



Meta-analysis

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Global, regional, and national burdens: An overlapping meta-analysis on *Staphylococcus aureus* and its drug-resistant strains

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ABSTRACT

Objective: To provide an inclusive blend of extant meta-analyses on the burden of *Staphylococcus* (*S.*) *aureus* and its resistant strains across diverse study populations, settings, and temporal contexts.

Methods: The study has adopted PRISMA 2020-based guides and registered its protocol on Open Science Framework with an extensive literature search. Study quality was assessed by QUOROM and AMSTAR techniques. Data analysis included parsing of study-level statistical power, assessment of primary study overlap, pooling of meta-analysis results, subgroup and temporal analysis.

Results: Totally 41 studies (64 meta-analyses) were selected by the inclusion criteria. The summary meta-analysis revealed global prevalence rates for *S. aureus* [24.8%, 95%CI 0.248(0.204–0.293), $I^2 = 93\%$], methicillin resistant *S. aureus* (MRSA) [5.8%, 95%CI 0.058(0.044–0.073), $I^2 = 92\%$], vancomycin intermediate *S. aureus* [1.7%, 95%CI 0.017(0.013–0.021), $I^2 = 36.4\%$], heterogeneous vancomycin intermediate *S. aureus* [5.2%, 95%CI 0.052(0.038–0.056), $I^2 = 36.4\%$], community-associated methicillin-resistant *S. aureus* [19.9%, 95%CI 0.199(-0.170–0.568), $I^2 = 96.67\%$], livestock-associated-MRSA [13.6%, 95%CI 0.136(-0.028–0.243), $I^2 = 97.7\%$], and mupirocin resistant *S. aureus* [7.6%, 95%CI 0.076(0.062–0.090), $I^2 = 0\%$]. Temporal analysis revealed that the burden community-associated methicillin-resistant *S. aureus* notably increased from 1.3% in 2003 to 39.0% in 2014. Coagulase-negative staphylococci rose from 23.2% in 2021 to 29.8% in 2022. Vancomycin resistant *S. aureus* peaked at 9.0% in 2018, declining to 2.6% in 2020. Livestock-associated-MRSA significantly increased to 19.0% in 2020. MRSA fluctuated, peaking at 52.7% in 2012 and 31.0% in 2022.

Conclusions: The study reveals a considerable global prevalence of

S. aureus at 24.8%. Regional differences were apparent, with Africa facing a high burden of MRSA at 40.8% of *S. aureus* and temporal trends exposed a dynamic state.

KEYWORDS: Vancomycin-resistant *Staphylococcus aureus*; Methicillin resistant *Staphylococcus aureus*; Livestock-associated (LA)-MRSA strain; Meta-analysis; Antimicrobial resistance

1. Introduction

Many meta-analyses on the incidences of *Staphylococcus* (*S.*) *aureus* and methicillin resistant *S. aureus* (MRSA) in human and animal environments have been conducted over the last three decades; there is still a knowledge vacuum in many nations. *S. aureus* is a prevalent pathogen isolated in hospitals globally[1]. Approximately 20% of healthy adults are chronic carriers of *S. aureus*, 30% are intermittent carriers, and 50% are immune for unexplained reasons[1]. The most pathogenic staphylococci are MRSA strains, which first developed

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in the 1960s, shortly after the methicillin was brought into clinical practice[2]. It has emerged as a major cause of antibiotic resistance and a global public health concern. Healthcare-associated MRSA, one of the most frequent pathogens in hospital settings, is a leading cause of skin and soft tissue infections as well as serious diseases such as pneumonia and sepsis[3]. MRSA infection affected 29% of MRSA carriers, lengthening hospital stays, increasing in-hospital costs, and causing thousands of deaths worldwide. MRSA epidemiology features altered dramatically during the 1990s[4]. Novel MRSA lineages have arisen, accumulating various types of resistance genes responsible for community-acquired infections [community-acquired MRSA (CA-MRSA)][5]. MRSA has also spread to livestock as a result of routine antibiotic use in livestock production. Livestock-associated (LA-MRSA) strains differ from human MRSA strains in that they can establish and propagate within livestock herds and have the potential to spread and cause infections in humans[6]. The international movement of livestock has accelerated the spread of LA-MRSA between animals and people[7]. Farmers are under pressure to raise animals more efficiently in order to meet rising global meat output and consumption[8]. This frequently entails the widespread administration of antibiotics, which can raise the risk of MRSA related with cattle production. Under selective pressure, *S. aureus* isolates that are susceptible to vancomycin can alter their cell wall structure, leading to reduced susceptibility to vancomycin[9].

Foodborne diseases are a constant threat to public health and a consistent cause of morbidity and mortality worldwide. It has been estimated that up to one-third of the developed countries population suffers a foodborne disease each year and it can be assumed that the prevalence is even higher in the developing countries[10].

S. aureus is a harmful bacterium that can be found in a variety of foods, including meat, poultry, fish, and dairy products. *S. aureus* and some other coagulase-positive or -negative staphylococcal species can cause Staphylococcal food poisoning by producing enterotoxins, which cause foodborne illness such as vomiting, gastroenteritis, and even systemic shock in primates[11].

It is believed that *S. aureus* was responsible for 20%-25% of foodborne illness outbreaks produced by bacteria in China, causing substantial harm to human health[12]. These antibiotic-resistant bacteria can be transmitted to humans *via* the food chain[13], and clinical antibiotic therapies for possible human illnesses may be ineffective or even ineffective due to antibiotic resistance[14].

Active surveillance cultures, pre-emptive isolation of high-risk patients, decolonization therapy, and contact isolation of patients colonized with MRSA are among the control strategies used to limit the occurrence of hospital-acquired infections caused by MRSA[15].

The role of these initiatives, however, is still being debated[15].

Mupirocin (Pseudomonic acid A) is an antibiotic approved for the decontamination of MRSA and methicillin-susceptible *S. aureus* (MSSA) in both patients and healthcare personnel. Resistance occurred shortly after long-term use of mupirocin was permitted, particularly during decolonization[16].

Antimicrobial resistance is a major issue in the treatment of *S. aureus* infections and is a global public health concern[3]. Glycopeptide antibiotics, such as vancomycin, are the first-line treatment for methicillin-resistant *S. aureus* (MRSA) infections[17]. Vancomycin glycopeptide has been recognized as the last line of defense in the treatment of infections caused by severe MRSA and other resistant Gram-positive bacteria[17]. Sadly, vancomycin-intermediate *S. aureus* (VISA) isolates with lower resistance to vancomycin exists.

Estimating the burden of any disease is difficult, and global and regional estimates of infections or risk factors are needed to inform public health policy[18]. This study can provide useful epidemiological context and contribute to worldwide statistics for estimating the burden of *S. aureus* and its drug-resistant strains.

A metanalysis of meta-analysis is a method for statistically synthesizing results from multiple meta-analyses that address similar research questions[19]. This study aims to provide an inclusive blend of extant meta-analyses on the burden of *S. aureus* and its resistant strains across diverse study populations, settings, and temporal contexts.

2. Methods

2.1. Information sources and protocol registration

The protocol for this study can be found at Open Science Framework at <https://osf.io/786zh/>.

To conduct this study, PRISMA-based guidelines for literature review were used[20].

2.2. Search Strategy

The databases including PubMed, Embase, MEDLINE, and Google Scholar were searched using all appropriate variations of the words: “meta-analysis”, “systematic reviews and metanalysis”, “*Staphylococcus aureus*”, “Methicillin resistant *Staphylococcus aureus*”, “MRSA”, “Vancomycin Intermediate *Staphylococcus aureus*”, “VISA”, “Vancomycin Resistant *Staphylococcus aureus*”, “VRSA”, “Heterogeneous vancomycin-intermediate

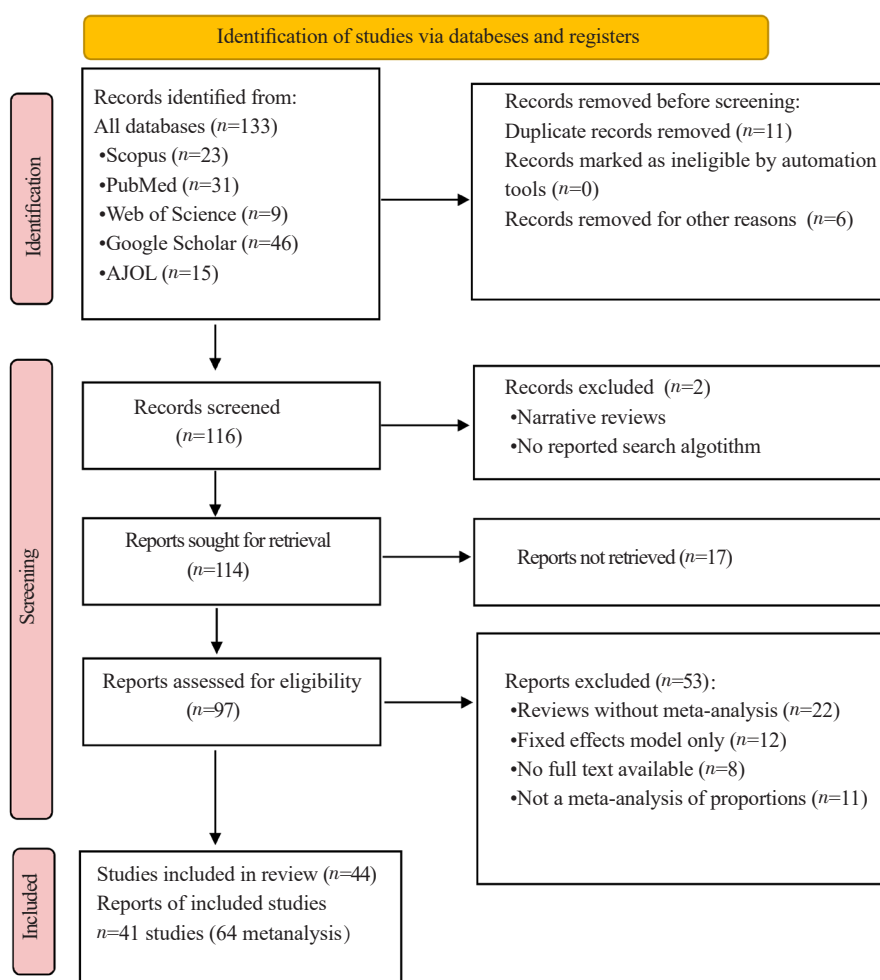


Figure 1. Selection of articles for inclusion. Note: While the number of studies were 41, Sixty-four (64) meta-analyses were parsed due to some studies reporting on multiple strains.

Staphylococcus", "hVISA", "Coagulase negative *Staphylococcus aureus*", "CoNS", "community-acquired *Staphylococcus aureus*", "CA-MRSA", "Livestock-Associated Methicillin-Resistant *Staphylococcus aureus*", "LA-MRSA", "hospital", "carriage", "infect*", "community", "surfaces" and "environment*".

2.3. Eligibility criteria

A study was considered if it was a meta-analysis of the prevalence of *S. aureus* and/or its drug resistant strains. Exclusion criteria included systematic reviews that did not include data pooling or meta-analysis, narrative reviews, reviews that did not include a search algorithm, and reviews that did not specify how studies were selected for review.

2.4. Selection process

Relevant manuscripts were separately rated, and there were no notable differences met in the literature parsing after deliberations,

indicative of a consensus in the study selection for inclusion in the meta-meta-analysis.

2.5. Data extraction and quality assessment

Data provided by an included meta-analysis comprises, first author, primary studies, confidence intervals, rates, study years, sample size, languages, database searches, publication dates, journals, protocols, models, and software[21,22]. To assess the validity and depths of the included meta-analyses, the Quality of Reporting of Meta-analyses (QUOROM) checklist and Assessment of Multiple Systematic Reviews (AMSTAR) techniques were used[23]. The assessment of primary study overlap involved the utilization of pairwise intersection heat maps, Corrected Covered Area (CCA), and a Citation matrix of evidence[24–26].

The 'metameta' package's functions[27] were used to compute and visualize study-level statistical power for a range of true effect sizes (a "Firepower" plot) [28].

Comprehensive meta-analyst program (V3) was used to meld

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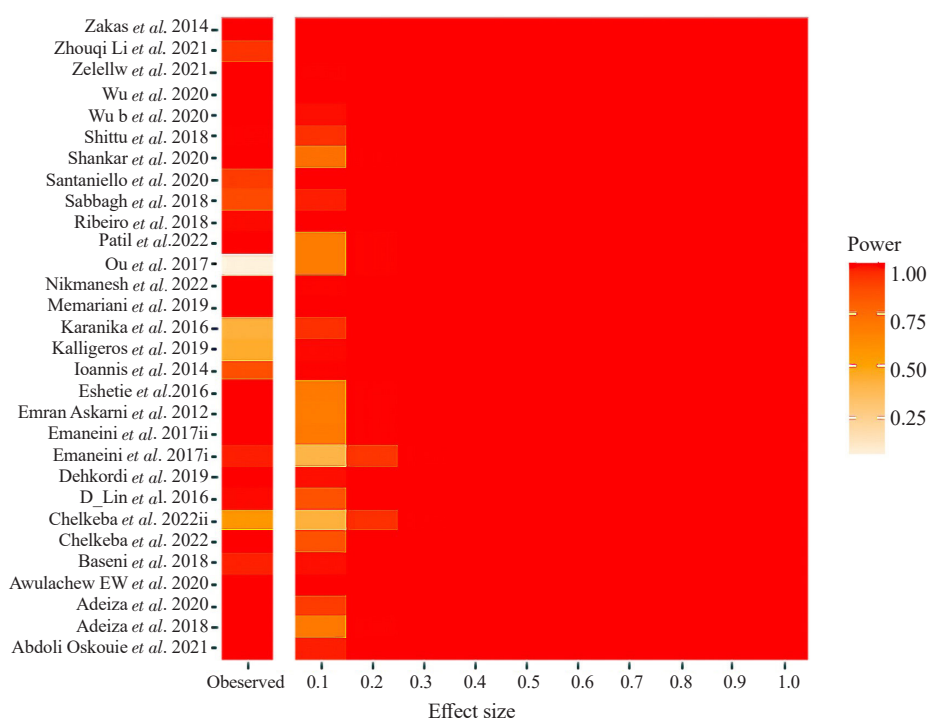


Figure 3. Firepower plot of study-level statistical powers of meta-analysis and range of effect sizes from 0.1 to 1 (in increments on 0.1). In the figure, Low =White, midpoint = 0.5 (0.5), Orange and High=Red

the outcomes of meta-analyses modeled by random effects with 95% confidence intervals[29]. Summary of calculations in the meta-analytical method includes DerSimonian-Laird estimate for τ^2 , the Jackson technique for calculating the confidence interval of τ^2 and τ , and the Clopper-Pearson confidence interval for individual studies. Cochran's Q statistic was used to determine whether effect sizes were consistent across studies. The degree of heterogeneity between studies was calculated using Higgins & Thompson's I^2 index[30,31]. The visualization of subgroup analysis for moderator variables was conducted using the Forester package in R software version 4.2.2.3.

3. Results

3.1. Search results

Initially 133 abstracts were identified. Forty-one out of 64 meta-analyses met the eligibility criteria and were included[7,32–59,59–70]. A flow diagram is shown in Figure 1. These studies were published between 2003 and 2023. Fourteen (34.2%) of them were published between 2020 and 2023 (Table 1). All of the studies performed proportional metanalysis with random effects model. Twenty five percent of included studies used Joanna Briggs Institute (JBI) for quality assessment, Newcastle-Ottawa Scale (NOS) 22.7%, Evidence-Based Mental Health (EMBH), 4.6%, Strengthening the Reporting of Observational studies in Epidemiology (STROBE)

6.8%, Critical Appraisal Skills Programme (CASP) 2.3%, Condition Context Population (Coco Pop) 2.3%; QUADAS 2.3%; Fixed rating scale (FRS) 2.3%. Methods of quality assessment were not reported in 34.1% of the studies. The most frequently used software for data pooling by the included meta-analysis were Stata of 47.6%; CMA 19.05%; R software 9.52%; and MedCalc 7.14%. Other softwares were Epi-Info, Meta-XL, Open Meta Analyst, REVMAN, Stats Direct and SAS with a frequency of 2.4%. The range of publication years of primary studies cited ranged from 1978 to 2022. The total number of primary studies cited was 1 683 and ranges from 10 to 152, with a median of 40 primary studies (Table 1).

The data obtained from the included studies comprised of general public ($n=946$ 187), patients ($n=299$ 992), hospital isolates ($n=55$ 185), clinicals specimen ($n=30$ 151), Animals ($n=18$ 022), healthcare workers ($n=27$ 859), asymptomatic athletes ($n=1$ 495), food ($n=66$ 769) and environmental samples ($n=4$ 449).

3.2. Search methodology and primary study overlap

All studies except those by Karanika *et al.* and Lin *et al.* utilized the Pubmed/Medline database in their literature search. Only two studies were found through the CINAHL database (Table 2). There was variation in the utilization of other databases but every study except Shipeng Li *et al.* used at least two electronic databases for searching. The percentage distribution of the databases are as follows: Medline/PubMed (95.1%, $n=39$), Embase (80.5%,

$n=33$), Google scholar (53.7%, $n=22$), Web of science (56.1%, $n=23$), Scopus (34.1%, $n=14$), Science direct (31.7%, $n=13$), Cochrane Library (9.8%, $n=4$), AJOL (14.6%, $n=6$), CNKI (7.3%, $n=3$), CINAHL (4.9%, $n=2$) and other databases (78.5%, $n=32$). All studies had language limitations in their search criteria except Shariati *et al.* which had no limitations[58]. There was some consistency in which primary studies were included with most of the reviews simply adding more recently published studies (Figure 2). There was slight overlap between the included primary studies and the CCA score was less than 5% (1.20%). Moreover, pooled effects of each included study have stated in Table 3.

3.3. Power evaluation

The power of the studies encompassed a range from 0.25 to 1, with most falling within the 0.5 (medium power) to 1.0 range (high power), assuming that the summary effect size is the true effect size. The findings indicate that the majority of the included studies are suitably powered to detect a wide range of meaningful effects, particularly in studies drawn from a universe of potential studies (Figure 3).

3.4. Study reporting and quality assessment (Validity)

The studies were evaluated for QUOROM scores, which varied between 10 and 15, and had a median score of 12.8 out of a possible 18. In the case of included meta-analyses, AMSTAR scores were assessed, ranging from 7 to 10 points, with a median score of 8.7 out of a maximum possible score of 11 points. No study had a priori published research objectives and rarely did quality factor into decision-making relative to conclusions and recommendations. AMSTAR and QUOROM scores showed that studies were not uniformly detailed the characteristics of the included studies and most performed a comprehensive literature search and assessed the methodology of included studies and publication bias (Supplementary Figure 1, 2 and Supplementary Table 1).

In a proportional meta-analysis, prevalence/incidence is reported in terms of their proportions and will always fall between the values of zero and one. For the sake of simplicity, the results of the summary metanalysis were communicated as a percentage.

3.5. Global, regional and national rates (Combined for humans, animal and food sources)

Figure 4 provides subgroup analysis of *S. aureus* prevalence/incidence at the global, national and regional levels. The summary metanalysis of 30 studies that reported global prevalence rates are

as follows: For *S. aureus*, seven studies reported a summary rate of 24.8% [95%CI, 0.248(0.204–0.293), $I^2 = 93\%$]; For MRSA, thirteen studies reported a rate of 5.8% [95%CI, 0.058 (0.044–0.073), $I^2 = 92\%$]; For VISA, three studies reported a rate of 1.7% [95%CI, 0.017 (0.013–0.021), $I^2 = 36.4\%$]; For hVISA, two studies reported a rate of 5.2% [95%CI, 0.052 (0.038–0.066), $I^2 = 36.4\%$]; For CA-MRSA, two studies reported a rate of 19.9% [95%CI, 0.199(-0.170–0.568), $I^2 = 96.67\%$]; For LA-MRSA, two studies reported a rate of 13.6% [95%CI, 0.136(-0.028–0.243), $I^2 = 97.7\%$]; For MuRSA, one study reported a rate of 7.6% [95%CI, 0.076 (0.062–0.090), $I^2 = 0\%$].

Regional data drawn from 31 meta-analysis, pooled a summary rate of 25.2% *S. aureus* burden in Africa [13 studies, 95%CI, 0.252(0.167–0.338), $I^2 = 93.82\%$]; 40.8% MRSA [4 studies, 95%CI, 0.408 (0.320–0.496), $I^2 = 66.40\%$]; 29.8% CoNS [2 studies, 95%CI, 0.298 (-0.091–0.688), $I^2 = 88.89\%$]; 14.0% MuRSA [1 study, 95%CI, 0.140(0.060–0.220), $I^2 = 0\%$] (Figure 4).

For Asia subgroup analysis of sixteen studies provides SA, MRSA, CA-MRSA and VISA prevalence/incidence of 21.7% [5 studies, 95%CI, 0.217 (0.173–0.261), $I^2 = 83.23\%$], 30.5% [8 studies, 95%CI, 0.305 (0.137–0.473), $I^2 = 98.70\%$], 3.1% [8 studies, 95%CI, 0.031 (0.004–0.059), $I^2 = 60.23\%$] and 9.0% [1 study, 95%CI, 0.090 (-0.009–0.190), $I^2 = 0\%$] respectively. The two-study summary prevalence of MRSA in the USA, UK and Russia was 15% [2 studies, 95%CI, 0.150 (-0.046–0.346), $I^2 = 96.40\%$].

In the national context, the prevalence of *S. aureus* in Iran, MRSA and VISA was 18.1, 44.7% and 9.0% [1 study, 95%CI, 0.090 (-0.009–0.190), $I^2 = 87.02\%$] (Figure 4). Prevalence rates of 22.5% [3 study, 95%CI, 0.225 (0.138–0.311), $I^2 = 87.02\%$], 39.1% [2 studies, 95%CI, 0.391 (0.225–0.557), $I^2 = 63.32\%$] and 29.8% [2 studies, 95%CI, 0.298 (-0.091–0.688), $I^2 = 88.90\%$] pooled for *S. aureus*, MRSA and CoNS respectively in Ethiopia. In China, *S. aureus* and MRSA prevalence rates were 21.0% [1 study, 95%CI, 0.210 (0.180–0.240), $I^2 = 0\%$] and 9.5% [2 study, 95%CI, 0.095(-0.009–0.199), $I^2 = 94.60\%$].

3.6. Categories of burden

Categories of burden in human, animal, food sources and environment are presented in Figure 4 jointly contribute to disease burden globally (Figure 4).

In humans, 24.9% [16 studies, 95%CI, 0.249 (0.215–0.282), $I^2 = 92.17\%$] of global prevalence was attributed to *S. aureus*, and prevalence 15.0% [1 study, 95%CI, 0.150 (0.120–0.180), $I^2 = 0\%$] from the environmental sources. A burden of 24.1% [3 studies, 95%CI, 0.241(0.129–0.353), $I^2 = 96.11\%$] was attributed to food sources.

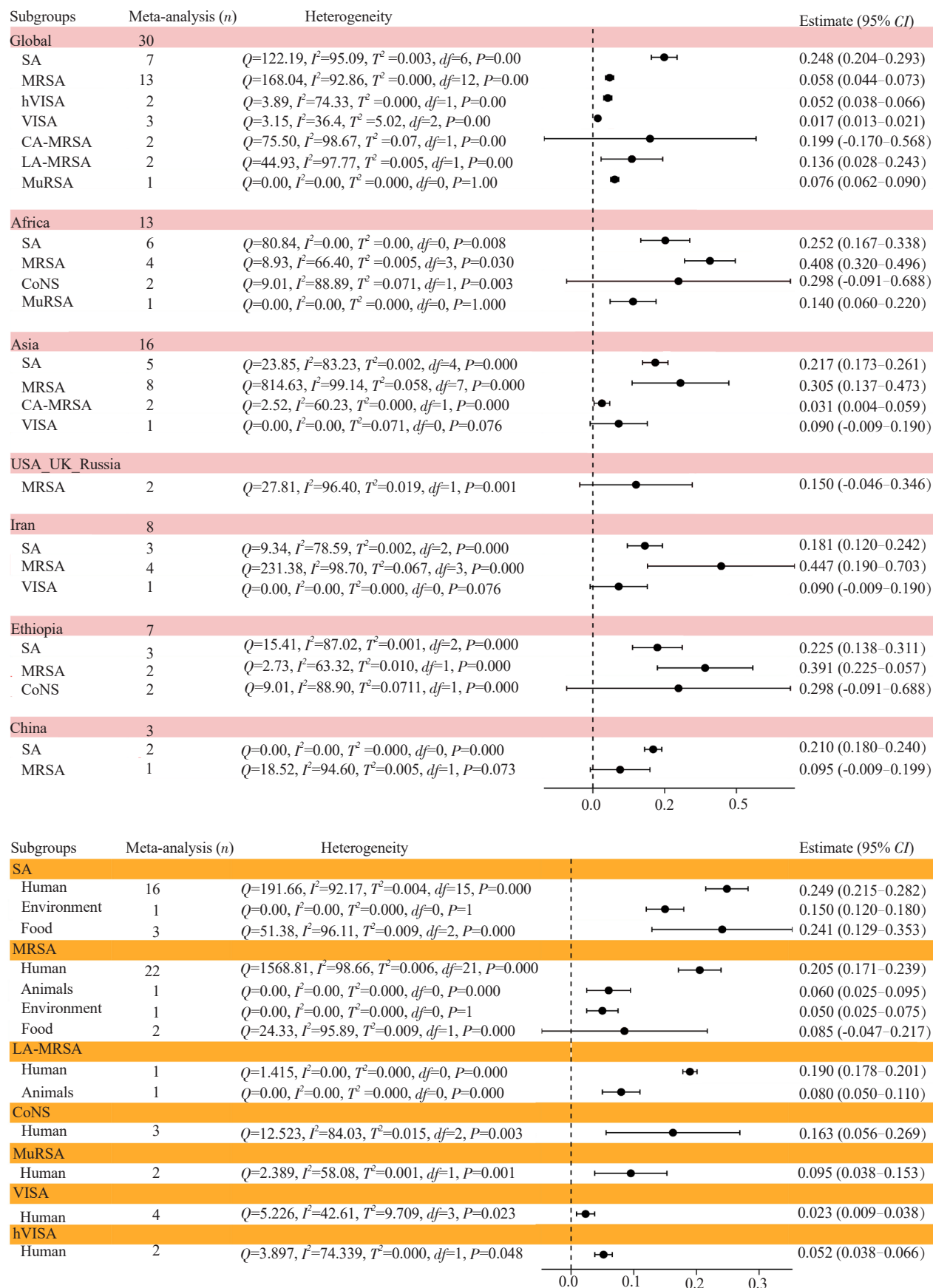


Figure 4. Subgroup analysis of point prevalence of *Staphylococcus (S.) aureus* (SA), Methicillin resistant *S. aureus* (MRSA), Mupirocin-resistant *S. aureus* (mupSA), Vancomycin-resistant *S. aureus* (VRSA), Vancomycin-intermediate *S. aureus* (VISA), Heterogeneous VISA (hVISA).

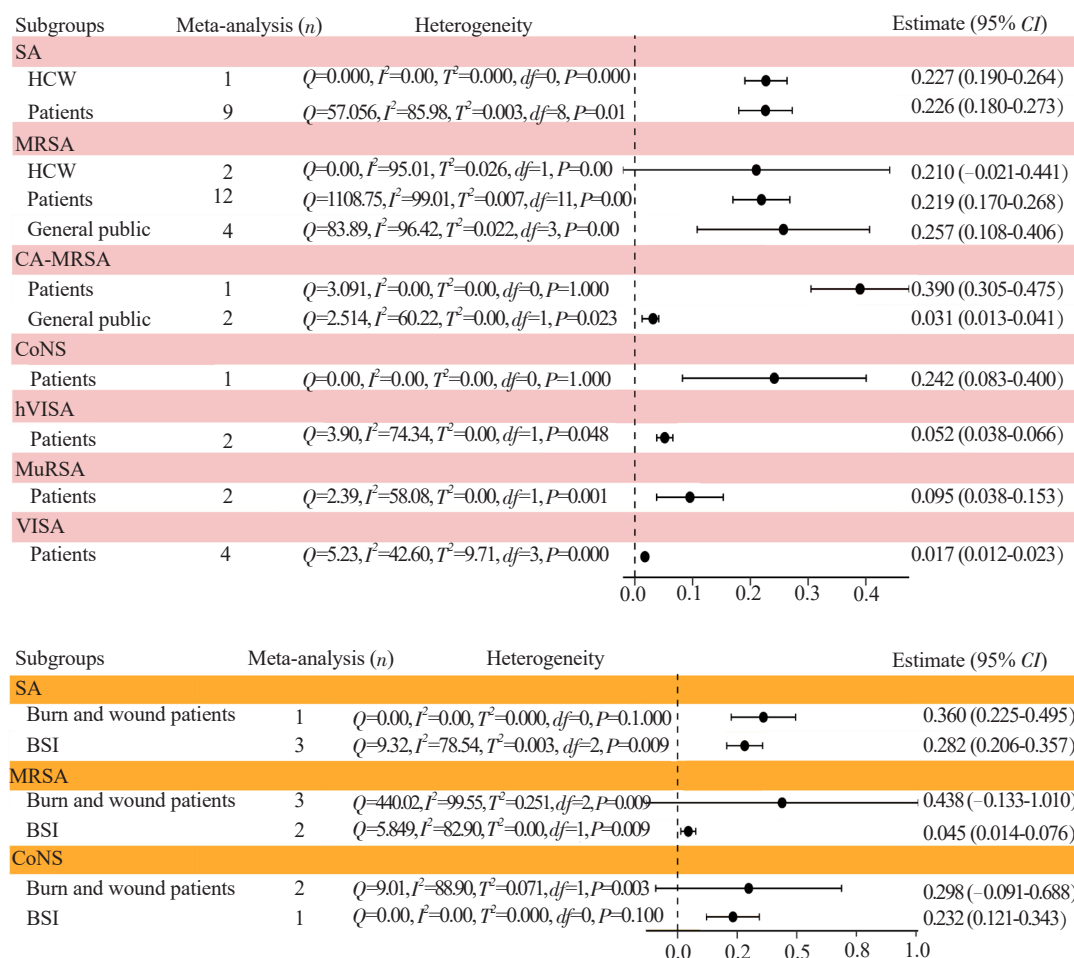


Figure 5. Subgroup analysis of point prevalence of *Staphylococcus (S.) aureus* (SA), Methicillin resistant *Staphylococcus aureus* (MRSA), Mupirocin-resistant *S. aureus* (mupSA), Vancomycin-resistant *S. aureus* (VRSA), Vancomycin-intermediate *S. aureus* (VISA), and Heterogeneous VISA (hVISA) [A] Patients, Healthcare workers(HCW) and general public (B) Burn and wound, and blood stream infected patients(BSI)].

The burden of MRSA in humans, animals, environment and food sources were reported as 20.5% [22 studies, 95%CI, 0.205(0.171–0.239), $I^2 = 98.66\%$], 6.0% [1 study, 95%CI, 0.06(0.025–0.095), $I^2 = 0\%$], 5.0% [1 study, 95%CI, 0.050(0.025–0.075), $I^2 = 0\%$] and 8.5% [2 studies, 95%CI, 0.085(-0.047–0.217), $I^2 = 95.89\%$] respectively. The burden of LA-MRSA, MuRSA, VISA and hVISA in humans were reported to be 19.0% [1 study, 95%CI, 0.190(-0.178–0.201), $I^2 = 0\%$], 9.5% [2 studies, 95%CI, 0.095(0.038–0.153), $I^2 = 50.08\%$], 2.3% [4 studies, 95%CI, 0.023(0.009–0.038), $I^2 = 42.61\%$] and 5.2% [2 studies, 95%CI, 0.052(0.038–0.066), $I^2 = 74.34\%$]. One study reported LA-MRSA in animals to be 8.0% [95%CI, 0.080(0.050–0.110), $I^2 = 0\%$].

3.7. Pathogen prevalence in patients, healthcare workers (HCW) and the general public

Figure 3 reports pooled pathogen prevalence associated with

patients, HCW and the general public. The proportions of *S. aureus* among HCW and patients are 22.7% [1 study, 95%CI, 0.227(0.190–0.264), $I^2 = 0\%$] and 22.6% [9 studies, 95%CI, 0.226(0.180–0.273), $I^2 = 85.98\%$] respectively. Pooled prevalence of MRSA was 21.0% [2 studies, 95%CI, 0.210(-0.021–0.441), $I^2 = 95.01\%$] for HCW; 21.9% [12 studies, 95%CI, 0.219(0.170–0.268), $I^2 = 99.01\%$] for patients; 25.7% [4 studies, 95%CI, 0.257(0.180–0.406), $I^2 = 96.42\%$] for the general public (Figure 5).

For CA-MRSA, summary metanalysis pooled prevalence rates of 39.0% [1 study, 95%CI, 0.390(0.305–0.475), $I^2 = 0\%$] and 3.1% [2 studies, 95%CI, 0.031(0.013–0.041), $I^2 = 66.22\%$] for patients and general public. Outcomes of patient's summary analysis reported prevalence rates of 24.2% [1 study, 95%CI, 0.242(0.083–0.400), $I^2 = 0\%$], 1.7% [4 studies, 95%CI, 0.017(0.012–0.023), $I^2 = 42.60\%$], 5.2% [2 study, 95%CI, 0.052(0.038–0.066), $I^2 = 74.34\%$] and 9.5% [2 study, 95%CI, 0.095 (0.038–0.153), $I^2 = 58.08\%$] for CoNS, VISA, hVISA and MuRSA respectively.

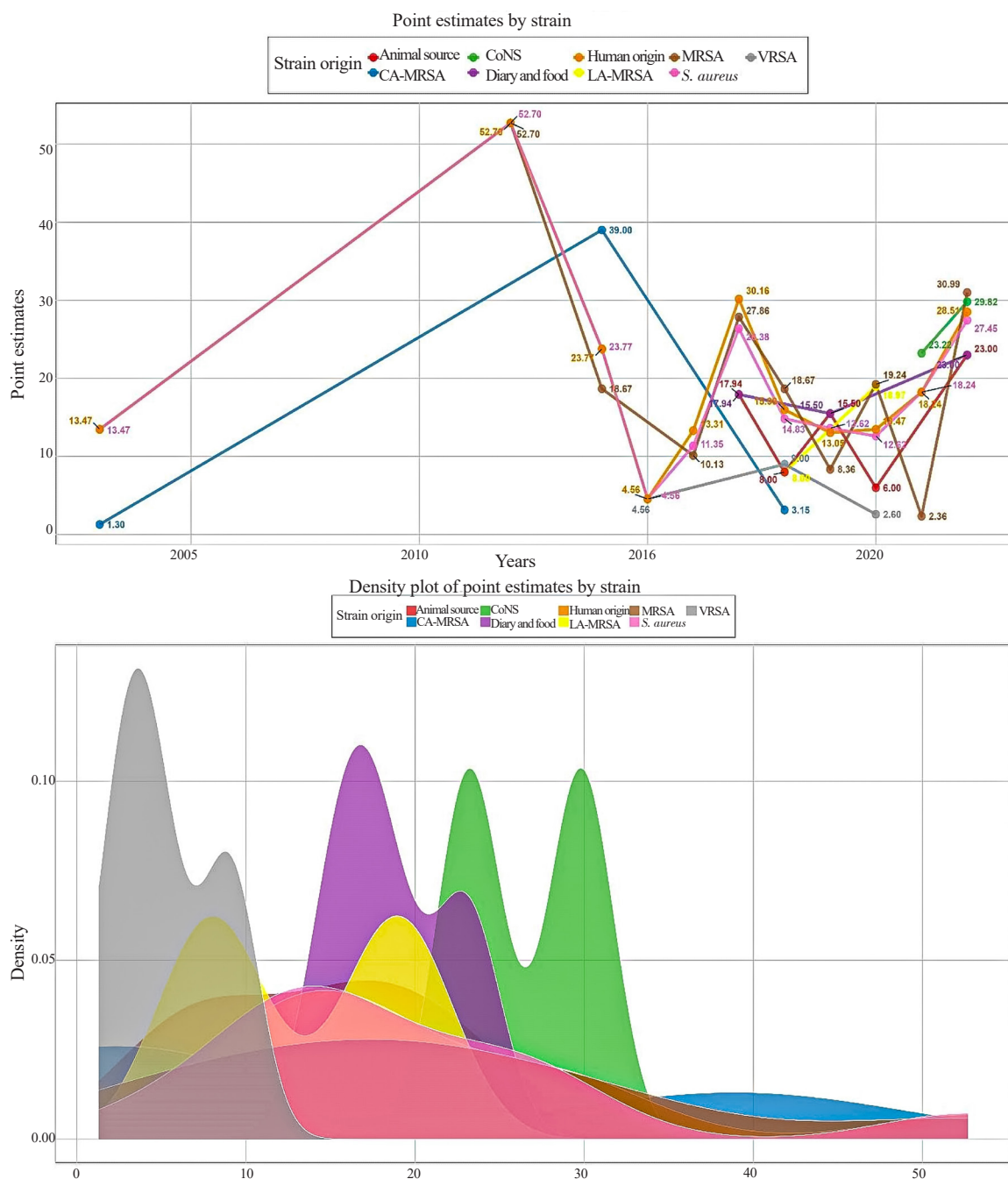


Figure 6. Temporal and density plot of point estimates.

3.8. Prevalence among burn and wound patients, and blood stream infected patients.

The prevalence of *S. aureus* among burn and wound patients was 36.0% [1 study, 95%CI, 0.360(0.225–0.495), $I^2 = 0\%$] while a rate of 28.2% [3 studies, 95%CI, 0.282(0.206–0.357), $I^2 = 78.54\%$] was reported among patients with blood stream infection (BSI)(Figure 5).

In terms of MRSA, a summary prevalence of 43.8% [3 studies, 95%CI, 0.438(-0.133–1.010), $I^2 = 99.5\%$] and 4.5% [2 studies, 95%CI, 0.045(0.014–0.076), $I^2 = 82.90\%$] was reported for burn and wound patients, and BSI patients.

For CoNS, burn and wound patients had a prevalence rate of 29.8% [2 studies, 95%CI, 0.298(-0.091–0.688), $I^2 = 88.90\%$] whereas BSI patients had a prevalence of 23.2% [1 study, 95%CI, 0.232(-0.121–0.343), $I^2 = 0\%$].

3.9. Temporal trends

CAMRSA notably increased from 1.3% (2003) to 39.0% (2014). CoNS ascended from 23.2% (2021) to 29.8% (2022). VRSA peaked at 9.0% (2018), declining to 2.6% (2020).

LAMRSA significantly increased to 18.97% (2020). MRSA

Table 1. Characteristics of included studies.

S/N	Authors	Journals	Range	Primary studies(n)	Protocol	Quality assessment	Software
P1	Shankar <i>et al.</i> 2020	International Journal of Infectious Diseases	2004-2018	19	PRISMA/ MOOSE	NR	Stata v12
P2	Chelkeba <i>et al.</i> 2022a	Journal of Global Antimicrobial Resistance	2008-2019	39	PRISMA	JB	Stata v14
P3	Chelkeba <i>et al.</i> 2022b	Journal of Global Antimicrobial Resistance	2008-2020	28	PRISMA	JB	Stata v14
P4	Chelkeba <i>et al.</i> 2022c	Journal of Global Antimicrobial Resistance	2008-2021	16	PRISMA	JB	Stata v14
P5	Chelkeba <i>et al.</i> 2022d	Journal of Global Antimicrobial Resistance	2008-2022	9	PRISMA	JB	Stata v14
P6	Baseri <i>et al.</i> 2018	Journal of Global Antimicrobial Resistance	2006-2017	40	PRISMA	NR	Stata v14
P7	Ribeiro <i>et al.</i> 2018	Journal of Food Protection	2003-2017	51	PRISMA	NR	MetaXL v1.0
P8	Zeilellw <i>et al.</i> 2021a	BioMed Research International	2009-2018	27	PRISMA	NOS	NR
P9	Zeilellw <i>et al.</i> 2021b	BioMed Research International	2013-2018	25	PRISMA	NOS	NR
P10	Wong <i>et al.</i> 2018a	Clinical Epidemiology	2000-2016	152	PRISMA	NOS	OpenMeta Analyst
P11	Wong <i>et al.</i> 2018b	Clinical Epidemiology	2000-2016	152	PRISMA	NOS	OpenMeta Analyst
P12	Emaneini <i>et al.</i> 2017a	Rev Soc Bras Med Trop	2003-2015	22	PRISMA	JB	CMA(V2.2)
P13	Emaneini <i>et al.</i> 2017b	Rev Soc Bras Med Trop	2003-2015	22	PRISMA	JB	CMA(V2.2)
P14	Emaneini <i>et al.</i> 2017	Journal of Global Antimicrobial Resistance	2006-2015	13	PRISMA	JB	CMA(V2.2)
P15	Karanika <i>et al.</i> 2016	Clinical Infectious Diseases	1996-2012	15	PRISMA/ MOOSE	NOS	Stata(v13)
P16	Wu <i>et al.</i> 2019	PLoS ONE	2005-2018	37	PRISMA/ MOOSE	EMB	Stata v12
P17	Wu <i>et al.</i> 2019	PLoS ONE	2005-2018	37	PRISMA/ MOOSE	EMB	Stata v12
P18	Gagnaire <i>et al.</i> 2017	Expert Review of Anti-infective Therapy	2004-2016	18	PRISMA	NR	MedCalc v17.6
P19	Gagnaire <i>et al.</i> 2017b	Expert Review of Anti-infective Therapy	2004-2016	17	PRISMA	NR	MedCalc v17.6
P20	Adeiza <i>et al.</i> 2020	GMS Hygiene and Infection Control	2020-2020	18	PRISMA	JB	CMA(V3.3)
P21	Adeiza <i>et al.</i> 2020b	GMS Hygiene and Infection Control	2020-2020	5	PRISMA	JB	CMA (V3.3)
P22	Emran Askari <i>et al.</i> 2012	Iranian Journal of Basic Medical Sciences	2004-2012	47	NR	NR	MetaAnalyst V3.1 and CMA (V2.0)
P23	Santaniello <i>et al.</i> 2020	Int. J. Environ. Res. Public Health (MDPI)	2002-2019	16	PRISMA	NR	R software
P24	Kalligeros <i>et al.</i> 2019[45]	Burns	1998-2018	16	PRISMA	NOS	Stata v15
P25	Memariani <i>et al.</i> 2019	Reviews in Medical Microbiology	2011-2018	14	PRISMA	NOS	MedCalc v18.9
P26	Awulachew EW <i>et al.</i> 2020	Journal of Bacteriology and Parasitology	2000-2020	60	PRISMA	CoCoPop	R software
P27	Ou <i>et al.</i> 2017	Critical Reviews in Food Science and Nutrition	2000-2016	72	PRISMA	STROBE	Stata v.13
P28	Ou <i>et al.</i> 2017b	Critical Reviews in Food Science and Nutrition	2000-2016	22	PRISMA	STROBE	Stata v.13
P29	Chelkeba <i>et al.</i> 2022ii	Archives of Gynecology and Obstetrics	2014-2020	18	PRISMA	JB	Stata v14
P30	Stacey <i>et al.</i> 2019	Acta Diabetologica	2002-2018	23	PRISMA	JB	MedCalc
P31	Eshetie <i>et al.</i> 2016	BMC Infectious Diseases	2007-2015	20	NR	NR	CMA (V3.3)
P32	Shittu <i>et al.</i> 2018	Antimicrobial Resistance and Infection Control	2006-2015	11	PRISMA	NR	Stats Direct
P33	Nikmanesh <i>et al.</i> 2022[52]	Journal of Health Population and Nutrition	1999-2016	12	PRISMA	CASP	CMA (V3.3)
P34	Sabbagh <i>et al.</i> 2018[53]	American Journal of Infection Control	1997-2017	69	PRISMA	NOS	Stata v.13
P35	Adeiza <i>et al.</i> 2018	Nigerian Journal of Microbiology	2003-2018	41	PRISMA	JB	CMA (V3.3)
P36	Adeiza <i>et al.</i> 2018b	Nigerian Journal of Microbiology	2003-2018	24	PRISMA	JB	CMA (V3.3)
P37	Dehkordi <i>et al.</i> 2019	Ann Ig	2008-2016	33	PRISMA	JB	CMA (V2.2)
P38	Dehkordi <i>et al.</i> 2019b	Ann Ig	2008-2016	11	PRISMA	JB	CMA (V2.2)
P39	Shipeng Li <i>et al.</i> 2014	Indian Journal of Pathology and Microbiology	1998-2013	33	PRISMA	NR	REVMAN V5.0
P40	Girmay 2022	Journal of Biotechnology & Bioinformatics Research	2011-2020	29	NR	NR	Stata v16
P41	Shariati <i>et al.</i> 2020a	Nature SCIENTIFIC REPORTS	1997-2019	23	NR	JB	Stata v14
P42	Shariati <i>et al.</i> 2020b	Nature SCIENTIFIC REPORTS	1997-2019	50	NR	JB	Stata v14
P43	Shariati <i>et al.</i> 2020c	Nature SCIENTIFIC REPORTS	1997-2019	82	NR	JB	Stata v14
P44	D_Lin <i>et al.</i> 2016a	American Journal of Infection Control	2002-2014	32	PRISMA	STROBE	Stata 13
P45	D_Lin <i>et al.</i> 2016b	American Journal of Infection Control	2002-2014	28	PRISMA	STROBE	Stata 13
P46	Cassandra <i>et al.</i> 2003	Clinical Infectious Diseases	1998-2001	10	NR	NR	Epi Info 2000
P47	Cassandra <i>et al.</i> 2003b	Clinical Infectious Diseases	1998-2001	10	NR	NR	Epi Info 2000
P48	Chen <i>et al.</i> 2020[7]	Occup Environ Med	2007-2018	37	PRISMA	NOS	CMA (V2.2)
P49	Uduak Okomo <i>et al.</i> 2019a	The lancet_infection	2008-2018	82	NR	STROBE	Stata v.13
P50	Uduak Okomo <i>et al.</i> 2019b	The lancet_infection	2008-2018	82	NR	STROBE	Stata v.13
P51	Lin J <i>et al.</i> 2016	PLoS ONE	2001-2014	13	PRISMA/ MOOSE	EMB	Stata v.13
P52	Oskouie <i>et al.</i> 2020a	Jundishapur J Microbiol	1994-2019	15	PRISMA	JB	Stata V16
P53	Oskouie <i>et al.</i> 2020b	Jundishapur J Microbiol	2008-2019	14	PRISMA	JB	Stata V16
P54	Zhouqi Li <i>et al.</i> 2021a	BMC Infectious Diseases	2003-2018	24	PRISMA	NOS	Stata V16
P55	Zhouqi Li <i>et al.</i> 2021b	BMC Infectious Diseases	2003-2018	24	PRISMA	NOS	Stata V16
P56	Patil <i>et al.</i> 2022	Oman Medical Journal	2015-2019	98	PRISMA	FRS	R software
P57	Zhang <i>et al.</i> 2015a	PLoS ONE	1997-2014	76	PRISMA	NR	Stata v12
P58	Zhang <i>et al.</i> 2015b	PLoS ONE	1997-2014	38	PRISMA	NR	Stata v12
P59	Zigmond <i>et al.</i> 2014	International Congress on Infectious Diseases	2013 only	114	NR	NR	SAS 9.3
P60	Giri <i>et al.</i> 2022	American Journal of Infection Control	2001-2021	32	PRISMA	JB	R software
P61	Ioannis <i>et al.</i> 2014	Journal of American Society of Nephrology	1978-2011	38	PRISMA	NOS	Stata v11
P62	Dadashi <i>et al.</i> 2019a	Journal of Global Antimicrobial Resistance	2004-2015	30	PRISMA	JB	Stata v14
P63	Dadashi <i>et al.</i> 2019b	Journal of Global Antimicrobial Resistance	1999-2016	63	PRISMA	JB	Stata v14
P64	Ziakas <i>et al.</i> 2014	Critical Care Medicine journal	1991-2009	51	PRISMA	QUADAS	Stata v11

Note: Newcastle-Ottawa Scale (NOS), Joanna Briggs Institute (JBI), Strengthening the Reporting of Observational studies in Epidemiology (STROBE), Critical Appraisal Skills Programme (CASP), Evidence-Based Mental Health (EMB), Condition Context Population (CoCoPop), Fixed Rating Scale (FRS), Quality Assessment Tool for Diagnostic Accuracy Studies (QUADAS), Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA), Meta-analyses of Observational Studies in Epidemiology (MOOSE), Not Reported (NR). Bibliography of included meta-analyses are documented in the supplementary reference file.

Table 2. Search methodology used by each included study.

S/N	Authors	Country	S	P/M	SD	WoS	G	E	CL	CI	CN	AJ	O	L
P1	Shankar <i>et al.</i> 2020	USA_Other	×	√	×	×	×	√	×	×	×	×	×	√
P2	Chelkeba <i>et al.</i> 2022a	Ethiopia	×	√	√	×	√	√	×	×	×	×	√	√
P3	Chelkeba <i>et al.</i> 2022b	Ethiopia	×	√	√	×	√	√	×	×	×	×	√	√
P4	Chelkeba <i>et al.</i> 2022c	Ethiopia	×	√	√	×	√	√	×	×	×	×	√	√
P5	Chelkeba <i>et al.</i> 2022d	Ethiopia	×	√	√	×	√	√	×	×	×	×	√	√
P6	Baseri <i>et al.</i> 2018	Iran	√	√	×	×	×	×	×	×	×	×	×	√
P7	Ribeiro <i>et al.</i> 2018	Africa_Americas_Asia_Europe	×	√	×	×	×	×	×	×	×	×	√	√
P8	Zeilellw <i>et al.</i> 2021a	Developing Countries	×	√	√	√	√	×	√	√	×	√	√	√
P9	Zeilellw <i>et al.</i> 2021b	Developing Countries	×	√	√	√	√	×	√	√	×	√	√	√
P10	Wong <i>et al.</i> 2018a	Asia-Pacific region	×	√	×	×	×	√	×	×	×	×	√	√
P11	Wong <i>et al.</i> 2018b	Asia-Pacific region	×	√	×	×	×	√	×	×	×	×	√	√
P12	Emaneini <i>et al.</i> 2017a	Iran	×	√	×	√	×	√	×	×	×	×	√	√
P13	Emaneini <i>et al.</i> 2017b	Iran	×	√	×	√	×	√	×	×	×	×	√	√
P14	Emaneini <i>et al.</i> 2017	Iran	×	√	×	√	×	√	×	×	×	×	√	√
P15	Karanika <i>et al.</i> 2016	USA_UK_Russia	×	×	×	×	×	√	×	×	×	×	√	√
P16	Wu <i>et al.</i> 2019a	China	×	√	×	×	×	×	×	×	×	×	√	√
P17	Wu <i>et al.</i> 2019b	China	×	√	×	×	×	×	×	×	×	×	√	√
P18	Gagnaire <i>et al.</i> 2017	Africa_Americas_Asia_Europe	×	√	√	√	×	×	×	×	×	×	√	√
P19	Gagnaire <i>et al.</i> 2017b	Africa_Americas_Asia_Europe	×	√	√	√	×	×	×	×	×	×	√	√
P20	Adeiza <i>et al.</i> 2020	Africa_Americas_Asia_Europe	√	√	×	√	√	×	×	×	×	×	×	√
P21	Adeiza <i>et al.</i> 2020b	Africa_Americas_Asia_Europe	√	√	×	√	√	×	×	×	×	×	×	√
P22	Emran Askari <i>et al.</i> 2012	Iran	×	√	×	×	√	×	×	×	×	×	√	√
P23	Santaniello <i>et al.</i> 2020	Africa_Americas_Asia_Europe_Oceania	√	√	×	×	×	×	×	×	×	×	×	√
P24	Kalligeros <i>et al.</i> 2019	Africa_Americas_Asia_Europe	×	√	×	×	×	√	×	×	×	×	×	√
P25	Memariani <i>et al.</i> 2019	Iran	×	√	×	×	√	×	×	×	×	×	×	√
P26	Awulachew EW <i>et al.</i> 2020	Africa_Americas_Asia_Europe	√	√	×	×	√	√	√	×	×	×	√	√
P27	Ou <i>et al.</i> 2017a	Multicountry	×	√	×	√	×	√	×	×	×	×	×	√
P28	Ou <i>et al.</i> 2017b	Multicountry	×	√	×	√	×	√	×	×	×	×	×	√
P29	Chelkeba <i>et al.</i> 2022ii	Ethiopia	×	√	×	√	√	×	×	×	×	×	×	√
P30	Stacey <i>et al.</i> 2019	Africa_Americas_Asia_Europe	×	√	×	×	×	√	×	×	×	×	×	√
P31	Eshetie <i>et al.</i> 2016	Ethiopia	×	√	×	×	√	×	×	×	×	×	√	√
P32	Shittu <i>et al.</i> 2018	Africa	√	√	×	√	√	×	×	×	×	×	√	√
P33	Nikmanesh <i>et al.</i> 2022	Middle East	√	√	×	√	×	×	×	×	×	×	×	√
P34	Sabbagh <i>et al.</i> 2018	Africa_Americas_Asia_Europe	√	√	×	√	×	√	×	×	×	×	×	√
P35	Adeiza <i>et al.</i> 2018	Nigeria	×	√	×	×	√	×	×	×	×	√	×	√
P36	Adeiza <i>et al.</i> 2018b	Nigeria	×	√	×	×	√	×	×	×	×	√	×	√
P37	Dehkordi <i>et al.</i> 2019	Iran	√	√	×	×	√	×	×	×	×	√	×	√
P38	Dehkordi <i>et al.</i> 2019b	Iran	√	√	×	×	√	×	×	×	×	√	×	√
P39	Shipeng Li <i>et al.</i> 2014	Asia_Europe_North America	×	√	×	×	×	×	×	×	×	×	×	√
P40	Girmay 2022	Ethiopia	×	√	×	×	√	×	×	×	×	×	×	√
P41	Shariati <i>et al.</i> 2020a	Africa_Americas_Asia_Europe_Oceania	×	√	√	√	×	√	×	×	×	×	×	×
P42	Shariati <i>et al.</i> 2020b	Africa_Americas_Asia_Europe_Oceania	×	√	√	√	×	√	×	×	×	×	×	×
P43	Shariati <i>et al.</i> 2020c	Africa_Americas_Asia_Europe_Oceania	×	√	√	√	×	√	×	×	×	×	×	×
P44	D_Lin <i>et al.</i> 2016a	Africa_Americas_Asia_Europe	√	√	√	×	×	×	×	×	×	×	√	√
P45	D_Lin <i>et al.</i> 2016b	Africa_Americas_Asia_Europe	√	√	√	×	×	×	×	×	×	×	√	√
P46	Cassandra <i>et al.</i> 2003a	Americas_Asia_Europe	×	√	×	×	×	×	×	×	×	×	×	√
P47	Cassandra <i>et al.</i> 2003b	Americas_Asia_Europe	×	√	×	×	×	×	×	×	×	×	×	√
P48	Chen <i>et al.</i> 2020	Americas_Asia_Europe	×	√	×	×	√	×	×	×	×	×	×	√
P49	Uduak Okomo <i>et al.</i> 2019a	Sub-Saharan Africa	×	√	×	×	×	√	×	×	×	×	√	√
P50	Uduak Okomo <i>et al.</i> 2019b	Sub-Saharan Africa	×	√	×	×	×	√	×	×	×	×	√	√
P51	Lin J <i>et al.</i> 2016	China	×	×	×	×	×	×	×	×	×	√	×	√
P52	Oskouie <i>et al.</i> 2020a	Africa_Americas_Asia_Europe_Oceania	√	√	×	√	×	√	×	×	√	×	√	√
P53	Oskouie <i>et al.</i> 2020b	Africa_Americas_Asia_Europe_Oceania	√	√	×	√	×	√	×	×	√	×	√	√
P54	Zhouqi Li <i>et al.</i> 2021a	Africa_Americas_Asia_Europe_Oceania	×	√	×	×	×	√	×	×	×	×	√	√
P55	Zhouqi Li <i>et al.</i> 2021b	Africa_Americas_Asia_Europe_Oceania	×	√	×	×	×	√	×	×	×	×	√	√
P56	Patil <i>et al.</i> 2022	India	×	√	×	×	√	×	×	×	×	×	√	√
P57	Zhang <i>et al.</i> 2015a	Americas_Asia_Europe_Oceania	×	√	×	×	×	√	×	×	×	×	×	√
P58	Zhang <i>et al.</i> 2015b	Americas_Asia_Europe_Oceania	×	√	×	×	×	√	×	×	×	×	×	√
P59	Zigmond <i>et al.</i> 2014	Africa	×	√	×	×	×	×	×	×	×	×	×	√
P60	Giri <i>et al.</i> 2022	South Asia	×	√	×	×	√	×	√	×	×	×	√	√
P61	Ioannis <i>et al.</i> 2014	Africa_Americas_Asia_Europe	×	√	×	×	×	√	×	×	×	×	×	√
P62	Dadashi <i>et al.</i> 2019a	Africa_Americas_Asia_Europe_Oceania	×	√	×	√	×	√	×	×	×	×	×	√
P63	Dadashi <i>et al.</i> 2019b	Africa_Americas_Asia_Europe_Oceania	×	√	×	√	×	√	×	×	×	×	×	√
P64	Ziakas <i>et al.</i> 2014	Americas_Asia_Europe_Oceania	×	√	×	×	×	√	×	×	×	×	×	√

Note: Scopus(S), Medline /PubMed (M/P), Science Direct (SD), Web of Science (WoS), Google scholar(G), Embase (E), Cochrane Library (CL) , CINAHL(CI), CNKI(CN), AJOL(AJ), Other Databases (O), and Language Limitations (L).

Table 3. Pooled effects of each included study.

S/N	Authors	Population	(n)	organism	Meta-analysis				
					Total	Fraction	effects	lower	upper
P1	Shankar <i>et al.</i> 2020	Household contacts	19	MRSA	NR	NR	0.25	0.2	0.3
P2	Chelkeba <i>et al.</i> 2022a	Wound infection	39	SA	5647	2033	0.36	0.23	0.5
P3	Chelkeba <i>et al.</i> 2022b	Wound infection	28	CoNS	4243	438	0.12	0.09	0.14
P4	Chelkeba <i>et al.</i> 2022c	Wound infection	16	MRSA	2033	1017	0.5	0.31	0.69
P5	Chelkeba <i>et al.</i> 2022d	Wound infection	9	MRSA-CoNS	438	228	0.52	0.26	0.78
P6	Baseri <i>et al.</i> 2018*	clinical specimens	40	VISA	13690	1213	0.09	0.001	0.02
P7	Ribeiro <i>et al.</i> 2018	Poultry	51	LA-MRSA	15794	1171	0.08	0.05	0.11
P8	Zelellw <i>et al.</i> 2021a	Neonatal Sepsis in children	27	SA	52582	12209	0.2322	0.1837	0.2807
P9	Zelellw <i>et al.</i> 2021b	Neonatal Sepsis in children	25	CoNS	27897	6477	0.2322	0.1215	0.3429
P10	Wong <i>et al.</i> 2018a	General public	152	CA-MRSA	808940	NR	0.021	0.009	0.037
P11	Wong <i>et al.</i> 2018b	General public	152	CA-MRSA	808940	NR	0.05	0.022	0.088
P12	Emaneini <i>et al.</i> 2017a	Iranian HCWs	22	SA	5819	1315	0.227	0.193	0.266
P13	Emaneini <i>et al.</i> 2017b	Iranian HCWs	22	MRSA	1315	419	0.328	0.26	0.404
P14	Emaneini <i>et al.</i> 2017	Burn patients	13	MRSA	1253	957	0.779	0.702	0.84
P15	Karanika <i>et al.</i> 2016	Asymptomatic Athletes	15	MRSA	1495	75	0.05	0.01	0.12
P16	Wu <i>et al.</i> 2019a	Healthy Chinese population	37	SA	50641	10536	0.21	0.18	0.24
P17	Wu <i>et al.</i> 2019b	Healthy Chinese population	37	MRSA	10536	2214	0.15	0.1	0.19
P18	Gagnaire <i>et al.</i> 2017	Patients and children	18	SA	2647	443	0.1674	0.208	0.291
P19	Gagnaire <i>et al.</i> 2017b	Intestinal carriage	17	MRSA	38327	1199	0.03128	0.03	0.033
P20	Adeiza <i>et al.</i> 2020a	COVID_19 infected patients	18	SA	3038	1192	0.256	0.156	0.39
P21	Adeiza <i>et al.</i> 2020b	COVID_19 infected patients	5	MRSA	181	66	0.539	0.245	0.809
P22	Emran Askari <i>et al.</i> 2012	Clinical isolates	47	MRSA	7464	3654	0.527	0.479	0.574
P23	Santaniello <i>et al.</i> 2020*	Dogs	16	MRSA	2228	101	0.06	0.03	0.1
P24	Kalligeros <i>et al.</i> 2019	Burn patients	16	MRSA	12086	NR	0.04	0.03	0.06
P25	Memariani <i>et al.</i> 2019	Hospital Patients	14	SA	31677	4136	0.13057	0.0293	0.28885
P26	Awulachew EW <i>et al.</i> 2020	Healthy People	60	SA	52544	10789	0.22	0.18	0.26
P27	Ou <i>et al.</i> 2017a	Cow milk	72	SA	50671	17228	0.34	0.3	0.38
P28	Ou <i>et al.</i> 2017b	Cow milk	22	MRSA	17228	346	0.02	0.01	0.04
P29	Chelkeba <i>et al.</i> 2022ii	Pregnant women	18	SA	781	131	0.15	0.12	0.18
P30	Stacey <i>et al.</i> 2019	Diabetic patients	23	MRSA	11577	1065	0.092	0.0626	0.1263
P31	Eshetie <i>et al.</i> 2016	Clinical specimens	20	MRSA	2254	704	0.325	0.241	0.409
P32	Shittu <i>et al.</i> 2018	Clinical isolates	11	MupSA	NR	NR	0.14	0.07	0.23
P33	Nikmanesh <i>et al.</i> 2022	Patients with cystic fibrosis	12	SA	1660	734	0.409	0.296	0.531
P34	Sabbagh <i>et al.</i> 2018	HIV patients	69	MRSA	3935	304	0.07	0.05	0.09
P35	Adeiza <i>et al.</i> 2018	General public	41	SA	6460	2579	0.414	0.362	0.469
P36	Adeiza <i>et al.</i> 2018b	General public	24	MRSA	1877	694	0.364	0.277	0.461
P37	Dehkordi <i>et al.</i> 2019	Food resources	33	SA	11261	1738	0.155	0.127	0.189
P38	Dehkordi <i>et al.</i> 2019b	Food resources	11	MRSA	995	149	0.155	0.111	0.214
P39	Shipeng Li <i>et al.</i> 2014	MRSA-infected patients	33	CA-MRSA	50737	19785	0.39	0.308	0.478
P40	Girmay 2022	Beef_milk and milk product	29	SA	4837	1113	0.23	0.19	0.28
P41	Shariati <i>et al.</i> 2020a	Clinical isolates	23	VRSA	5855	NR	0.015	0.01	0.02
P42	Shariati <i>et al.</i> 2020b	Clinical isolates	50	VISA	22277	NR	0.017	0.013	0.02
P43	Shariati <i>et al.</i> 2020c	Clinical isolates	82	hVISA	47721	NR	0.046	0.041	0.051
P44	D_Lin <i>et al.</i> 2016a	Hospital Environmental objects	32	SA	4449	744	0.15	0.98	0.21
P45	D_Lin <i>et al.</i> 2016b	Hospital Environmental objects	28	MRSA	4449	187	0.05	0.027	0.077
P46	Cassandra <i>et al.</i> 2003a	Community members	10	SA	8125	2085	0.2566	0.2457	0.2679
P47	Cassandra <i>et al.</i> 2003b	Community members	10	CA-MRSA	8125	106	0.013	0.0104	0.0153
P48	Chen <i>et al.</i> 2020	Occupational workers and veterinarians	37	LA- MRSA	5714	1084	0.1897	0.1786	0.2013
P49	Uduak Okomo <i>et al.</i> 2019a	Neonatal infections BSI	82	SA	NR	2080	0.25	0.21	0.29
P50	Uduak Okomo <i>et al.</i> 2019b	Neonatal infections Meningitis	82	SA	NR	92	0.12	0.03	0.25
P51	Lin J <i>et al.</i> 2016	Chinese Children	13	MRSA	19477	NR	0.044	0.02.7	0.062
P52	Oskouie <i>et al.</i> 2020a	Medical Students	15	SA	NR	NR	0.28	0.021	0.034
P53	Oskouie <i>et al.</i> 2020b	Medical Students	14	MRSA	NR	NR	0.02	0.01	0.03
P54	Zhouqi Li <i>et al.</i> 2021a	Patients with malignancy BSI	24	SA	10550	3690	0.44	0.32	0.57
P55	Zhouqi Li <i>et al.</i> 2021b	Patients with malignancy BSI	24	MRSA	10550	310	0.03	0.02	0.05
P56	Patil <i>et al.</i> 2022	Community members	98	MRSA	20493	6583	0.37	0.32	0.41
P57	Zhang <i>et al.</i> 2015a	Clinical samples	76	hVISA	NR	99042	0.0605	0.0478	0.0748
P58	Zhang <i>et al.</i> 2015b	Clinical samples	38	VISA	NR	68792	0.0301	0.0162	0.0483
P59	Zigmond <i>et al.</i> 2014	Clinical sample	114	MRSA	NR	26943	0.488	0.404	0.572
P60	Giri <i>et al.</i> 2022	Healthcare workers	32	MRSA	5423	NR	0.0923	0.065	0.01235
P61	Ioannis <i>et al.</i> 2014	Dialysis Patients	38	MRSA	NR	5596	0.062	0.042	0.085
P62	Dadashi <i>et al.</i> 2019a	Patients and healthcare personnel	30	MuRSA	10903	NR	0.076	0.062	0.09
P63	Dadashi <i>et al.</i> 2019b	Patients and healthcare personnel	63	MuMRSA	10524	NR	0.138	0.12	0.156
P64	Ziakas <i>et al.</i> 2014	ICU admission	51	MRSA	63740	NR	0.0703	0.058	0.083

Note: *Staphylococcus (S.) aureus* (SA), Methicillin resistant *S. aureus* (MRSA), Mupirocin-resistant *S. aureus* (mupSA), Vancomycin-resistant *S. aureus* (VRSA), Vancomycin-intermediate *S. aureus* (VISA), Heterogeneous VISA (hVISA).

fluctuated, peaking at 52.70% (2012) and 30.99% (2022). Animal source, Human origin, and Dairy and Food strains varied, with peaks in 2017 and 2022 (Figure 6).

4. Discussion

S. aureus epidemiology and pathotypes have evolved dramatically over time. As a result, various meta-analytic investigations have been carried out to track its occurrence. *S. aureus* is the most common nosocomial pathogen in the world. *S. aureus* infection is associated with a significant morbidity and mortality rate[71]. Because of the significant consequences of this infection, effective preventative efforts are critical. This research appears to be the first systematic review of overlapping meta-analysis to integrate existing evidence on the prevalence of *S. aureus* and its pathotypes to date, based on evidence from 41 meta-analytic investigations.

Although resistance is a typical evolutionary process for microorganisms, it has been further exacerbated by the continual use of antimicrobial medications in treating infections, which has resulted in the formation of resistance among varied strains. Antimicrobial resistance (AMR) is caused by a variety of factors, ranging from a lack of infection prevention to the inappropriate use of antimicrobials by health professionals and patients[72].

A variety of variables contribute to AMR. First, a lack of infection prevention adds to repeated infection, which in turn contributes to the emergence of resistant strains. Second, antibiotic abuse from prescription to patient usage[73]. The third issue could be antibiotic overuse by health practitioners and non-standardized practice. The fourth issue could be unsanitary hospital settings. Another issue that may be a lack of routine antimicrobial susceptibility testing, which leads to empiric therapy. There is a need for creative ways to stop AMR in line with *S. aureus* prevention and containment techniques. Combination therapy and the availability of novel anti-MRSA medicines will be critical in the fight against *S. aureus* AMR[14].

S. aureus becomes resistant to different antibiotics through various ways. These include creating alternative pathways for sulphonamides, producing β -lactamase to counteract β -lactam-sensitive antibiotics, improving the removal of tetracycline, having acetyltransferase for chloramphenicol, reducing the build-up of macrolide antibiotics, making aminoglycoside-modifying enzymes for aminoglycosides, changing the expression of topoisomerase IV and DNA gyrase for fluoroquinolones, and activating the *mec* gene, which alters penicillin binding protein for β -lactam antibiotics. Per our analysis, prevalence rates varied across all moderators analyzed. A recent meta-analysis, not included in this study[74], found that milk samples had an *S. aureus* prevalence rate of 29.1%, which is consistent with the pooled rate in this study, which was reported at

24.1% (12.9%–35.3%) for food sources.

Also, a summary MRSA rate in human samples was reported to be 20.5% in this study, which is comparable to the 14.7%, observed by Hasanpour AH in another meta-analysis of aged care center residents[75]. The implication of high prevalence of MRSA for suspected or verified *S. aureus* infections such as common skin and wound infections and surgical prophylaxis is that there is a need for better alternatives drugs. Alternative drugs needed to treat or prevent *S. aureus* infections are more expensive and, because of their adverse effects, monitoring during treatment is advisable which increases the costs even further.

Several natural and technical factors that are known to cause variation in microbiome outcomes might have influenced our results. First, in some studies the number of samples and surveyed population are not enough. Second, the conditions (such as the specimen types, testing methodologies used and laboratory conditions) are not the same in different studies[76].

Another possible explanation for the above variations could be due to methodological differences (*i.e.* Microbiological isolation and detection techniques), variation in sociodemographic characteristics, economic, and health service utilization, health infrastructure and health policy implementation across different regions[77].

In various urban and national settings, there can be variations in densely populated areas, public health regulations, and the approach to prudent antimicrobial management. The unique characteristics of highly populated cities and countries may contribute to an environment conducive to the spread of microorganisms.

Also, countries and cities with high public hygiene standards and more control of infections are more successful in the control of *S. aureus* transmission. These differences highlight the importance of interpreting the results carefully, taking the methods used into consideration.

One of the problems of combining data from multiple centers is that it can obscure trends that may exist within a given institution or country, because of differences in patient populations and drug-usage patterns.

The diminished occurrence of MRSA in European nations could be attributed to heightened public consciousness regarding MRSA and the implementation of subsequent public health initiatives to manage it. Our research also revealed that healthcare professionals face a risk of carrying MRSA, likely due to their frequent and close interactions with patients in medical settings. Despite the considerable variation in MRSA molecular types across different regions globally, the elevated relative frequency of MRSA emphasizes the importance of clinicians being vigilant in prescribing and utilizing medications both in community and hospital contexts.

There is widespread recognition that numerous prescription recommendations rely on outdated information obtained from small-scale observational studies[77]. Additionally, efforts in

infection control serve as a pivotal framework and strategy to reduce the occurrence and spread of MRSA strains. In contrast to hospital-acquired MRSA, which can be effectively managed through rigorous hand hygiene, antimicrobial stewardship, and barrier precautions, community-acquired MRSA lacks easily identifiable prevention strategies.

CA-MRSA, unlike hospital-acquired MRSA which could be effectively controlled by vigorous hand hygiene, antimicrobial stewardship, and barrier precautions, lacks easily targeted prevention strategies. The likelihood of CA-MRSA strains spreading is higher in densely populated areas, suggesting that continuous monitoring and early intervention could be effective in controlling its spread. This observation may contribute to the observed rate of CA-MRSA in our analysis.

The observed rate of VISA and hVISA in our analysis may indicate a rapid rise and spread of vancomycin resistant *S. aureus* strains associated to more use of vancomycin in hospital settings. The diminished sensitivity to vancomycin is linked to various changes in both observable traits and genetic elements, such as the *vanA* gene[78]. The emergence of selective pressure on Vancomycin is seen as a significant challenge to the already complex treatment of MRSA. This situation underscores the need to incorporate potent new anti-MRSA antimicrobial agents into the national medicine list, along with the implementation of robust antimicrobial stewardship programs. These measures are crucial for preventing and containing antimicrobial resistance in the context of staphylococcal infections[79].

We observed a moderate prevalence of CoNS in this study. The lower frequency of CoNS infections in comparison to *S. aureus* may contribute to reduced exposure to antimicrobials. Nonetheless, CoNS is undergoing a transformation from being commensal staphylococci to becoming invasive pathogens, potentially evolving into resistant strains and acquiring resistance genes from *S. aureus*[80].

MuRSA observed in this study highlights the relatively low prevalence of MuRSA strains. One potential explanation for this is a significant increasing trend among overall *S. aureus* infections and a shift in antibiotic pressures[69]. Although mupirocin as a cornerstone of decolonization regimens is widely used for eradication of *S. aureus* nasal colonization and the control of MRSA transmission in healthcare settings, the emergence of mupirocin resistance among *S. aureus* isolates will result in a decrease in the efficacy of this antibiotic. Control measures as a powerful framework and strategy for reducing the prevalence of MuMRSA strains should also be taken into consideration.

At farm level, differences in flock size, antimicrobial drug use, animal movement or type of housing might be responsible for the observed LA-MRSA rates reported here. Pigs and cattle are considered the main reservoir for the LA-MRSA, and people having professional contact with farm animals or living at industrial farms

are considered to have increased risk for colonization. LA-MRSA incidences vary considerably, depending on the country and patient population in humans[7]. The emergence of LA-MRSA may pose a potential public health hazard that requires continuously monitoring.

The observed temporal trends point to the multifaceted interplay of aspects shaping epidemiological dynamics, the enduring challenge of evolving antimicrobial resistance, and alterations in their clinical implication.

Interpretation of the findings of this meta-analysis requires considering the limitations thereof. The limitations arise from the inherent characteristics of the included individual studies. First, this is *in vitro* antimicrobial resistance testing and its direct translation to clinical effectiveness requires caution. Second, Numerous investigations were conducted in restricted geographical areas, predominantly within prominent urban teaching hospitals specializing in the treatment of patients experiencing advanced, severe, and recurrent infections. Consequently, there is a possibility that the observed resistance levels may have been overemphasized.

5. Conclusions

The study revealed a considerable global prevalence of *S. aureus* at 24.8%, indicative of the prevalent influence of this pathogen. Regional differences were apparent, with Africa facing a particularly high burden of MRSA at 40.8% of *S. aureus*. Temporal trends exposed a dynamic state, such as the noteworthy surge in community-associated MRSA from 1.30% in 2003 to 39.00% in 2014. This implies that regulatory authorities, governments, and hospitals should enable access to newer, safer, and easier treatment options. Furthermore, resistance to newer medications is essentially inevitable in the course of time. As a result, the need for antibiotics with novel targets is evident.

Conflict of interest statement

The authors claim there is no conflict of interest.

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This study receives no extramural funding.

Data availability statement

The data supporting the findings of this study are available from the corresponding author upon request.

Authors' contributions

The work undertaken by Adeiza SS included conceptualization, data curation, formal analysis, investigation, methodology, and writing of the original draft, as well as review and editing. Shittu A, Adeiza SS and Islam MA contributed to methodology, provided resources, managed software, supervised the project, ensured validation, and participated in reviewing and editing the manuscript.

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Review Article

One Health Bulletin

Global, regional, and national burdens: An overlapping meta-analysis on *Staphylococcus aureus* and its drug-resistant strains

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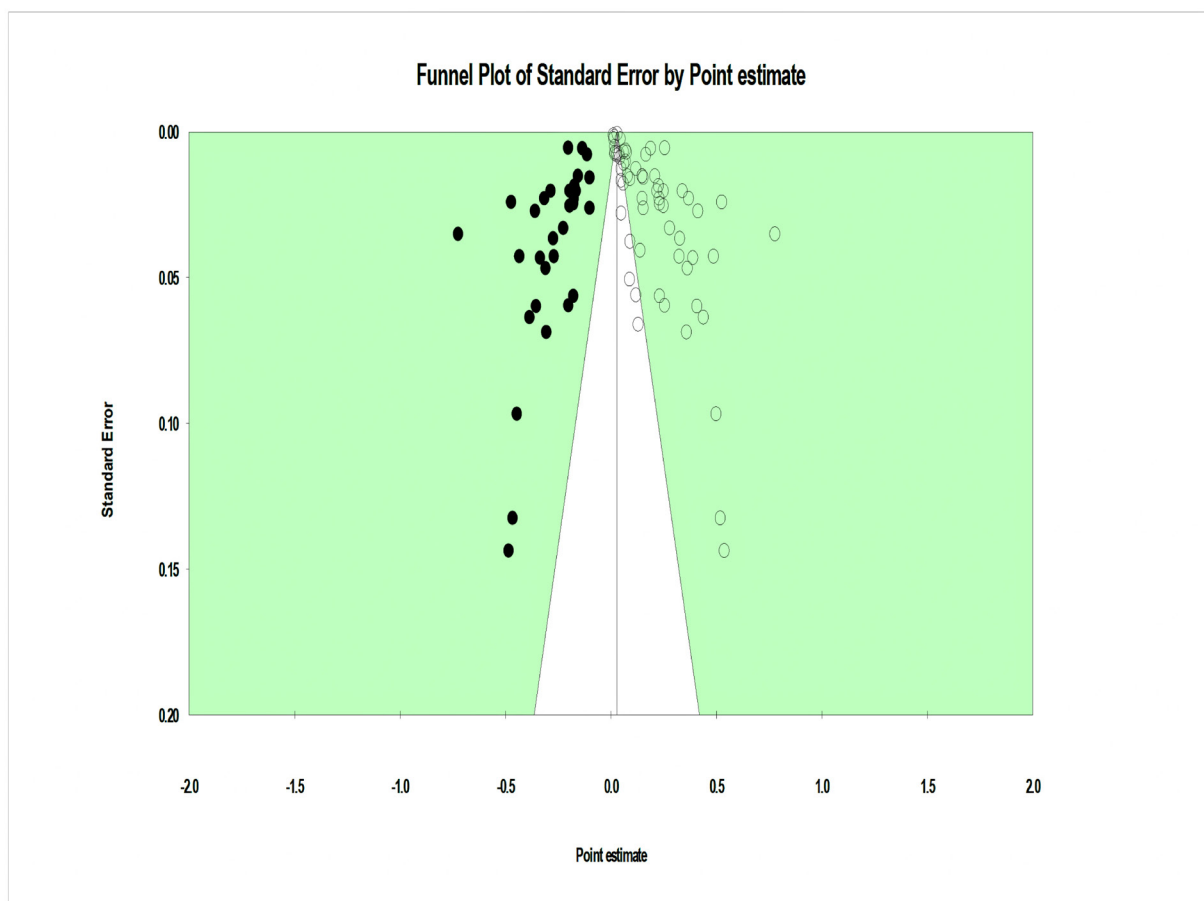
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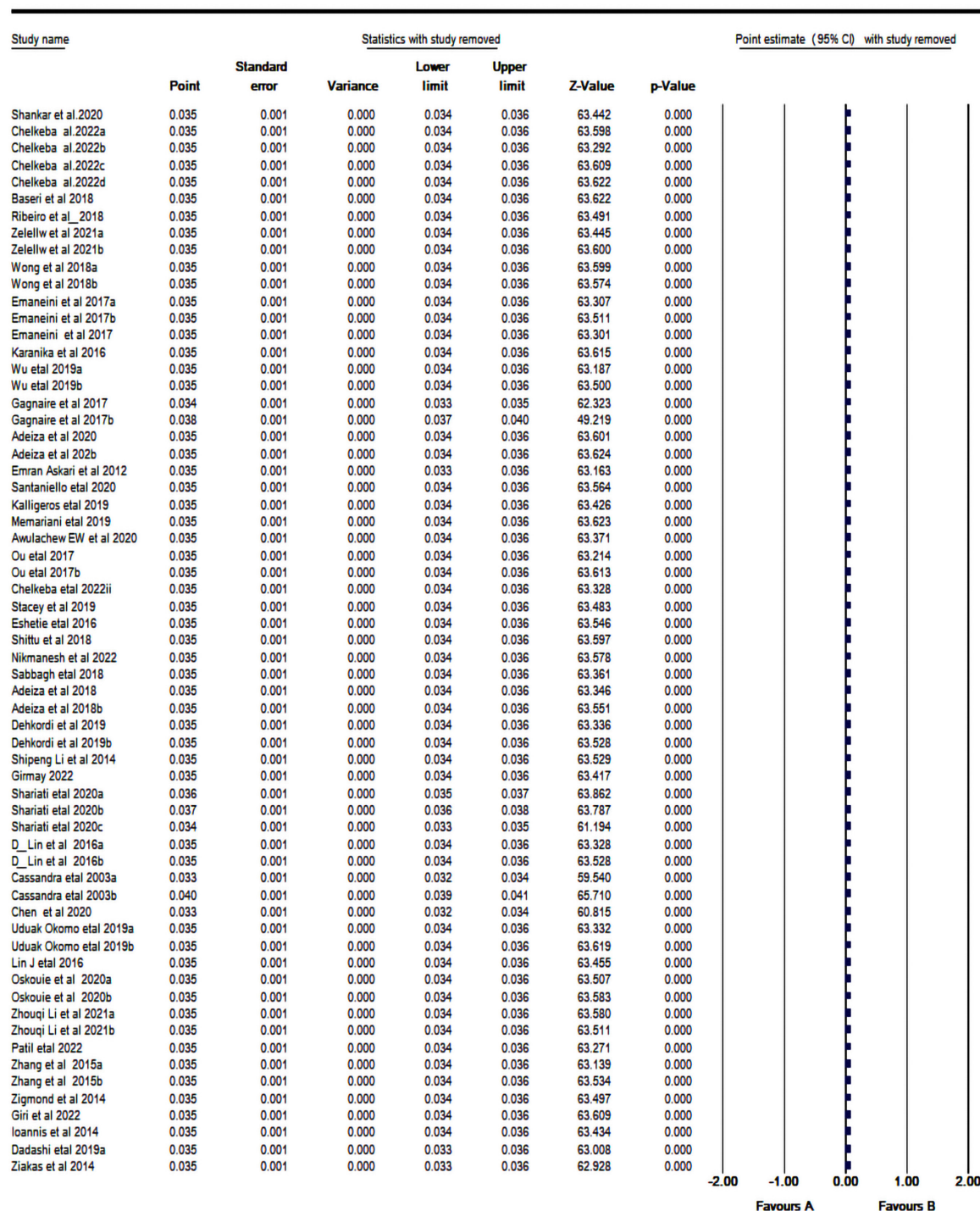
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Supplementary Figures and Table



Supplementary Figure 1. Funnel plot of standard error denoting publication bias.



Sensitivity analysis (one study Removed)

Supplementary Figure 2. Sensitivity analysis.

Supplementary Table 1. AMSTAR Criteria and QUOROM Score

Paper ID	Items/ study	Priori design?	Duplicate study selection and data extraction?	Comprehensive search?	Publication status used as inclusion criterion?	Studies list provided?	Characteristics of studies provided?	Scientific quality assessed and documented?	Scientific quality used conclusions?	Methods used to combine findings, correct?	Publication bias assessed?	Conflict of interest stated?	Total AMSTAR score	QUOROM score
P1	Shankar <i>et al.</i> 2020	0	1	1	1	1	1	1	1	1	1	1	10	15
P2	Chelkeba <i>et al.</i> 2022	0	1	1	0	1	0	1	1	1	1	1	8	13
P3	Baseri <i>et al.</i> 2018	0	1	1	0	1	1	1	1	1	1	1	9	12
P4	Ribeiro <i>et al.</i> 2018	0	1	1	1	1	1	1	1	1	1	1	10	14
P5	Zeilellw <i>et al.</i> 2021	0	1	1	0	1	0	1	1	1	1	1	8	12
P6	Wong <i>et al.</i> 2018	0	1	1	0	1	1	1	1	1	0	1	8	12
P7	Emaneni <i>et al.</i> 2017	0	1	1	1	0	1	1	1	1	1	1	9	14
P8	Karanika <i>et al.</i> 2016	0	1	1	1	1	1	1	0	1	0	1	8	11
P9	Wu <i>et al.</i> 2019	0	1	1	0	0	1	1	1	1	0	1	7	10
P10	Gagnaire <i>et al.</i> 2017	0	1	1	0	1	1	1	1	1	1	1	9	14
P11	Adeiza <i>et al.</i> 2020	0	1	1	0	1	1	1	1	1	1	1	9	13
P12	Emran Askari <i>et al.</i> 2012	0	1	1	0	1	1	1	1	1	0	1	8	12
P13	Santaniello <i>et al.</i> 2020	0	1	1	0	0	1	1	1	1	0	1	7	11
P14	Kalligeros <i>et al.</i> 2019	0	1	1	0	1	1	1	1	1	1	1	9	14
P15	Memariani <i>et al.</i> 2019	0	1	1	1	1	1	1	1	1	1	1	10	15
P16	Awulachew <i>et al.</i> 2020	0	1	1	0	1	1	1	1	1	0	1	8	11
P17	Ou <i>et al.</i> 2017	0	1	1	1	1	1	1	1	1	1	1	10	14
P18	Stacey <i>et al.</i> 2019	0	1	1	0	1	1	1	1	1	1	1	10	15
P19	Eshetie <i>et al.</i> 2016	0	1	1	0	1	1	1	1	1	0	1	8	12
P20	Shittu <i>et al.</i> 2018	0	1	1	1	1	1	1	1	1	1	1	10	15
P21	Nikmanesh <i>et al.</i> 2022	0	1	1	0	1	1	1	1	1	1	1	9	14
P22	Sabbagh <i>et al.</i> 2018	0	1	1	1	1	1	1	1	1	1	1	10	14
P23	Adeiza <i>et al.</i> 2018	0	1	1	0	1	1	1	1	1	1	1	10	13
P24	Dehkordi <i>et al.</i> 2019	0	1	1	1	1	1	1	1	1	0	1	9	12
P25	Shipeng Li <i>et al.</i> 2014	0	1	1	0	0	1	1	1	1	0	1	7	11
P26	Girmay 2022	0	1	1	1	1	1	1	1	1	0	1	9	13
P27	Shariati <i>et al.</i> 2020	0	1	1	0	0	1	1	1	1	1	1	8	13
P28	D_Lin <i>et al.</i> 2016	0	1	1	0	1	1	1	1	1	1	1	9	14
P29	Cassandra <i>et al.</i> 2003	0	1	0	0	1	1	1	1	1	0	1	7	11
P30	Chen <i>et al.</i> 2020	0	1	1	0	1	1	1	1	1	0	1	8	11
P31	Uduak Okomo <i>et al.</i> 2019	0	1	1	0	0	1	1	1	1	0	1	7	11
P32	Lin J <i>et al.</i> 2016	0	1	1	1	1	1	1	1	1	0	1	9	14
P33	Oskouie <i>et al.</i> 2021	0	1	1	1	1	1	1	1	1	1	1	10	14
P34	Zhouqi Li <i>et al.</i> 2021	0	1	1	1	1	1	1	1	1	1	1	10	15
P35	Patil <i>et al.</i> 2022	0	1	1	1	1	1	1	1	1	1	1	10	14
P36	Zhang <i>et al.</i> 2015	0	1	1	0	1	1	1	1	1	0	1	8	13
P37	Zigmond <i>et al.</i> 2014	0	1	1	1	1	1	1	1	1	0	1	9	12
P38	Giri <i>et al.</i> 2022	0	1	1	0	0	1	1	1	1	1	1	8	13
P39	Ioannis <i>et al.</i> 2014	0	1	1	0	1	1	1	1	1	0	1	8	12
P40	Dadashi <i>et al.</i> 2019	0	1	1	0	1	1	1	1	1	0	1	8	12
P41	Ziakas <i>et al.</i> 2014	0	1	1	0	1	1	1	1	1	1	1	9	13

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