1%–86.8%) and 57% for male urine (95% CI 36%–75%; range 20.0%–82.6%). For NAAT-based POCTs, the pooled sensitivity was 94% (95% CI 90%–96%) for cervical swabs, 94% (95% CI 86%–98%) for vaginal swabs, 95% (95% CI 91%–97%) for urine specimens and 93% (95% CI 87%–96%) for anorectal swabs.

Interpretation: NAAT-based POCTs for CT have a significantly better performance particularly in sensitivity for diagnosing the infection with CT than the AD-based POCTs. Screening strategy with AD-based POCTs may potentially result in a substantial under-detection of the infections.

1. Introduction

Chlamydia trachomatis (CT) infection is one of the most prevalent sexually transmitted infections (STIs) globally. The World Health Organization (WHO) estimates that 127.2million new cases of CT occur globally every year and most of them come from the resource-limited countries [1]. Untreated CT infection in women can lead to

* Corresponding author at: Institute of Dermatology, Chinese Academy of Medical Sciences & Peking Union Medical College, 12 Jiangwangmiao Street, Nanjing 210042, China
E-mail address: chenxs@ncstdlc.org (X.-S. Chen).
[1] These authors contributed equally to this work.

https://doi.org/10.1016/j.eclinm.2021.100961

Research in context

Evidence before this study

Point-of-care tests (POCTs) are critical for filling the gaps in diagnosis of infections with *Chlamydia trachomatis*, particularly in many settings where laboratory-based tests are usually not available but performance of the available POCTs for detecting CT at genital, rectal and oropharyngeal sites or using different types of specimens is not well known. Three systematic reviews were published in 2010, 2016 and 2017 respectively but none of them include a meta-analysis assessing nucleic acid amplification test (NAAT)-based POCTs for CT across different types of specimens or the specimens from different anatomical sites potentially exposed to the sexual contacts.

Added value of this study

This systematic review and meta-analysis includes a comprehensive set of published studies on evaluating performance of POCTs for detecting antigen or nucleic acid of CT using different types of specimens and/or specimens collected from different anatomical sites. This study indicates that the sensitivity of NAAT-based POCTs was significantly superior to that of antigen-based POCTs, highlighting the importance to introduce NAAT-based POCTs for overcoming underperformance of antigen detection (AD)-based POCTs. Approaches to improve the quality of specimen collection could substantially improve the sensitivity of AD-based POCTs.

Implications of all the available evidence

NAAT-based POCTs have acceptable performance in terms of identifying and excluding chlamydial infections in comparison with the laboratory-based nucleic acid amplification tests. AD-based POCTs which are widely used in many resource-limited settings are not efficient to identify the infections, resulting in half of infections to be missed. However, high cost of NAAT-based POCTs may be one of barriers to prevent the introduction of this approach particularly in resource-limited settings.

serious complications, including pelvic inflammatory disease (PID), ectopic pregnancy, tubal infertility, and chronic pelvic pain [2,3]. Among men CT infection is associated with non-gonococcal urethritis and epididymitis [4]. CT infection in pregnant women can contribute to the incidence of adverse obstetric outcomes such as preterm birth and low birthweight [5]. In addition, genital CT infection significantly increases the risk of HIV transmission and human papillomavirus (HPV)-associated cervical carcinoma development [6,7]. Because over 70% of CT infections in women and 50% in men are asymptomatic [8], effective control of the infections often relies on screening for CT followed by treatment of the infected cases. Benefits of CT screening in women have been demonstrated a reduction in rates of PID [9], and prevention of adverse obstetric outcomes among pregnant women [10,11]. Screening for CT is largely subject to the tests available and accessible to the target populations. Laboratory-based nucleic acid amplification tests (NAATs) provide a highly accurate diagnosis but are usually neither affordable nor accessible in the developing countries because they require laboratory infrastructure and trained personnel and have a high cost [12]. In addition, delay in report of the test results may lead to the impossibility to provide timely treatment intervention. In contrast, point--of--care tests (POCTs) can be used in either clinic or out-of-clinic settings and allow diagnosis and treatment decisions to be made at the same visit, ensuring the immediate treatment and preventing the losses of follow-ups [13].

A few published systematic reviews have summarized the accuracy of POCTs for the diagnosis of urogenital CT infections using vaginal, cervical, urethral or urine samples [12,14,15]. However, most of the POCTs included into these reviews were mainly based on antigen detection in lateral flow format (AD-based POCTs). Since the publication of the latest review [12], many studies on performance of POCTs, particularly NAAT-based POCTs, have been published. Additionally, increasing rates of anorectal CT infections among men and women call for requirement of these diagnostics to be applied in rectal specimens [16,17]. Accordingly, we conducted a systematic review and meta-analysis to update the diagnostic performance of AD- and NAAT-based POCTs for diagnoses of urogenital, anorectal or oropharyngeal CT infections.

2. Methods

2.1. Search strategy

The present systematic review and meta-analysis was conducted in accordance with the MOOSE (Meta-analysis Of Observational Studies in Epidemiology) and PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analysis) guidelines [18,19]. We systematically searched the PubMed/Medline and Embase for studies published from January 2004 (the year in which WHO published its pivotal report on POCTs for sexually transmitted infections) to May 2021. No restrictions were applied concerning language. The following combinations of search terms were used: (*Chlamydia trachomatis* OR chlamydia* OR (*C. trachomatis*)) AND ((point-of-care test*) OR POC* OR assay* OR diagnostic* OR RDT*) AND (performance OR accuracy OR sensitivit* OR specificit*). We also manually searched the relevant references to identify potential articles.

2.2. Study selection and data extraction

The full text of the studies deemed relevant were reviewed to determine eligibility. The studies were included using the following criteria: (1) any sexually active populations in any geographical location; (2) technology in POCT or near POCT format used as the index test for evaluating the performance in diagnosis of CT infection; (3) sufficient data, including the absolute numbers of true positives, false positives, true negatives, and false negatives, to construct 2×2 contingency tables regarding sensitivity and specificity; (4) laboratory-based NAAT assay used as the reference standard; and (5) publications between January 2004 and May 2021. The exclusion criteria were as follows: (1) without defined outcome measure for validating the performance (i.e. defined reference assay); (2) insufficient data to construct contingency tables; (3) duplicated studies using the same index test and the same population; (4) case report, or review article; (5) inappropriate reference standard such as culture; and (6) inappropriate POCT such as gram stain or enzyme detection assay. In the case of any overlapping study, only the largest and most informative study was included. Two investigators (YZ, JL) independently applied inclusion and exclusion criteria to screen the titles and abstracts of studies retrieved to exclude the irrelevant articles. Subsequently, full-text publications were reviewed to decide whether the study fitted the eligibility criteria of the review. Discrepancies were resolved through discussion and mutual agreement between the two investigators. For eligible studies, the following baseline characteristics of included studies were extracted by two investigators (YZ, JL) independently using the standardized form: first author's last name, year of publication, type of test, type of specimen, reference standard, sample size, economic category of the country where the evaluation was conducted, and data for determining the outcomes of interests (absolute number of true positive, false positive, true negative, and false negative results), as shown in Tables S1 and S2. If the exact value for each outcome was not clearly reported through the included

studies, it was estimated from the related percentage. For each study, the sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and diagnostic odds ratio (DOR), compared with the reference standard, were calculated. Any discrepancies in data extraction were resolved through consensus.

2.3. Quality assessment

The methodological quality of each included study was independently assessed by two reviewers (YZ and TTJ) using the QUADAS-2 (quality assessment of diagnostic accuracy studies) tool [20]. This checklist consists of four key domains: patient selection, index test, reference standard and flow and timing. Within each study, the domains were assessed in terms of risk of bias and the first three of these domains were assessed in terms of concerns about applicability. Risk of bias (involved all four domains) and applicability (involved three domains) were scored using low risk, high risk or unclear. Disagreements on determining risk between YZ and TTJ were discussed to achieve consensus.

2.4. Statistical analysis

For each included study, sensitivity, specificity, and diagnostic odds ratios (DORs), along with their 95% confidence intervals (CIs), were calculated to express performance of the evaluated assay for diagnosing CT infection using laboratory-based NAAT as a reference standard. Heterogeneity across the included studies was assessed using Cochran's Q statistic and the I^2 test [21]. Heterogeneity was indicative when P-value<0.05 (Q statistic) and/or $I^2 > 50\%$, and then a random effects model was performed to calculate the performance estimates including the pooled sensitivity and specificity, and DOR which represents the overall diagnostic accuracy. A fixed effect model would be used when P-value≥ 0.05 (Q statistic) and $I^2 \leq 50\%$. We defined sources of heterogeneity a priori and we included the following factors: POCT type (AD-based versus NAAT-based), POCT specimen (cervical, vaginal, rectal or urine), and study setting (low/middle-income versus high-income countries). In addition, the estimate of summary receiver operating characteristics (SROC) curve was plotted and the area under SROC curve (AUC) served as a proxy of diagnostic accuracy. An area under the SROC curve between 0.90 and 1.00 is considered as excellent diagnostic accuracy, between 0.80 and 0.90 as very good, between 0.70 and 0.80 as good, between 0.60 and 0.70 as sufficient, between 0.50 and 0.60 as bad and less than 0.5 as not useful [22]. Using the Moses–Littenberg method, Q^* values were calculated from the SROC curve by the point where sensitivity equaled specificity and values of Q^* near 1.0 indicate that SROC curves are snugged up near the desirable northwest corner where sensitivity and specificity are both 1.00 [23]. A two-sample Z-test was conducted to evaluate a significant difference in AUC and Q^* values between two diagnostic modalities (AD-based POCTs using cervical specimens vs. AD-based POCTs using vaginal specimens), and P-value<0.05 was considered statistically significant. Probability of publication bias was also considered and evaluated by Deeks et al. funnel plot [24], and P-value<0.05 was considered indicative of publication bias. All analysis were performed by using STATA version 14.0 (Stata Corporation, College Station, TX, USA), Meta-DiSc version 1.4 and Review Manager version 5.3 [25]. The study protocol is registered with PROSPERO, number CRD42019140544.

2.5. Role of the funding source

The funder of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

3. Results

3.1. Study selection

A total of 3,038 articles were identified from the PubMed/Medline ($n = 992$) and the Embase ($n = 2,046$) during the initial literature search. After excluding duplicated articles (951 articles), 2,087 publications were kept for screening, of which 2,032 articles were subsequently discarded after reviewing titles and abstracts. Through mutual search of review articles, another 3 articles were added in the study. Therefore, a total of 58 full-text articles were then assessed for their eligibility for inclusion in the final meta-analysis, and 19 of them were excluded because of insufficient data to construct contingency tables ($n = 2$), inappropriate reference standard ($n = 4$, including culture), inappropriate index POC test ($n = 10$, including gram stain or enzyme detection), modeling research or cost-effectiveness analysis ($n = 2$) and case report or review articles ($n = 1$) (Fig. 1). Finally, 39 articles were included in this systematic review and meta-analysis [26–64].

3.2. Characteristics of included studies

A total of 14 studies evaluated the performance of 10 brands of AD-based POCTs in 14,582 specimens from 11 countries. Among the 14 studies included, half of them were from the high-income countries according to the World Bank's classification of countries by income [65], namely the United Kingdom, the United States, Netherlands and the Republic of Korea, and another half from the low and middle-income countries including China, Guatemala, Vanuatu, Zambia, Philippines, Colombia and South Africa. Twenty-five studies evaluated NAAT-based POCTs in 27,754 specimens from 10 countries, and majority (84.0%) of these studies were conducted in high-income countries, namely the United Kingdom, the United States, Australia,

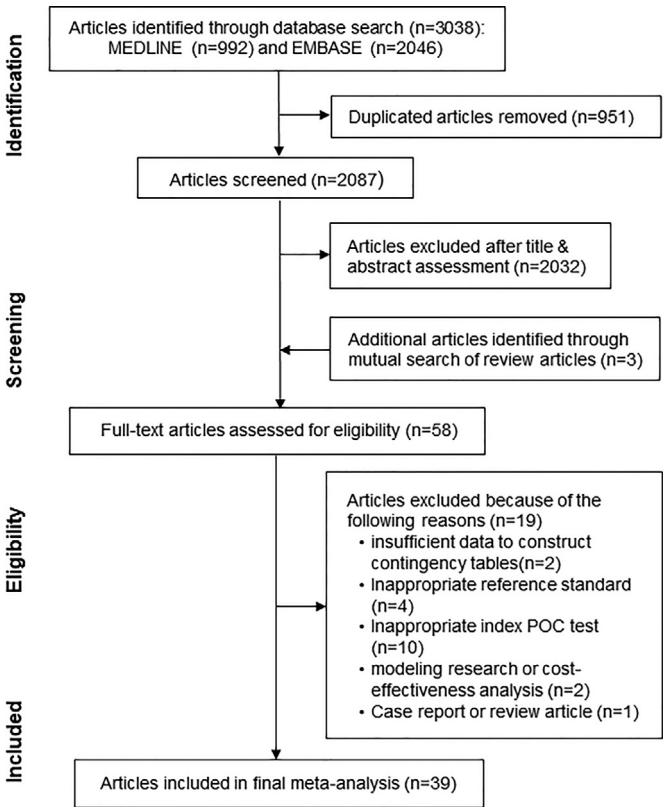

Fig. 1. PRISMA flow diagram for article search and selection.

Finland, Estonia and Japan, and the remaining studies were from Papua New Guinea, Thailand, India and China. The laboratory-based assays used as the reference standard included polymerase chain reaction (PCR) assay (Roche Molecular Systems, USA), ligase chain reaction (LCR) assay (Abbott Diagnostics, USA), strand displacement amplification (SDA) assay (ProbeTec ET, Becton Dickinson, USA) and transcription-mediated amplification (TMA) assay (Aptima, GenProbe, now Hologic, USA), and real-time PCR assay (AccuPower, Bioneer, Inc., Daejeon, Korea). Tables S1 and S2 summarized the data extracted from the studies, including first author, year of publication, type of test, type of specimen, reference criteria, sample size, and sensitivity, specificity, positive predictive value, and negative predictive value.

3.3. Study quality

The proportion of studies that fulfill each QUADAS-2 criterion is summarised in Fig. S1. Of the 39 studies, 17 (43.6%) [28,29,32,34–37,39–42,45,49,51,57,58,62] satisfy all of the criteria in the QUADAS-2 [20]. In the patient selection domain, one (2.6%) study [54] is classified at a high risk of bias for employing a case-control design. In the index test domain, 10 (25.6%) studies [30,31,53–57,59,63,64] did not clearly report if the index test had been conducted and interpreted before the reference standard. In the reference standard domain, three (7.7%) study [31,63,64] does not clarify if the reference standard results are interpreted without knowledge of infection status. In the flow and timing domain, no study is considered to be at high risk of bias. In terms of applicability no studies are considered to be at risk of bias for either patient selection, the reference standard or index test domains. As a result, the overall quality of the included studies was considered adequate, with the exception of only one study that demonstrated a high risk of bias.

3.4. Diagnostic performance

Table 1 shows the data of sensitivity and specificity from 14 studies on AD-based POCTs and 25 on NAAT-based POCTs. The overall sensitivity ranged from 17.1% to 93.8% with a median of 51.6% for AD-based POCTs and from 50.0% to100.0% with a median of 95.6% for NAAT-based POCTs. The overall specificity was generally high for either AD-based (range 89.0%–100.0%) or NAAT-based POCTs (range 89.4%–100.0%). Table 2 shows the pooled sensitivity, specificity and DOR estimates of AD-based POCTs and NAAT-based POCTs. According to the results, the overall estimates of pooled sensitivity, specificity and DOR were 56% (95% CI 45%–67%), 99% (95% CI 98%–99%) and 86 (95% CI 46–163), respectively, for AD-based POCTs, and 94% (95% CI 91%–96%), 99% (95% CI 99%–99%) and 1933 (95% CI 1018–3669) for NAAT-based POCTs. AUCs were 0.941 (95% CI 0.858–1.024) and 0.996 (95% CI 0.991–0.999) for AD-based POCTs and NAAT-based POCTs, respectively; the pooled diagnostic accuracy (Q*) were 0.878 (95% CI 0.772–0.984) and 0.975 (95% CI 0.964–0.986), respectively (Fig. 2). The diagnostic sensitivity of NAAT-based POCTs was significantly higher than AD-based POCTs ($P < 0.05$).

3.5. Subgroup analysis

The forest plots of AD-based POCTs and NAAT-based POCTs for different specimen types are given in Figs. 3 and 4. Although AD-based POCTs exhibited high specificity across all specimen types (range 89%–100%), the pooled sensitivity was 46% for cervical swabs (95% CI 37%–56%; range 22.7%–71.4%), 52% for vaginal swabs (95% CI 34%–70%; range 17.1%–86.8%) and 57% for male urine (95% CI 36%–75%; range 20.0%–82.6%). AUCs were 0.87 (95% CI 0.68–1.06) and 0.95 (95% CI 0.83–1.07) for AD-based POCTs using cervical and vaginal specimens, respectively; Q^* values were 0.80 (95% CI 0.62–0.98) and 0.89 (95% CI 0.72–1.06), respectively (Fig. 5). There were no significant differences between AD-based POCTs using cervical and vaginal specimens for both AUC and Q^* values ($P = 0.47$). For NAAT-based POCTs, as shown in Fig. 4, the pooled sensitivity was 93% (95% CI 87%–96%) for anorectal swabs, 94% (95% CI 90%–96%) for cervical swabs, 94% (95% CI 86%–98%) for vaginal swabs and 95% (95% CI 91%–97%) for urine specimens with a pooled specificity ranging from 99% to 100%. AUCs were above 0.99 and Q^* values were above 0.95 for NAAT-based POCTs regardless of the specimen types used (Fig. 6). Two studies evaluated the performance of NAAT-based POCT for pharyngeal swabs from the USA. One study reported that the Cepheid Xpert CT/NG assay had a sensitivity of 50% (1 of 2 positive samples of pharyngeal infection were detected) and another study reported a sensitivity of 100% (8 of 8 positive samples of pharyngeal infection were detected).

For AD-based POCTs, a further subgroup analysis was performed according to the income variation between countries (Table 2), and the results indicate that the pooled sensitivity of AD-based POCTs may be higher in high-income countries (65%, 95% CI 44%–82%) than low and middle-income countries (50%, 95% CI 40%–61%). For NAAT-based POCTs, we sub-grouped them into commercial availability and unavailability (Table 2), and found that the NAAT-based POCTs which were not commercially available had a similar pooled sensitivity (95%, 95% CI 92%–97%) to those commercially available (94%, 95% CI 90%–96%).

3.6. Publication bias

Deeks et al. funnel plot, seen in Fig. S2, was used to assess publication bias. The funnel plot had a slope coefficient of 9.86 ($P = 0.55$) and −16.15($P = 0.15$) for AD-based POCTs and NAAT-based POCTs, respectively, suggesting a low likelihood of publication bias in this meta-analysis.

4. Discussion

Chlamydial infections are still a major public health problem globally and the importance of introducing POCTs as one of strategic components for prevention and control of sexually transmitted infections has been widely recognized, particularly in the resource-limited countries. Advancement of POCTs would allow the delivery of etiology-based diagnosis to move from centralised laboratory-based testing to a clinic-based approach closer to the setting in which patients seek healthcare or community-based approach through self-testing of target populations. Hence, these approaches with POCTs would offer an important opportunity to make a rapid diagnosis of the infections for treatment, and initiate partner notification or other interventions in the same clinic visit.

In 2017, Kelly et al. [12] published a systematic review of rapid POCTs of CT in the urogenital tract, which included 12 studies on AD-based POCTs from 2006 to 2016, and 2 studies on NAAT-based POCTs (Cepheid GeneXpert CT/NG) from 2012 to 2013. Since then, a couple of studies on evaluation of AD-based POCTs including the *Chlamydia* Rapid Test (CRT) Device in South Africa in 2016 [41] and the Cortez OneStep *Chlamydia* RapiCard™ insta test in Zimbabwe in 2017 [44] and more studies on NAAT-based POCTs including commercial NAAT-based POCT (Cepheid GeneXpert CT/NG and binx CT/NG assay) and NAAT-based POCTs under development had been published. In our systematic review and meta-analysis, we identified 39 studies with 68 records assessing the performance of AD- or NAAT-based POCTs for diagnosis of CT infections in different anatomical sites in men and women, published over the past 17 years from January 2004 to May 2021.

Our finding that AD-based POCTs had generally low sensitivity for identifying CT infections was consistent with the three systematic reviews previously published [12,14,15], indicating that AD-based POCTs lacked sufficient sensitivity to be recommended as screening

Table 1.
Data on sensitivity and specificity of 39 studies included in the systematic review.

	AD-based point-of-care tests			NAAT-based point-of-care tests		
	No. studies*	Sensitivity% (median, range)	Specificity% (median, range)	No. studies*	Sensitivity% (median, range)	Specificity% (median, range)
Overall	14	51.6 (17.1–93.8)	98.8 (89.0–100.0)	25	95.6 (50.0–100.0)	99.4 (89.4–100.0)
Specimen by sex						
Cervical swab in females	8	51.6 (22.7–71.4)	99.5 (97.9–100)	7	95.7 (84.1–97.4)	99.6 (98.6–100.0)
Vaginal swab in females	10	54.0 (17.1–86.8)	97.7 (91.3–99.7)	10	96.1 (58.8–99.3)	98.7 (92.9–100.0)
Urine in males	6	45.4 (20.0–82.6)	98.7 (89.0–100.0)	7	94.4 (80.0–100.0)	99.5(97.5–100.0)
Urine in females	0	NA	NA	4	94.3 (80.9–97.6)	99.7 (99.3–99.9)
Urine in males and females	1	88.2	94.7	2	91.0 (83.3–98.6)	98.7 (97.3–100.0)
Rectal swab in males	0	NA	NA	3	86.0 (85.7–88.2)	99.2 (99.4–100.0)
Rectal swab in females	0	NA	NA	1	96.7	97.7
Rectal swab males and females	0	NA	NA	3	95.5 (94.4–96.6)	98.3 (89.4–99.7)
Pharyngeal swab in males	0	NA	NA	1	50.0	100.0
Pharyngeal swab in males and females	0	NA	NA	1	100.0	99.5
Swab in males and females	1	93.8	96.8	2	98.1 (96.2-98.0)	99.0 (98.0-100.0)
Urine or vaginal swab	0	NA	NA	1	98.6	99.5
Study location						
High−income country	7	70.7 (17.1–93.8)	98.5 (93.7–99.7)	21	94.9 (50.0–100.0)	99.4 (92.9–100.0)
Low- and middle-income country	7	46.8 (20.0–86.8)	99.2 (89.0–100.0)	5	96.6 (95.8–100.0)	99.1 (89.4–100.0)
Product						
Clearview Chlamydia MF (Clearview,Unipath Ltd, Bedford, UK)	4	41.3 (31.1–53.5)	98.5 (95.2–99.2)	NA	NA	NA
Chlamydia Rapid Test (CRT) (DRW, Cambridge, UK)	10	72.6 (20.0–86.8)	98.8 (89.0–100.0)	NA	NA	NA
Chlamydia test card (Ultimed Products GmbH, Ahrensburg Germany)	1	63.0	99.6	NA	NA	NA
Biorapid CHLAMYDIA Ag test (Biokit, Barcelona, Spain)	1	17.1	93.7	NA	NA	NA
QuickVue Chlamydia test (Quidel Corporation, San Diego, USA)	2	31.4 (25.0–37.7)	99.6 (99.4–99.7)	NA	NA	NA
ACON Chlamydia Rapid Test Device (ACON, San Diego, USA)	3	43.8 (22.7–66.7)	98.3 (91.3–100.0)	NA	NA	NA
CT Duo test combo (ACON Laboratories, San Diego, USA)	1	30.5	99.8	NA	NA	NA
Cortez Onestep Chlamydia RapicardTM insta test (Cortez Diagnostics, Inc., Woodland Hills, USA)	1	71.4	99.6	NA	NA	NA
BioStar Chlamydia OIA (Biostar, Inc., Boulder, USA)	1	59.4	98.4	NA	NA	NA
aQcare Chlamydia TRF kit (Medisensor, Inc., Daegu, Korea)	2	91.0 (88.2–93.8)	95.8 (94.7–96.8)	NA	NA	NA
GeneXpert CT/NG (Cepheid, Sunnyvale, USA)	NA	NA	NA	18	95.0 (50.0–100.0)	99.5 (89.4–100.0)
*Atlas Genetics io® platform (Atlas Genetics Ltd., Bath, UK)	NA	NA	NA	2	90.0 (83.9–96.1)	98.3 (97.7–98.8)
*the binx health ioCT/NG assay (binx health,USA)	NA	NA	NA	2	94.3 (92.5–96.1)	99.2 (99.1–99.3)
Other uncommercial NAAT-based products	NA	NA	NA	19	95.9 (75.5–100.0)	99.6 (92.9–100.0)

AD: antigen detection; NAAT: Nucleic acid amplification test; NA: Not applicable. * the Atlas assay is the same as the binx assay (the company renamed).

Table 2.
Pooled sensitivity and specificity, and DOR of antigen- and NAAT-based point-of-care tests.

	No. subjects (No. studies)	Pooled sensitivity (95% CI)	Pooled specificity (95% CI)	Pooled DOR (95% CI)
AD-based POCTs				
Overall	14,582(14)	56% (45%–67%)	99% (98%–99%)	86(46–163)
Subgroup by specimen				
Cervical swabs	4482 (8)	46% (37%–56%)	99% (98%–100%)	102 (57–184)
Vaginal swabs	6990 (10)	52% (34%–70%)	98% (96%–99%)	58(18–183)
Urine subtotal	2760 (7)	62% (41%–79%)	98% (96%–99%)	78(19–316)
Urine from males	2667 (6)	57% (36%–75%)	98% (96%–99%)	71 (15–345)
cup-collected urine	766 (3)	NA	NA	NA
First Burst-collected urine	1901 (3)	NA	NA	NA
Urine from a mixed sample of males or females	93 (1)	NA	NA	NA
Swabs from a mixed sample of males and females	348 (1)	NA	NA	NA
Subgroup by country category				
High-income country	6716 (7)	65% (44%- 82%)	98% (97%–99%)	97 (28–330)
Low- and middle-income country	7866 (7)	50% (40%–61%)	99% (98%–99%)	77 (38–154)
NAAT-based POCTs				
Overall	27,754 (25)	94% (91%–96%)	99% (99%–99%)	1933 (1018–3669)
Subgroup by specimen				
Cervical swabs	4886(7)	94% (90%–96%)	100% (99%–100%)	3648 (1425–9341)
Vaginal swabs	8591 (10)	94% (86%–98%)	99% (98%–99%)	1216 (407–3635)
Urine subtotal	9214 (13)	95% (91%–97%)	100% (99%–100%)	4146(1697–10,131)
Urine from males	3925 (7)	95% (92%–97%)	100% (99%–100%)	5257 (981–28,189)
Urine from females	5071 (4)	96% (85%–99%)	100% (99%–100%)	50,823 (244–110,000)
Urine from a mixed sample of males and females	218 (2)	NA	NA	NA
Rectal swabs	2069 (7)	93% (87%–96%)	99% (97%–100%)	977 (501–1900)
Pharyngeal swabs	538 (2)	NA	NA	NA
Swabs from a mixed sample of males or females	150 (2)	NA	NA	NA
Urine or vaginal swabs	2486 (1)	NA	NA	NA
Subgroup by commercial availability				
Availability (GeneXpert CT/NG and Atlas Genetics and binx health ioCT/NG assay)	16,614 (12)	94% (90%–96%)	99% (99%–100%)	2277(1141–4544)
Unavailability (others)	11,140 (13)	95% (92%–97%)	99% (99%–100%)	2291 (926–5666)

DOR: diagnostic odds ratio; AD: antigen detection; NAAT: nucleic acid amplification test; POCT: point-of-care test; NA: not applicable because of insufficient number of studies (less than 4 studies) for the analysis.

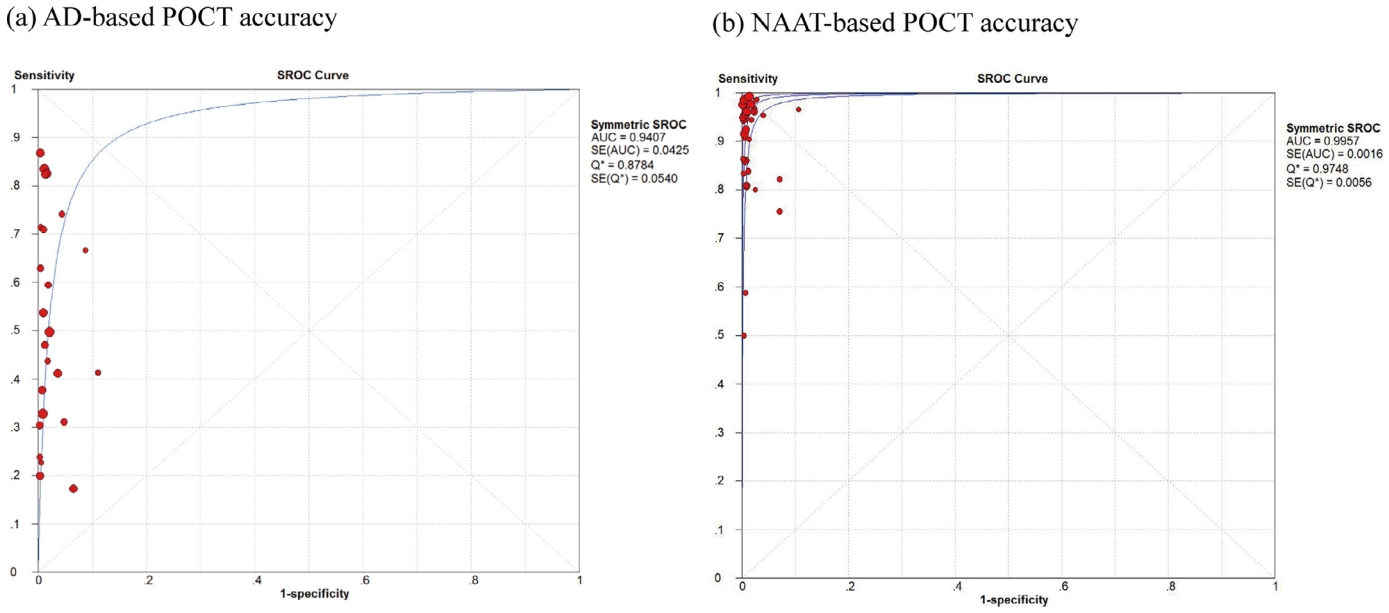

Fig. 2. Summary receiver operating characteristic (SROC) curve of the performance of (a) antigen detection (AD)-based POCTs, (b) NAAT-based POCTs for detection Chlamydia trachomatis (CT) infection.

AUC, area under the curve; Q*, Q* value. Dots' number and area size mean the number and sample size of observed data, respectively.

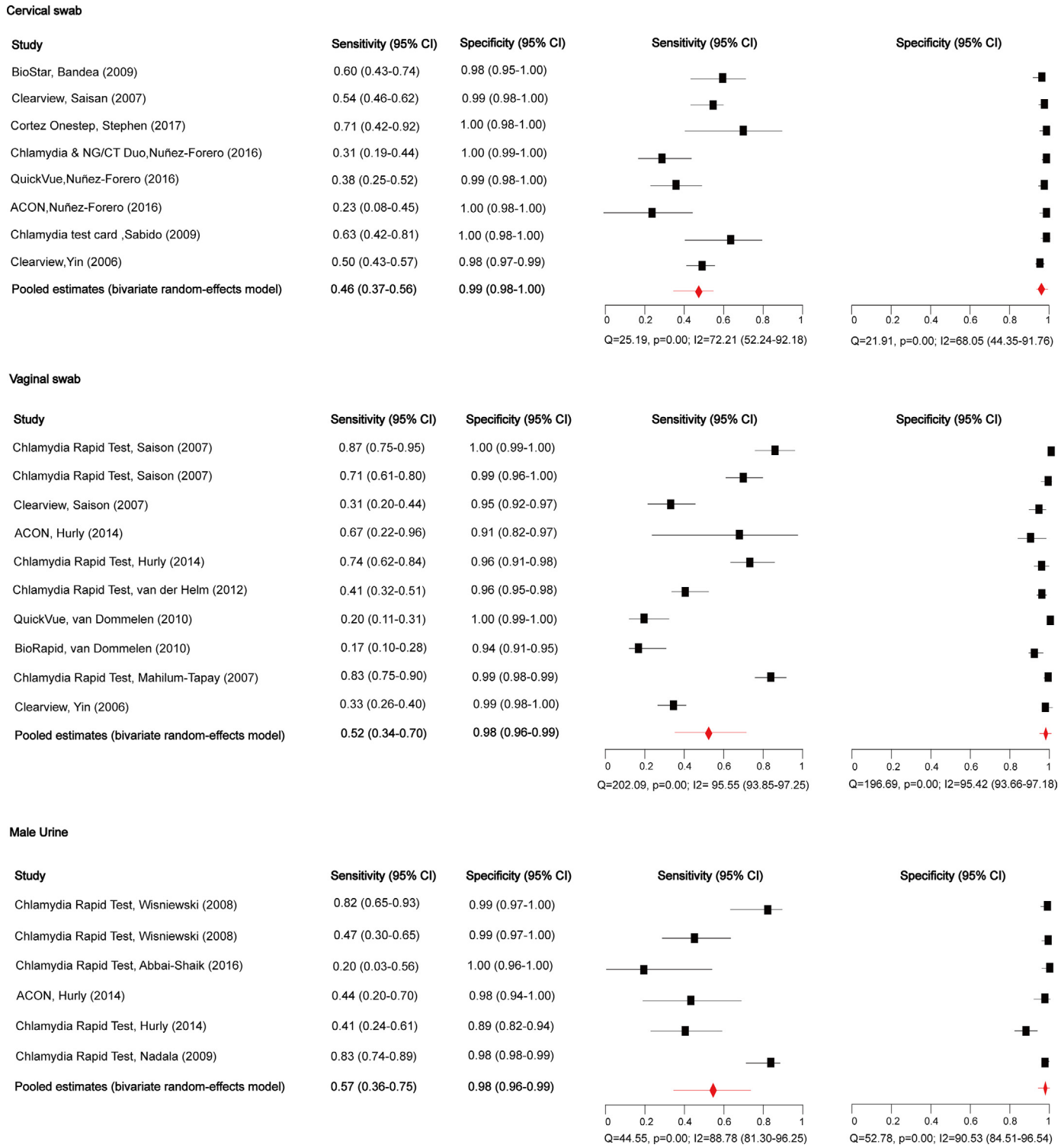

Fig. 3. Forest plots of sensitivity and specificity of antigen detection (AD)-based point-of-care tests by specimen. Red diamonds and lines represent subtotal sensitivities and specificities and their 95% confidence intervals.

test. Nevertheless, AD-based POCTs are being used, especially in low and middle-income countries, because of their advantage of relative cheapness as compared with NAAT-based POCTs [66]. However, the trade-off between accuracy and affordability needs to be considered when we consider a POCT for CT screening particularly in resource-constrained settings. We compared the performance of AD-based POCTs for different specimen types and found no significant difference between AD-based POCTs using cervical and vaginal specimens in terms of diagnostic accuracy, which revealed that the performance of cervical specimen was not necessarily superior to vaginal specimen in testing for CT infection as previously thought [12]. It is noted that three studies testing on first-void specimens showed a sensitivity of more than 80%, indicating the prospect of developing similar collection devices to increase the sensitivity of AD-based POCTs in urine samples in the future. In addition, a Qcare Chlamydia TRF kit, which uses europium-chelated nanoparticles instead of conventional

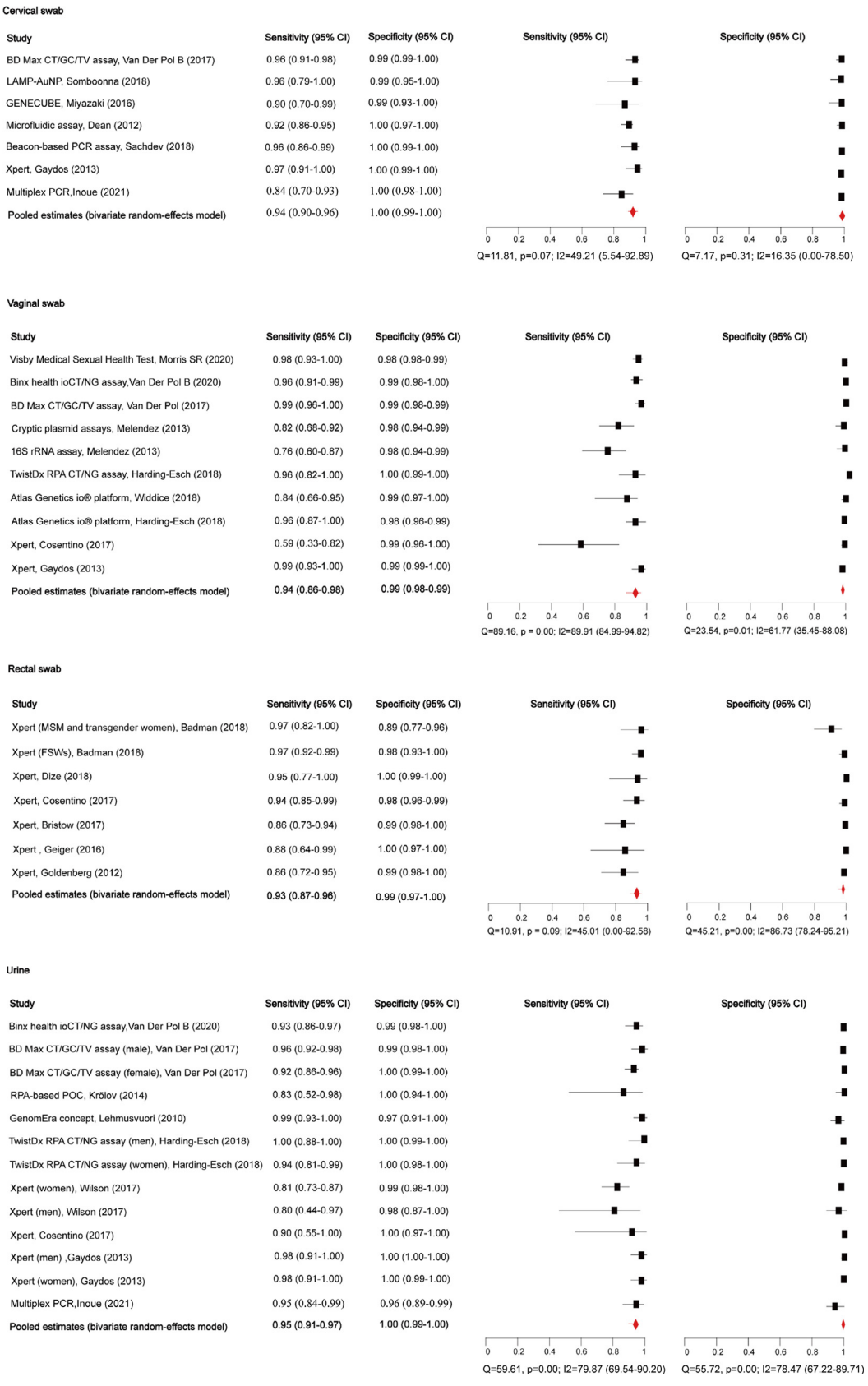

Fig. 4. Forest plots of sensitivity and specificity of nucleic acid amplification testing (NAAT)-based point-of-care tests by specimen.
Red diamonds and lines represent subtotal sensitivities and specificities and their 95% confidence intervals.
MSM=men who have sex with men. FSWs=female sex workers. CI=confidence interval.

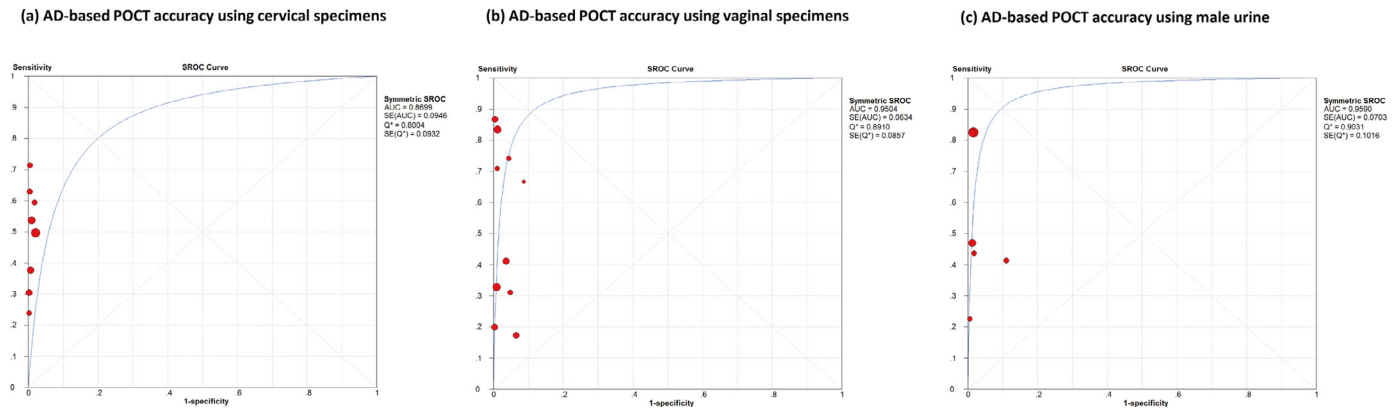

Fig. 5. Summary receiver operating characteristic (SROC) curve of the performance of (a) antigen detection (AD)-based POCTs using cervical specimens, (b) AD-based POCTs using vaginal specimens, (c) AD-based POCTs using male urine for detection Chlamydia trachomatis (CT) infection.

AUC, area under the curve; Q^*, Q^* value. Dots' number and area size mean the number and sample size of observed data, respectively.

colloidal gold or latex as the labeling substance, had good sensitivity and specificity, indicating a promising novel lateral flow immunoassay-based POCT kit for detecting CT. However, it should be mentioned that this kit was only evaluated in one trial [33] and further evaluation may be needed to confirm its performance across settings and sub-populations. The pooled sensitivity of AD-based POCTs was higher in high-income countries than that in low and middle-income countries although the difference was not statistically significant. This was probably due to different medical and health services among different countries. Since AD-based POCTs are mostly being used in low and middle-income countries, future real-world studies are needed to assess the performance of AD-based POCTs and compare evidence across studies.

Regarding NAAT-based POCTs, 23 articles published since 2012 were included in our study and 18 of them were published since 2016. NAAT-based POCTs showed excellent accuracy for urine specimen (with pooled sensitivity of 95%, specificity of 100%, AUC of 1.00). However, extra-urogenital (rectal and pharyngeal) infections with CT are more common among MSM and other sub-populations [67,68]. According to a systematic review of studies published between 1981 and 2015, the median prevalences of rectal and pharyngeal CT were 8.9% and 1.7% among men who have sex with men (MSM), 8.7% and 1.7% among women and 7.7% and 1.6% among men who have sex only with women (MSW), respectively [16]. NAAT-based POCTs have been approved for use with extragenital specimens by the Food and Drug Administration (FDA) in 2019 [69]. Our systematic review included 7 and 2 studies on evaluation of rectal and pharyngeal NAAT-based POCTs and was the first study to do a meta-analysis on performance of rectal NAAT-based POCTs. Our results showed that the NAAT-based POCTs had adequate performance with rectal swabs (with pooled sensitivity of 93%, specificity of 99%, AUC of 0.99). However, it was hard to make inferences about the sensitivity of the NAAT-based POCT product (Cepheid Xpert CT/NG assay) for pharyngeal swabs due to the number of truly pharyngeal infection was small in the two published studies [42,43].

In 2006, the World Health Organization (WHO) proposed the ASSURED (Affordable, Sensitive, Specific, User-friendly, Rapid and robust, Equipment-free and Deliverable to end-users) criteria as a benchmark for developing and introducing the most appropriate diagnostic tests for resource-constrained settings [70]. Recently, two additional criteria of *R* (real-time connectivity) and E (ease of specimen collection and environmental friendliness) into the original ASSURED to create a new acronym of REASSURED [71]. Although significant progress has been made in the POC diagnostic tests for syphilis, chlamydia, gonococcal infections, and trichomonas, no POC diagnostic tests that fully meet all these criteria have been completed to date [71]. Most of AD-based POCTs for CT meet the following criteria: affordable, specific, user-friendly, rapid and robust, and equipment free, but the common drawback is the low sensitivity. The currently commercially available NAAT-based POCTs (such as Cepheid GeneXpert CT/NG assay) are more sensitive and specific than antigen detection assays and meet many of the desirable characteristics defined by WHO for a POC devices, but affordability may be a critical concern for their introduction into the low-resource settings. To speed up the development of sexual transmitted infections (STI) POC diagnostic tests, the WHO organized an expert consultation to formulate the target product profiles (TPP) of the ideal POC diagnostic tests for CT and other STIs [72]. TPP requires that the sensitivity of NAAT-based POCT for CT should be at least 90% and ideally 100%. The lowest specificity should be 98% and ideally 100%. The minimal acceptable time to result is up to 60 min and optimally 30 min or shorter. The currently commercially available NAAT-based POCTs for CT (such as Cepheid GeneXpert CT/NG assay) in rectal swabs or urine specimens could meet the minimal requirement of the TPP in terms of the sensitivity and specificity. However, the run- time for the Cepheid GeneXpert CT/NG assay is 90 min and the turn-around time between sample collection and getting the result of these POCTs is even longer. Recently, some new molecular POC diagnostic technology (such as the io CT/NG Assay, the Visby Medical Sexual Health Test and the rapid multiplex PCR assays.) has been developed and meets many of the requirements of the TPP for a POC device (sensitive, specific, rapid), which could represent important advances in the development of rapid diagnostics for sexually transmitted infections [61,62,64].

The advantage of this study is that it is a comprehensive meta-analysis of published studies on evaluating performance of POCTs for detecting the antigen or nucleic acid of CT using the different types of specimens and/or specimens collected from the different anatomical sites. However, our study has several limitations to be mentioned. First, only two major databases (PubMed and EmBase) were selected for searching the published studies and the search terms might not comprehensive enough, which may lead to an incomplete literature retrieval. Second, no study on evaluating AD-based POCTs on urethral swabs was found from the literature retrieval although such specimens had been recommended for detection of CT infection among males [73]. In addition, our study did not address the sensitivity and specificity of community-based CT testing with either AD- or NAAT-based POCTs. Application of POCTs in this purpose might have different test characteristics.

In conclusion, evidence from our systematic review and meta-analysis indicates that the diagnostic performance of NAAT-based POCT is significantly better than that of AD-based POCT, especially in terms of the diagnostic sensitivity across specimens collected from different anatomic sites. Our study also highlights several areas that

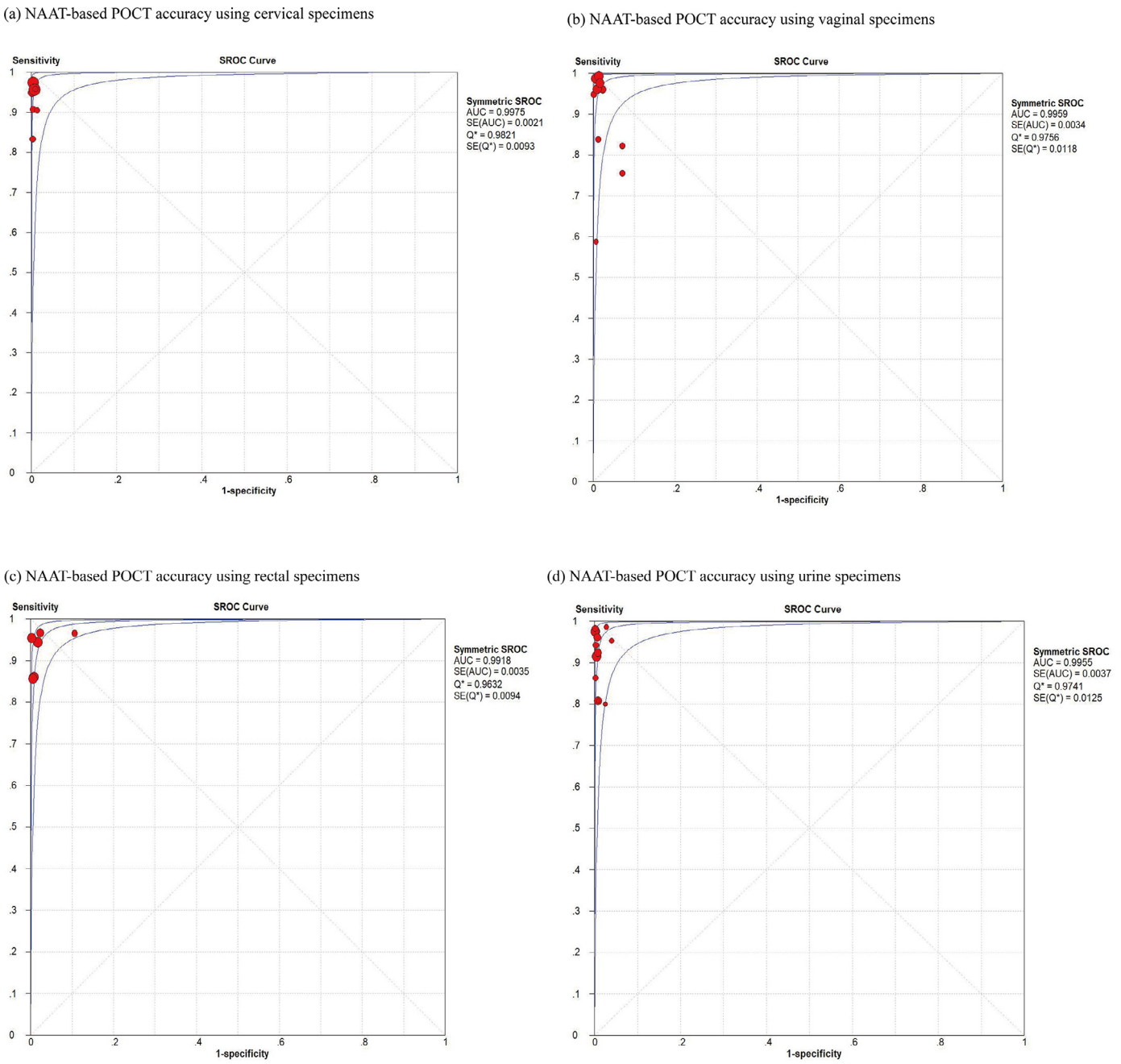

Fig. 6. Summary receiver operating characteristic (SROC) curve of the performance of (a) nucleic acid amplification testing (NAAT)-based POCTs using cervical specimens, (b) NAAT-based POCTs using vaginal specimens, (c) NAAT-based POCTs using rectal specimens, (d) NAAT-based POCTs using urine specimens for detection Chlamydia trachomatis (CT) infection.

AUC, area under the curve; Q*, Q* value. Dots' number and area size mean the number and sample size of observed data, respectively.

merit further studies. In addition to an ideal performance in terms of sensitivity and specificity, further evaluation on cost-effectiveness of NAAT-based POCTs are needed because affordability has crucial implications for scaling-up this technology particularly in areas with low resources but a heavy burden of CT infection. Further efforts to address the sensitivity of the current AD-based POCTs by improving quality of specimen collection and/or result reading may be also valuable.

5. Funding

The National Science and Technology Major Project for Belt and Road Initiative (2018ZX10101001), the Chinese Academy Medical Sciences Initiative for Innovative Medicine (2016-I2M-3-021) in China and the World Health Organization (agreement 2019/883266-0).

6. Contributors

XSC conceived the idea for the review. YZ and JL designed and undertook the literature review and extracted the data with help from XSC. YZ, TTJ and XSC analyzed and interpreted the data. YZ and TTJ prepared the tables, figures, and appendix with support from XSC. YZ wrote the first draft of the manuscript with input from TTJ. XSC made a critical revision of the drafts. All authors reviewed and revised subsequent versions of the manuscripts.

7. Data sharing

Extracted data for all included studies are available as an appendix online. All figures and statistical outputs are available in online.

Declaration of Competing Interest

We declare no competing interests.

Acknowledgments

We thank Qi Li (Library Manager, Chinese Academy of Medical Sciences Institute of Dermatology) for his assistance in literature searches. XSC (grant 2018ZX10101001-001-001) and YPY (grant 2018ZX10101001-004-003) are funded by the National Science and Technology Major Project for Belt and Road Initiative. XSC and YPY (grant 2016-I2M-3-021) are funded by the Chinese Academy Medical Sciences Initiative for Innovative Medicine. XSC and TTJ (agreement 2019/883266-0) are funded by the World Health Organization.

Supplementary materials

Supplementary material associated with this article can be found, in the online version at doi:10.1016/j.eclinm.2021.100961.

References

[1] Rowley J, Vander Hoorn S, Korenromp E, et al. Chlamydia, gonorrhoea, trichomoniasis and syphilis: global prevalence and incidence estimates, 2016. Bull World Health Organ 2019;97:548–562P.
[2] Price MJ, Ades AE, Soldan K, et al. The natural history of *Chlamydia trachomatis* infection in women: a multi-parameter evidence synthesis. Health Technol Assess 2016;20:1–250.
[3] Price MJ, Ades AE, De Angelis D, et al. Risk of pelvic inflammatory disease following Chlamydia trachomatis infection: analysis of prospective studies with a multistate model. Am J Epidemiol 2013;178:484–92.
[4] Taylor BD, Haggerty CL. Management of Chlamydia trachomatis genital tract infection: screening and treatment challenges. Infect Drug Resist 2011;4:19–29.
[5] Olson-Chen C, Balaram K, Hackney DN. Chlamydia trachomatis and adverse pregnancy outcomes: meta-analysis of patients with and without infection. Matern Child Health J 2018;22:812–21.
[6] Zhu H, Shen Z, Luo H, Zhang W, Zhu X. Chlamydia Trachomatis infection-associated risk of cervical cancer: a meta-analysis. Medicine 2016;95:e3077. (Baltimore).
[7] Castellsagué X, Pawlita M, Roura E, et al. Prospective seroepidemiologic study on the role of human papillomavirus and other infections in cervical carcinogenesis: evidence from the EPIC cohort. Int J Cancer 2014;135:440–52.
[8] Low WE, et al. Chlamydia trachomatis infections of the adult. In: Holmes KK, Sparling PF, Mardh P, editors. Sexually transmitted diseases. New York: McGraw-Hill; 1999. p. 407–22.
[9] Wong WCW, Lau STH, Choi EPH, et al. A systematic literature review of reviews on the effectiveness of chlamydia testing. Epidemiol Rev 2019;41:168–75.
[10] Reekie J, Roberts C, Preen D, et al. Chlamydia trachomatis and the risk of spontaneous preterm birth, babies who are born small for gestational age, and stillbirth: a population-based cohort study. Lancet Infect Dis 2018;18:452–60.
[11] Folger AT. Maternal Chlamydia trachomatis infections and preterm birth: the impact of early detection and eradication during pregnancy. Matern Child Health J 2014;18:1795–802.
[12] Kelly H, Coltart CEM, Pant Pai N, et al. Systematic reviews of point-of-care tests for the diagnosis of urogenital Chlamydia trachomatis infections. Sex Transm Infect 2017;93(S4):S22–30.
[13] Hocking JS, Guy R, Walker J, et al. Advances in sampling and screening for chlamydia. Future Microbiol 2013;8(3):367–86.
[14] Hislop J, Quayyum Z, Flett G, Boachie C, Fraser C, Mowatt G. Systematic review of the clinical effectiveness and cost-effectiveness of rapid point-of-care tests for the detection of genital chlamydia infection in women and men. Health Technol Assess 2010;14:1–97.
[15] Herbst de Cortina S, Bristow CC, Joseph Davey D, Klausner JD. A systematic review of point of care testing for chlamydia trachomatis, neisseria gonorrhoeae, and trichomonas vaginalis. Infect Dis Obstet Gynecol 2016;2016:4386127.
[16] Chan PA, Robinette A, Montgomery M, et al. Extragenital infections caused by chlamydia trachomatis and neisseria gonorrhoeae: a review of the literature. Infect Dis Obstet Gynecol 2016;2016:5758387.
[17] Nwokolo NC, Dragovic B, Patel S, et al. 2015 UK national guideline for the management of infection with Chlamydia trachomatis. Int J STD AIDS 2016;27:251–67.
[18] Stroup DF, Berlin JA, Morton SC, et al. Meta-analysis of observational studies in epidemiology: a proposal for reporting. meta-analysis of observational studies in epidemiology (MOOSE) group. JAMA 2000;283:2008–12.
[19] Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015: elaboration and explanation. BMJ 2016;354:i4086.
[20] Whiting PF, Rutjes AW, Westwood ME, et al. QUADAS-2: a revised tool for the quality assessment of diagnostic accuracy studies. Ann Intern Med 2011;155:529–36.
[21] Higgins JP, Thompson SG. Quantifying heterogeneity in a meta-analysis. Stat Med 2002;21:1539–58.
[22] Šimundić AM. Measures of diagnostic accuracy: basic definitions. EJIFCC 2009;19:203–11.
[23] Moses LE, Shapiro D, Littenberg B. Combining independent studies of a diagnostic test into a summary ROC curve: data-analytic approaches and some additional considerations. Stat Med 1993;12:1293–316.
[24] Deeks JJ, Macaskill P, Irwig L. The performance of tests of publication bias and other sample size effects in systematic reviews of diagnostic test accuracy was assessed. J Clin Epidemiol 2005;58:882–93.
[25] Zamora J1, Abraira V, Muriel A, Khan K, Coomarasamy A. Meta-DiSc: a software for meta-analysis of test accuracy data. BMC Med Res Methodol 2006;6:31.
[26] Bristow CC, McGrath MR, Cohen AC, et al. Comparative evaluation of 2 nucleic acid amplification tests for the detection of chlamydia trachomatis and neisseria gonorrhoeae at extragenital sites. Sex Transm Dis 2017;44:398–400.
[27] Yin YP, Peeling RW, Chen XS, et al. Clinic-based evaluation of clearview chlamydia mf for detection of chlamydia trachomatis in vaginal and cervical specimens from women at high risk in China. Sex Transm Infect 2006;82(5):v33–7 Suppl.
[28] Saison F, Mahilum-Tapay L, Michel CE, et al. Prevalence of Chlamydia trachomatis infection among low- and high-risk Filipino women and performance of Chlamydia rapid tests in resource-limited settings. J Clin Microbiol 2007;45:4011–7.
[29] Mahilum-Tapay L, Laitila V, Wawrzyniak JJ. New point of care Chlamydia rapid test–bridging the gap between diagnosis and treatment: performance evaluation study. BMJ 2007;335:1190–4.
[30] Wisniewski CA, White JA, Michel CE, et al. Optimal method of collection of first-void urine for diagnosis of Chlamydia trachomatis infection in men. J Clin Microbiol 2008;46:1466–9.
[31] Bandea CI, Koumans EH, Sawyer MK, et al. Evaluation of the rapid BioStar optical immunoassay for detection of Chlamydia trachomatis in adolescent women. J Clin Microbiol 2009;47:215–6.
[32] Sabido M, Hernandez G, Gonzalez V, et al. Clinic-based evaluation of a rapid point-of-care test for detection of Chlamydia trachomatis in specimens from sex workers in Escuintla, Guatemala. J Clin Microbiol 2009;47:475–6.
[33] Ham JY, Jung J, Hwang BG, et al. Highly sensitive and novel point-of-care system, aQcare Chlamydia TRF kit for detecting Chlamydia trachomatis by using europium(Eu) (III) chelated nanoparticles. Ann Lab Med 2015;35:50–6.
[34] Nadala EC, Goh BT, Magbanua JP, et al. Performance evaluation of a new rapid urine test for chlamydia in men: prospective cohort study. BMJ 2009;339:b2655.
[35] van Dommelen L, van Tiel FH, Ouburg S, et al. Alarmingly poor performance in Chlamydia trachomatis point-of-care testing. Sex Transm Infect 2010;86:355–9.
[36] van der Helm JJ, Sabajo LO, Grunberg AW, et al. Point-of-care test for detection of urogenital chlamydia in women shows low sensitivity. A performance evaluation study in two clinics in Suriname. PLoS ONE 2012;7:e32122.
[37] Goldenberg SD, Finn J, Sedudzi E, et al. Performance of the GeneXpert CT/NG assay compared to that of the Aptima AC2 assay for detection of rectal Chlamydia trachomatis and Neisseria gonorrhoeae by use of residual Aptima Samples. J Clin Microbiol 2012;50:3867–9.
[38] Gaydos CA, Van Der Pol B, Jett-Goheen M, et al. Performance of the cepheid CT/NG Xpert rapid PCR test for detection of chlamydia trachomatis and neisseria gonorrhoeae. J Clin Microbiol 2013;51:1666–72.
[39] Hurly DS, Buhrer-Skinner M, Badman SG, et al. Field evaluation of the CRT and ACON chlamydia point-of-care tests in a tropical, low-resource setting. Sex Transm Infect 2014;90:179–84.
[40] Nunez-Forero L, Moyano-Ariza L, Gaitan-Duarte H, et al. Diagnostic accuracy of rapid tests for sexually transmitted infections in symptomatic women. Sex Transm Infect 2016;92:24–8.
[41] Abbai-Shaik NS, Reddy T, Govender S, Ramjee G. Poor performance of the chlamydia rapid test device for the detection of asymptomatic infections in South African men: a pilot study. J Sex Transm Dis 2016;2016:8695146.
[42] Geiger R, Smith DM, Little SJ, et al. Validation of the GeneXpert® CT/NG assay for use with male pharyngeal and rectal swabs. Austin J HIV AIDS Res 2016;3:1021.
[43] Cosentino LA, Danby CS, Rabe LK, et al. Use of nucleic acid amplification testing for diagnosis of extragenital sexually transmitted infections. J Clin Microbiol 2017;55:2801–7.
[44] Stephen S, Muchaneta-Kubara C, Munjoma MW, et al. Evaluation of cortez one-step chlamydia rapicard insta test for the detection of chlamydia trachomatis in pregnant women at mbare polyclinic in Harare, Zimbabwe. Int J MCH AIDS 2017;6:19–26.
[45] Wilson SP, Vohra T, Goldberg J, et al. Reliable rapid assay for gonorrhea and chlamydia in the emergency department. J Emerg Med 2017;53:890–5.
[46] Dize L, Silver B, Gaydos C. Comparison of the cepheid GeneXpert CT/NG assay to the hologic aptima combo2 assay for the detection of chlamydia trachomatis and neisseria gonorrhoeae in self-collected rectal swabs. Diagn Microbiol Infect Dis 2018;90:83–4.
[47] Causer LM, Guy RJ, Tabrizi SN, et al. Molecular test for chlamydia and gonorrhoea used at point of care in remote primary healthcare settings: a diagnostic test evaluation. Sex Transm Infect 2018;94:340–5.

[48] Badman SG, Willie B, Narokobi R, et al. A diagnostic evaluation of a molecular assay used for testing and treating anorectal chlamydia and gonorrhoea infections at the point-of-care in Papua New Guinea. Clin Microbiol Infect 2019;25:623–7.
[49] Widdice LE, Hsieh YH, Silver B, et al. Performance of the Atlas genetics rapid test for chlamydia trachomatis and women's attitudes toward point-of-care testing. Sex Transm Dis 2018;45:723–7.
[50] Harding-Esch EM, Cousins EC, Chow SC, et al. A 30-min nucleic acid amplification point-of-care test for genital chlamydia trachomatis infection in women: a prospective, Multi-center Study of Diagnostic Accuracy. EBioMedicine. 2018;28:120–7.
[51] Harding-Esch EM, Fuller SS, Chow SC, et al. Diagnostic accuracy of a prototype rapid chlamydia and gonorrhoea recombinase polymerase amplification assay: a multicentre cross-sectional preclinical evaluation. Clin Microbiol Infect 2019;25:380. e1-380.e7.
[52] Sachdev D, Wasnik K, Patel AL, et al. Multi-centric validation of an in-house-developed beacon-based PCR diagnostic assay kit for Chlamydia and Neisseria and portable fluorescence detector. J Med Microbiol 2018;67:1287–93.
[53] Lehmusvuori A, Juntunen E, Tapio AH, et al. Rapid homogeneous PCR assay for the detection of Chlamydia trachomatis in urine samples. J Microbiol Methods 2010;83:302–6.
[54] Pearce DM, Shenton DP, Holden J, Gaydos CA. Evaluation of a novel electrochemical detection method for Chlamydia trachomatis: application for point-of-care diagnostics. IEEE Trans Biomed Eng 2011;58:755–8.
[55] Dean D, Turingan RS, Thomann HU, et al. A multiplexed microfluidic PCR assay for sensitive and specific point-of-care detection of Chlamydia trachomatis. PLoS ONE 2012;7:e51685.
[56] Melendez JH, Huppert JS, Jett-Goheen M, et al. Blind evaluation of the microwave-accelerated metal-enhanced fluorescence ultrarapid and sensitive Chlamydia trachomatis test by use of clinical samples. J Clin Microbiol 2013;51:2913–20.
[57] Van Der Pol B, Williams JA, Fuller D, Taylor SN, Hook 3rd. EW. Combined testing for Chlamydia, Gonorrhea, and Trichomonas by Use of the BD Max CT/GC/TV assay with genitourinary specimen types. J Clin Microbiol 2016;55:155–64.
[58] Krölov K, Frolova J, Tudoran O, et al. Sensitive and rapid detection of Chlamydia trachomatis by recombinase polymerase amplification directly from urine samples. J Mol Diagn 2014;16:127–35.
[59] Miyazaki N, Yamagishi Y, Izumi K, Kawashima Y, Suematsu H, Mikamo H. Evaluation of rapid measurement of chlamydia trachomatis and neisseria gonorrhoeae by using automatic gene analyzer "GENECUBE". Jpn J Antibiot 2016;69:291–8.
[60] Somboonna N, Choopara I, Arunrut N, et al. Rapid and sensitive detection of Chlamydia trachomatis sexually transmitted infections in resource-constrained settings in Thailand at the point-of-care. PLoS Neglected Trop Dis 2018;12:e0006900.
[61] Van Der Pol B, Taylor SN, Mena L, et al. Evaluation of the performance of a point-of-care test for chlamydia and gonorrhea. JAMA Netw Open 2020;3:e204819.
[62] Morris SR, Bristow CC, Wierzbicki MR, et al. Performance of a single-use, rapid, point-of-care PCR device for the detection of Neisseria gonorrhoeae, Chlamydia trachomatis, and Trichomonas vaginalis: a cross-sectional study. Lancet Infect Dis 2020 S1473-3099(20)30734-9.
[63] Ye X, Li Y, Wang L, et al. All-in-one microfluidic nucleic acid diagnosis system for multiplex detection of sexually transmitted pathogens directly from genitourinary secretions. Talanta 2021;221:121462.
[64] Inoue T, Chihara Y, Kiba K, et al. Rapid multiplex PCR assay for simultaneous detection of Neisseria gonorrhoeae and Chlamydia trachomatis in genitourinary samples: a 30-minute assay. J Microbiol Methods 2021;180:106103.
[65] Fantom N, Serajuddin U. The World bank's classification of countries by income. Policy Res Work Pap Ser 2016;7528 The World Bank.
[66] Wi TE, Ndowa FJ, Ferreyra C, et al. Diagnosing sexually transmitted infections in resource-constrained settings: challenges and ways forward. J Int AIDS Soc 2019;22(6):e25343. Suppl.
[67] Leon SR, Segura ER, Konda KA, et al. High prevalence of Chlamydia trachomatis and Neisseria gonorrhoeae infections in anal and pharyngeal sites among a community-based sample of men who have sex with men and transgender women in Lima, Peru. BMJ Open 2016;6:e008245.
[68] Andersson N, Boman J, Nylander E. Rectal chlamydia-should screening be recommended in women? Int J STD AIDS 2017;28:476–9.
[69] US Food & Drug Administration. FDA news release: FDA clears first diagnostic tests for extragenital testing for chlamydia and gonorrhea. silver spring. FDA; 2019. Available online at: https://www.fda.gov/news-events/press-announcements/fda-clears-firstdiagnostic-tests-extragenital-testing-chlamydia-and-gonorrhea [verified 20 June 2019].
[70] Peeling RW, Holmes KK, Mabey D, et al. Rapid tests for sexually transmitted infections (STIs): the way forward. Sex Transm Infect 2006;82(5):v1–6 Suppl.
[71] Land KJ, Boeras DI, Chen XS, et al. REASSURED diagnostics to inform disease control strategies, strengthen health systems and improve patient outcomes. Nat Microbiol 2019;4:46–54.
[72] Toskin I, Murtagh M, Peeling RW, et al. Advancing prevention of sexually transmitted infections through point-of-care testing: target product profiles and landscape analysis. Sex Transm Infect 2017;93(S4):S69–80.
[73] Potter Y. Self-screening for sexually transmitted infections. Nurs Stand 2014;28:37–43.