Prevalence of methicillin-resistant *Staphylococcus aureus* in healthy Chinese population: A system review and meta-analysis

Man Wu, Xiang Tong, Sitong Liu, Dongguang Wang, Lei Wang, Hong Fan*

Department of Respiratory and Critical Care Medicine, West China Hospital/West China School of Medicine, Sichuan University, Chengdu, China

* fanhongfan@qq.com

Abstract

Objective

To comprehensively determine the prevalence of MRSA in healthy Chinese population, the influencing factors of MRSA colonization and its antibiotic resistance.

Methods

Articles that studied prevalence or influencing factors of MRSA carriage in healthy Chinese population were retrieved from PubMed, Ovid database, three Chinese electronic databases. The pooled prevalence of MRSA, its antibiotic resistance and influencing factors were analyzed by STATA12.0.

Results

37 studies were included. The pooled prevalence of MRSA was 21.2% (95% CI: 18.5%-23.9%), and the prevalence of *S. aureus* was 15% (95% CI: 10%-19%), with a significant heterogeneity (MRSA: $I^2 = 97.6\%$, $P < 0.001$; *S. aureus*: $I^2 = 98.4\%$, $P < 0.001$). In subgroup analysis, the pooled prevalence of MRSA was 28% (95%CI: 10%-51%) for Livestock-related workers, 18% (95%CI: 11%-26%) for children, 20% (95%CI: 12%-29%) for healthcare workers, 7% (95%CI: 3%-13%) for community residents. The prevalence of MRSA in studies with oxacillin disk diffusion method (28%, 95%CI: 21%-35%) seemed higher than that with the mecA gene method(12%, 95%CI: 7%-19%). MRSA in studies conducted in Taiwan was more common than in Mainland China and Hong Kong. Similar results were found in meta-regression. Influencing factors for MRSA colonization were noted in seven eligible studies, they included younger age (OR: 3.54, 95% CI: 2.38–5.26; OR: 2.24, 95% CI: 1.73–2.9), attending day care centers (DCCs) (OR: 1.95, 95% CI: 1.4–2.72; OR: 1.53, 95% CI: 1.2–1.95), flu vaccination (OR:1.73, 95% CI: 1.28–2.35), using antibiotics within the past year (OR: 2.05, 95% CI:1.35–3.11), residing in northern Taiwan (OR: 1.45, 95% CI: 1.19–1.77), regular visits to health care facility (OR: 23.83, 95% CI: 2.72–209.01), household member working in health care facility (OR: 8.98, 95% CI:1.4–55.63), and contact with
livestock (OR: 6.31, 95% CI: 3.44–11.57). Moreover, MRSA was found to be highly resistant to penicillin, ampicillin, erythromycin, and clindamycin, with a pooled resistance ratio of 100, 93, 88, and 75%, respectively. However, no resistance were noted to vancomycin.

Conclusion

The pooled prevalence of MRSA was considerably high in health Chinese population. Additionally, these strains showed extreme resistance to penicillin, ampicillin, erythromycin and clindamycin. Public MRSA protection measures and the surveillance of MRSA should be strengthened to reduce the spread of MRSA among hospitals, communities, and livestock.

Background

*Staphylococcus aureus* (*S. aureus*) is one of the main causes of hospital and community-acquired infections, resulting in serious consequences, and the disease ranges from skin infections to Septic shock[1]. Following the introduction of penicillin in 1940, *S. aureus* resistance appeared, leading to the development of semisynthetic penicillins such as methicillin. In 1960, methicillin-resistant *Staphylococcus aureus* (MRSA) was clinically identified. Poor infection control measures and continued indiscriminate exposure to antibiotics in humans and animals lead to MRSA transmission[2]. In recent years, the prevalence of MRSA is rising. The infection due to the MRSA strains has a higher mortality rate than the infection caused by the methicillin-sensitive *Staphylococcus aureus* (MSSA) strains, which brings great difficulty to treatment [3, 4].

MRSA acquires methicillin resistance by expressing a penicillin-binding protein (PBP2a) with reduced affinity for most available beta-lactam agents, including methicillin, which is encoded by mecA gene located in a mobile genomic element known as the staphylococcal cassette chromosome mec (SCCmec). New drug resistance genes have been discovered in recent years (mecB, mecC, and/or mecD)[2]. The MRSA colonization and infection has appeared from hospitals to the community and further to animals, so MRSA is no longer only anosocomial pathogen. Depending on the genotype, MRSA can be divided into community-acquired MRSA (CA-MRSA) and hospital-acquired MRSA (HA-MRSA), CA-MRSA strains are commonly sensitive to a variety of non-beta-lactam antibiotics and usually carry SCCmec type IV (less common, type V) and Panton-Valentine leukocidin (PVL) gene. While HA-MRSA strains are resistant to a variety of antibiotics, and are most associated with type I, II and III SCCmec[5, 6].

*S. aureus* colonization is a global phenomenon affected by various factors, not limited to age, health, economic status and country. *S. aureus* may be colonized in multiple body parts, but the anterior nares are the most stable colonization site. *S. aureus* colonization has been identified as an important risk factor for the development of *S. aureus* infection in community and hospital settings[7, 8]. In the past few years, the colonization rate of MRSA in healthy hosts increased significantly and may play an important role in the spread of MRSA in community and hospital settings[9]. Previous studies have shown that the demographic (e.g. age, gender, region), environmental (e.g. crowded or medical environments, animal contact), and host factors (e.g. immunity, received antibiotics) may be influence factors for MRSA carriage [7, 10]. Therefore, it is important to understand the prevalence of MRSA in healthy population at the country level to support effective prevention and control strategies.
In recent years, extensive investigative researches were performed in China on the prevalence of MRSA in healthy people, but the results are quite different with limited sample sizes. Therefore, it is necessary to conduct a systematic review and meta-analysis to comprehensively determine the prevalence of MRSA in healthy Chinese population, the influencing factors of MRSA colonization and its antibiotic resistance, which may help to establish public health interventions to reduce MRSA infection.

Materials and methods

Inclusion criteria

The following are the inclusion criteria in our meta-analysis: (1) the subjects were healthy Chinese population (Eligible participants with no acute medical problem); (2) observational studies including cross-sectional, prospective, and retrospective study (e.g. cohort and case-control studies); (3) provided total number of *S. aureus* and MRSA strains, and the total sample size; (4) Nasal or nasopharyngeal specimens. The following exclusion criteria were applied: (1) the study objects were special population (pregnant women, residents of nursing homes, infants); (2) previous studies were repeated; (3) editorial articles, meta-analyses, abstracts, letters or reviews; and (4) reported outbreak epidemiological data.

Search strategy

This meta-analysis followed PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses)[S1 Table] and MOOSE (Meta-analysis of Observational Studies in Epidemiology) statement. We searched PubMed, Ovid database, China National Knowledge Internet (CNKI), VIP Chinese Science and Technique Journals Database, and Wanfang Database on MRSA (the last search conducted on July 20, 2019) using the following search terms: (“methicillin-resistant *Staphylococcus aureus*” or “MRSA”) and (“nasal” or “nasopharyngeal”) and “China”. The references listed in all included articles were also searched to identify additional relevant articles. The language of publication was in English or Chinese.

Data extraction

Two authors (Man Wu, Xiang Tong) independently extracted data from all eligible publications. Each study provided the following information: the first author, year of publication, study area/cities, study time, study period, study population, sample size, total numbers of *S. aureus* and MRSA, or resistant of MRSA isolates to commonly available antimicrobial agents, or influencing factors. When the data for analysis was missing in the study, we contacted the author by email. If the author did not respond, the article was excluded. Any disagreement was also resolved through the discussion of the entire group.

Quality assessments

Two authors independently assessed the quality of included studies using a validated prevalence study quality assessment tool[11], which based on the following eight components: (1) a clear definition of the target population; (2) representative of probability sampling; (3) sample characteristics matching the overall population; (4) adequate response rate (If the sample sociodemographic characteristics match the overall population, the minimum rate should be set at 70%, otherwise 80%); (5) standardized data Collection methods; (6) reliability of survey instruments; (7) validation of survey instruments; and (8) appropriate statistical methods. For "No" and "Yes", the answers were scored 0 or 1. The total quality score for each study varied from 0 to 8. The total scores of 0–4 and 5–8 were considered to be low and non-low quality,
respectively. Two authors assessed the quality scores for each study separately and resolved any disagreement through the discussion of the entire group.

**Statistical analysis**

All statistical analyses were performed by STATA 12.0. A random effects model (DerSimonian Laird method) was used to obtain a pooled prevalence and a corresponding 95% confidence interval (CI). In a secondary analysis, we also calculated the resistance of MRSA to specific antibiotics. Statistical heterogeneity between groups and within groups was estimated using Chi-square based Q statistic, with $P$ values $< 0.1$ or $I^2 > 50\%$ as statistically significant heterogeneity. Freeman-Tukey double arcsine transformation was used to address both the problem of CIs outside the 0..1 range and that of variance instability. Meta-regression analysis was used to analyze the influencing factors of inter-heterogeneity. We defined $\logit(P)$ as the dependent variable ($P$ referred to the prevalence of MRSA). All the independent factors were selected based on the availability of relevant information in the included studies, including the region (Mainland China, Taiwan, Hong Kong), age range (children, non-children), Study population (Livestock-related workers, children, community residents, healthcare workers, medical students), study period (2001–2010, 2011–2016), and method ($meca$ gene, cefoxitin disk diffusion method, oxacillin disk diffusion method, oxacillin agar dilution method, and others). The factors were included into the random effects meta-regression model with restricted maximum likelihood (REML) method and were analyzed by Odds Ratios (ORs) and 95% CIs. The subgroup analysis was based on the study population, age range, region, study period, and method. A Q-test for heterogeneity was used to compare the effect size in two or more subgroups by assessing the dispersion of the summary effects about the combined effect. Begg’s test and Egger’s test were used to assess potential publication bias, with $P < 0.05$ indicating potential bias. In addition, sensitivity analysis was used to assess the influence of each study.

**Results**

**Characteristics of the studies and assessment of quality**

A total of 694 studies were initially identified from different databases. 130 studies were excluded because they were duplicated across the databases. After reading their titles and abstracts, we excluded 467 reviews, meta-analyses, and articles that were not relevant to our study. After the full-text versions were read, we further excluded 36 studies that did not offer usable data (unreported the total number of $S.aureus$ or MRSA, repeatability reports). Finally, 37 studies met our inclusion criteria and were included in the meta-analysis. The prevalenc e of MRSA in healthy Chinese population
Overall pooled prevalence. In the 37 studies included in the meta-analysis, 10536 S. aureus strains were detected from 50639 samples. There was a high level of heterogeneity ($I^2 = 98.4\%, P < 0.001$), therefore, a random effects model was conducted to obtain the pooled prevalence of S. aureus among the population (21.2\%, 95\% CI: 18.5\%-23.9\%) (Fig 2). Moreover, we performed a sensitivity analysis to explore the effect of every study on the pooled prevalence of S. aureus, and no substantial differences were found in the conclusions, indicating the stability of our meta-analysis (Fig 3). No publication bias was detected in Begg’s test ($P = 0.927$) or Egger’s test ($P = 0.874$).

2214 MRSA strains were detected in the included articles, we observed the prevalence of MRSA among S. aureus ranging from 0\% to 52.7\%. A significant heterogeneity was found among the 37 studies ($I^2 = 97.56\%, P < 0.01$), thus, the pooled prevalence of MRSA colonization was 15\% (95\% CI: 10\%-19\%) (Fig 4) by a random effect method. No publication bias was detected in Begg’s test ($P = 0.855$).
Table 1. Characteristics of all the included studies.

| First author, publication year | Study period | region | Study population | Age range | Sample size, N | No of SA | MRSA prevalence, n(%) | Study type | Score |
|--------------------------------|--------------|--------|------------------|-----------|----------------|----------|----------------------|------------|-------|
| Ye XH, 2015 [15]               | 2013–11 to 2014–11 | Guangdong | Livestock-related workers / Community residents | 15-60y | 682/1178 | 91/109 | 48 (52.7)/16 (14.7) | cross-sectional | 8     |
| Fan J, 2011 [16]               | 2005–9 to 2005–9 | Sichuan | Healthy children | 2-7y | 801 | 147 | 9 (6.1) | cross-sectional | 7     |
| Zhang WJ, 2011 [17]            | 2008–10 to 2009–11 | BJ, SH, GZ, IN, YZ | Livestock-related workers | - | 51 | 12 | 1 (8.3) | cross-sectional | 5     |
| Ma XX, 2011 [18]               | 2008–5 to 2009–10 | Shenyang | Medical students | 19-23y | 2103 | 234 | 22 (9.4) | cross-sectional | 7     |
| Ma XX, 2011 [19]               | 2010 | Shenyang | Medical students | 21.1y | 1634 | 115 | 24 (20.9) | cross-sectional | 7     |
| Chen B, 2015 [20]              | 2013–10 to 2014–3 | Guangzhou | Community residents / Healthcare workers | >17y | 297/292 | 75/63 | 1 (1.3)/3 (4.8) | cross-sectional | 8     |
| Du J, 2011 [21]                | 1 month period | Wenzhou | Medical students | - | 935 | 144 | 28 (19.4) | cross-sectional | 7     |
| O’Donoghue MM, 2004 [22]       | - | Hong Kong | community residents | 11-60y | 653 | 186 | 9 (4.8) | cross-sectional | 6     |
| Xie XY, 2018 [23]              | 2016–2 to 2016–3 | Guangzhou | Healthcare workers | 20-56y | 434 | 87 | 10 (11.5) | cross-sectional | 8     |
| Yan X, 2015 [24]               | 2009 to 2011 | BJ, HRB | Community residents | 18-74y | 2448 | 403 | 8 (2) | cross-sectional | 8     |
| Chen BJ, 2017 [25]             | 2014–10 to 2015–5 | Guangzhou | Medical students | 10-76y | 295 | 73 | 1 (1.4) | cross-sectional | 7     |
| Chen CH, 2018 [26]             | 2005–10 to 2010–12 | Taiwan | Healthy children | 2-60y | 3020 | 840 | 246 (29.3) | prospective | 8     |
| Deng JJ, 2012 [27]             | 2005 to 2007, 2008 to 2010 | Chengdu | Healthy children | 2-18y | 2373 | 430 | 27 (6.3) | cross-sectional | 6     |
| Zhang M, 2011 [28]             | - | Hong Kong | Community residents / Healthcare workers | - | 775/249 | 186/51 | 4 (2.2)/8 (15.7) | cross-sectional | 8     |
| Ho PL, 2012 [29]               | 2009–9 to 2010–4 | Hong Kong | Healthy children | 2-6y | 2211 | 610 | 28 (4.6) | cross-sectional | 8     |
| Chen CJ, 2011 [7]              | 2005–7 to 2008–6 | Taiwan | Healthy children | 2-60m | 6057 | 1404 | 473 (33.7) | cross-sectional | 7     |
| Gong ZR, 2017 [30]             | 2012–10 to 2012–11 | Tibetan | Healthy children | 6-11y | 314 | 16 | 3 (18.8) | cross-sectional | 7     |
| Boost M.V, 2011 [31]           | - | Hong Kong | Livestock-related workers | 20-59y | 150 | 22 | 2 (9.1) | cross-sectional | 7     |
| Fu JJ, 2015 [32]               | 2011–3 to 2011–5 | Guangzhou | Healthy children | 2.5-12y | 1475 | 550 | 28 (5.1) | cross-sectional | 5     |
| Ge YL, 2012 [33]               | 2009–7 to 2010–6 | Shanghai | Healthcare workers | - | 2653 | 152 | 48 (31.6) | cross-sectional | 6     |
| Liu H, 2016 [34]               | 2007 to 2014 | Tianjin | Healthcare workers | 20-62y | 1085 | 89 | 12 (13.5) | cross-sectional | 6     |
| Zhong JJ, 2016 [35]            | 2013–10 to 2013–12 | Guangdong | Livestock-related workers | 17-67y | 411 | 51 | 20 (39.2) | cross-sectional | 7     |
| Huang YC, 2007 [36]            | 2005–7 to 2006–10 | Taiwan | Healthy children | 2m-5y | 3046 | 713 | 221 (31) | cross-sectional | 8     |
| Lu PL, 2005 [37]               | 2001–4 to 2001–10 | Taiwan | Community residents / Healthy children / Healthcare workers | 1-90y/2-18y/17-60y | 851/987/137 | 149/314/31 | 31 (20.8)/33 (10.5)/7 (22.6) | cross-sectional | 7     |
| Lo WT, 2006 [38]               | 2003–12 to 2005–11 | Taiwan | Healthy children | <14y | 1195 | 300 | 89 (29.7) | prospective | 7     |
| Huang YC, 2005 [39]            | 2001–11 to 2002–6 | Taiwan | Healthy children / health care workers | -/- | 262/137 | 95/38 | 5 (3.3)/18 (47.4) | cross-sectional | 6     |
| Chen CS, 2012 [40]             | - | Taiwan | Medical students | 18-41y | 322 | 62 | 7 (11.3) | cross-sectional | 6     |

(Continued)
Subgroup analyses. Subgroup analyses were conducted by age range, region, study period, method, and study population. All the pooled prevalence of MRSA and corresponding 95% CI of subgroups were obtained, which were showed in Table 2. Among these subgroups, heterogeneity did still exist, except in Hong Kong. Significant differences were also found across study population (P = 0.03), methods (P < 0.001), and regions (P < 0.001). The pooled prevalence of MRSA was 28% (95%CI: 10%-51%, I^2 = 86.9%) for Livestock-related workers, 18% (95%CI: 11%-26%, I^2 = 98.53%) for children, 20% (95%CI: 12%-29%, I^2 = 82.61%) for healthcare workers, 7% (95%CI: 3%-13%, I^2 = 94.88%) for community residents and 11% (95%CI: 6%-18%, I^2 = 84.76%) for medical students (Fig 5). In view of different MRSA identification methods, the pooled prevalence in studies was 28% (95%CI: 21%-35%) with oxacillin disk diffusion method, followed by others (22%, 95%CI: 14%-31%, I^2 = 96.3%), meca gene method (12%, 95%CI: 7%-19%, I^2 = 93.91%), cefoxitin disk diffusion method (10%, 95%CI: 4%-18%, I^2 = 95.43%), and the minimum was 8% (95%CI: 3%-16%) with oxacillin agar dilution method (Fig 6). In addition, MRSA proportion was higher in studies conducted in Taiwan than Mainland China and Hong Kong (Fig 7). On the other hand, significant differences were not found across the study period and age ranges (S1 File).

Meta-regression for the prevalence of MRSA. The meta-regression was performed to identify related potential influencing factors of inter-heterogeneity, which was showed in Table 3. The meta-regression (residual I^2 = 99.49%, adj R^2 = 12.15%, P = 0.028 in the test for the goodness of model fit) showed that compared with Taiwan, the prevalence of MRSA was significantly lower in Mainland China (OR = 0.43, 95%CI: 0.2-0.92, P = 0.003), and Hong Kong (OR = 0.26, 95%CI: 0.08–0.84, P = 0.026). In addition, the prevalence of MRSA was higher among Livestock-related workers (OR = 4.54, 95%CI: 1.23–16.77, P = 0.024), children (OR = 2.85, 95%CI: 1.19–6.83, P = 0.02) and healthcare workers(OR = 3.67, 95%CI: 1.31–9.79, P = 0.011) than community residents.

Influencing factors. Among the 37 articles, only seven studies reported risk factors for MRSA carriage among healthy Chinese population. The significant risk factors were identified

---

**Table 1. (Continued)**

| First author, publication year | Study period | region | Study population | Age range | Sample size, N | No of SA | MRSA prevalence, n(%) | Study type | Score |
|-------------------------------|--------------|--------|------------------|-----------|---------------|---------|----------------------|------------|-------|
| Wang JT, 2009[41]            | 2007–10 to 2007–12 | Taiwan | Community residents | >18y       | 3098          | 686     | 119 (17.3)           | cross-sectional | 7     |
| Pan HH, 2017[42]             | 2005–7 to 2010–12 | Taiwan | Healthy children  | 2-60m      | 3144          | 545     | 165 (30.3)           | prospective  | 7     |
| Wang HK, 2017[43]            | 2013–6 to 2013–9 | Taiwan | Community residents | 18-35y     | 259           | 58      | 4 (6.9)              | cross-sectional | 6     |
| Wu TH, 2018[44]              | 2015–2 to 2015–6 | Taiwan | Healthcare workers | 19-91y     | 326           | 85      | 20 (23.5)           | prospective  | 7     |
| Lo WT, 2010[45]              | 2004 to 2009 | Taiwan | Healthy children | 1m-14y     | 3200          | 824     | 371 (45)            | prospective  | 7     |
| Huang YC, 2015[46]           | 2011         | Taiwan | Community residents | -          | 262           | 73      | 21 (28.8)           | prospective  | 7     |
| Lu PL, 2008[47]              | 2002–9       | Taiwan | Community residents | -          | 410           | 112     | 7 (6.3)             | prospective  | 7     |
| Qu F, 2010[48]               | 2007–5 to 2007–7 | Guangzhou | Community residents | 18-31y     | 1044          | 209     | 0 (0)               | cross-sectional | 7     |
| Chen CJ, 2013[49]            | 2010–8 to 2011–7 | Taiwan | Healthy children | -          | 154           | 75      | 12 (16)             | prospective  | 8     |
| Chang CJ, 2015[50]           | 2014–6 to 2014–8 | Taiwan | Community residents / Healthcare workers | 21-77y     | 75/111        | 10/17   | 1 (10)/4 (23.5)     | cross-sectional | 6     |

https://doi.org/10.1371/journal.pone.0223599.t001
through univariable or multivariable logistic regression models, and they included younger age (OR: 3.54, 95% CI: 2.38–5.26; OR: 2.24, 95% CI: 1.73–2.9), attending day care centers (DCCs) (OR: 1.95, 95% CI: 1.4–2.72; OR: 1.53, 95% CI: 1.2–1.95), flu vaccination (OR: 1.73, 95% CI: 1.28–2.35), residing in northern Taiwan (OR: 1.45, 95% CI: 1.19–1.77) in children, contact with livestock (OR: 6.31, 95% CI: 3.44–11.57) in Livestock-related workers, regular visits to health care facility (OR: 23.83, 95% CI: 2.72–209.01), household member working in health care facility (OR: 8.98, 95% CI:1.4–55.63), and using antibiotics within the past year (OR: 2.05, 95% CI:1.35–3.11). While colonization by S.pneumoniae (OR: 0.7, 95% CI: 0.52–0.94), Smoking habits (OR:0.44, 95% CI: 0.24–0.82) and breastfeeding (OR: 0.69, 95% CI: 0.516–0.93; OR: 0.65, 95% CI: 0.53–0.8) were protective factors in against MRSA carriage. Other influencing factors were reported in Table 4.
Furthermore, 10 studies were included for meta-analysis of the antimicrobial resistance of MRSA isolates. The pooled prevalence of MRSA resistance for 11 antibiotics included in the meta-analysis were presented in Table 5. High prevalence of resistance was observed to penicillin (100%, 95% CI: 99%-100%, P<0.001), erythromycin (88%, 95% CI: 79%-95%, P<0.001), Clindamycin (75%, 95% CI: 60%-87%, P<0.001). However, linezolid had a low rate of resistance (0%, 95% CI: 0%-4%, P<0.001), and the resistance of MRSA to Vancomycin has not been found in healthy people.

Discussion

Nasal MRSA carriage has been extensively studied in a variety of study populations with significant heterogeneous prevalence and influencing factors. We conducted this meta-analysis to summarize the prevalence of MRSA, antibiotic resistance and influencing factors of MRSA carriage in healthy Chinese population. The main findings were as follows: the pooled prevalence of MRSA was about 21%, and the prevalence of S.aureus was about 15%. When performing a subgroup analysis by study population, children (18%), Livestock-related workers (28%) and healthcare workers (20%) presented higher prevalence of MRSA compared with community residents (7%). When classifying studies by region, the prevalence of MRSA carriage in Taiwan (22%) was higher than in mainland China (11%) and Hong Kong (4%). The risk factors of MRSA carriage were including living in northern Taiwan, younger age, attending
DCCs, flu vaccination, using antibiotics within the past year, working in hospital, and contact Livestock or medical environment. These MRSA strains also showed extreme resistance to penicillin, ampicillin, erythromycin and clindamycin (100%, 93%, 88%, and 75%).

The prevalence of *S. aureus* was lower in our meta-analysis compared to diabetes population that was investigated by Lin J *et al* in the US (21.2% vs 28.3%)[51]. The prevalence of MRSA among *S. aureus* was about 15%, which was far lower than the average prevalence of clinical isolate MRSA reported by CHINET surveillance of bacterial resistance across China (38.4% between January 1, 2016 to December 31, 2016)[52]. However, Den Heijer CD *et al* conducted a study to find that the highest prevalence of MRSA was 2.1% and prevalence of *S. aureus* was 21.6% (ranging from 12.1% to 29.4%) for healthy people in nine European countries[53]. The lower prevalence of MRSA in European countries may be the result of increased public awareness of MRSA and subsequent public health measures to control MRSA.
As showed in subgroup analysis by region, the prevalence of MRSA in Taiwan was 22%, which was higher than the mainland and Hong Kong (11%, 4%). Meta-regression suggested that Taiwan was an risk factor of MRSA nasal carriage, which may be due to genetic variability or infection control measures. Further research is needed. In addition, the highest prevalence of MRSA was observed in the Livestock-related workers, followed by healthcare workers, children, medical students, community residents (28%, 20%, 18%, 11%, 7%). In this meta-regression, contact animals, children and working in hospital were risk factors for MRSA carriage. Several recent studies have shown that occupational livestock contact might lead to livestock-associated methicillin-resistant Staphylococcus aureus (LA-MRSA) transmission to humans, and LA-MRSA strains were associated with severe and lethal infections in humans[15, 54, 55]. Therefore, the emergence of LA-MRSA may pose a potential public health hazard that requires continuously monitoring. In addition, a review conducted by Dulon M et al found that carriage prevalence among healthcare works are much higher than among community members in Europe and the United States[56]. Not surprisingly, we also found Healthcare workers was the risk of MRSA carriage, which may be explained by the frequent and intimate contact with patient in the medical environment. Children were also considered to be a risk factor of MRSA in our meta-analysis, and may be a reservoirs of MRSA and play an important role in MRSA dissemination[57]. As for subgroup of methods to identify MRSA, The prevalence of MRSA in studies with oxacillin disk diffusion method (28%) seemed higher than that with the mecA gene method (12%), however, there was not statistically significant by meta-regression analysis. It is well known that the mecA gene method is recognized as the gold standard for diagnosing MRSA, which is generally only suitable to identification of purified staphylococcus cultures.

Table 2. Pooled prevalence of MRSA among S. aureus estimates by subgroups.

| Subgroups                        | Number of studies | MRSA prevalence(%) | 95%Confidence Interval | I²(P-value) | P-value * |
|----------------------------------|-------------------|--------------------|------------------------|-------------|-----------|
| **Age range**                    |                   |                    |                        |             |           |
| Children                         | 14                | 18                 | 11–26                  | 98.53 (P<0.001) | 0.4       |
| Non-children                     | 30                | 13                 | 9–18                   | 93.7 (P<0.001) |           |
| **Region**                       |                   |                    |                        |             |           |
| Mainland China                   | 17                | 11                 | 6–17                   | 94.99 (P<0.001) | <0.001    |
| Taiwan                           | 16                | 22                 | 17–27                  | 95.26 (P<0.001) |           |
| Hong Kong                        | 4                 | 4                  | 3–6                    | 0 (P = 0.74) |           |
| **Study population**             |                   |                    |                        |             |           |
| Community residents              | 12                | 7                  | 3–13                   | 94.88 (P<0.001) | 0.03      |
| Livestock-related workers        | 4                 | 28                 | 10–51                  | 86.9 (P<0.001) |           |
| Children                         | 14                | 18                 | 11–26                  | 98.53 (P<0.001) |           |
| Healthcare workers               | 9                 | 20                 | 12–29                  | 82.61 (P<0.001) |           |
| Medical students                 | 5                 | 11                 | 6–18                   | 84.76(P<0.001) |           |
| **Study period**                 |                   |                    |                        |             |           |
| 2001–2010                        | 19                | 16                 | 11–23                  | 98.2 (P<0.001) | 0.43      |
| 2011–2016                        | 18                | 13                 | 8–19                   | 92.77 (P<0.001) |           |
| **Method**                       |                   |                    |                        |             |           |
| mecA gene                        | 15                | 12                 | 7–19                   | 93.91 (P<0.001) | <0.001    |
| cefoxitin disk diffusion         | 8                 | 10                 | 4–18                   | 95.43 (P<0.001) |           |
| oxacillin disk diffusion         | 3                 | 28                 | 21–35                  | -           |           |
| others                           | 8                 | 22                 | 14–31                  | 96.3 (P<0.001) |           |
| oxacillin agar dilution          | 3                 | 8                  | 3–16                   | -           |           |

* a Q-test for heterogeneity between subgroups

https://doi.org/10.1371/journal.pone.0223599.t002
[58]. However, conventional antibiotic susceptibility tests, such as cefoxitin and oxacillin disc diffusion, have become the mainstream of diagnostic MRSA[59].
Moreover, seven articles discussed the influencing factors for MRSA nasal carriage in healthy Chinese populations. Younger age, attending DCCs, flu vaccination, living in northern Taiwan, using antibiotics within the past year, and frequent contact with livestock and medical environment are independent predictors of MRSA carriage. Among environmental factors, crowded environments, such as attending DCCs and living in northern Taiwan with the smaller mean house size compared with southern Taiwan, were associated risk for subsequent MRSA colonization. Antibiotic usage was an independent risk of MRSA colonization, so,
health care providers should promote the rational use of antibiotic. One of the seven studies unexpectedly found that influenza vaccination were significantly associated with MRSA colonization without confirmed by any research [26]. However, colonization by S. pneumoniae and breastfeeding are protective factors. Host innate immunity is associated with S. aureus nasal colonization, and breastfeeding may play a protective role in MRSA colonization through immunity[7, 60]. Additionally, the relationship between the prevalence of MRSA carriage and colonization by S. pneumoniae may be elucidated by S. pneumoniae-S. aureus interference, which could be mediated by hydrogen peroxide in the vitro study conducted by Gili RY et al [61]. Smoking habits appeared to be a protective factor of MRSA carriage in our study, while
parental smoking were independent risk factors in children[62]. Clearly, the impact of smoking on MRSA colonization needs further research.

Based on the above discussion, public health departments should focus on the results of meta-regression analysis and significant influencing factors when establishing public health interventions to reduce MRSA infection. Public health departments should pay more attention to healthy population in China with younger age, attending DCCs, flu vaccination, using antibiotics within the past year, working in hospital, and contact Livestock or medical environment.

In this meta-analysis, we also estimated the pooled prevalence of MRSA resistance to 11 different antimicrobial agents commonly used in China. It was found that MRSA resistance to commonly available antimicrobial agents in China was ranging from 0% to vancomycin to 100% to penicillin. MRSA resistance to beta-lactam antibiotics (penicillin, ampicillin) is understood via expressing PBP2a[63]. In addition, MRSA was highly resistant to erythromycin and clindamycin (88%, 75%). Several previous studies have found that MRSA resistance to erythromycin is also associated with resistant to clindamycin, this cross-resistance can be mediated by erythromycin ribosomal methylase encoding genes[64, 65]. In 2002, the first vancomycin-resistant S. aureus strain was reported in the United States[66]. Fortunately, no resistance to vancomycin was found in our meta-analysis. However, more and more vancomycin intermediate-resistant S. aureus (VISA) was reported with increasing frequency in the use of vancomycin, which may pose severe challenges to public health security in the future[67]. At present, vancomycin remains the first choice for the treatment of serious MRSA infection. In addition, Linezolid and daptomycin are considered as the first-line drugs for some selected patients, such as skin and skin structure infections[68].

There are some strengths. Firstly, the included studies have provided sufficient simple size. Secondly, all subjects were healthy Chinese people, thus excluding the impact of ethnic, which

| Table 3. Summary results of meta-regression for the prevalence of MRSA. |
|---|---|---|---|---|
| Factor | Coefficient | OR | 95% CI (OR) | P-value |
| **Age range** | | | | |
| Non-children | - | 1 | - | - |
| children | 0.405 | 1.499 | 0.623−3.301 | 0.307 |
| **Region** | | | | |
| Taiwan | - | 1 | - | - |
| Mainland | -0.84 | 0.432 | 0.203−0.919 | 0.003 |
| Hong Kong | -1.359 | 0.257 | 0.078−0.842 | 0.026 |
| **Study population** | | | | |
| Community residents | - | 1 | - | - |
| Children | 1.048 | 2.851 | 1.191−6.825 | 0.02 |
| Livestock-related workers | 1.512 | 4.537 | 1.228−16.769 | 0.024 |
| Medical students | 0.417 | 1.517 | 0.415−5.544 | 0.519 |
| Healthcare workers | 1.296 | 3.655 | 1.314−9.794 | 0.011 |
| **Study period** | | | | |
| 2001–2010 | - | 1 | - | - |
| 2011–2018 | -0.314 | 0.73 | 0.349−1.53 | 0.396 |
| **method** | | | | |
| mecA gene | - | 1 | - | - |
| cefoxitin disk diffusion | -0.381 | 0.683 | 0.253−1.844 | 0.442 |
| oxacillin disk diffusion | 1.117 | 3.054 | 0.939−9.936 | 0.063 |
| others | 0.706 | 2.026 | 0.82−5.005 | 0.122 |

https://doi.org/10.1371/journal.pone.0223599.t003
Table 4. Risk factors of MRSA nasal carriage in healthy Chinese population reported in the selected studies.

| Influencing Factors, Odds ratio (95% CI) | Univariable logistic regression models | Multivariable logistic regression models |
|----------------------------------------|----------------------------------------|----------------------------------------|
|                                        | Xie XY, 2018 [23]                      | Chen CH, 2018 [26]                      | Chen CJ, 2011 [7]                      | Chen CJ, 2013 [49]                      | Ye XH, 2015 [15]                      | Wang JT, 2009 [41]                      | Pan HH, 2017 [42]                      |
| Gender (male vs female)                | 0.88 (0.24–3.16)                      | -                                      | -                                      | -                                      | -                                      | 0.99 (0.72–1.36)                      |
| Age (2–6 m vs 0.5–5y)                  | -                                      | 3.54 (2.38–5.26)                      | 2.24 (1.73–2.9)                       | -                                      | -                                      | -                                      |
| Current smoking statue (yes vs no)     | 2.03 (0.25–16.75)                     | -                                      | -                                      | -                                      | -                                      | -                                      |
| Residing in northern Taiwan (yes vs no)| -                                      | -                                      | 1.45 (1.19–1.77)                      | -                                      | -                                      | -                                      |
| Department (microbiological laboratory vs other laboratory) | 0.58 (0.12–2.76) | -                                      | -                                      | -                                      | -                                      | -                                      |
| Nasal cleaning habit (daily or weekly vs rarely or never) | 1.34 (0.34–5.26) | -                                      | -                                      | -                                      | -                                      | -                                      |
| Underlying disease (yes vs no)         | 1.88 (0.39–9.2)                       | -                                      | -                                      | -                                      | -                                      | -                                      |
| Colonization by S. pneumoniae (yes vs no) | -                                      | -                                      | 0.7 (0.52–0.94)                      | -                                      | -                                      | -                                      |
| Breastfeeding (yes vs no)              | -                                      | 0.69 (0.52–0.93)*                     | 0.65 (0.53–0.8)*                     | -                                      | -                                      | 0.85 (0.60–1.20)                      |
| Day care attendance (yes vs no)        | -                                      | 1.95 (1.4–2.72)                       | 1.53 (1.2–1.95)*                     | -                                      | -                                      | 0.78 (0.48–1.24)                      |
| Flu vaccination (yes vs no)            | -                                      | 1.73 (1.28–2.35)*                     | -                                      | -                                      | -                                      | -                                      |
| Contact with livestock (yes vs no)     | -                                      | -                                      | -                                      | 6.31 (3.44–11.57)*                    | -                                      | -                                      |
| Contact with pig (yes vs no)           | -                                      | -                                      | -                                      | 6.58 (3.50–12.38)*                    | -                                      | -                                      |
| Contact with poultry (yes vs no)       | -                                      | -                                      | -                                      | 4.94 (1.32–18.41)*                    | -                                      | -                                      |
| Contact with other animal (yes vs no)  | -                                      | -                                      | -                                      | 4.50 (0.88–22.98)*                    | -                                      | -                                      |
| Living with hospital staff (yes vs no) | 0.83(0.21–3.27)                       | -                                      | -                                      | -                                      | -                                      | -                                      |
| Smoking habits (yes vs no)             | -                                      | -                                      | -                                      | -                                      | 0.44(0.24–0.82)*                      | -                                      |
| Passive smoking (yes vs no)            | -                                      | -                                      | -                                      | -                                      | 1.16 (0.84–1.60)                      | -                                      |
| Using antibiotics within the past year (yes vs no) | -                                      | -                                      | -                                      | -                                      | 2.05 (1.35–3.11)*                     | -                                      |
| Presence of household members aged under 7 | -                                      | -                                      | -                                      | -                                      | 2.24 (1.53–3.29)*                    | -                                      |
| Received antibiotics within 2 weeks (yes vs no) | -                                      | -                                      | -                                      | -                                      | -                                      | 1.78 (0.92–3.46)                      |
| URI within 2 weeks (yes vs no)         | -                                      | -                                      | -                                      | -                                      | -                                      | 1.270(0.88–1.84)                     |
| Pneumococcal vaccination(yes vs no)    | -                                      | -                                      | -                                      | -                                      | -                                      | 1.38(0.89–2.14)                     |
| Regular visits to health care facility(yes vs no) | -                                      | -                                      | -                                      | -                                      | 23.83(2.72–209.01)*                | -                                      |
| Household member working in health care facility(yes vs no) | -                                      | -                                      | -                                      | -                                      | 8.98 (1.4–55.63)*                    | -                                      |

*Statistical significance

Underlying disease: hypertension, diabetes, chronic rhinitis, urticaria, hyperthyroidism

https://doi.org/10.1371/journal.pone.0223599.t004
was considered as a major potential confounding factor. Most importantly, MRSA poses a serious threat to public health. MRSA colonization in healthy hosts is a risk factor in causing infection and may play an important role in the dissemination of MRSA in community and hospital settings. This meta-analysis is the first to focus on the prevalence of MRSA in healthy Chinese populations, and could provide some epidemiological information about MRSA and the influencing factors, as well as antibiotic resistance.

However, there are also some limits in our meta-analysis. Firstly, the significant heterogeneity of prevalence of MRSA in the included studies was observed. There was no doubt that we should pay attention to heterogeneity. However, our subgroup analysis by age, study population, region, and method did not significantly reduce heterogeneity, except in Hong Kong. Because sufficient data in primary studies were lacking, we failed to perform further subgroup analyses to investigate the other factors, such as gender, history of previous antibiotic usage, smoking, which may also be the cause of such heterogeneity. Secondly, we only focus on nasopharyngeal colonization, however, Bitterman et al indicated that multiple sites should be used to detect carry-over status[69]. In addition, the included studies are cross-sectional studies, which make it difficult to distinguish between persistent carriers and intermittent carriers[70]. Finally, all the studies are mainly carried out in high-level general hospitals, and the study areas are unevenly distributed in the mainland, mainly in Beijing, Shanghai, Guangzhou, Sichuan, Shenyang and Jinan. Therefore, it is impossible to represent population distribution of the whole country. Despite the above weaknesses of the study, all studies were of non-low quality (score > 5). Additionally, publication bias did not found according to the Begg’s test and Egger’s test. So the results of this study are reliability and accuracy. In the future, prospective studies may need to verify these results, to guide the development of measures to control the spread of MRSA.

**Conclusion**

In this meta-analysis, the pooled prevalence of S. aureus was about 21%, and the pooled MRSA prevalence was considerably high, reaching 15%. MRSA was also found to be highly resistant

Table 5. Pooled prevalence of MRSA resistance to different antimicrobial agents in healthy Chinese population.

| Antibiotics | Fan J, 2011 | Chen B, 2015 | Du J, 2011 | Fu J, 2015 | Zhong JJ, 2016 | Huoang YC, 2007 | Huoang YC, 2005 | O’Donohue MM, 2004 | Chen CS, 2012 | Pan HH, 2017 | Pooled resistance rate, (95% CI) | $I^2$ (P-value) |
|-------------|-------------|-------------|-------------|-------------|---------------|-----------------|-----------------|-----------------|-------------|-------------|-----------------|-----------------|
| Penicillin  | 9 (100)     | -           | 28 (100)    | 25 (89.3)   | 20 (100)      | 210 (99.1)     | 23 (100)        | 9 (100)         | -             | 162 (98.2)   | 1 (0.99–1)     | 0 (P = 0.48)    |
| Ampicillin  | -           | -           | 26 (92.9)   | -           | -             | -               | -               | -               | -             | -            | 0.93 (-)       | -               |
| Erythromycin| 7 (77.8)    | 4 (100)     | 21 (75)     | 23 (82.1)   | 12 (60)       | 198 (93.4)     | 23 (100)        | 7 (77.8)        | 5 (71.4)     | 153 (92.7)   | 0.88 (0.79–0.95) | 71.89 (P<0.001) |
| Gentamicin  | -           | 1 (25)      | 8 (28.6)    | 2 (10)      | -             | -               | 5 (55.6)        | -               | -             | -            | 0.26 (0.09–0.47) | 53.13 (P = 0.09) |
| Clindamycin | 2 (22.2)    | 4 (100)     | 15 (53.6)   | 22 (78.6)   | 13 (65)       | 193 (91)       | 7 (77.8)        | 5 (71.4)        | 147 (89.1)   | 0.75 (0.6–0.87) | 84.23 (P<0.001) |
| Tetracycline| -           | 1 (25)      | 8 (28.6)    | 8 (28.6)    | 10 (50)       | -               | -               | -               | -             | -            | 0.33 (0.22–0.44) | 0 (P = 0.42)    |
| Ciprofloxacin| -           | 15 (53.6)   | 3 (15)      | -           | -             | 5 (55.6)        | -               | -               | -             | -            | 0.39 (0.13–0.69) | 77.04 (P = 0.01) |
| Levofloxacin| -           | 11 (39.3)   | 1 (3.6)     | -           | -             | -               | -               | -               | -             | 0.18 (0.09–0.3) | -             |
| Doxycycline | -           | -           | -           | -           | 5 (2.4)       | -               | -               | 0 (0)           | 8 (4.9)      | 0.02 (0–0.04)   | 0 (P = 0.43)   |
| Vancomycin  | 0 (0)       | 0 (0)       | 0 (0)       | 0 (0)       | 0 (0)         | -               | -               | 0 (0)           | 0 (0)        | 0 (0–0)       | 0 (P = 0.93)   |
| Linezolid   | 1 (11.1)    | 0 (0)       | 0 (0)       | 1 (5)       | -             | -               | -               | 0 (0)           | -            | 0 (0–0.04)     | 0 (P = 0.41)   |

https://doi.org/10.1371/journal.pone.0223599.t005
to penicillin, ampicillin, erythromycin and clindamycin. In contrast, MRSA was not found to be resistant to vancomycin in healthy Chinese population. In addition, to control MRSA carriage and infection, Public MRSA protection measures should be required in Livestock-related workers and children with younger age or attending DCCs. Healthcare workers should take strict disinfection measures, and strengthen the surveillance of MRSA. Additionally, the supervision of antibiotics also should be strengthened in both hospitals and communities.

**Supporting information**

S1 File. Subgroup analyses. (DOCX)

S1 Table. PRISMA checklist. (DOC)

S2 Table. Quality assessment of the included studies. (DOCX)

**Author Contributions**

Conceptualization: Hong Fan.

Data curation: Man Wu, Sitong Liu, Dongguang Wang, Lei Wang.

Methodology: Man Wu, Xiang Tong, Sitong Liu.

Resources: Hong Fan.

Software: Dongguang Wang.

Writing – original draft: Man Wu, Xiang Tong, Sitong Liu, Lei Wang.

Writing – review & editing: Man Wu, Xiang Tong.

**References**

1. Hassoun A, Linden PK, Friedman B. Incidence, prevalence, and management of MRSA bacteremia across patient populations—a review of recent developments in MRSA management and treatment. Critical Care. 2017; 21:211. https://doi.org/10.1186/s13054-017-1801-3 PMID: 28807042

2. Sahreena L, Zhang KY. Methicillin-Resistant Staphylococcus aureus: Molecular Characterization, Evolution, and Epidemiology. Clin Microbiol Rev, 2018, 12; 31(4).

3. Hurley JC. Risk of death from methicillin-resistant Staphylococcus aureus bacteraemia: a meta-analysis. Med J Aust. 2002; 176:264–267.

4. Jokinen E, Laine J, Huttunen R, Rahikka P, Huhtala H, Vuento R, et al. Comparison of outcome and clinical characteristics of bacteremia caused by methicillin-resistant, penicillin-resistant and penicillin-susceptible Staphylococcus aureus strains. Infect Dis. 2017; 49:493–500.

5. Stryzewski ME, Corey GR. Methicillin-resistant Staphylococcus aureus: an evolving pathogen. Clinical Infectious Diseases. 2014; 58 Suppl 1:S10.

6. Abdulgader SMA, Shittu A, Nicol MP, Kaba M. Molecular epidemiology of methicillin-resistant Staphylococcus aureus in Africa: a systematic review of the published literature. International Journal of Infectious Diseases. 2014; 21:107–107.

7. Chih-Jung C, Kuang-Hung H, Tzou-Yien L, Kao-Pin H, Po-Yen C, Yhu-Chering H. Factors associated with nasal colonization of methicillin-resistant Staphylococcus aureus among healthy children in Taiwan. Journal of Clinical Microbiology. 2011; 49:131. https://doi.org/10.1128/JCM.01774-10 PMID: 21084507

8. Philippe C, Hélène M, Olivier J, Josiane C, Anne-Laure BU. Molecular evidence that nasal carriage of Staphylococcus aureus plays a role in respiratory tract infections of critically ill patients. Journal of Clinical Microbiology. 2005; 43:3491–3. https://doi.org/10.1128/JCM.43.7.3491-3493.2005 PMID: 16000487
The prevalence of MRSA in healthy Chinese population

9. Yhu-Chereng H, Chen-Fang H, Chi-Jung C, Lin-Hui S, Tiou-Yien L. Nasal carriage of methicillin-resistant Staphylococcus aureus in household contacts of children with community-acquired diseases in Taiwan. Pediatric Infectious Disease Journal. 2007; 26:1066–1068. https://doi.org/10.1097/INF.0b013e31813429e8 PMID: 17984820

10. Liu W, Liu Z, Yao Z, Fan Y, Ye X, Chen S. The prevalence and influencing factors of methicillin-resistant Staphylococcus aureus carriage in people in contact with livestock: A systematic review. Ajic American Journal of Infection Control. 2015; 43:469–475.

11. Boyle MH. Guidelines for evaluating prevalence studies. Evidence-Based Mental Health. 1998; 1:37–39.

12. Dersimonian R, Nan L. Meta-analysis in clinical trials revisited. Contemporary Clinical Trials. 2015; 45:139–145. https://doi.org/10.1016/j.cct.2015.09.002 PMID: 26343745

13. Higgins JP, Thompson SG. Quantifying heterogeneity in a meta-analysis. Statistics in Medicine. 2002.

14. Barendregt JJ, Doi SA, Yong YL, Norman RE, Yos T. Meta-analysis of prevalence. J Epidemiol Community Health. 2013; 67:974–978. https://doi.org/10.1136/jech-2013-203104 PMID: 23963506

15. Ye X, Liu W, Fan Y, Wang X, Zhou J, Yao Z, et al. Frequency-risk and duration-risk relations between occupational livestock contact and methicillin-resistant Staphylococcus aureus carriage among workers in Guangdong, China. Ajic American Journal of Infection Control. 2015; 43:676–681.

16. Fan J, Zhou W, Shu M, DengJJ, Zhu Y, Deng SY, et al. Nasal carriage of community-acquired methicillin-resistant Staphylococcus aureus clones. Diagn Microbiol Infect Dis. 2011; 70:22–30.

17. Zhang W, Hao Z, Wang Y, Cao X, Logue CM, Wang B, et al. Molecular characterization of methicillin-resistant Staphylococcus aureus strains from pet animals and veterinary staff in China. Veterinary Journal. 2011; 190:e125–e129.

18. Xiao XM, Sun DD, Wang S, Wang ML, Li M, Shang H, et al. Nasal carriage of methicillin-resistant Staphylococcus aureus among preclinical medical students: epidemiologic and molecular characteristics of methicillin-resistant S. aureus clones. Diag Microbiol Infect Dis. 2011; 70:22–30. https://doi.org/10.1016/j.diagmicrobio.2010.12.004 PMID: 21513841

19. Ma XX, Luo EJ. Distribution of Staphylococcus aureus strains colonized in healthy community population and molecular epidemiological characteristics for MRSA strains. Chin J Epidemiol. 2011; 32:804–807.

20. Chen B, Dai X, He B, Pan K, Li H, Liu X, et al. Differences in Staphylococcus aureus nasal carriage and molecular characteristics among community residents and healthcare workers at Sun Yat-Sen University, Guangzhou, Southern China. Bmc Infectious Diseases. 2015; 15:303. https://doi.org/10.1186/s12879-015-1032-7 PMID: 26223250

21. Jimei D, Chun C, Baixing D, Jinjing T, Zhiqiang Q, Chris P, et al. Molecular characterization and antimicrobial susceptibility of nasal Staphylococcus aureus isolates from a Chinese medical college campus. Plos One. 2011; 6:e27328. https://doi.org/10.1371/journal.pone.0027328 PMID: 22114670

22. O’Donoghue MM, Boost MV. The prevalence and source of methicillin-resistant Staphylococcus aureus (MRSA) in the community in Hong Kong. Epidemiology & Infection. 2004; 132:1091–1097.

23. Xie X, Dai X, Ni L, Chen B, Luo Z, Yao Y, et al. Molecular epidemiology and virulence characteristics of Staphylococcus aureus nasal colonization in medical laboratory staff: comparison between microbiological and non-microbiological laboratories. Bmc Infectious Diseases. 2018; 18:122. https://doi.org/10.1186/s12879-018-3024-x PMID: 29529992

24. Yan X, Song Y, Yu X, Tao X, Yan J, Luo F, et al. Factors associated with Staphylococcus aureus nasal carriage among healthy people in Northern China. Clinical Microbiology & Infection the Official Publication of the European Society of Clinical Microbiology & Infectious Diseases. 2015; 21:157–162.

25. Chen BJ, Xie XY, Ni LJ, Dai XL, Lu Y, Wu XQ, et al. Factors associated with Staphylococcus aureus nasal carriage and molecular characteristics among the general population at a Medical College Campus in Guangzhou, South China. Annals of Clinical Microbiology & Antimicrobials. 2017; 16:28.

26. Chen CH, Kuo KC, Hwang KP, Lin TY, Huang YC. Risk factors for and molecular characteristics of methicillin-resistant Staphylococcus aureus nasal colonization among healthy children in southern Taiwan, 2005–2010. Journal of Microbiology, Immunology and Infection.

27. Deng JJ, Wan CM, Mu D Z, Zhou w, Xu AL, Fan J, et al. Nasal Carriage of Community-acquired Staphylococcus aureus and Drug Sensitivity Testsin Healthy Children in Chengdu. J Sichuan Univ (MedSci). 2012; 45:139–145.

28. Zhang M, O’Donoghue MM, Ito T, Hiramatsu K, Boost MV. Prevalence of antiseptic-resistance genes in Staphylococcus aureus and coagulase-negative staphylococci colonising nurses and the general population in Hong Kong. Journal of Hospital Infection. 2011; 78:113–117. https://doi.org/10.1016/j.jhin.2011.02.018 PMID: 21507521
29. Ho PL, Chiu SS, Chan MY, Gan Y, Chow KH, Lai EL, 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. Journal of Infection. 2012; 64:500–506. https://doi.org/10.1016/j.jinf.2012.02.018 PMID: 22406412

30. Gong Z, Shu M, Xia Q, Tan S, Zhou W, Zhu Y, et al. Staphylococcus aureus nasal carriage and its antibiotic resistance profiles in children in high altitude areas of Southwestern China. Archives Argentinos De Pediatría. 2017; 115:274. https://doi.org/10.1055/aap.2017.06.027 PMID: 28504494

31. Boost MV, So SYC, Perreten V. Low rate of methicillin-resistant coagulase-positive staphylococcal colonization of veterinary personnel in Hong Kong. Zoonoses & Public Health. 2011; 58:36–40.

32. Jin-Jian FU, Xiao-Hua YE, Yao ZJ, Fan YP, Chen SD. Antibiotic resistance of Staphylococcus aureus from the nasal carriage in healthy school children. Modern Preventive Medicine. 2015.

33. Ge YL, Chen YH, Zhu SY, Shen W. Study on Methicillin—Resistant Staphylococcus aureus Carrying and Drug—Resistance Related Genes In Medical Staff. Chin J Disinfection. 2012; 29:565–568.

34. Liu H, Fei CN, Dong J, Shen P, Liu J, Ji XY, et al. Study of bacterium drug—resistance in nasal vestibular of medical staff. Chin J Disinfection. 2016; 33:983–985.

35. Zhong J, Zhang C, Lai L, Yu X, Wang X, Ye X. Carriage and antibiotic resistance of methicillin resistant Staphylococcus aureus colonies among meat processing and sales workers. Chin J Nosocomiology. 2016; 26:5315–5317.

36. Yhu-Che ring H, Kao-Pin H, Po-Yen C, Chih-Jung C, Tzou-Yien L. Prevalence of methicillin-resistant Staphylococcus aureus nasal colonization among Taiwanese children in 2005 and 2006. Journal of Clinical Microbiology. 2007; 45:3992–5. https://doi.org/10.1128/JCM.01202-07 PMID: 17942647

37. Po-Liang L, Lien-Chun C, Chien-Fang P, Yi-Hsiung C, Tyen-Po C, Ling M, et al. Risk factors and molecular analysis of community methicillin-resistant Staphylococcus aureus carriage. Journal of Clinical Microbiology. 2005; 43:132. https://doi.org/10.1128/JCM.43.1.132-144.2005 PMID: 15634961

38. Wen-Tsung L, Wei-Jen L, Min-Hua T, Chih-Chien W, Chih-Chien W. Methicillin-resistant Staphylococcus aureus in children. Taiwan. Emerging Infectious Diseases. 2006; 12:1267–1270. https://doi.org/10.3201/eid1208.051570 PMID: 16965712

39. Huang YC, Su LH, Chen CJ, Lin TY. Nasal carriage of methicillin-resistant Staphylococcus aureus in school children without identifiable risk factors in northern taiwan. Pediatric Infectious Disease Journal. 2005; 24:276–278. https://doi.org/10.1097/01.inf.0000154333.46032.0f PMID: 15750471

40. Chen CS, Chen CY, Huang YC. Nasal carriage rate and molecular epidemiology of methicillin-resistant Staphylococcus aureus among medical students at a Taiwanese university. International Journal of Infectious Diseases Ijid Official Publica tion of the International Society for Infectious Diseases. 2012; 16:e799–e803. https://doi.org/10.1016/j.ijid.2012.07.004 PMID: 22878173

41. Wang JT, Liao CH, Fang CT, Chie WC, Lai MS, Lauderdale TL, et al. Prevalence of and risk factors for colonization by methicillin-resistant Staphylococcus aureus among adults in community settings in Taiwan. Journal of Clinical Microbiology. 2009; 47:2957. https://doi.org/10.1128/JCM.00853-09 PMID: 19625471

42. Pan HH, Huang YC, Chen CJ, Huang FL, Ting PJ, Huang JY, et al. Prevalence of and risk factors for nasal methicillin-resistant Staphylococcus aureus colonization among children in central Taiwan. Journal of Microbiology Immunology & Infection. 2017S16841 18217300634.

43. Wang HK, Huang CY, Chen CJ, Huang YC. Nasal Staphylococcus aureus and methicillin-resistant Staphylococcus aureus carriage among college student athletes in northern Taiwan. Journal of microbiology, immunology, and infection = Wei mi an yu gan ran za zhi. 2017; 50:S1684118217300749.

44. Wu TH, Lee CY, Yang HJ, Fang YP, Chang YF, Tzeng SL, et al. Prevalence and molecular characteristics of methicillin-resistant Staphylococcus aureus among nasal carriage strains isolated from emergency department patients and healthcare workers in central Taiwan. Journal of Microbiology, Immunology and Infection.

45. Wen-Tsung L, Chih-Chien W, Wei-Jen L, Sheng-Ru W, Ching-Shen T, Ching-Feng H, et al. Changes in the nasal colonization with methicillin-resistant Staphylococcus aureus in children: 2004–2009. Plos One. 2010; 5:e15791–e15791. https://doi.org/10.1371/journal.pone.0015791 PMID: 21209954

46. Huang Y-C, Chen C-J. Nasal Carriage of Methicillin-Resistant Staphylococcus aureus During the First 2 Years of Life in Children in Northern Taiwan. Pediatric Infectious Disease Journal. 2015; 34:131–5. https://doi.org/10.1097/INF.0000000000000517 PMID: 25144800

47. Lu PL, Tsai J-C, Chiu Y-W, Chang F-Y, Chen Y-W, Hsiao C-F, et al. Methicillin-resistant Staphylococcus aureus nasal carriage, infection and transmission in dialysis patients, healthcare workers and their family members. Nephrology, dialysis, transplantation: official publication of the European Dialysis and Transplant Association—European Renal Association. 2008; 23:1659.
48. Qu F, Cui E, Guo T, Li H, Chen S, Liu L, et al. Nasal Colonization of and Clonal Transmission of Methicillin-Susceptible Staphylococcus aureus among Chinese Military Volunteers. Journal of Clinical Microbiology. 2010; 48:64–9. https://doi.org/10.1128/JCM.01572-09 PMID: 19889899

49. Chen CJ, Wang S-C, Chang H-Y, Huang Y-C. Longitudinal Analysis of Methicillin-Resistant and Methicillin-Susceptible Staphylococcus aureus Carriage in Healthy Adolescents. Journal of Clinical Microbiology. 2013; 51:2506–2514. https://doi.org/10.1128/JCM.00572-13 PMID: 23678067

50. Chun-Jui C, Ning-Chun C, Chong-Kei L, Yhu-Chering H, Srinand S. Nasal Staphylococcus aureus and Methicillin-Resistant S. aureus Carriage among Janitors Working in Hospitals in Northern Taiwan. Plos One. 2015; 10:e0138971. https://doi.org/10.1371/journal.pone.0138971 PMID: 26407070

51. Prevalence, Influencing Factors, Antibiotic Resistance, Toxin and Molecular Characteristics of Staphylococcus aureus and MRSA Nasal Carriage among Diabetic Population in the United States, 2001–2004

52. Hu FP, Guo Y, Zhu DM, Wang F, Jiang XF, Xu YC, et al. CHINET surveillance of bacterial resistance across China: report of the results in 2016. Chin J of Infect Chemother. 2017; 17:7–17.

53. Heijer CDJ, Den, Bijnen EME, Van W John P, Mike P, Herman G, Bruggeman CA, et al. Prevalence and resistance of commensal Staphylococcus aureus, including meticillin-resistant S aureus, in nine European countries: a cross-sectional study. Lancet Infectious Diseases. 2013; 13:409–415. https://doi.org/10.1016/S1473-3099(13)70036-7 PMID: 23473661

54. Wang XL, Li L, Li SM, Huang JY, Fan YP, Yao ZJ, et al. Phenotypic and molecular characteristics of Staphylococcus aureus and methicillin-resistant Staphylococcus aureus in slaughterhouse pig-related workers and control workers in Guangdong Province, China. Epidemiology and Infection.

55. Chen CJ, Lauderdale TY, Lu CT, Chuang YY, Yang CC, Wu TS, et al. Clinical and molecular features of Methicillin-Resistant S. aureus Carriage among Janitors Working in Hospitals in Northern Taiwan. Plos One. 2015; 10:e0138971. https://doi.org/10.1371/journal.pone.0138971 PMID: 26407070

56. Dulon M, Peters C, Schablon A, Nienhaus A. MRSA carriage among healthcare workers in non-outbreak settings in Europe and the United States: a systematic review. Bmc Infectious Diseases. 2014; 14:1–14. https://doi.org/10.1186/1471-2334-14-1

57. Ken H, Kyoko KA, Munetaka Y, Teruyo I, Yasuo N, Longzhu C, et al. Dissemination of methicillin-resistant staphylococci among healthy Japanese children. Journal of Clinical Microbiology. 2005; 43:3364–3372. https://doi.org/10.1128/JCM.43.7.3364-3372.2005 PMID: 16000461

58. Brown J. DF. Guidelines for the laboratory diagnosis and susceptibility testing of methicillin-resistant Staphylococcus aureus (MRSA). Journal of Antimicrobial Chemotherapy. 2005; 56:1000. https://doi.org/10.1093/jac/dki372 PMID: 16293678

59. Kali A, Stephen S, Umadevi S. Laboratory Evaluation of Phenotypic Detection Methods of Methicillin-Resistant Staphylococcus Aureus. Biomedical Journal. 2014; 37:411–414. https://doi.org/10.4103/2319-4170.132907 PMID: 25179712

60. Quinn GA, Cole AM. Suppression of innate immunity by a nasal carriage strain of Staphylococcus aureus increases its colonization on nasal epithelium. Immunology. 2010; 122:80–89.

61. Gili RY, Krzysztof T, Thompson CM, Richard M, Marc L. Interference between Streptococcus pneumoniae and Staphylococcus aureus: In vitro hydrogen peroxide-mediated killing by Streptococcus pneumoniae. Journal of Bacteriology. 2006; 188:4996. https://doi.org/10.1128/JB.00317-06 PMID: 16786209

62. Soltani B, Arakani AT, Moravveji A, Erami M, Rezaei MH, Moniri R, et al. Risk Factors for Methicillin Resistant Staphylococcus aureus Nasal Colonization of Healthy Children. Jundishapur Journal of Microbiology. 2014; 7:e20025. https://doi.org/10.5812/jjm.20025 PMID: 25485071

63. Waters EM, Rudkin JK, Coughlan S, Clair GC, Adkins JN, Gore S, et al. Redeploying β-Lactam Antibiotics as a Novel Antivirulence Strategy for the Treatment of Methicillin-Resistant Staphylococcus aureus Infections. Journal of Infectious Diseases. 2017; 215:80. https://doi.org/10.1093/infdis/jiw461 PMID: 28077586

64. Jarajreh D, Aqel A, Alzoubi H, Al-Zereini W. Prevalence of inducible clindamycin resistance in methicillin-resistant Staphylococcus aureus: the first study in Jordan. Journal of Infection in Developing Countries. 2017; 11:350. https://doi.org/10.3855/jidc.8310 PMID: 28459227

65. Lail M, Sahni AK. Prevalence of inducible clindamycin resistance in Staphylococcus aureus isolated from clinical samples. Medical Journal Armed Forces India. 2014; 70:43–47.

66. Sievert DM, Rudrik JT, Patel JB, Mcdonald LC, Wilkins MJ, Hageman JC. Vancomycin-resistant Staphylococcus aureus in the United States, 2002–2006. Clinical Infectious Diseases. 2008; 46:668–674. https://doi.org/10.1086/527392 PMID: 18257700

67. Susana G, Alexander T. Mechanisms of vancomycin resistance in Staphylococcus aureus. Journal of Clinical Investigation. 2014; 124:2836. https://doi.org/10.1172/JCI68834 PMID: 24983424
68. Rodvold KA, Mcconeghy KW. Methicillin-resistant Staphylococcus aureus therapy: past, present, and future. Clinical Infectious Diseases. 2014; 58 Suppl 1:S20.

69. Bitterman Y, Laor A, Itzhaki S, Weber G. Characterization of the best anatomical sites in screening for methicillin-resistant Staphylococcus aureus colonization. European Journal of Clinical Microbiology & Infectious Diseases. 2010; 29:391–397.

70. Wertheim HF, Melles DC, Leeuwen WV, Belkum AV, Verbrugh HA, et al. The role of nasal carriage in Staphylococcus aureus infections. Lancet Infectious Diseases. 2005; 5:751–762. https://doi.org/10.1016/S1473-3099(05)70295-4 PMID: 16310147