Clinical Relevance of Xpert MRSA/SA in Guiding Therapeutic Decisions for Staphylococcal Infections: A Diagnostic Test Accuracy Analysis

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ABSTRACT

Introduction: Rapid identification of the causal organism and antibiotic resistance is crucial for guiding targeted therapy in patients with suspected staphylococcal infection. A meta-analysis was carried out to evaluate the diagnostic relevance of Xpert™ MRSA/SA (Xpert) from clinical samples of various origins for limiting the use of unnecessary empirical methicillin-resistant *Staphylococcus aureus* (MRSA) therapy.

Methods: Five databases, including the Cochrane Library, Scopus, PubMed, Web of Science, and Embase, were comprehensively inspected from inception to October 12, 2021.

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The pooled summary estimates were evaluated using a bivariate random-effects model.

Results: Our inclusion criteria were met by 49 publications containing 68 datasets out of 735 citations. A total of 21 studies ($n = 4996$) examined the accuracy of Xpert in detecting methicillin-sensitive *S. aureus* (MSSA), while 47 studies ($n = 45,430$) examined the accuracy of Xpert in detecting MRSA. As compared to MRSA, Xpert's diagnostic performance for MSSA detection was markedly higher [sensitivity: 0.97 (0.96–0.98), specificity: 0.97 (0.97–0.98), area under curve (AUC): 0.99 (0.99–1.0)]. Xpert's pooled sensitivity and specificity differed marginally across sample types, including screening of colonization, lower respiratory tract (LRT), osteoarticular, and bloodstream samples. Notably, the Xpert pooled specificity was consistently $\geq 92\%$ against microbiological culture across all sample types. The diagnostic efficiency heterogeneity was not explained by a meta-regression and subgroup analysis of research design, sample conditions, and sampling methods ($P > 0.05$).

Conclusion: Our findings suggest that Xpert could be used as the favoured screening test for the early detection of staphylococcal infection in a variety of sample types, with the goal of guiding therapeutic decisions.

Keywords: Bacteremia; Osteoarticular infection; Respiratory infection; Staphylococcal infection; Xpert accuracy

Key Summary Points

Rapid identification of the causal organism and antibiotic resistance is crucial for guiding treatment.

Evaluation of Xpert accuracy in various sample settings including nasal, blood, lower respiratory tract (LRT), and osteoarticular.

Detection of methicillin-sensitive and-methicillin resistant *S. aureus* to guide therapeutic decisions.

Utilization of Xpert as the preferred early diagnostic test for staphylococcal infection to avoid empiric broad-spectrum antibiotics.

INTRODUCTION

Staphylococcus aureus is both a commensal and an opportunistic human pathogen that may cause anything from minor skin blemishes to life-threatening conditions like sepsis [1]. Approximately 20–40% of adults carry staphylococcal strains on various body sites, which could lead to subsequent infection [2]. MRSA infection continues to be a major threat globally [3, 4], with higher morbidity and mortality than methicillin-sensitive *S. aureus* (MSSA) [5], leading to the recommendation of vancomycin as empirical antimicrobial therapy. Other antibiotics used as an alternative therapy for MRSA include linezolid, teicoplanin, daptomycin, and delafloxacin [6, 7]. Although there are no known immediate hazards to this method, patients may ultimately end up taking too many broad-spectrum antibiotics, which may modify the patient's microflora, expose individuals to the dangers of drug toxicity, and maximize the rate of drug-resistant bacteria [8]. Also, vancomycin is less effective than anti-staphylococcal penicillin in treating MSSA infections [9]. If the primary medications are

insufficient and are changed after diagnostic procedures are accessible, the fatality rate does not significantly improve. All these conditions eventually contribute to extended hospital stays and higher treatment costs.

The current intervention of staphylococcal infections has primarily relied on gram stain and detection of pathogenic organisms using traditional culture-based methods. However, due to gram stain's low sensitivity, diagnosing staphylococcal infection remains challenging [10, 11], and a microbiological diagnosis takes approximately 48–72 h to provide a result and has reduced sensitivity compared to amplification assays [12, 13]. Poor bacterial culture detection rates may be ascribed to a combination of previous antibiotic medication before acquiring specimens [14], low bacterial concentration in fluid samples, and perhaps causative agents that are difficult to discern in the laboratory owing to rigorous criteria. The limited sensitivity of these tests hinders patient care and antibiotic selection, causing patients to lose out on the most effective treatment alternatives. Therefore, rapid identification of causative agents and prompt contact precautions are crucial for infection control and transmission prevention.

Xpert[TM] MRSA/SA (Xpert) (Cepheid, Sunnyvale, CA) has been shown to detect *S. aureus*, MRSA, and non-staphylococcal strains in a timely and efficient manner and is unaffected by prior antibiotic exposure [15, 16]. According to Brown and Paladino (2010), using the Xpert assay and implementing directed therapy based on test findings can reduce costs and mortality rates compared to empiric therapy alone [17]. The Xpert assay employs an automated real-time polymerase chain reaction (PCR)-based system that integrates sample purification and amplification and detects MSSA and MRSA in clinical specimens within 1 h [15]. This assay requires minimal training and biosafety facilities, avoids cross-contamination, and has a high responsiveness in culture negative specimens [15, 16, 18]. Xpert detects MSSA by detecting the staphylococcal protein A (*spa*) gene and can distinguish MSSA from MRSA given the presence of both the methicillin-resistant gene (*mecA*) and the staphylococcal cassette

chromosome *mec* (SCCmec) embedded into the *S. aureus* chromosome *attB* site [19]. *Spa*-negative gram-positive cocci in clusters can be assumed to be coagulase-negative staphylococci because internal control detects assay failures [20]. In recent years, Xpert has been extensively documented to identify staphylococcal infection [21–69]; however, the literature on the usefulness of these tests for prompt staphylococcal infection care is widely dispersed. We therefore aimed to conduct a diagnostic test accuracy meta-analysis based on the most up-to-date research evidence to inform support in clinical decisions.

METHODS

Data Sources and Searches

This study was carried out following the guidelines by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses of Diagnostic Test Accuracy (PRISMA-DTA) (*see* Supplementary Table 1) [70]. Five databases, including the Cochrane Library, Scopus, PubMed, Web of Science, and Embase, were methodically inspected using electronic databases from the library's inception until October 12, 2021. The search strategy was developed based on broader terms used in literature for staphylococcal infections, which include: ('*Staphylococcus aureus*' OR '*S. aureus*' OR 'Methicillin-resistant *Staphylococcus aureus*' OR 'MRSA') AND ('Xpert' OR 'GeneXpert' OR 'Roche' OR 'Cepheid' OR 'Abbott') AND ('Sensitivity' OR 'Specificity' OR 'Accuracy'). Furthermore, references of reviews and included papers were searched for possibly relevant research. This article is based on previously conducted studies and does not contain any new studies with human participants or animals performed by any of the authors.

Study Selection

All search results were imported into the citation manager (EndNote X9, Thomson Reuters, New York, USA), and duplicates were carefully filtered to ensure no overlapping publications. Two authors (S.C. Ojha and K. Chen) independently assessed citations by title and abstract according to preset eligibility criteria, and unrelated papers were eliminated. All studies requesting a diagnosis, whether for colonization screening or determining the causal agent of suspected staphylococcal infections, were included. The full text of all qualifying studies was reviewed for diagnostic accuracy data and that any differences of opinion were settled through mutual agreement.

Inclusion Criteria

Inclusion criteria comprised: (i) Xpert accuracy as an index test in various specimens; (ii) patients clinically or radiographically suspected of having a staphylococcal infection; (iii) implication of traditional culture as the reference standard; (iv) comprises data for specificity and sensitivity or provides adequate information to construct 2×2 contingency tables.

Exclusion Criteria

Exclusion criteria involved meta-analyses, conference proceedings and abstracts, reviews, letters to the editor, animal experiments, editorials, commentaries, case reports, and mechanism studies, as were studies with fewer than ten participants. Studies that failed to detect staphylococcal strains in clinically suspected patients using the index test and the microbiological reference standard were excluded.

Data Extraction

Two independent analysts (S.C. Ojha and K. Chen) piloted the data extraction form. The investigating authors independently extracted results from all selected studies using a predefined strategy. Findings were compared after data extraction, and disputes were resolved by consultation with a third investigator (C. Sun). When accuracy data or sample preparation processes were ambiguous, the authors of published research were approached. Using data

from the publications, we constructed two-by-two contingency tables for Xpert performance against the microbiological culture reference standard. Investigations that included the identification of both MSSA and MRSA were regarded as distinct studies.

Quality Assessment

Independent studies were evaluated for bias using the Quality Assessment of Diagnostic Accuracy Studies (QUADAS-2) tool [71]. The methodological quality was evaluated independently by two investigating analysts. Molecular approaches as a reference standard were not considered. The risk of bias was judged in four QUADAS-2 domains (reference standard, flow and timing, patient selection, and index test), and applicability concerns were judged through three domains (reference standard, index test, and patient selection). The spectrum and selection biases of individuals were identified. The risk of bias in each domain was evaluated by asking signaling queries to which the answer could be "yes" or "no". The signaling questions were deemed "unclear" due to a lack of information that could not be answered as "yes" or "no".

Statistical Analysis

Data obtained from 2×2 contingency tables were utilized to compute pooled summary estimates and the related confidence intervals (CIs). Missing values were substituted with 0.5 to attain a zero correction in the contingency tables. RevMan (version 5.4; Nordic Cochrane Centre, Copenhagen, Denmark) was employed to evaluate the quality of studies and generate summary plots [72]. As per random-effects model, Xpert's diagnostic accuracy with a was calculated against a culture reference standard. Meta-DiSc 1.4 (from the Cochrane Colloquium in Barcelona, Spain) was used to get pooled summary estimates of factors like the likelihood ratios, sensitivity, area under the curve (AUC), specificity, and diagnostic odds ratio (DOR) [73]. In addition, I-square (I^2) statistics was used to determine the degree of

data heterogeneity among the studies [74]. Meta-regression and subgroup analyses were used to examine for probable causes of heterogeneity in different research designs (prospective/other), sample conditions (fresh/frozen), and sampling methods (consecutive/ convenience). To assess publication bias, Deek's funnel asymmetry test was used [75]. Generally, a P value of < 0.05 was regarded as statistically relevant.

RESULTS

Literature Selection

A total of 735 distinct publications were searched (PubMed, 259; Scopus, 185; the Cochrane Library, 6; Web of Science, 135; Embase, 150) (Fig. 1). Of these, 262 records were eliminated owing to database duplication. After evaluating the titles and abstracts of 473 papers, 125 studies that were judged possibly relevant were submitted for full-text review. Supplementary Table 1 summarizes the papers that were examined as well as the reasons why those studies were eliminated. Finally, future analyses included 49 papers that met all of the inclusion criteria [21–69].
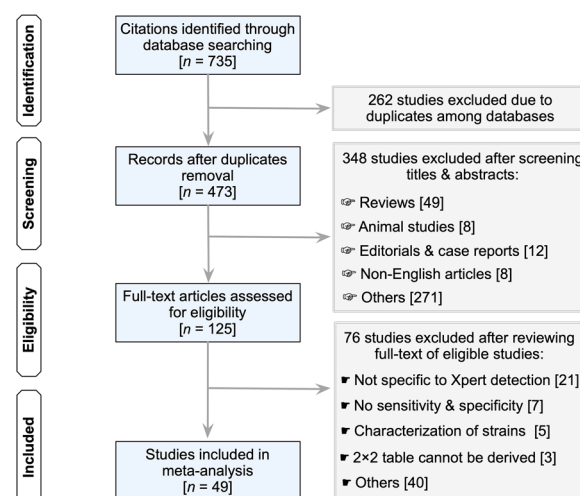
Fig. 1 Flow chart of study selection

Table 1 Baseline characteristics of included studies

Author [Ref.]	Year	Location	Setting	Pros enroll	Patient selection	Specimen condition	Total Sample	Sample type	Reported feature
Allmen [1]	2019	Germany	TCC	Yes	Consecutive	Fresh/frozen	1671	Nasal/throat	Colonization
Anderson [2]	2010	Norway	TCC	No	Convenience	Fresh	669	Swab	Colonization
Arcenas [3]	2012	USA	TCC	Yes	Consecutive	Fresh/frozen	1202	Nasal	Colonization
Bebko [4]	2015	USA	TCC	Yes	Convenience	Fresh/frozen	217	Nasal/groin	Colonization
Blanc [5]	2013	Switzerland	TCC	No	Convenience	Fresh	5546	Swab	Colonization
Bulliard [6]	2019	Switzerland	UHL	Yes	Consecutive	Fresh/frozen	9531	Swab	Colonization
Creamer [7]	2010	Ireland	TCC	Yes	Convenience	Fresh	696	Nasal/groin	Colonization
Dewar [8]	2019	UK	TCC	Yes	Convenience	Fresh	605	Nasal	Colonization
Gray [9]	2012	UK	TCC	No	Consecutive	Fresh	1282	Nasal/throat	Colonization
Hombach [10]	2010	Switzerland	TCC	Yes	Convenience	Fresh/frozen	168	Nasal/groin	Colonization
Jacqmin [11]	2017	Belgium	TCC	No	Convenience	Fresh	6473	Swab	Colonization
Jonckheere [12]	2015	Belgium	TCC	No	Convenience	Fresh	115	Swab	Colonization
Kelley [13]	2009	Australia	TCC	Yes	Convenience	Fresh	208	Nasal/groin	Colonization
Lee [14]	2013	Korea	TCC	No	Consecutive	Fresh	401	Nasal	Colonization
Lepainteur [15]	2015	France	UHL	Yes	Convenience	Fresh/frozen	154	Nasal	Colonization
Malhotra-Kumar [16]	2010	Belgium	UHL	Yes	Convenience	Fresh	52	Nasal/groin	Colonization
May [17]	2014	USA	UHL	Yes	Convenience	Fresh/frozen	115	Swab	Colonization
May [18]	2015	USA	UHL	Yes	Consecutive	Fresh/frozen	142	Swab	Colonization
Nielsen [19]	2017	Denmark	TCC	Yes	Convenience	Fresh/frozen	444	Swab	Colonization
Nulens [20]	2010	Belgium	TCC	No	Convenience	Fresh/frozen	496	Nares/throat	Colonization
Parcell [21]	2014	UK	TCC	Yes	Convenience	Fresh	1134	Swab	Colonization
Patel [22]	2015	USA	UHL	No	Convenience	Fresh/frozen	971	Nasal	Colonization
Patel [23]	2014	USA	UHL	No	Convenience	Fresh/frozen	1230	Nasal	Colonization
Roisin [24]	2012	Belgium	UHL	Yes	Convenience	Fresh/frozen	2292	Swab	Colonization

Table 1 continued

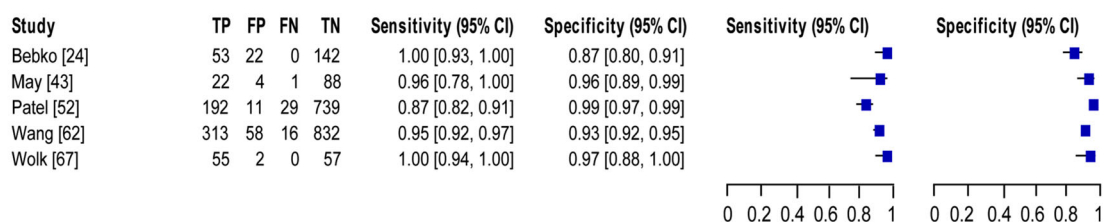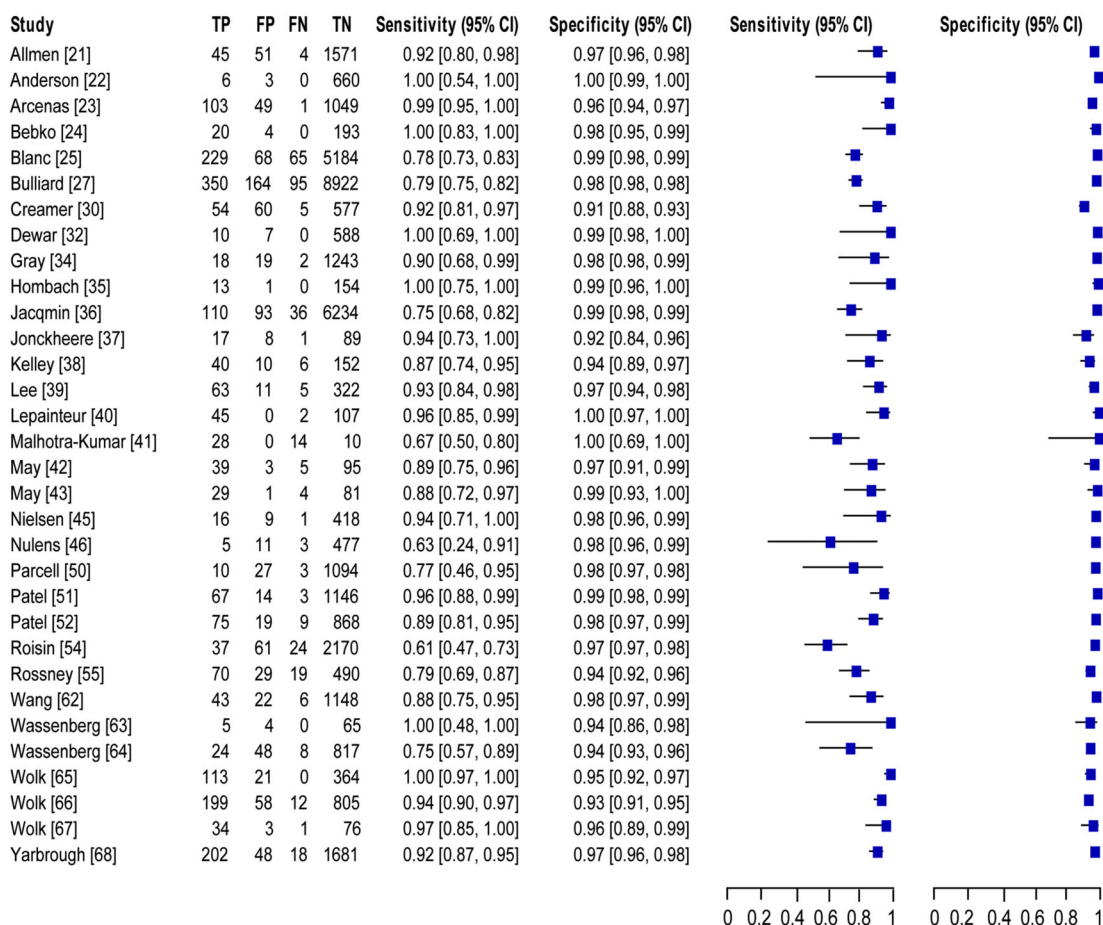| Author [Ref.]	Year	Location	Setting	Pros enroll	Patient selection	Specimen condition	Total Sample	Sample type	Reported feature
Rossney [25]	2008	Ireland	TCC	No	Convenience	Fresh/frozen	608	Swab	Colonization
Wang [26]	2021	USA	TCC	No	Convenience	Fresh	1219	Nasal	Colonization
Wassenberg [27]	2012	Netherland	UHL	Yes	Convenience	Fresh	897	Swab	Colonization
Wassenberg [28]	2010	Netherland	UHL	Yes	Convenience	Fresh	74	Swab	Colonization
Wolk [29]	2009	USA	TCC	No	Convenience	Fresh	498	Nasal	Colonization
Wolk [30]	2009	USA	TCC	Yes	Convenience	Fresh	1074	Swab	Colonization
Yarbrough [31]	2017	USA	UHL	Yes	Convenience	Fresh	1949	Nasal	Colonization
Wolk [32]	2009	USA	TCC	No	Convenience	Fresh	520	Pus/ Blood	Colonization
Author [Ref.]	**Year**	**Location**	**Setting**	**Pros enroll**	**Patient selection**	**Specimen condition**	**Total Sample**	**Sample type**	**Reported feature**
Cercenado [33]	2012	Spain	TCC	No	Consecutive	Fresh	135	LRT	VAP
Coppens [34]	2019	Belgium	UHL	No	Convenience	Fresh/frozen	79	EA	VAP
Oh [35]	2013	Korea	TCC	No	Convenience	Fresh	129	LRT	RTI
Paonessa [36]	2019	USA	TCC	Yes	Consecutive	Fresh	465	BAL	Pneumonia
Trevino [37]	2016	USA	TCC	Yes	Convenience	Fresh/frozen	100	LRT	LRTI
Dubouix-bourandy [38]	2011	France	TCC	Yes	Convenience	Fresh	135	Synovial fluid	BJI
Sambri [39]	2016	Italy	TCC	Yes	Convenience	Fresh	70	Swab	BJI
Searns [40]	2019	USA	TCC	No	Convenience	Fresh/frozen	182	Swab	BJI
Valour [41]	2014	France	TCC	No	Convenience	Fresh/frozen	91	Osteoarticular	BJI
Buchan [42]	2015	USA	UHL	Yes	Convenience	Fresh/frozen	792	Blood	Bacteremia
Davies [43]	2012	Australia	TCC	Yes	Convenience	Fresh	151	Blood	Bacteremia
McHugh [44]	2020	Scotland	TCC	Yes	Convenience	Fresh	256	Blood	Bacteremia
Page [45]	2017	Ireland	TCC	No	Convenience	Fresh	35	Blood	Bacteremia
Reddy [46]	2021	South Africa	TCC	Yes	Consecutive	Fresh	225	Blood	Bacteremia
Spencer [47]	2011	USA	TCC	No	Consecutive	Fresh	259	Blood	Bacteremia

Table 1 continued

Author [Ref.]	Year	Location	Setting	Pros enroll	Patient selection	Specimen condition	Total Sample	Sample type	Reported feature
Wade-Cummings [48]	2021	Canada	TCC	No	Convenience	Fresh	441	Blood	Bacteremia
Zboromyrska [49]	2016	Spain	TCC	Yes	Convenience	Fresh	92	Blood	Bacteremia

BAL bronchoalveolar lavage; *BJI* bone and joint infection; *EA* endotracheal aspirates; *LRT* lower respiratory tract; *Pros enroll* prospective enrollment; *RTI* respiratory tract infection; *TCC* tertiary care center; *UHL* university hospital laboratory

## Characteristics of the Included Studies

The characteristic features of the studies that were included are shown in Table 1 [21–69]. The majority of the research was carried out in high-income states, with one study being carried out in a lower-middle-income nation [53]. A single study that assessed Xpert accuracy for both MSSA and MRSA against a microbiological culture was treated as two investigations. Based on this proposition, this meta-analysis comprised 49 studies with a total of 68 datasets. Of 49 publications, 20 articles comprising 21 datasets ($n = 4996$) evidenced the Xpert's pooled summary estimates for MSSA detection [24, 26, 28, 29, 31, 33, 43, 44, 49, 52, 53, 56–62, 67, 69], while 47 publications ($n = 45,430$) evidenced the Xpert's accuracy for detection of MRSA [21–28, 30–60, 62–68]. For *S. aureus* diagnostic assessment, the median sample size per study was 182 (interquartile range: 107–333), whereas for MRSA clinical assessment, the median number of samples per study was 401 (interquartile range: 135–1074). Likewise, five publications ($n = 2636$) evaluated the Xpert's accuracy for screening MSSA colonization [24, 43, 52, 62, 67], whereas 32 studies ($n = 42,247$) assessed MRSA colonization [21–25, 27, 30, 32, 34–43, 45, 46, 50–52, 54, 55, 62–68]. Four publications ($n = 480$) investigated the Xpert's accuracy in detecting bone and joint infection caused by MSSA, while other publications ($n = 478$) assessed the Xpert's accuracy in detecting MRSA in osteoarticular samples [33, 56, 57, 60]. Xpert was also evaluated for lower respiratory tract (LRT) infections. Four publications ($n = 561$) evaluated the Xpert's MSSA detection accuracy [28, 29, 49, 59], while four other publications ($n = 582$) evaluated MRSA in LRT specimens [28, 47, 49, 59]. The remaining studies assessed Xpert's accuracy in bloodstream infections. The Xpert's accuracy to detect bloodstream MSSA was evaluated in eight publications ($n = 2622$) [26, 31, 44, 53, 58, 61, 67, 69], while MRSA in blood samples was evaluated in seven publications ($n = 2123$) [26, 31, 44, 48, 53, 58, 67]. In all cases, the research was carried out in referral hospitals or academic research laboratories. Up

(A)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Bebko [24]	53	22	0	142	1.00 [0.93, 1.00]	0.87 [0.80, 0.91]
May [43]	22	4	1	88	0.96 [0.78, 1.00]	0.96 [0.89, 0.99]
Patel [52]	192	11	29	739	0.87 [0.82, 0.91]	0.99 [0.97, 0.99]
Wang [62]	313	58	16	832	0.95 [0.92, 0.97]	0.93 [0.92, 0.95]
Wolk [67]	55	2	0	57	1.00 [0.94, 1.00]	0.97 [0.88, 1.00]

(B)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Allmen [21]	45	51	4	1571	0.92 [0.80, 0.98]	0.97 [0.96, 0.98]
Anderson [22]	6	3	0	660	1.00 [0.54, 1.00]	1.00 [0.99, 1.00]
Arcenas [23]	103	49	1	1049	0.99 [0.95, 1.00]	0.96 [0.94, 0.97]
Bebko [24]	20	4	0	193	1.00 [0.83, 1.00]	0.98 [0.95, 0.99]
Blanc [25]	229	68	65	5184	0.78 [0.73, 0.83]	0.99 [0.98, 0.99]
Bulliard [27]	350	164	95	8922	0.79 [0.75, 0.82]	0.98 [0.98, 0.98]
Creamer [30]	54	60	5	577	0.92 [0.81, 0.97]	0.91 [0.88, 0.93]
Dewar [32]	10	7	0	588	1.00 [0.69, 1.00]	0.99 [0.98, 1.00]
Gray [34]	18	19	2	1243	0.90 [0.68, 0.99]	0.98 [0.98, 0.99]
Hombach [35]	13	1	0	154	1.00 [0.75, 1.00]	0.99 [0.96, 1.00]
Jacqmin [36]	110	93	36	6234	0.75 [0.68, 0.82]	0.99 [0.98, 0.99]
Jonckheere [37]	17	8	1	89	0.94 [0.73, 1.00]	0.92 [0.84, 0.96]
Kelley [38]	40	10	6	152	0.87 [0.74, 0.95]	0.94 [0.89, 0.97]
Lee [39]	63	11	5	322	0.93 [0.84, 0.98]	0.97 [0.94, 0.98]
Lepainteur [40]	45	0	2	107	0.96 [0.85, 0.99]	1.00 [0.97, 1.00]
Malhotra-Kumar [41]	28	0	14	10	0.67 [0.50, 0.80]	1.00 [0.69, 1.00]
May [42]	39	3	5	95	0.89 [0.75, 0.96]	0.97 [0.91, 0.99]
May [43]	29	1	4	81	0.88 [0.72, 0.97]	0.99 [0.93, 1.00]
Nielsen [45]	16	9	1	418	0.94 [0.71, 1.00]	0.98 [0.96, 0.99]
Nulens [46]	5	11	3	477	0.63 [0.24, 0.91]	0.98 [0.96, 0.99]
Parcell [50]	10	27	3	1094	0.77 [0.46, 0.95]	0.98 [0.97, 0.98]
Patel [51]	67	14	3	1146	0.96 [0.88, 0.99]	0.99 [0.98, 0.99]
Patel [52]	75	19	9	868	0.89 [0.81, 0.95]	0.98 [0.97, 0.99]
Roisin [54]	37	61	24	2170	0.61 [0.47, 0.73]	0.97 [0.97, 0.98]
Rossney [55]	70	29	19	490	0.79 [0.69, 0.87]	0.94 [0.92, 0.96]
Wang [62]	43	22	6	1148	0.88 [0.75, 0.95]	0.98 [0.97, 0.99]
Wassenberg [63]	5	4	0	65	1.00 [0.48, 1.00]	0.94 [0.86, 0.98]
Wassenberg [64]	24	48	8	817	0.75 [0.57, 0.89]	0.94 [0.93, 0.96]
Wolk [65]	113	21	0	364	1.00 [0.97, 1.00]	0.95 [0.92, 0.97]
Wolk [66]	199	58	12	805	0.94 [0.90, 0.97]	0.93 [0.91, 0.95]
Wolk [67]	34	3	1	76	0.97 [0.85, 1.00]	0.96 [0.89, 0.99]
Yarbrough [68]	202	48	18	1681	0.92 [0.87, 0.95]	0.97 [0.96, 0.98]

Fig. 2 Forest plot for detection of (**A**) MSSA; pooled sensitivity: 0.93 (0.91–0.95), pooled specificity: 0.95 (0.94–0.96) and (**B**) MRSA, pooled sensitivity: 0.86 (0.84–0.87), pooled specificity: 0.98 (0.97–0.98) in nasal samples. The square stands for the sensitivity and specificity of a particular study; the black line represents its confidence interval. *TP* true positive, *FP* false positive, *FN* false negative, *TN* true negative, *CI* confidence interval
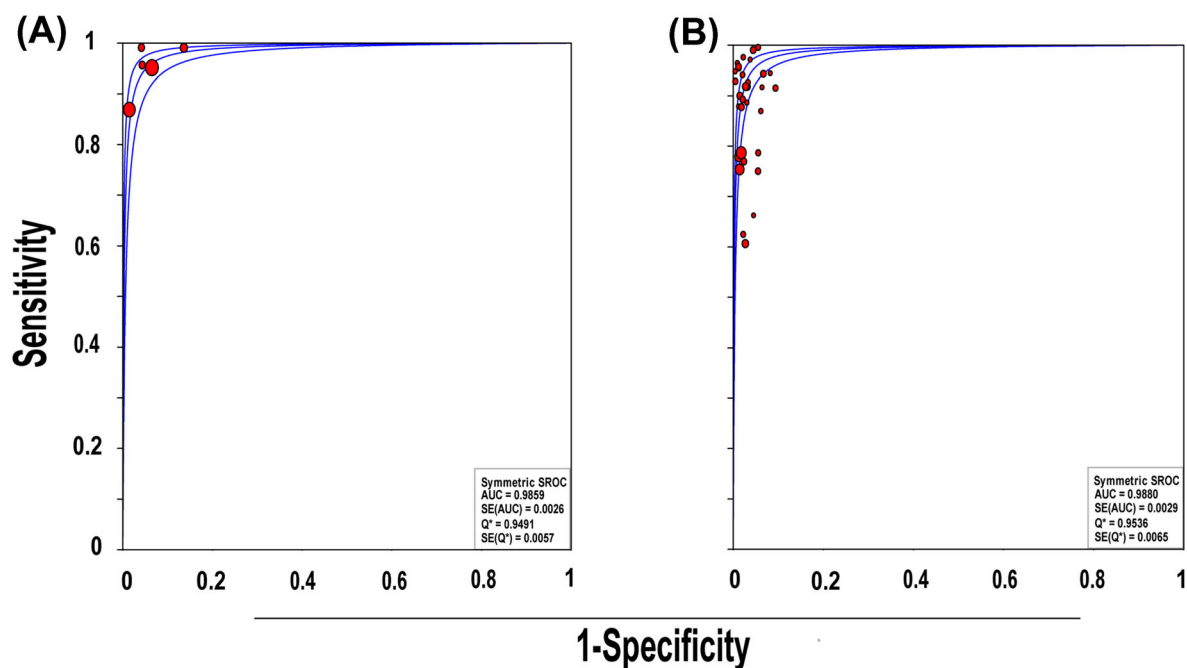
Fig. 3 SROC plot of Xpert for (A) MSSA and (B) MRSA detection in nasal samples. Red circles indicate the data point from each of the investigations, and the solid blue line represents the SROC curve

to October 12, 2021, all articles published in English were included.
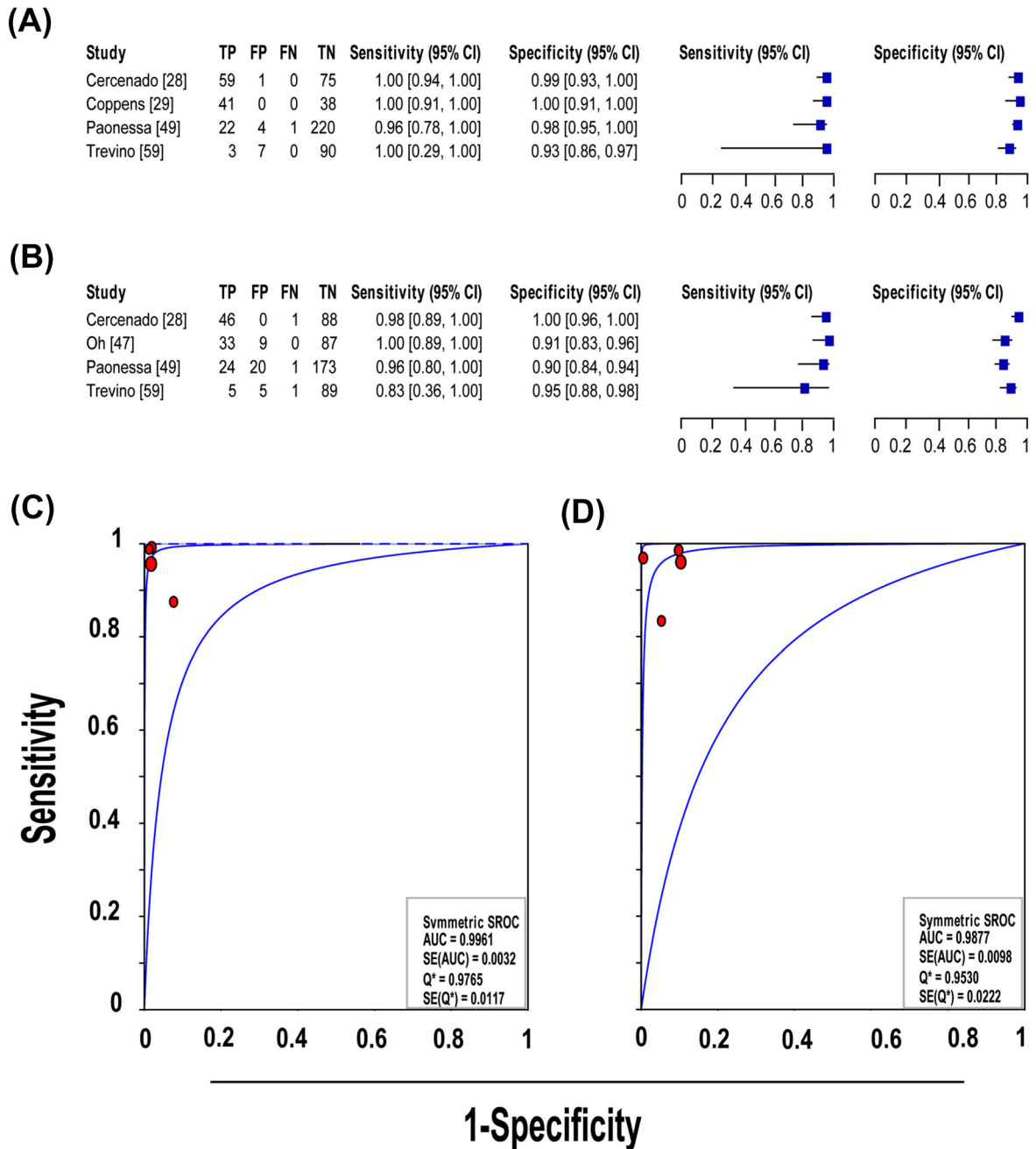
Quality Appraisal

The quality of included studies was demonstrated using QUADAS-2 tool (see Supplementary Fig. 1A, 1B). Twenty-four publications demonstrated a high risk of bias in the patient selection domain, as the studies were unable to prevent improper sample exclusion [23–28, 32, 34, 35, 37, 38, 40, 43, 44, 46, 51–54, 56, 57, 62, 68]. Applicability concern in the patients' selection domain was not a concern as all publications used samples from patients with possible infections, signaling a low risk of bias. Regarding index tests, all studies did not report about blinding of index tests except for three studies [65–67]; therefore, the risk of bias in the index test domain was considered unclear. The index test's applicability for all studies was considered unclear since there is not a globally accepted test methodology. The reference standard domain was said to have a low risk of bias due to the Xpert's use of pre-established binary

dependent inquiry standards. The reference standards for all publications were performed in either referral hospitals or academic research laboratories, so we do not expect operator error bias to be an issue. Finally, because the reference standards and the index test were performed on the same samples, there was no possibility of bias in the flow and timing domains or their applicability.

Summary Estimates

Because the studies were heterogeneous, combining all of them to obtain Xpert accuracy estimates for total staphylococcal infections was not considered to be meaningful for guiding therapy choices. To restrict the spread of staphylococcal infection within clinical settings, we examined the accuracy of Xpert for MSSA and MRSA in samples from diverse sample settings. Based on the availability of data for various samples such as nasal, LRT, osteoarticular, and bloodstream samples, we sorted studies into subgroups to assess the Xpert's accuracy against a microbiological reference standard in

(A)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Cercenado [28]	59	1	0	75	1.00 [0.94, 1.00]	0.99 [0.93, 1.00]
Coppens [29]	41	0	0	38	1.00 [0.91, 1.00]	1.00 [0.91, 1.00]
Paonessa [49]	22	4	1	220	0.96 [0.78, 1.00]	0.98 [0.95, 1.00]
Trevino [59]	3	7	0	90	1.00 [0.29, 1.00]	0.93 [0.86, 0.97]

(B)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Cercenado [28]	46	0	1	88	0.98 [0.89, 1.00]	1.00 [0.96, 1.00]
Oh [47]	33	9	0	87	1.00 [0.89, 1.00]	0.91 [0.83, 0.96]
Paonessa [49]	24	20	1	173	0.96 [0.80, 1.00]	0.90 [0.84, 0.94]
Trevino [59]	5	5	1	89	0.83 [0.36, 1.00]	0.95 [0.88, 0.98]

(C)

Symmetric SROC
AUC = 0.9961
SE(AUC) = 0.0032
Q* = 0.9765
SE(Q*) = 0.0117

(D)

Symmetric SROC
AUC = 0.9877
SE(AUC) = 0.0098
Q* = 0.9530
SE(Q*) = 0.0222

Fig. 4 Detection of staphylococcal strains in LRT samples. **A** Forest plot for MSSA; pooled sensitivity: 0.99 (0.96–1.0), pooled specificity: 0.97 (0.95–0.99). **B** Forest plot for MRSA; pooled sensitivity: 0.97 (0.92–0.99), pooled specificity: 0.93 (0.90–0.95). The black line shows the study's confidence interval, while the blue square reflects its sensitivity and specificity. **C** SROC plot for MSSA; **D** SROC plot for MRSA. Red circles in SROC curve represent each investigation's data point, while the solid blue line shows the SROC curve. *TP* true positive; *FP* false positive; *FN* false negative; *TN* true negative; *CI* confidence interval; *LRT* lower respiratory tract; *AUC* area under the curve

(A)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Dubouix-Bourandy [33]	16	2	0	119	1.00 [0.79, 1.00]	0.98 [0.94, 1.00]
Sambri [56]	7	0	0	63	1.00 [0.59, 1.00]	1.00 [0.94, 1.00]
Searns [57]	41	3	7	131	0.85 [0.72, 0.94]	0.98 [0.94, 1.00]
Valour [60]	59	0	4	28	0.94 [0.85, 0.98]	1.00 [0.88, 1.00]

(B)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Dubouix-Bourandy [33]	2	0	0	133	1.00 [0.16, 1.00]	1.00 [0.97, 1.00]
Sambri [56]	4	0	0	66	1.00 [0.40, 1.00]	1.00 [0.95, 1.00]
Searns [57]	9	0	2	171	0.82 [0.48, 0.98]	1.00 [0.98, 1.00]
Valour [60]	9	0	0	82	1.00 [0.66, 1.00]	1.00 [0.96, 1.00]

(C)

Symmetric SROC
AUC = 0.9969
SE(AUC) = 0.0046
Q* = 0.9795
SE(Q*) = 0.0185

(D)

Symmetric SROC
AUC = 0.9969
SE(AUC) = 0.0046
Q* = 0.9795
SE(Q*) = 0.0185

Sensitivity — 1-Specificity

Fig. 5 Detection of staphylococcal strains in osteoarticular samples. **A** Forest plot for MSSA; pooled sensitivity: 0.92 (0.86–0.96), pooled specificity: 0.99 (0.97–1.0). **B** Forest plot for MRSA; pooled sensitivity: 0.92 (0.75–0.99), pooled specificity: 1.0 (0.99–1.0). The black line shows the study's confidence interval, while the blue square reflects its sensitivity and specificity. **C** SROC plot for MSSA; **D** SROC plot for MRSA. Red circles in SROC curve represent each investigation's data point, while the solid blue line shows the SROC curve. *TP* true positive; *FP* false positive; *FN* false negative; *TN* true negative; *CI* confidence interval; *AUC* area under the curve

(A)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Buchan [26]	235	3	1	553	1.00 [0.98, 1.00]	0.99 [0.98, 1.00]
Davies [31]	22	0	0	129	1.00 [0.85, 1.00]	1.00 [0.97, 1.00]
McHugh [44]	38	0	0	218	1.00 [0.91, 1.00]	1.00 [0.98, 1.00]
Reddy [53]	42	0	0	183	1.00 [0.92, 1.00]	1.00 [0.98, 1.00]
Spencer [58]	33	0	0	226	1.00 [0.89, 1.00]	1.00 [0.98, 1.00]
Wade-Cummings [61]	441	0	0	0	1.00 [0.99, 1.00]	Not estimable
Wolk [67]	120	4	0	282	1.00 [0.97, 1.00]	0.99 [0.96, 1.00]
Zboromyrska [69]	4	2	0	86	1.00 [0.40, 1.00]	0.98 [0.92, 1.00]

(B)
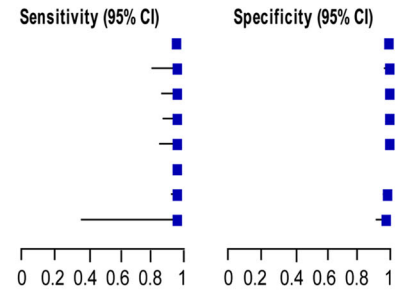
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Buchan [26]	103	3	2	684	0.98 [0.93, 1.00]	1.00 [0.99, 1.00]
Davies [31]	11	0	0	139	1.00 [0.72, 1.00]	1.00 [0.97, 1.00]
McHugh [44]	1	0	0	255	1.00 [0.03, 1.00]	1.00 [0.99, 1.00]
Page [48]	1	0	0	34	1.00 [0.03, 1.00]	1.00 [0.90, 1.00]
Reddy [53]	15	0	0	210	1.00 [0.78, 1.00]	1.00 [0.98, 1.00]
Spencer [58]	19	0	0	240	1.00 [0.82, 1.00]	1.00 [0.98, 1.00]
Wolk [67]	57	2	1	346	0.98 [0.91, 1.00]	0.99 [0.98, 1.00]

(C)

Symmetric SROC
AUC = 0.9989
SE(AUC) = 0.0005
Q* = 0.9906
SE(Q*) = 0.0034

(D)

Symmetric SROC
AUC = 0.9993
SE(AUC) = 0.0004
Q* = 0.9939
SE(Q*) = 0.0037
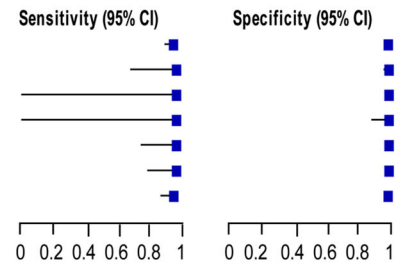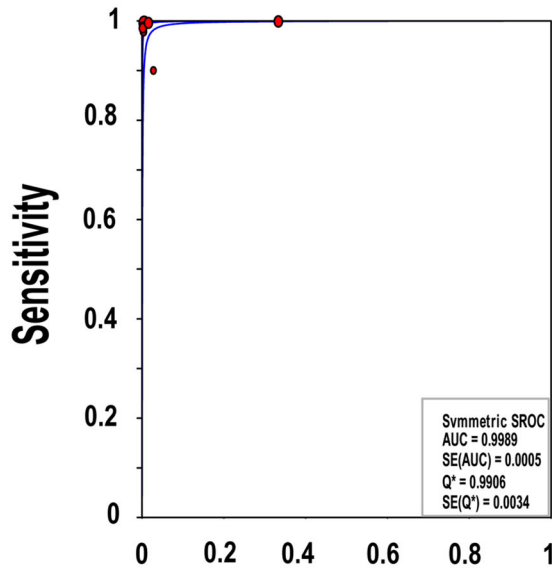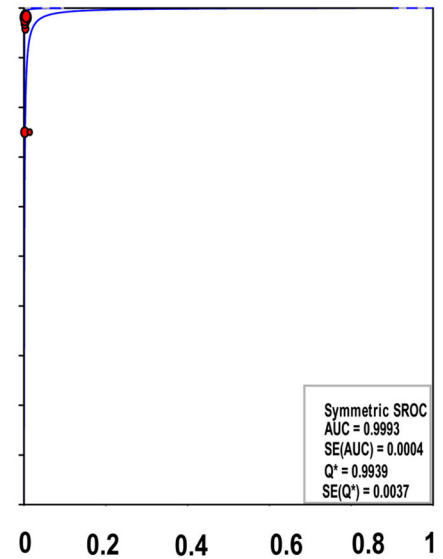
◀**Fig. 6** Detection of staphylococcal strains in blood samples. **A** Forest plot for MSSA; pooled sensitivity: 1.0 (0.99–1.00), pooled specificity: 1.0 (0.99–1.00). **B** Forest plot for MRSA; pooled sensitivity: 0.99 (0.96–1.0), pooled specificity: 1.0 (0.99–1.00). The black line shows the study's confidence interval, while the blue square reflects its sensitivity and specificity. **C** SROC plot for MSSA; **D** SROC plot for MRSA. Red circles in SROC curve represent each investigation's data point, while the solid blue line shows the SROC curve. *TP* true positive; *FP* false positive; *FN* false negative; *TN* true negative; *CI* confidence interval; *AUC* area under the curve

diverse samples and obtained pooled summary estimates.

Detection of Staphylococcal Infections

A total of 20 publications (n = 4996) compared Xpert to traditional culture for MSSA detection [24, 26, 28, 29, 31, 33, 43, 44, 49, 52, 53, 56–62, 67, 69], while 47 publications (n = 45,430) evidenced the Xpert's accuracy in detecting MRSA [21–28, 30–60, 62–68]. The Xpert's MSSA detection sensitivity and specificity varied from 0.85 (0.72–0.94) to 1.0 (0.97–1.0) and from 0.87 (0.8–0.91) to 1.00 (0.98–1.0), respectively (*see* Supplementary Fig. 2A). To detect MSSA, the Xpert's pooled estimates in overall samples were [specificity: 0.97 (0.96–0.98), sensitivity: 0.97 (0.96–0.98), negative likelihood ratio (NLR): 0.033 (0.02–0.06), positive likelihood ratio (PLR): 40.95 (23.5–71.45), DOR: 1452.6 (670.14–3148.8)]. Significant heterogeneity was seen in the I^2 statistics, where the sensitivity and specificity are 84.1% and 86.8%, respectively. With an area under the curve (AUC) of 0.99 (0.99–1.0), the summary receiver-operating characteristics (SROC) were found to have high overall clinical utility (*see* Supplementary Fig. 3A).

Similarly, 47 publications [21–28, 30–60, 62–68] with a total of 45,430 samples fulfill the criteria for MRSA diagnosis in suspected patients. The Xpert's MSSA detection sensitivity and specificity varied from 0.6 (0.47–0.73) to 1.0 (0.97–1.0) and from 0.9 (0.84–0.94) to 1.0

(0.99–1.0), respectively (*see* Supplementary Fig. 2B). The Xpert's pooled estimates to detect MRSA were [specificity: 0.98 (0.97–0.98), sensitivity: 0.87 (0.86–0.88), NLR: 0.11 (0.09–0.14), PLR: 33.78 (26.8–42.57), and DOR: 352.42 (249.33–498.13)]. Significant heterogeneity was seen in the I^2 statistics, where the sensitivity and specificity are 83.4% and 90.3%, respectively. With an AUC of 0.99 (0.98–1.0), the SROC were found to have high overall clinical utility (*see* Supplementary Fig. 3B).

Detection of Staphylococcal Colonization

A total of 2636 swabs from five publications were used to detect MSSA in clinically suspected patients [24, 43, 52, 62, 67] that met the criteria for contrasting Xpert with culture standard. The Xpert's MSSA detection sensitivity and specificity varied from 0.87 (0.82–0.91) to 1.0 (0.94–1.0) and from 0.87 (0.80–0.91) to 0.99 (0.97–0.99), respectively (Fig. 2A). The Xpert's pooled estimates to detect MSSA in swabs were [specificity: 0.95 (0.94–0.96), sensitivity: 0.93 (0.91–0.95), NLR: 0.06 (0.02–0.13), PLR: 19.3 (9.18–40.6), DOR: 359.64 (234.78–559.9)]. Significant heterogeneity was seen in the I^2 statistics, where the specificity and sensitivity were 90.3% and 83.4%, respectively. With an AUC of 0.99 (0.98–1.0), the SROCs were found to have higher clinical utility (see Fig. 3A).

Correspondingly, 32 publications with 42,247 samples examined MRSA colonization in clinically suspected patients [21–25, 27, 30, 32, 34– 43, 45, 46, 50–52, 54, 55, 62–68]. The Xpert's MRSA detection sensitivity and specificity varied from 0.6 (0.47–0.73) to 1.0 (0.97–1.0) and from 0.91 (0.88–0.93) to 1.0 (0.97–1.0), respectively (Fig. 2B). The pooled estimates for detecting MRSA in swabs were [specificity: 0.98 (0.97–0.98), sensitivity: 0.86 (0.84–0.87), NLR: 0.13 (0.1–0.17), PLR: 30.64 (24.13–38.92), and DOR: 252.91 (181.41–352.57)]. Considerable heterogeneity was seen in the I^2 statistics, where the specificity and sensitivity were 90.9% and 85.3%, respectively. With an AUC of 0.99 (95% CI: 0.98–0.99), the SROC were found to have greater clinical diagnostic value (see Fig. 3B).

Table 2 Diagnostic accuracy of Xpert MRSA/SA against traditional reference standard in various sample types: summary of results

Index test	Diagnostic target	Sample type	No. of data	% Sensitivity (95% CI)	% Specificity (95% CI)	PLR (95% CI)	NLR (95% CI)	DOR (95% CI)	AUC (95% CI)
Xpert MRSA/ SA	MSSA	Total	20	0.97 (0.96–0.98)	0.97 (0.96–0.98)	4.95 (23.5–71.45)	0.03 (0.02–0.06)	1452.6 (670.14–3148.8)	0.99 (0.99–1.0)
		Nasal	5	0.93 (0.91–0.95)	0.95 (0.94–0.96)	19.3 (9.18–40.6)	0.06 (0.02–0.13)	359.64 (234.78–559.9)	0.99 (0.98–1.0)
		LRT	4	0.99 (0.96–1.0)	0.97 (0.95–0.99)	34.15 (8.81–132.43)	0.03 (0.01–0.11)	1204.6 (188.1–7715.6)	0.99 (0.99–1.0)
		Osteoarticular	4	0.92 (0.86–0.96)	0.99 (0.97–1.0)	46.48 (21.66–99.76)	0.11 (0.06–0.18)	445.72 (145.19–1368.3)	1.0 (0.99–1.0)
		Blood	8	1.0 (0.99–1.00)	1.0 (0.99–1.00)	90.1 (31.86–254.75)	0.01 (0.004–0.03)	11,653.5 (3311.8–41,006.4)	1.0 (0.99–1.0)
	MRSA	Total	47	0.87 (0.86–0.88)	0.98 (0.97–0.98)	33.78 (26.8–42.57)	0.11 (0.09–0.14)	352.42 (249.33–498.13)	0.99 (0.98–1.0)
		Nasal	32	0.86 (0.84–0.87)	0.98 (0.97–0.98)	30.64 (24.13–38.92)	0.13 (0.1–0.17)	252.91 (181.41–352.57)	0.99 (0.98–0.99)
		LRT	4	0.97 (0.92–0.99)	0.93 (0.90–0.95)	13.04 (6.16–27.62)	0.05 (0.02–0.14)	374.04 (76.19–1836.3)	0.99 (0.99–1.0)
		Osteoarticular	4	0.92 (0.75–0.99)	1.0 (0.99–1.0)	184.07 (45.74–740.74)	0.16 (0.07–0.39)	1560.1 (241.57–10,075.9)	1.0 (0.99–1.0)
		Blood	7	0.99 (0.96–1.0)	1.0 (0.99–1.00)	218.05 (106.36–447.01)	0.04 (0.02–0.10)	7328.5 (2366.0–22,699.0)	1.0 (0.99–1.0)

CI confidence interval; *DOR* diagnostic odds ratio; *LRT* lower respiratory tract; *MSSA* methicillin-sensitive *S. aureus*; *MRSA* methicillin-resistant *S. aureus*; *NLR* negative likelihood ratio; *PLR* positive likelihood ratio

Detection of Staphylococcal Infection in LRT Specimens

Four publications [28, 29, 49, 59] assessed the Xpert's MSSA detection accuracy using 561 LRT specimens, while four publications [28, 47, 49, 59] demonstrated the Xpert's MRSA detection accuracy using 582 specimens. The Xpert's MSSA detection sensitivity and specificity varied from 0.96 (0.78–1.0) to 1.0 (0.94–1.00) and 0.93 (0.86–0.97) to 1.00 (0.91 to 1.00), respectively (Fig. 4A), while MRSA detection sensitivity and specificity varied from 0.83 (0.36–1.0) to 1.0 (0.90–1.00) and from 0.90 (0.84–0.94) to 1.00 (0.96–1.0), respectively (Fig. 4B). The Xpert's pooled MSSA detection estimates were comparable [specificity: 0.97 (0.95–0.99), sensitivity: 0.99 (0.96–1.0), NLR: 0.03 (0.01–0.11), PLR: 34.15 (8.81–132.43), and DOR: 1204.6 (188.1–7715.6)] to MRSA [specificity: 0.93 (0.90–0.95), sensitivity: 0.97 (0.92–0.99), NLR: 0.05 (0.02–0.14), PLR: 13.04 (6.16–27.62), and DOR: 374.04 (76.19–1836.3)]. Low to moderate heterogeneity was seen in the I^2 statistics for MSSA detection, where the specificity and sensitivity were 65.8% and 12.7%, respectively, while the I^2 statistical values of Xpert sensitivity and specificity for MRSA identification were 26.8 and 82.2%, respectively, suggesting low to moderate heterogeneity. With an AUC of 0.99 (0.99–1.00), the SROCs were found to have greater clinical diagnostic value for both MSSA and MRSA (Fig. 4C, 4D).

Detection of Staphylococcal Infection in Osteoarticular Samples

In four publications [33, 56, 57, 60], the accuracy of Xpert was tested in osteoarticular samples for both MSSA ($n = 480$) and MRSA ($n = 478$). The Xpert's MSSA detection sensitivity and specificity varied from 0.85 (0.72–0.94) to 1.0 (0.79–1.00) and 0.98 (0.94–1.0) to 1.0 (0.94–1.0), respectively (Fig. 5A). For MRSA identification, the Xpert's sensitivity and specificity varied from 0.82 (0.48–0.98) to 1.0 (0.66–1.0) and 1.00 (0.95–1.00) to 1.00 (0.98–1.00), respectively (Fig. 5B). The Xpert's pooled diagnostic accuracy was comparable for

both MSSA [specificity: 0.99 (0.97–1.0), sensitivity: 0.92 (0.86–0.96), NLR: 0.11 (0.06–0.18), PLR: 46.48 (21.66–99.76), DOR: 445.72 (145.19–1368.3)] and MRSA [specificity: 1.0 (0.99–1.0), sensitivity: 0.92 (0.75–0.99), NLR: 0.16 (0.07–0.39), PLR: 184.07 (45.74–740.74), DOR: 1560.1 (241.57–10,075.9)]. The I^2 statistical scores for MSSA detection specificity and sensitivity were 6.0% and 53.1%, respectively, suggesting low to moderate heterogeneity, whereas the I^2 MRSA statistical scores were < 18.3%, indicating low heterogeneity across studies. Both MSSA and MRSA had an AUC of 1.0 (0.99–1.00), denoting remarkably higher diagnostic value (Fig. 5C, D).

Detection of Bloodstream Staphylococcal Infection

Eight publications [26, 31, 44, 53, 58, 61, 67, 69] with a total of 2622 specimens analyzed the Xpert's MSSA detection accuracy in blood specimens, whereas seven studies [26, 31, 44, 48, 53, 58, 67] with a total of 2123 samples evaluated the Xpert's accuracy for MSSA detection in samples from bloodstream. The Xpert's MSSA detection sensitivity and specificity varied from 0.99 (0.98–1.0) to 1.0 (0.99–1.00) and 0.98 (0.92–1.0) to 1.00 (0.98 to 1.00) and 0.98 (0.92–1.0) to 1.00 (0.98 to 1.00), respectively (Fig. 6A). On the other hand, Xpert's MRSA detection sensitivity and specificity varied from 0.98 (0.93–1.00) to 1.0 (0.82–1.00) and 0.99 (0.98–1.0) to 1.00 (0.99–1.00), respectively (Fig. 6B). Xpert evidenced roughly similar diagnostic value for both MSSA [specificity: 1.0 (0.99–1.00), sensitivity: 1.0 (0.99–1.00), NLR: 0.01 (0.004–0.03), PLR: 90.1 (31.86–254.75), DOR: 11,653.5 (3311.8–41,006.4)] and MRSA [specificity: 1.0 (0.99–1.00), sensitivity: 0.99 (0.96–1.0), NLR: 0.04 (0.02–0.10), PLR: 218.05 (106.36–447.01), DOR: 7328.5 (2366.0–22,699.0)]. In the case of MSSA detection, the I^2 scores for sensitivity and specificity were 0% and 48.7%, reflecting low to substantial heterogeneity, whilst the Xpert's MRSA detection sensitivity and specificity were 0% and 3.9%, reflecting low heterogeneity. With an AUC of 1.0 (0.99–1.00), the SROCs

were found to have greater clinical diagnostic value for both MSSA and MRSA (Fig. 6C, 6D).

Meta-Regression and Subgroup Analysis

Because there was high heterogeneity across studies, a meta-regression test was utilized to inspect the source of heterogeneity in designated subgroups. Meta-regression analysis demonstrated that except for the sampling methods (consecutive/convenience; $P = 0.03$), all other factors including research design (prospective/others) and sample conditions (fresh/frozen) were not major contributors to heterogeneity (meta-regression $P = 0.86$ and $P = 0.6$, respectively).

Publication Bias

Deek's funnel plot asymmetry analysis was conducted to examine publication bias of all included studies. In our study, we found no evidence of significant publication bias ($P > 0.05$).

DISCUSSION

Timely and efficient microbiological detection of staphylococcal infection is critical in the care of both colonized and infected patients to choose suitable therapy and avoid infection transmission via the use of appropriate barrier measures. However, the various studies' use of distinct case definitions and samples makes comparing study results difficult and limits illness treatment. Staphylococcal infections are traditionally tested using culture-based approaches, which are time-consuming (48–72 h) and need further phenotypic assessments. In fact, a 24–48-h period is generally predicted between the detection of gram-positive cocci in clusters on gram-stain and the results of antibiotic susceptibility testing. According to the existing literature, prompt selection of the best suitable antibacterial may minimize mortality and expenses [76, 77]. One effective tool that may aid with this is an Xpert MRSA/SA system (Cepheid, Sunnyvale, CA), which is a unique,

completely automated approach that distinguishes MRSA from MSSA in < 1 h after acquiring gram stain. This technique has been successfully examined for the identification of *Clostridium difficile* [78], group B *Streptococci* [79], *Bacillus anthracis* [80], Staphylococcal strains [21–69], and others from clinical specimens. Nonetheless, there is a paucity of data to decide on the accuracy of the Xpert MRSA/SA assay for the diagnosis of staphylococcal infections to facilitate the targeted administration of the most appropriate antibiotic.

Based on our findings, Xpert was better at detecting MSSA [specificity: 0.97 (0.96–0.98), sensitivity: 0.97 (0.96–0.98), AUC: 0.99 (0.99–1.0)] than MRSA [specificity: 0.98 (0.97–0.98), sensitivity: 0.87 (0.86–0.88), AUC: 0.99 (0.99–1.0)]. It should be emphasized that there was substantial diversity in the number of studies included and sample settings, which may not necessarily depict the true scenario and aid in pragmatic therapeutic advice. Therefore, we initially aimed to screen colonization of both MSSA and MRSA in carriers, who can then be subjected to contact precautions to prevent spread to other patients. We observed that a larger number of studies were conducted for screening colonization and were mostly compared to direct culture, which demonstrated sensitivity of 86% and specificity of 98%, which correlated well to the overall summary estimates of staphylococcal strains (Table 2). Low sensitivity for Xpert might be attributed to patient features, sampling error, and low bacterial load in swab samples. Conversely, Xpert's ability to correctly identify patients who did not have an infection was consistently above 95%, depicting Xpert's ability to identify patients without infection correctly. Compared to previous studies, an investigation by Parente and coworkers [81] found that MRSA nares screening can be useful to rule out MRSA pneumonia, but the study was not unique in its ability to accurately diagnose staphylococcal colonization.

Similarly, diagnosing the causative organism and administering appropriate antibiotic therapy are critical in treating staphylococcal BJI in osteoarticular specimens. Traditional bacterial culture and gram stain tests have low to

moderate sensitivity, which impedes the treatment strategy of staphylococcal BJI [12, 82], leading to delays in the administration of antibacterial medications against the causative microorganisms. Numerous recent studies have shown that Xpert may be useful for distinguishing staphylococcal BJI from other pathogenic microbes [33, 56, 57, 60]; however, the findings of these studies have not been fully examined. According to the results of this investigation, the testing of Xpert in osteoarticular samples compared to those using the culture technique demonstrated great sensitivity and specificity for distinguishing MSSA and MRSA (Table 2). It should be mentioned that in patients with suspected staphylococcal BJI, identifying staphylococcal species and resistance markers as soon as possible is critical, as a timely therapy may significantly increase overall life expectancies and minimize hospital burden.

The role of the diagnostic laboratory in the treatment of LRT infection is critical. Traditional testing method of the respiratory secretions is still the best way to look for pathogenic microorganisms [83]. However, a positive test can only be made in about 30% of cases [13], with a high rate of false negatives due to normal flora complicating the analysis and necessitating a significant amount of samples to start culture, which is not ideal. Several studies have examined the Xpert's ability to distinguish between MSSA and MRSA in possible LRT specimens [28, 29, 47, 49, 59]; nevertheless, a clear understanding of Xpert accuracy has not been demonstrated. According to the findings of this study, the pooled estimates of Xpert's MSSA detection [specificity: 0.97 (0.95–0.99), sensitivity: 0.99 (0.96–1.0), AUC: 1.0 (0.99–1.00)] were relatively similar to the MRSA detection [specificity: 0.93 (0.90–0.95), sensitivity: 0.97 (0.92–0.99), AUC: 1.0 (0.99–1.00)], exemplifying Xpert's impressive overall performance. In contrast to previously published systematic reviews, a publication by Chen et al. reported on the effective diagnostic relevance of NAAT for staphylococcal strains in LRT specimens [18], which is similar to the results of our investigation.

We also compared the Xpert assay to established reference standards for detecting staphylococcal strains in blood specimens, where most studies employed gram-positive cocci culture broths. The Xpert assay demonstrated statistically equivalent sensitivities and specificities for identifying MSSA and MRSA in positive blood cultures compared to the culture method (Fig. 6). The superior sensitivity of Xpert across enrichment samples, as well as the fairly low non-interpretable data, encourage the Xpert's utility for monitoring bloodstream infections. A potential advantage of the Xpert assay is the simplified sample-to-result workflow and on-demand flexibility, which minimizes turnaround time for blood cultures. The advantages of quick diagnosis of MSSA and MRSA with the deployment of a molecular test straight from positive blood culture broths have been extensively established in terms of reduced patient numbers, time to commence treatment, duration of hospital stay, and related healthcare expenditures [20, 84]. Table 2 shows the pooled Xpert estimates for distinguishing MSSA and MRSA across all specimens. Importantly, these benefits can only be realized when molecular testing is available on demand and the findings are actively disclosed to the clinician.

Our research strengths include a thorough search approach that retrieved all relevant publications from five of the most often used databases. The searches were carried out methodically, and at least two investigators examined the titles and abstracts of all publications. Following a group discussion, the authors' collective opinion was represented in the publications included in this meta-analysis. The PRISMA-DTA criteria for systematic reviews and the QUADAS-2 tool were applied to ascertain the included publications quality. In the following analysis, publications that did not satisfy the conditions for identifying staphylococcal BJI were exempted. Furthermore, studies that compared different genera of Xpert with the same sample were aggregated rather than included as separate studies, which could have resulted in an overestimation of the clinical outcomes of index tests.

This research has certain limitations that should be considered. Despite doing a thorough

search of databases, it is conceivable that we overlooked a few pertinent studies. We also could not address the impact of attributes such as specimen volume, non-standardized processing, amplification protocols, expert knowledge with the Xpert test, and research laboratory facilities on the Xpert's accuracy because of the high level of discrepancies in reporting of these factors in the publications. Also, we did not evaluate the accuracy of Xpert among independent traditional reference standards, including direct and enrichment cultures, which could be probable reasons for the heterogeneity. Studies comparing different generations of Xpert assay with culture were averaged for their representation in our meta-analysis. Although the research design, sampling condition, and test methods were not a major source of inconsistency in the meta-regression analysis, these factors may have elevated variability and limited the Xpert's universal applicability. It is also worth noting that most studies were conducted in high-income countries, with only one study conducted in a lower-middle income country, which may limit the generalizability of the study. Furthermore, there was also a limited availability of osteoarticular and LRT-related publications, which should be considered when interpreting the results of this study.

CONCLUSIONS

To the best of the author's knowledge, this is the first study of its kind to evaluate Xpert's diagnostic accuracy across multifaceted specimens to guide appropriate therapeutic decisions. Our findings suggest that Xpert is a reliable and robust automated assay for distinguishing staphylococcal strains from potentially infected patients in diverse sample settings. This research suggests that if a short time delay (≤ 60 min) does not influence mortality, as no literature has claimed so far, then commencing suitable medication may be more important than immediately starting empiric use of broad-spectrum antibiotics. Xpert can be utilized as the preferable first testing method for a point-of-care diagnosis of staphylococcal

infection to avoid costly anti-MRSA therapy. Whenever possible, the use of Xpert in conjunction with microbiological culture should be considered, as susceptibilities must be obtained to properly guide treatment. Furthermore, Xpert results and local clinical data should be taken into account when developing new guidelines for anti-staphylococcal medication use. Given the paucity of Xpert data across osteoarticular and LRT sample types, a thorough examination involving a relatively large number of prospective studies may be helpful in determining the best sample type for future implications. It should also be noted that, compared to traditional methods, the use of molecular techniques incurs additional costs and necessitates substantial facilities, and only a limited number can be tested at any given time, which could be interesting to estimate in future studies. Furthermore, future investigations are required to thoroughly substantiate the treatment benefit associated with Xpert's cost-effectiveness, mortality prediction, and time to antibiotic discontinuation.

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Compliance with Ethics Guidelines. This article is based on previously conducted studies and does not contain any new studies with human participants or animals performed by any of the authors.

Data Availability . All data generated or analyzed during this study are included in the manuscript.

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