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# Global epidemiology of asymptomatic colonisation of methicillin-resistant *Staphylococcus aureus* in the upper respiratory tract of young children: a systematic review and meta-analysis

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## ABSTRACT

**Objective** To estimate the global prevalence of asymptomatic colonisation, and determine the associated risk factors, antibiotic resistance and genotypes of methicillin-resistant *Staphylococcus aureus* (MRSA) in the upper respiratory tract of young children.

**Design** Four bibliometric databases were searched for publications between 2010 and 2022 according to the protocol registered in PROSPERO. Cross-sectional or cohort studies describing the prevalence of asymptomatic colonisation of *S. aureus* and MRSA in young children were included. Data extraction and analysis were carried out by two reviewers independently according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses 2020 statement. Pooled prevalence was estimated using a random effects model.

**Setting and studies** We included studies where children without respiratory tract infection or Staphylococcal infection were recruited from the community, children's institutions (ie, nurseries, kindergartens, daycare centres and preschools) and healthcare centre visits and assessed for asymptomatic colonisation with *S. aureus* and MRSA.

**Main outcome measures** The pooled prevalence of asymptomatic colonisation of *S. aureus* and MRSA of young children globally.

**Results** In this systematic review and meta-analysis of 21416 young children, the pooled global prevalence of asymptomatic *S. aureus* colonisation was 25.1% (95% CI 21.4 to 28.8) and MRSA colonisation was 3.4% (95% CI 2.8 to 4.1). The clones of MRSA strains included healthcare-associated MRSA, community-associated MRSA and livestock-associated MRSA.

**Conclusion** This study provides evidence of increased MRSA colonisation globally among young children, underlining the critical role of asymptomatic carriers in MRSA transmission and the need for control measures.

**PROSPERO registration number** CRD 42022328385.

## WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ The prevalence of methicillin-resistant *Staphylococcus aureus* (MRSA) colonisation and infection was 2.8% (95% CI 1.6 to 4.0) among children (0–5 years old) between 2000 and 2010 reported in a meta-analysis and systematic review. The prevalence of MRSA among young children was higher than among healthy adults (0.8%; 95% CI 0.0 to 17.5), which may be due to their immature immune system and interaction with asymptomatic MRSA carriers.

## WHAT THIS STUDY ADDS

⇒ Asymptomatic MRSA colonisation among young children may have increased in the last decade. Available studies were mostly regional, and more data on a global scale are needed. To the best of our knowledge, this study is the first systematic review and meta-analysis on the global prevalence and epidemiology of asymptomatic MRSA colonisation in young children.

## HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Public health policymakers should take asymptomatic MRSA transmission into consideration to implement antibiotic regulatory and infection control measures that will limit the spread, and protect children.

MRSA (CA-MRSA) infection is often reported among healthy children under 6 years of age.<sup>2</sup>

Colonisation is defined as the presence of bacteria on the human body's surface (eg, airway, skin and mouth) without displaying disease symptoms and is regarded as a prerequisite for infection.<sup>3</sup> However, many publications confuse 'colonisation' with 'infection'.<sup>3</sup> Therefore, 'asymptomatic colonisation' is adopted to distinguish it from infection, as defined by Chisholm, Campbell.<sup>4</sup>

The respiratory tract of humans, particularly the anterior nares, serves as the primary ecological reservoir for *S. aureus*.<sup>5</sup> *S. aureus* can adhere and multiply in the nose and transmit among the



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human nose via hands and air.<sup>6</sup> Individuals who are persistently colonised by MRSA are at an increased risk for MRSA infection.<sup>7</sup> The rate of invasive CA-MRSA infection cases among children rose from 1.1 cases per 100 000 children in 2005 to 1.7 cases per 100 000 children in 2010 according to a population-based active surveillance programme in the USA, with a modelled yearly increase of 10.2% (95% CI 2.7 to 18.2).<sup>8</sup> Most studies were conducted nationally, while aggregate global data on asymptomatic MRSA colonisation among children are lacking. Hence, the role of 'asymptomatic MRSA colonisation' in MRSA transmission could be underestimated in surveillance programmes and in developing policies and programmes on infection control.<sup>4</sup> Thus, understanding the prevalence and epidemiology of asymptomatic MRSA colonisation in the upper respiratory tract of young children could provide better evidence for developing infection control and prevention strategies locally and globally.

To the best of our knowledge, this is the first systematic review and meta-analysis focused on the global prevalence and epidemiology of asymptomatic MRSA colonisation in young children. The study aimed to identify the prevalence of *S. aureus* and MRSA asymptomatic colonisation and risk factors associated with asymptomatic MRSA colonisation in the upper respiratory tract of young children and to characterise the antibiotic resistance and genetic characteristics of relevant MRSA isolates.

## METHOD

The systematic review and meta-analysis followed the guideline of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses 2020 statement<sup>9</sup> and registered on PROSPERO.

### Searching strategies and eligible criteria

All review authors collaboratively developed the search strategies (online supplemental appendix I) for publications. A comprehensive publication search was conducted on Medline, Embase, Web of Science and CINAHL on 3 March 2022. All the records were exported to Covidence (<https://www.covidence.org/>). Studies had to report prevalence data on both *S. aureus* and MRSA in young children to be eligible, and other eligibility criteria are listed in online supplemental appendix II.

### Data extraction

A data collection form (online supplemental appendix III) was designed for data extraction. Missing data were extracted from figures if possible. The primary outcomes of interest were the prevalence of asymptomatic *S. aureus* and MRSA carriage among young children without infection. For cohort studies, if specimens for *S. aureus* and MRSA screening were collected from a subject more than once, only the first screening outcomes were extracted. As for the secondary outcomes, significant risk factors for asymptomatic colonisation, antibiotic resistance and genetic characteristics of MRSA in young children were extracted. Basic information about the studies was also extracted, including author names, publication year, country/continent, economic status of countries, screening setting, study design, sampling sites, total number of target subjects, age/age group, health status, *S. aureus* screening method, MRSA confirmation method and whether combining pre-enrichment (ie, broth enrichment to enhance the sensitivity of detection) before *S. aureus* detection.

### Bias assessment and data analysis

The risk of bias in publications was assessed using Joanna Briggs Institution (JBI) standardised critical appraisal checklist for both cross-sectional and cohort studies. The checklist comprised nine

questions to determine the possible bias in the design, conduct, and analysis experiment.<sup>10</sup>

The 'meta' package<sup>11</sup> in R software (V.4.1.2) was employed for all the statistical analyses. As a binary primary outcome, the overall pooled prevalence and the 95%CI for asymptomatic *S. aureus* and MRSA colonisation were calculated with a random-effects model and visualised in forest plots. Statistical heterogeneity between studies was assessed by  $I^2$  statistics and interpreted according to the Cochrane Collaboration.<sup>12</sup> The possible causes of heterogeneity were examined using subgroup analysis based on certain potential independent factors. The estimated prevalence of each subgroup was reported. As part of the secondary outcomes, the available quantitative data on antibiotic resistance and genetic characteristics of MRSA isolates were analysed using a random effects model. A p-value less than 0.05 was considered statistically significant.

## RESULTS

### Study selection and data extraction

A total of 12 974 publication records were initially collected (figure 1). Of these, 8843 unique records were screened by title and abstract, and 1190 were subjected to full-text screening. After excluding those not fulfilling the inclusion criteria, 35 articles were identified (34 peer-reviewed articles and one letter to the editor).

The prevalence of *S. aureus* and MRSA was extracted from all included publications. Of the 35 studies,<sup>13–47</sup> seven<sup>13 15 17 20 23 24 27</sup> reported significant risk factors or predictors of asymptomatic MRSA colonisation in young children.

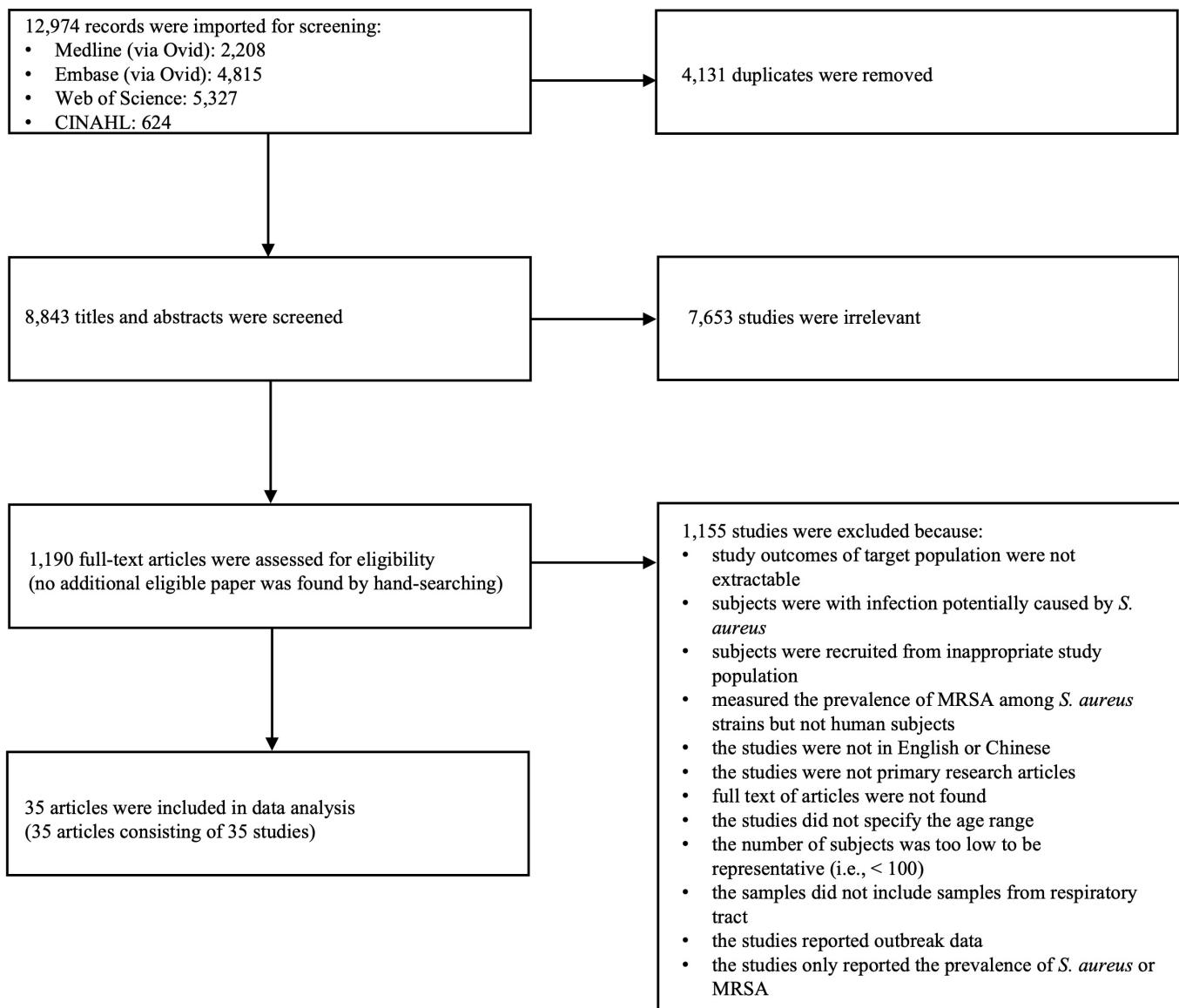
### Study characterisation

The included studies were conducted from 2004 to 2019 in 22 countries on five continents (detailed in online supplemental appendix IV). Among them, non-duplicate subjects from three publications from Taiwan were eligible.<sup>44–46</sup> Most included studies were cross-sectional studies (31/35), while the remainder were cohort studies. *S. aureus* and MRSA screening were conducted among children from children's institutions (20/35), followed by healthcare centres and communities. A total of 18 190 subjects were young children (0–8 years old) without respiratory infections or other potential infections caused by *S. aureus* infections.

From the studies, only five had more than 1000 subjects, and the majority (20/35) had fewer than 500 subjects. Most screening specimens (23/35) were mainly collected from nares only and followed by nasopharynx only. Moreover, the risk of bias in all included studies assessed with the JBI standardised critical appraisal checklist for included studies was with an overall score (yes%) higher than 60%, which was with acceptable publication quality (detailed in online supplemental appendix V).

### Overall pooled prevalence

All studies (n=35) were included in the pooled prevalence analysis using a random effects model. The pooled prevalence of asymptomatic *S. aureus* colonisation was 25.1% (95% CI 21.4 to 28.8) (figure 2). The prevalence of each study derived largely from 3.7% to 48.6% with a significant degree of statistical heterogeneity ( $I^2$ : 97.9% (97.6 to 98.2);  $p\leq 0.0001$ ). The highest prevalence was observed in studies conducted in Portugal (48.6%),<sup>39</sup> followed by Brazil (48.0% and 47.3%).<sup>15 16</sup> For MRSA, the pooled prevalence was 3.4% (95% CI 2.8 to 4.1) (figure 3). The prevalence of each study ranged from 0.0% to 29.4% with significant heterogeneity ( $I^2$ : 96.7% (96.0 to 97.2));



**Figure 1** Flow diagram for publications screening. MRSA, methicillin-resistant *Staphylococcus aureus*.

$p \leq 0.0001$ ). The highest prevalence of asymptomatic MRSA colonisation was reported in Taiwan (29.4%),<sup>44</sup> followed by Iran (16.7%).<sup>42</sup>

#### Subgroup analysis for the prevalence of MRSA

Subgroup analyses for the prevalence of asymptomatic MRSA colonisation were conducted using nine independent factors (online supplemental appendix VI). Among them, the pooled prevalence of each subgroup differed significantly when the subgroups were divided by continent ( $p < 0.0001$ ), screening setting ( $p < 0.0001$ ) and age group ( $p < 0.0001$ ). As shown in figure 4, MRSA prevalence was higher in Asia (5.8%;  $I^2 = 97.6\%$ ) and South America (5.6%;  $I^2 = 2.5\%$ ) compared with European countries (0.6%;  $I^2 = 85.0\%$ ). Higher MRSA prevalence was reported by studies conducted in the community (5.7%;  $I^2 = 96.7\%$ ) and healthcare centres (6.4%;  $I^2 = 98.0\%$ ) when compared with children's institutions (ie, nurseries, kindergartens, daycare centres and preschools) (1.5%;  $I^2 = 89.9\%$ ). Although these significant factors can partially explain the heterogeneity, there is still relatively high heterogeneity within different subgroups.

#### Significant risk factors

Seven of the 35 included observational studies reported the significant risk factors/predictors of asymptomatic MRSA colonisation for the target population. Specifically, previous antibiotic intake history and having an MRSA-colonised mother were significantly associated with asymptomatic MRSA colonisation in young children. Other significant risk factors are reported in table 1.

#### Antibiotic resistance characterisation

Antibiotic resistance characteristics of MRSA isolates were extracted from a total of 14 studies out of 35 studies (detailed in online supplemental appendix VII). High pooled resistance rates (ie, higher than 60%) were observed for antibiotics, such as ampicillin (93.3%;  $I^2 = 44.7\%$ ) and erythromycin (63.0%;  $I^2 = 89.6\%$ ), while the resistance rates to some important antibiotics remained low, such as rifampin (0.3%;  $I^2 = 0.0\%$ ) and fusidic acid (0.0%;  $I^2 = 0.0\%$ ). Only one isolate found by Sedighi *et al*<sup>40</sup> was resistant to vancomycin.

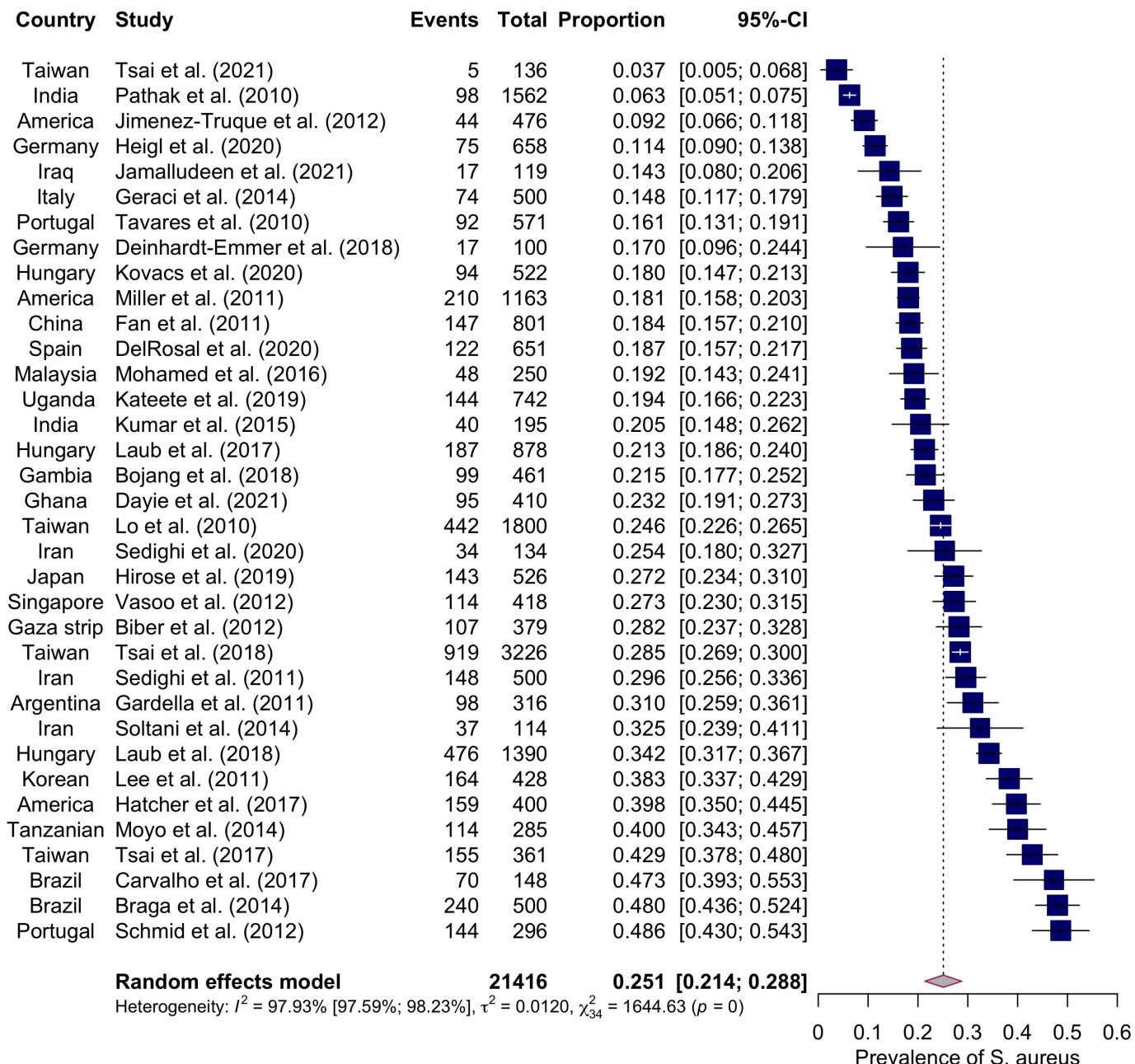


Figure 2 Forest plot for the prevalence of *S. aureus* asymptomatic colonisation (n=35).

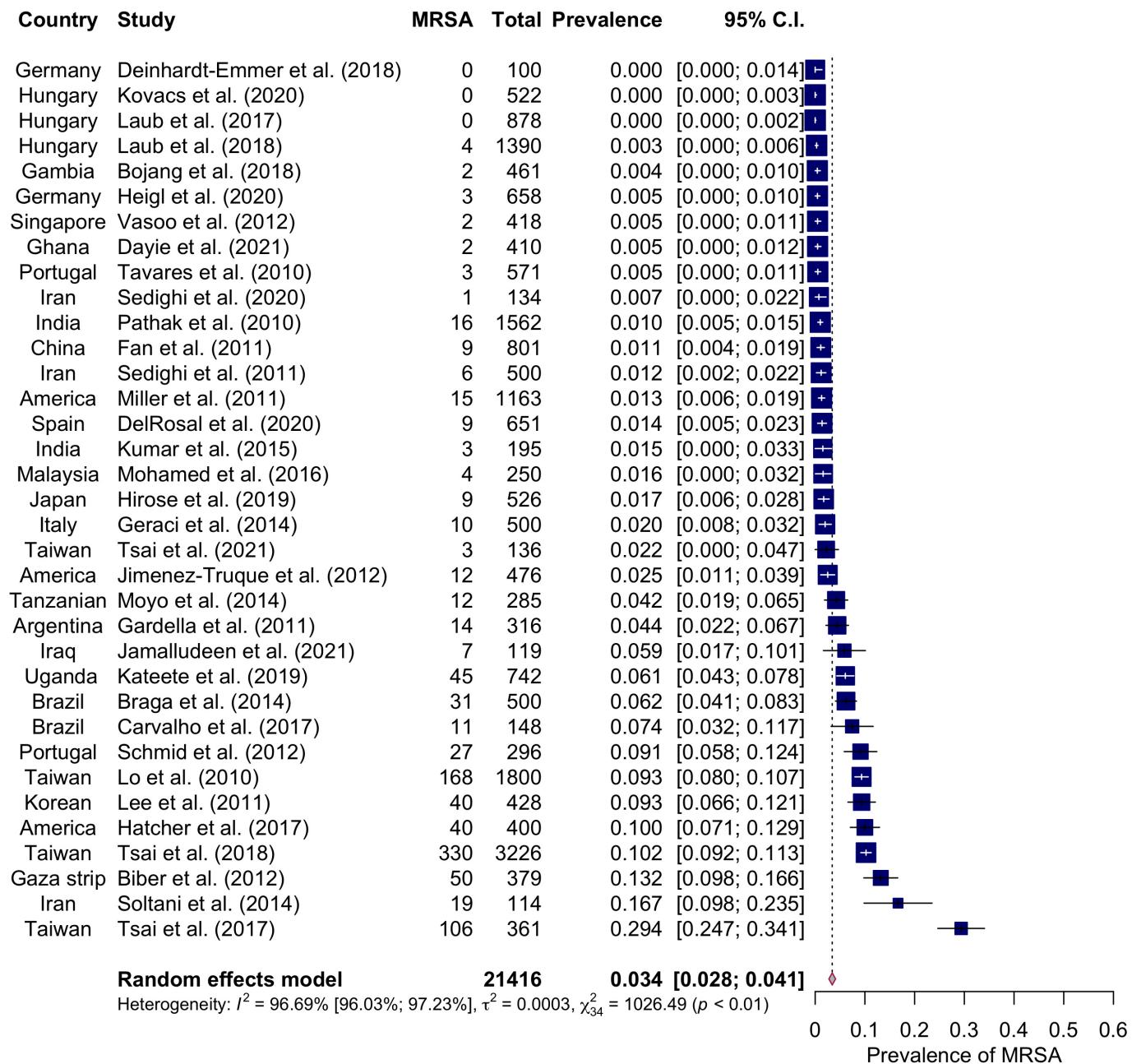
### Molecular genetic characterisation

Only a few studies characterised the molecular genetic characteristics of MRSA isolates from their target population. Among 13 studies that tested for the *mecA* gene, all isolates were positive (539/539).<sup>20 21 23 25 27 28 32 33 36 39 43 46</sup> Yet, the pooled positive rate of the Panton-Valentine leucocidin (PVL) gene was 14.7% (95% CI 4.3 to 25.0) with high heterogeneity ( $I^2=89.1\%$ ) among 493 MRSA isolates from 13 studies.<sup>16 17 20-22 25 28 33 35 36 43 46 47</sup> Tsai et al<sup>46</sup> found that the PVL gene was predominantly associated with SCC*mec* type V<sub>T</sub> or IV isolates. Different MRSA variations were reported in different studies. In particular, ST59 was the most commonly observed isolate in Taiwan, and sporadic MRSA isolates (ie, single locus variants of ST9) belonging to livestock-associated MRSA (LA-MRSA) clones were found in two children.<sup>46</sup> *Scn*-negative MRSA

(a putative marker for LA-MRSA) was observed in a child from a family involved in industrial hog farming and processing<sup>23</sup> and one ST398-MRSA-V was detected in a child without exposure to livestock.<sup>22</sup>

### DISCUSSION

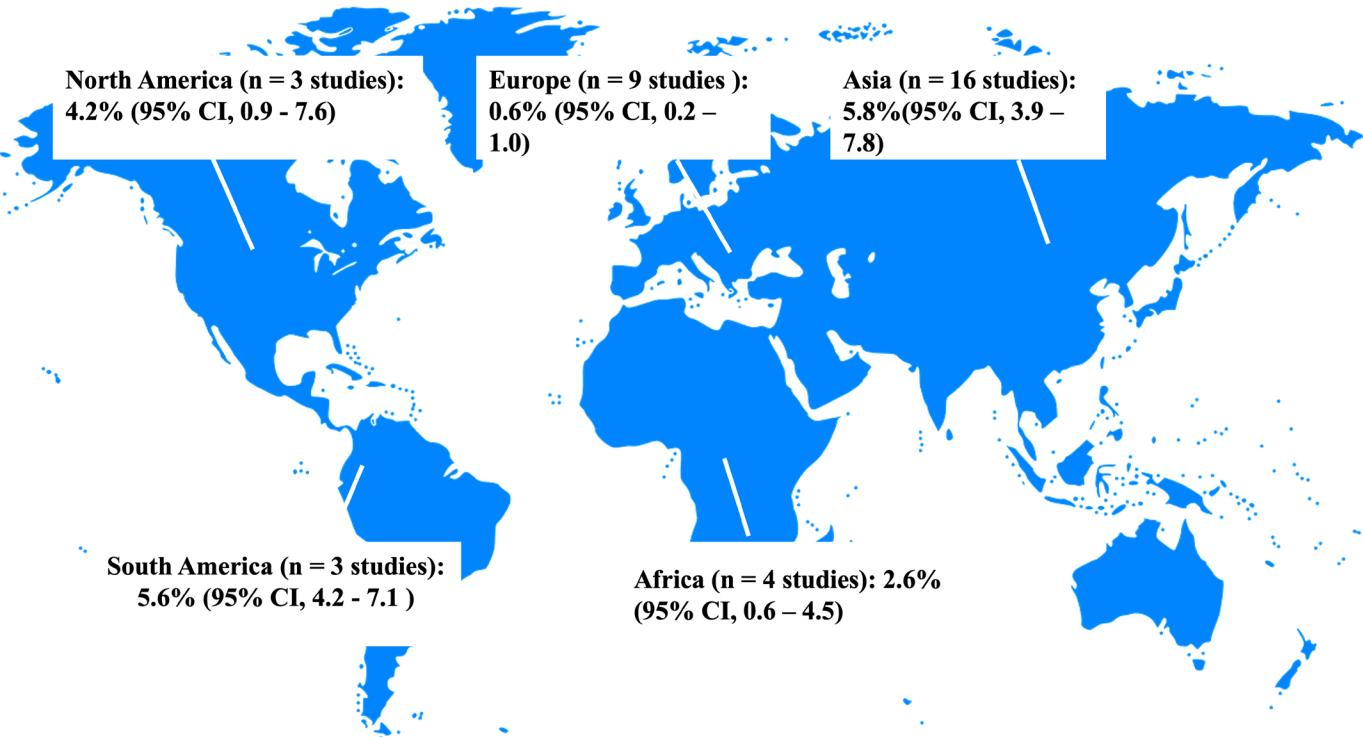
To the best of our knowledge, this is the first systematic review and meta-analysis on the global prevalence and epidemiology of asymptomatic MRSA colonisation in young children. This study estimated the global asymptomatic MRSA colonisation in children using 35 studies published between 2010 and 2021. The pooled prevalence of asymptomatic *S. aureus* and MRSA colonisation was 25.1% (95% CI 21.4 to 28.8) and 3.4% (95% CI 2.8 to 4.1) in young children, respectively. Compared with pooled MRSA colonisation and infection prevalence of 2.8% (95% CI 1.6 to 4.0) among children (0–5 years old) in a systematic



**Figure 3** Forest plot for the prevalence of MRSA asymptomatic colonisation (n=35). MRSA, methicillin-resistant *Staphylococcus aureus*.

review using data published between 2000 and 2010,<sup>48</sup> the overall asymptomatic colonisation prevalence increased among young children in the last 10–15 years. Furthermore, the prevalence was higher in young children than in healthy people, with a prevalence of 5.9% (95% CI 2.3 to 79.6) and 0.8% (95% CI 0.0 to 17.5) for *S. aureus* and MRSA colonisation, respectively, for the latter cohort.<sup>49</sup> It is also supported by a meta-analysis conducted for the Asia-Pacific region reporting higher CA-MRSA prevalence in young children under 6 years old with less mature immune systems than older children or adults.<sup>50</sup> This is a warning finding as a study conducted by von Eiff *et al*<sup>51</sup> presented evidence to support that *S. aureus* in the nasal mucosa could be an endogenous origin for bacteraemia. Compared with non-carriers, both low ( $Ct > 24$  cycles) burden and high burden ( $Ct \leq 24$  cycles) of nasal colonisation was associated with subsequent MRSA infection.<sup>52</sup>

Considerable heterogeneity in estimates of prevalence is mainly related to the continent, age of subjects and screening setting. MRSA became more prevalent in some Asian and Latin American countries.<sup>53 54</sup> A much higher MRSA prevalence in Asia (5.8%) and in South America (5.6%) was reported compared with Europe (0.6%). Studies conducted in mainland China and Taiwan<sup>34 44 46</sup> reported a higher prevalence of asymptomatic MRSA colonisation than others, while studies conducted in Hungary reported a lower prevalence.<sup>31 32</sup> It is important to note that a proportion of children recruited in a study conducted in the US was from households of industrial hog operation workers, which has been considered to be a risk factor for MRSA colonisation.<sup>23</sup> Therefore, the prevalence of MRSA colonisation reported in this study was much higher than the prevalence reported in other publications from the North America.<sup>27 35</sup> Furthermore, a higher prevalence of asymptomatic MRSA colonisation was



**Figure 4** Prevalence of asymptomatic colonisation of MRSA in the upper respiratory tracts of young children in five continents. MRSA, methicillin-resistant *Staphylococcus aureus*.

observed among young children recruited from communities and healthcare centres (without infections caused by *S. aureus*) than in children's institutions, although this classification may partially overlap due to the difficulty in clearly separating them based on the description in the original research publications.

Nonetheless, children attending child care centres are usually with a higher risk to of MRSA infection<sup>55</sup> and can be a potential reservoir for emerging MRSA genotypes.<sup>56</sup> More importantly, a previous study suggested that CA-MRSA infections were more likely to occur in children under 3 years old than in older

**Table 1** Reported significant risk factors/predictors of the asymptomatic colonisation of MRSA in the upper respiratory tract in young children

Study	Study design	Setting (country)	Age	Statistical analysis	Risk factors/predictors	Relevant statistical data
Fan et al <sup>20</sup>	Cross-sectional	Kindergartens (China)	2–7 years	Univariate	<ul style="list-style-type: none"> <li>▶ Attending day kindergartens compared with full day kindergartens;</li> <li>▶ Antibiotic intake within 6 months.</li> </ul>	<ul style="list-style-type: none"> <li>▶ Pearson <math>\chi^2</math>; p=0.027</li> <li>▶ Data not shown</li> </ul>
Jimenez-Truque <sup>27</sup>	Prospective	Obstetrics Clinic of Hospitals (America)	At birth (within 2 hours)	Univariate	<ul style="list-style-type: none"> <li>▶ Have an Africa American mother;</li> <li>▶ Have been born vaginally.</li> </ul>	<ul style="list-style-type: none"> <li>▶ Pearson <math>\chi^2</math>; p&lt;0.001</li> <li>▶ Pearson <math>\chi^2</math>; p=0.018</li> </ul>
Biber et al <sup>13</sup>	Cross-sectional	Neighbourhoods and village (Gaza Strip)	0–5.5 years	Multivariate	<ul style="list-style-type: none"> <li>▶ Having a MRSA carrier parent.</li> </ul>	<ul style="list-style-type: none"> <li>▶ OR=25.5; p=0.0004</li> </ul>
Braga et al <sup>15</sup>	Cross-sectional	Public daycare centres (Brazil)	3 months to 6 years	Bivariate	<ul style="list-style-type: none"> <li>▶ Use <math>\beta</math>-Lactam antibiotic in the previous 30 days;</li> <li>▶ Attend daycare centres located in aglomerado subnormal (AGSN) census tract.</li> </ul>	<ul style="list-style-type: none"> <li>▶ Pearson <math>\chi^2</math>; p=0.003</li> <li>▶ Pearson <math>\chi^2</math>; p&lt;0.001</li> </ul>
Hatcher et al <sup>23</sup>	Cross-sectional	Industrial hog operations (IHOs) families and non-IHOs families (America)	0–7 years	Bivariate	<ul style="list-style-type: none"> <li>▶ Live with IHO workers;</li> <li>▶ Occupational activities of IHO workers.</li> </ul>	<ul style="list-style-type: none"> <li>▶ Adjusted risk ratio=2.37 (95% CI, 1.14 to 4.92)</li> <li>▶ Crude risk ratio<sup>a</sup></li> </ul>
Heigl et al <sup>24</sup>	Cross-sectional	Hospitals (Germany)	At birth and 3 days after birth	Univariate	<ul style="list-style-type: none"> <li>▶ Have a MRSA colonised mother.</li> </ul>	<ul style="list-style-type: none"> <li>▶ Risk ratio=216.3 (95% CI, 69.59 to 672.53).</li> </ul>
Dayie et al <sup>17</sup>	Cross-sectional	Nurseries and kindergartens (Ghana)	0–5 years	Univariate	<ul style="list-style-type: none"> <li>▶ Age group (the prevalence of age between 37 and 48 months was the highest).</li> </ul>	<ul style="list-style-type: none"> <li>▶ Pearson <math>\chi^2</math>; p=0.003</li> </ul>

<sup>a</sup> take PPE (personal protective equipment) home: 12.07 (95% CI, 3.78 to 38.60); use disinfectant: 6.25 (95% CI, 1.95 to 20.01); work with nursery pigs: 2.23 (95% CI, 1.12 to 4.45); handle dead pigs: 3.21 (95% CI, 1.01 to 10.19).

MRSA, methicillin-resistant *Staphylococcus aureus*.

children.<sup>57</sup> Similarly, in this study, the prevalence of asymptomatic MRSA colonisation in newborns (within the first month) was significantly higher than in the older children, which is consistent with a meta-analysis that suggested the prevalence of MRSA colonisation in newborns (within 28 days) was significantly higher than in young children (within 5 years old), regardless of the subject's health status of subjects at the sampling time.<sup>48</sup> This finding highlights the importance of monitoring the prevalence and persistence of asymptomatic MRSA colonisation in children, particularly in the younger age group. However, it should be noted that the subgroup analysis for age in our study was largely influenced by a longitudinal study conducted in Keelung City, Taiwan.<sup>44</sup> In this cohort, 29.4% of the newborns were colonised by MRSA at the age of 1 month. Interestingly, the colonisation rate of both *S. aureus* and MRSA gradually decreased in the first year of their life, which may be due to the pneumococcal competition in the nasopharyngeal space.<sup>44</sup>

Genetically, SCCmec type IV or V<sub>T</sub> remained the predominant SCCmec type and was mainly associated with the presence of the PVL gene,<sup>46</sup> consistent with the genetic pattern observed 10–15 years ago.<sup>48</sup> The predominant SCCmec type IV, V<sub>T</sub> and V are associated with CA-MRSA, while type I is associated with hospital-acquired MRSA (HA-MRSA).<sup>58 59</sup> In addition, LA-MRSA was reported in young children, though the prevalence was low.<sup>22 23 46</sup> Therefore, it suggests that either CA-MRSA, HA-MRSA or LA-MRSA may be present in the upper respiratory tracts of young children without respiratory infection symptoms.

There are several limitations in this study. First, the languages of the included publications were restricted to English and Chinese, which may introduce bias to the prevalence estimates. Second, the substantial heterogeneity and publication bias across included studies may affect the estimation precision. However, since it is a small meta-analysis with 35 studies, it should be noted that the I<sup>2</sup> is known to be inevitably less precise in practice.<sup>60</sup> In addition, a large proportion of isolates (330 isolates) in our study was contributed by Tsai and colleagues,<sup>46</sup> which may cause systematic errors in estimating the resistance rate to some antibiotics and genetic characterisation. Third, the prevalence of MRSA colonisation in the respiratory tract may be underestimated in this meta-analysis because all included studies used culture-based methods with lower sensitivity instead of the PCR method to detect *S. aureus*.<sup>61</sup> Finally, considering that MRSA prevalence varies widely across different regions, and a higher number of studies may be conducted in regions with higher reported infection cases, more cross-regional routine surveillance studies are expected.

## CONCLUSION

In conclusion, our study provides evidence from an important aspect for establishing MRSA infection control among young children. The prevalence of asymptomatic MRSA colonisation was associated with geography, screening setting, children with younger age, previous antibiotic intake history. The increasing colonisation rate and considerable heterogeneity in prevalence estimates highlighted the need for more cross-regional active surveillance on asymptomatic colonisation in early childhood care to avoid a wider spread of MRSA and subsequent infections.

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## REFERENCES

- World Health Organization. WHO publishes list of bacteria for which new antibiotics are urgently needed 2017. 2017 Available: <https://www.who.int/news-room/27-02-2017-who-publishes-list-of-bacteria-for-which-new-antibiotics-are-urgently-needed>
- Yamamoto T, Nishiyama A, Takano T, et al. Community-acquired methicillin-resistant *staphylococcus aureus*: community transmission, pathogenesis, and drug resistance. *J Infect Chemother* 2010;16:225–54.
- Dani A. Colonization and infection. *Cent European J Urol* 2014;67:86–7.
- Chisholm RH, Campbell PT, Wu Y, et al. Implications of asymptomatic carriers for infectious disease transmission and control. *R Soc Open Sci* 2018;5:172341.
- Ciftci IH, Koken R, Bukulmez A, et al. Nasal carriage of *staphylococcus aureus* in 4–6 age groups in healthy children in afyonkarahisar, Turkey. *Acta Paediatr* 2007;96:1043–6.
- Wertheim HF, Melles DC, Vos MC, et al. The role of nasal carriage in *staphylococcus aureus* infections. *Lancet Infect Dis* 2005;5:751–62.
- Bradley SF. MRSA colonisation (eradicating colonization in people without active invasive infection). *BMJ Clin Evid* 2015;2015:0923.
- Iwamoto M, Mu Y, Lynfield R, et al. Trends in invasive methicillin-resistant *staphylococcus aureus* infections. *Pediatrics* 2013;132:e817–24.
- PRISMA. PRISMA statement. 2021. Available: <https://www.prisma-statement.org/PRISMAStatement/PRISMAStatement>
- Munn Z, Moola S, Lisy K, et al. Methodological guidance for systematic reviews of observational epidemiological studies reporting prevalence and cumulative incidence data. *Int J Evid Based Healthc* 2015;13:147–53.
- Schwarzer G. Package 'meta'. 2022. Available: <https://cran.r-project.org/web/packages/meta/meta.pdf>

- 12 The Cochrane Collaboration. Cochrane handbook for systematic reviews of interventions (version 5.1.0). 2011. Available: [https://handbook-5-1.cochrane.org/chapter\\_9/9\\_5\\_2\\_identifying\\_and\\_measuring\\_heterogeneity.htm](https://handbook-5-1.cochrane.org/chapter_9/9_5_2_identifying_and_measuring_heterogeneity.htm)
- 13 Biber A, Abuelaish I, Rahav G, et al. A typical hospital-acquired methicillin-resistant staphylococcus aureus clone is widespread in the community in the Gaza strip. *PLoS ONE* 2012;7:e42864.
- 14 Bojang A, Camara B, Jagne Cox I, et al. Long-term impact of oral azithromycin taken by Gambian women during labor on prevalence and antibiotic susceptibility of streptococcus pneumoniae and staphylococcus aureus in their infants: follow-up of a randomized clinical trial clinical infectious diseases. *Clin Infect Dis* 2018;67:1191–7.
- 15 Braga EDV, Aguiar-Alves F, de Freitas M de FN, et al. High prevalence of staphylococcus aureus and methicillin-resistant S. aureus colonization among healthy children attending public daycare centers in informal settlements in a large urban center in Brazil. *BMC Infect Dis* 2014;14:538.
- 16 Carvalho S de, Almeida J de, Andrade Y, et al. Community-acquired methicillin-resistant staphylococcus aureus carrying SCCmec type IV and V isolated from healthy children attending public daycares in northeastern Brazil. *Braz J Infect Dis* 2017;21:464–7.
- 17 Dayie N, Osei M-M, Opintan JA, et al. Nasopharyngeal carriage and antimicrobial susceptibility profile of staphylococcus aureus among children under five years in Accra. *Pathogens* 2021;10:1–12.
- 18 Deinhardt-Emmer S, Sachse R, Geraci J, et al. Virulence patterns of staphylococcus aureus strains from nasopharyngeal colonization. *J Hosp Infect* 2018;100:309–15.
- 19 Del Rosal T, Méndez-Echavarria A, García-Vera C, et al. Staphylococcus aureus nasal colonization in Spanish children. The COSACO nationwide surveillance study. *Infect Drug Resist* 2020;13:4643–51.
- 20 Fan J, Zhou W, Shu M, et al. Nasal carriage of community-acquired methicillin-resistant staphylococcus aureus in healthy children from Chengdu. *Zhongguo Dang Dai Er Ke Za Zhi* 2011;13:16–9.
- 21 Gardella N, Murzicato S, Di Gregorio S, et al. Prevalence and characterization of methicillin-resistant staphylococcus aureus among healthy children in a city of Argentina. *Infect Genet Evol* 2011;11:1066–71.
- 22 Geraci DM, Bonura C, Giuffrè M, et al. Tst1-positive St22-MRSA-IVa in healthy Italian preschool children. *Infection* 2014;42:535–8.
- 23 Hatcher SM, Rhodes SM, Stewart JR, et al. The prevalence of antibiotic-resistant *staphylococcus aureus* nasal carriage among industrial hog operation workers, community residents, and children living in their households: North Carolina, USA. *Environ Health Perspect* 2017;125:560–9.
- 24 Heigl K, Zamfir M, Adler AC, et al. Prevalence of methicillin-sensitive, methicillin-resistant staphylococcus aureus, and extended-spectrum beta-lactamase-producing escherichia coli in newborns: a cross-sectional study. *J Matern Fetal Neonatal Med* 2022;35:4243–9.
- 25 Hirose M, Aung MS, Fukuda A, et al. Prevalence and genetic characteristics of methicillin-resistant staphylococcus aureus and coagulase-negative staphylococci isolated from oral cavity of healthy children in Japan. *Microb Drug Resist* 2019;25:400–7.
- 26 Jamalludeen NM. Nasal carriage of staphylococcus aureus in healthy children and its possible bacteriophage isolates in Basrah, Iraq. *Biomed Pharmacol J* 2021;14:467–75.
- 27 Jimenez-Truque N, Tedeschi S, Saye Ej, et al. Relationship between maternal and neonatal staphylococcus aureus colonization. *Pediatrics* 2012;129:e1252–9.
- 28 Katee DP, Asimwe BB, Mayanja R, et al. Nasopharyngeal carriage, Spa types and antibiotic susceptibility profiles of staphylococcus aureus from healthy children less than 5 years in Eastern Uganda. *BMC Infect Dis* 2019;19:1023.
- 29 Kovács E, Sahin-Tóth J, Tóthpál A, et al. Co-carriage of staphylococcus aureus, streptococcus pneumoniae, haemophilus influenzae and moraxella catarrhalis among three different age categories of children in Hungary. *PLoS ONE* 2020;15:e0229021.
- 30 Kumar H, Palaha R, Kaur N, et al. Prevalence of multidrug-resistant, coagulase-positive staphylococcus aureus in nasal carriage, food, wastewater and paper currency in Jalandhar city (North-Western), an Indian state of Punjab. *Environ Monit Assess* 2015;187:4134.
- 31 Laub K, Tóthpál A, Kardos S, et al. Epidemiology and antibiotic sensitivity of staphylococcus aureus nasal carriage in children in Hungary. *Acta Microbiol Immunol Hung* 2017;64:51–62.
- 32 Laub K, Tóthpál A, Kovács E, et al. High prevalence of staphylococcus aureus nasal carriage among children in Szolnok, Hungary. *Acta Microbiol Immunol Hung* 2018;65:59–72.
- 33 Lee J, Sung JY, Kim YM, et al. Molecular characterization of methicillin-resistant staphylococcus aureus obtained from the anterior nares of healthy Korean children attending daycare centers. *Int J Infect Dis* 2011;15:e558–63.
- 34 Lo W-T, Wang C-C, Lin W-J, et al. Changes in the nasal colonization with methicillin-resistant staphylococcus aureus in children: 2004–2009. *PLoS ONE* 2010;5:e1579112.
- 35 Miller MB, Weber DJ, Goodrich JS, et al. Prevalence and risk factor analysis for methicillin-resistant staphylococcus aureus nasal colonization in children attending child care centers. *J Clin Microbiol* 2011;49:1041–7.
- 36 Mohamed NA, Ramli S, Amin NNZ, et al. Staphylococcus aureus carriage in selected kindergartens in Klang valley. *Med J Malaysia* 2016;71:62–5.
- 37 Moyo SJ, Aboud S, Blomberg B, et al. High nasal carriage of methicillin-resistant staphylococcus aureus among healthy tanzanian under-5 children. *Microb Drug Resist* 2014;20:82–8.
- 38 Pathak A, Marothi Y, Iyer RV, et al. Nasal carriage and antimicrobial susceptibility of staphylococcus aureus in healthy preschool children in Ujjain, India. *BMC Pediatr* 2010;10:100.
- 39 Schmid H, Lôpo N, Castro A, et al. Characterization of *Staphylococcus Aureus* isolated from healthy children in Portugal. 2012: 509–12.
- 40 Sedighi I, Faradmal J, Alikhani MY, et al. The comparison of staphylococcus aureus nasal colonization and its antibiotic resistance patterns in children of health careworkers (Hcws) and non-Hcws. *J Compr Ped* 2020;11.
- 41 Sedighi I, Moez HJ, Alikhani MY. Nasal carriage of methicillin resistant staphylococcus aureus and their antibiotic susceptibility patterns in children attending day-care centers. *Acta Microbiol Immunol Hung* 2011;58:227–34.
- 42 Soltani B, Taghavi Ardakan A, Moraveji A, et al. Risk factors for Methicillin resistant staphylococcus aureus nasal colonization of healthy children. *Jundishapur J Microbiol* 2014;7:e20025.
- 43 Tavares DA, Sá-Leão R, Miragaia M, et al. Large screening of CA-MRSA among staphylococcus aureus colonizing healthy young children living in two areas (urban and rural) of Portugal. *BMC Infect Dis* 2010;10:110.
- 44 Tsai M-H, Chiu C-Y, Shih H-J, et al. Longitudinal investigation of nasopharyngeal methicillin-resistant staphylococcus aureus colonization in early infancy: the patch birth cohort study. *Clin Microbiol Infect* 2017;23:S1198-743X(16)30509-2:121..
- 45 Tsai M-H, Chiu C-Y, Su K-W, et al. Community-associated Methicillin-resistant staphylococcus aureus colonization in a birth cohort of early childhood: the role of maternal carriage. *Front Med (Lausanne)* 2021;8:738724.
- 46 Tsai M-S, Chen C-J, Lin T-Y, et al. Nasal methicillin-resistant staphylococcus aureus colonization among otherwise healthy children aged between 2 months and 5 years in northern Taiwan, 2005–2010. *J Microbiol Immunol Infect* 2018;51:756–62.
- 47 Vasoo S, Singh K, Chow C, et al. Health care-associated Methicillin-resistant staphylococcus aureus colonization in children attending day care centers in Singapore. *Pediatr Infect Dis J* 2012;31:213–4.
- 48 Gesualdo F, Bongiorno D, Rizzo C, et al. MRSA nasal colonization in children: prevalence meta-analysis, review of risk factors and molecular Genetics. *Pediatr Infect Dis J* 2013;32:479–85.
- 49 Abdullahi IN, Lozano C, Ruiz-Ripa L, et al. Ecology and genetic lineages of nasal staphylococcus aureus and MRSA carriage in healthy persons with or without animal-related occupational risks of colonization: a review of global reports. *Pathogens* 2021;10:1000.
- 50 Wong JW, Ip M, Tang A, et al. Prevalence and risk factors of community-associated methicillin-resistant staphylococcus aureus carriage in Asia-Pacific region from 2000 to 2016: a systematic review and meta-analysis. *Clin Epidemiol* 2018;10:1489–501.
- 51 von Eiff C, Becker K, Machka K, et al. Nasal carriage as a source of staphylococcus aureus bacteraemia. *N Engl J Med* 2001;344:11–6.
- 52 Stenehjem E, Rimland D. MRSA nasal colonization burden and risk of MRSA infection. *Am J Infect Control* 2013;41:405–10.
- 53 Kang C-I, Song J-H. Antimicrobial resistance in Asia: current epidemiology and clinical implications. *Infect Chemother* 2013;45:22.
- 54 Guzmán-Blanco M, Mejía C, Ithuriz R, et al. Epidemiology of methicillin-resistant staphylococcus aureus (MRSA) in Latin America. *Int J Antimicrob Agents* 2009;34:304–8.
- 55 Centers for Disease Control and Prevention. Methicillin-resistant staphylococcus aureus (MRSA). 2019. Available: <https://www.cdc.gov/mrsa/community/index.html>
- 56 Ho P-L, Chiu SS, Chan MY, et al. Molecular epidemiology and nasal carriage of staphylococcus aureus and Methicillin-resistant S. aureus among young children attending day care centers and kindergartens in Hong Kong. *J Infect* 2012;64:500–6.
- 57 Yang X, Qian S, Yao K, et al. Multiresistant St59-Sccmec IV-T437 clone with strong biofilm-forming capacity was identified predominantly in MRSA isolated from Chinese children. *BMC Infect Dis* 2017;17:733.
- 58 Pan S-C, Wang J-T, Lauderdale T-L, et al. Epidemiology and staphylococcal cassette chromosome MEC typing of methicillin-resistant staphylococcus aureus isolates in Taiwan: a multicenter study. *J Formos Med Assoc* 2014;113:409–16.
- 59 Ahmad N, Ruzan IN, Abd Ghani MK, et al. Characteristics of community-and hospital-acquired Meticillin-resistant Staphylococcus aureus strains carrying SCC MEC type IV isolated in Malaysia. *J Med Microbiol* 2009;58(Pt 9):1213–8.
- 60 von Hippel PT. The heterogeneity statistic I<sub>2</sub> can <sup>b</sup>E biased in small meta-analyses. *BMC Med Res Methodol* 2015;15:1–8.
- 61 Luteijn JM, Hubben GAA, Pechivanoglou P, et al. Diagnostic accuracy of culture-based and PCR-based detection tests for methicillin-resistant staphylococcus aureus: a meta-analysis. *Clin Microbiol Infect* 2011;17:146–54.