Proportions of *Staphylococcus aureus* and Methicillin-Resistant *Staphylococcus aureus* in Patients with Surgical Site Infections in Mainland China: A Systematic Review and Meta-Analysis

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Abstract

**Background**

Sufficient details have not been specified for the epidemiological characteristics of *Staphylococcus aureus* (*S. aureus*) and methicillin-resistant *Staphylococcus aureus* (MRSA) among surgical site infections (SSIs) in mainland China. This systematic review aimed to estimate proportions of *S. aureus* and MRSA in SSIs through available published studies.

**Methods**

PubMed, Embase and four Chinese electronic databases were searched to identify relevant primary studies published between 2007 and 2012. Meta-analysis was conducted on the basis of logit-transformed metric for proportions of *S. aureus* and MRSA, followed by predefined subgroup meta-analysis. Random-effects meta-regression was also conducted to explore the impact of possible factors on *S. aureus* proportions.

**Results**

106 studies were included, of which 38 studies involved MRSA. *S. aureus* accounted for 19.1% (95%CI 17.2-21.0%; I² = 84.1%) of all isolates in SSIs, which was roughly parallel to 18.5% in the United States (US) (P-value = 0.57) but significantly exceeded those calculated through the surveillance system in China (P-value <0.001). In subgroup analysis, *S. aureus* in patients with thoracic surgery (41.1%, 95%CI 26.3-57.7%; I² = 74.4%) was more common than in those with gynecologic surgery (20.1%, 95%CI 15.6-25.6%; I² = 33.0%) or abdominal surgery (13.8%, 95%CI 10.3-18.4%; I² = 70.0%). Similar results were found in meta-regression. MRSA accounted for 41.3% (95%CI 36.5-46.3%; I² = 64.6%) of *S. aureus*,
 Competing Interests: This study was partly supported by MedImmune LLC, a wholly owned subsidiary of AstraZeneca, mainly for literature search and data collection. The funding was received directly by Peking University Health Science Center. None was paid individually to the researchers in this study for any employment or consultancy for the company. Antibiotics discussed in this review were not the patents of the company or its products in development or on market. There is no further relevant information about the conflicts of interest to declare. This does not alter the authors’ adherence to all the PLOS ONE policies on sharing data and materials, as detailed online in the guide for authors.

significantly lower than that in the US (P-value = 0.001). MRSA was sensitive to vancomycin (522/522) and linezolid (93/94), while 79.9% (95% CI 67.4-88.4%; I² = 0%) and 92.0% (95% CI 80.2-97.0%; I² = 0%) of MRSA was resistant to clindamycin and erythromycin respectively.

**Conclusion**

The overall proportion of *S. aureus* among SSIs in China was similar to that in the US but seemed higher than those reported through the Chinese national surveillance system. Proportions of *S. aureus* SSIs may vary with different surgery types. Commonly seen in SSIs, MRSA tended to be highly sensitive to vancomycin and linezolid but mostly resistant to clindamycin and erythromycin.

**Introduction**

It has been widely accepted that surgical site infections (SSIs) are an important component of all the nosocomial infection. Three types of SSIs are defined by the Centers for Disease Control and Prevention (CDC), including superficial, deep incisional SSIs and organ-space SSIs, depending on the sites and the extent of infection [1], among which superficial incisional SSIs are more common than the other two types [2]. In the United States (US) 2%-5% of patients undergoing surgeries develop SSIs of varying severity [3]. In studies from Europe, SSIs have a similar incidence, hovering at 3%-5% among patients undergoing surgery [4, 5]. SSIs are associated with increased morbidity and mortality rate [6]. In addition, patients with SSIs have a heavy economic burden in terms of extended length of stay and increased costs of treatment [7].

Various pathogens can contribute to SSIs, but significant concern has been raised for *Staphylococcus aureus* (*S. aureus*) and methicillin-resistant *Staphylococcus aureus* (MRSA). As the primary pathogen, *S. aureus* constitute approximately 20% of SSIs cases among hospitals according to the CDC [8]. From 1992 to 2002 the proportion of SSIs caused by *S. aureus* increased from 16.6% to 30.9%, during which time MRSA isolates increased from 9.2% to 49.3% [9]. The 90 days post-operative mortality was 6.7% and 20.7% for SSIs patients with methicillin-susceptible *S. aureus* (MSSA) and MRSA, respectively [10]. Compared with MSSA, the additional hospital charge associated with MRSA was at least $40,000 [10].

In China, the proportions of *S. aureus* in SSIs have been available from the Nosocomial Infection Surveillance System since 1990s; however, the system which covers a wide range of nosocomial infections is not specific to SSIs and the statistics reported from the system to date remain far from sufficient to describe the epidemiology of *S. aureus* or MRSA in SSIs across the country. Up to now, only three studies [11–13] have been published on the basis of this system, reporting the proportion of *S. aureus* in SSIs. According to the data from 79 hospitals in the system *S. aureus* accounted for 12.7% (377/2,971) between 1999 and 2001 [11] and 13.5% (515/3812) between 1999 and 2005 [12] among pathogens in SSIs. The proportions of *S. aureus* in patients with superficial incisional, deep incisional and organ-space infections were 14.1%, 12.8% and 7.4% respectively between 1999 and 2007 based on the data from 110 hospitals [13]. Furthermore, several limitations of the publications from this system existed. Firstly, the selected hospitals in the studies seemed unable to represent all the nationwide hospitals. The number of hospitals within the system had amounted to 134 in 2001 [14], but none of the studies involved all or a random sample of the hospitals to estimate the proportion of *S. aureus* in SSIs patients, which may introduce selection bias. Secondly, the exact data about the proportions of MRSA and the proportions of drug resistance of MRSA in SSIs, which should be the main
concern from the perspective of clinical practice, are not accessible in the studies. In addition, this system only provided the overall proportion of \textit{S. aureus} rather than proportions by year, region, hospital level, and surgery type, which are likely to have more significant impact on decision-making for clinical practice and public health.

Understanding the nationwide epidemiological situation of \textit{S. aureus} and MRSA in SSIs is vital for policy makers and clinicians to develop appropriate preventive countermeasures. As the national data in China remain inadequate, this systematic review aimed to estimate the proportions of \textit{S. aureus} and MRSA in SSIs, by summarizing and assessing the available observational studies in China published from 2007 to 2012, to provide further evidence.

**Methods**

**Information sources and search strategy**

We performed systematic search in six electronic databases, including PubMed, Embase (OVID), Chinese BioMedical Database (CBM), China National Knowledge Infrastructure (CNKI), VIP Chinese Science and Technique Journals Database, and Wanfang Database, to identify the relevant studies. Since the focus in the review was on the epidemiological characteristics of \textit{S. aureus} and MRSA in SSIs during recent years, search was limited to the publication date from January 2007 to November 2012. A combination of Mesh words and free text words applied to PubMed, Embase and CBM, and free text words were used to search CNKI, VIP and Wanfang database. The following search terms were mainly used: "surgery", "wound infection\*", "postoperative wound infection\*", "surgical site infection\*", "\textit{S. aureus}.", "\textit{Staphylococcus aureus}"", "methicillin", “MSSA” and “MRSA”. Details of the search strategies for each database were summarized in S1 Table.

**Eligibility criteria**

Criteria of inclusion:

- Patients: those with SSIs regardless of other characteristics;
- Outcomes: \textit{S. aureus} and MRSA isolates identified from SSIs;
- Study types: observational studies including cross-sectional, monitoring, prospective, ambispective and retrospective study.

Criteria of exclusion:

- Duplicate studies;
- Involvement of studied population from outside mainland China;
- Therapeutic study including randomized controlled trial and observational research for comparative effectiveness;
- Studies with data from the China Nosocomial Infection Surveillance System.

**Study selection**

According to the criteria of inclusion and exclusion, two reviewers independently screened each record by the title, keywords and abstract. The eligibility was determined further through the full texts if selection cannot be made only based on the screening. Any disagreement was resolved by the third reviewer.
Data extraction

An original extraction form was designed and then modified following a pilot test. The revised extraction form encompassed three parts: general information, clinical characteristics and numbers for calculating proportions of *S. aureus* and MRSA isolates. Two reviewers extracted information from each study independently. Any disagreement was also resolved by the third reviewer.

Assessment of risk of bias

As there were no acknowledged or standardized quality assessment tools for the included study designs, we used a checklist with 8 items adapted from a scale for case series [15], which was originally developed by the National Institute for Health and Care Excellence (NICE), a special health authority in the UK which is committed to providing national guidance and advice to improve health and social care. Low, high or unclear risk of bias for each item was determined according to the pre-specified criteria (S2 Table) and the graph of summary of risk of bias was developed with Revman 5.1. One point was scored if an item was judged low risk of bias. We defined study of higher quality with a total of at least 4 points.

Dealing with missing data

When information of the variables for analysis was missing from publications, the correspondent authors were contacted by email every one week. If the authors did not reply to the emails after our second contact attempt, the publications were excluded when the related variables were analyzed.

Statistical analysis

We conducted all the data analyses using R (Version 3.1.2, The R Foundation for Statistical Computing).

Calculation formula for the proportions of *S. aureus* and MRSA

Proportions of *S. aureus* and MRSA isolates were calculated by the following formula for each related study:

\[
\text{Proportion of } S.\text{aureus} = \frac{\text{Number of } S.\text{aureus isolates detected}}{\text{Number of all the detected isolates}} \times 100\%
\]

\[
\text{Proportion of MRSA} = \frac{\text{Number of MRSA isolates detected}}{\text{Number of } S.\text{aureus isolates detected}} \times 100\%
\]

Proportion of antibiotics–resistant MRSA

\[
\text{Proportion of antibiotics–resistant MRSA} = \frac{\text{Number of detected MRSA isolates resistant to a given antibiotic}}{\text{Number of MRSA isolates detected}} \times 100\%
\]

Incremental 0.5 was added to both the numerator and denominator in studies with zero or all events. 95% CI for the proportion in each study was calculated based on the logit-transformed metric.

Pooled overall proportions

Meta-analysis was conducted for the pooled estimates, followed by comparison between our overall estimate of *S. aureus* and MRSA and the corresponding proportions in the US and in
the China Nosocomial Infection Surveillance System. Statistical difference between the proportions in such comparisons was tested by Q statistic for heterogeneity [16]. P-value of less than 0.05 indicated statistical significance. Considering probable heterogeneity across all the observational studies, random-effects model with Der-Simonian Laird method was used \textit{a priori} throughout the data analyses.

Heterogeneity and subgroup analysis

Q test and I$^2$ statistic were used to examine and quantify the heterogeneity of the logit-transformed proportion across the studies. P-value of less than 0.05 or I$^2$ statistic of more than 50\% were regarded as substantial heterogeneity [17]. Subgroup analysis was conducted to explore the possible sources of heterogeneity based on the pre-defined variables including study quality, sample size, region, level of hospital, provincial economic condition, types of surgeries. A map for the distribution of \textit{S. aureus} was drawn through MapInfo Professional 11.0 according to the subgroup analysis by provinces. We determined small sample size if at most 20 bacteria isolates or \textit{S. aureus} isolates were included in analysis for primary studies respectively reporting the proportion of \textit{S. aureus} or MRSA. Based on whether the annual Gross Domestic Product (GDP) per capita of each province in 2011 was higher or lower than the national average (35,181RMB) in China, provinces were categorized into higher or lower provincial economic condition [18].

Informal comparisons were made between subgroups for the proportions of \textit{S. aureus} and MRSA by directly comparing the magnitudes of proportions between different subgroups instead of significance tests which tend to be misleading for the comparison in subgroup analysis. Statistical significance was defined as non-overlap of the confidence intervals of the proportions between the subgroups [19].

Meta-regression for the proportion of \textit{S. aureus} isolates

Meta-regression was used to explore the impact of pre-defined factors on the proportion of \textit{S. aureus} isolates. We defined logit($P$) as the dependent variable where $P$ referred to proportion of \textit{S. aureus} isolates. All the independent factors were initially selected based on the expertise in clinical microbiology and the availability of related information in the included articles, including study quality, sample size, region, level of hospital, provincial economic condition and type of surgery, all of which were defined as dummy variables. The factors without colinearity indicated by no correlation to each other (P-value $> 0.10$) were finally included into the random-effects meta-regression model with restricted maximum likelihood (REML) method. The statistical significance of any single coefficient was tested by Z-test and 0.05 was used as the threshold of P-value for statistically significant difference.

Publication bias

Egger’s test served to assess the probability of publication bias for the overall \textit{S. aureus} and MRSA proportion [20]. The test was based on the logit-transformed proportion and corresponding standard error. A P-value of less than 0.10 was regarded as statistical significance, indicating probable publication bias.

Results

General information about included studies

We retrieved 2904 references from six databases, of which 106 studies were eligible for inclusion (Fig. 1). All the studies, 105 published in Chinese and one in English, were hospital-based. Table 1, Table 2 and S3 Table show detailed characteristics of included studies.
Methodological quality of studies

The methodological quality of studies was displayed in Fig. 2 with more details in S2 Table, S1 Fig. The maximum score that studies achieved was 7 while the minimum was 0. We finally identified 38 studies with relatively high quality which reached at least 4 scores in our quality assessment scale.

Overall proportions

106 studies, including a total of 13,608 isolates, reported proportions of \textit{S. aureus} isolates. The pooled proportion of \textit{S. aureus} isolates among patients with SSIs was 19.1\% (95\%CI 17.2–21.0\%; \(I^2 = 84.1\%\)) (Fig. 3). The proportion was similar to 18.5\% (1,452/7,848, 95\%CI 17.7–19.4\%) (\(Q = 0.32, \text{df} = 1, \text{P-value} = 0.570\)) in the US, but significantly exceeded the proportions of 12.7\% (377/2,971, 95\%CI 11.5–13.9\%) (\(Q = 33.4, \text{df} = 1, \text{P-value}<0.001\)) and 13.5\% (515/3,812, 95\%CI 12.5–14.6\%) (\(Q = 28.3, \text{df} = 1, \text{P-value}<0.001\)) reported through the China Nosocomial Infection Surveillance System.

With respect to the proportion of MRSA, 1,502 isolates of \textit{S. aureus} in 38 studies were included. The overall proportion of MRSA isolates was 41.3\% (95\%CI 36.5–46.3\%; \(I^2 = 64.6\%\)) (Fig. 4). The proportion was significantly lower (\(Q = 10.3, \text{df} = 1, \text{P-value} = 0.001\)) than that of 53.9\% in the US (150/278, 95\%CI 48.1–59.7\%).

No evidence in Egger’s test suggested publication bias for the overall proportion of \textit{S. aureus} (t=-1.10, \text{P-value} = 0.275) and MRSA (t = 0.46, \text{P-value} = 0.651).

Subgroup analysis

All the results of subgroup analysis were summarized in Table 3 and the forest plots were presented in S1 File.

The pooled proportion was 41.1\% (95\%CI 26.3–57.7\%; \(I^2 = 74.4\%\)) for thoracic surgeries, 20.4\% (95\%CI 15.3–26.7\%; \(I^2 = 87.8\%\)) for orthopedics surgery, 20.1\% (95\%CI 26.3–57.7\%; \(I^2 = 74.4\%\)) for gynecologic surgery and 13.8\% (95\%CI 10.3–18.4\%; \(I^2 = 70.0\%\)) for abdominal surgeries. In addition, \textit{S. aureus} proportion was higher in studies conducted in low economic condition, rural or non-tertiary hospitals or with small sample size (at most 20 isolates of bacteria), although significant differences between subgroups were not found. On the other hand, the proportions seemed similar in studies with high and low quality, those with retrospective and non-retrospective design, or those beginning before and since 2007 (Fig. A-I in S1 File).

Geographical differences in \textit{S. aureus} proportions by different provinces or municipalities across China were shown in Fig. 5. Among 21 areas the maximum point estimate of \textit{S. aureus} proportion among all the provinces with available data was 33.3\% (95\%CI 15.8–57.1\%) in Ningxia province, followed by Tianjin municipality (30.2\%, 95\%CI 21.9–40.1\%) and Jiangxi province (30.0\%, 95\%CI 16.9–47.4\%) and the minimum was 11.5\% (95\%CI 8.1–16.1\%) in Gansu province. However, there was only one study available, respectively, for the proportion estimate in Ningxia, Jiangxi and Gansu.

Regarding the pooled proportion of MRSA isolates (Fig. J–R in S1 File), the proportion was 55.0\% (95\%CI 21.4–84.5\%, \(I^2 = 74.1\%\)) for abdominal surgeries, 41.0\% (95\%CI 23.5–61.1\%, \(I^2 = 0\%\)) for gynecologic surgeries, 39.1\% (95\%CI 3.8–91.2\%, \(I^2 = 94.0\%\)) for thoracic surgeries and 26.6\% (95\%CI 15.3–42.2\%, \(I^2 = 56.9\%\)) for orthopedics surgery. Furthermore, despite insignificant difference between subgroups, MRSA proportion tended to be higher in low economic condition, urban and tertiary hospitals as well as in studies with small sample size (at most 20 \textit{S. aureus} isolates). Similar proportions can be found between studies with higher and lower quality, studies with retrospective and non-retrospective design, or studies with the start time of before 2007 and since 2007.
Proportions of S. aureus and MRSA among SSIS in China

Figure 1. Flow diagram of study inclusion.

doi:10.1371/journal.pone.0116079.g001
Table 1. General information of all the included studies.

| Study ID | Province | Start          | Finishing       | Number of centers | Study type       | Number of SSIs patients | Surgery type* | Relevance to MRSA | Region      | Hospital level | Economy Score | Score for risk of bias |
|----------|----------|----------------|-----------------|-------------------|------------------|-------------------------|---------------|-------------------|-------------|-----------------|-----------------|------------------------|
| Ao 2007  | Jiangxi  | March 2005     | March 2007      | 1                 | Retrospective    | 89                      | Orthopedic    | No                | Urban       | Tertiary        | Lower 3         | 3                       |
| Chang 2010| Shanxi   | January 2007   | December 2009   | 1                 | Ambispective     | 95                      | Multiple      | No                | Urban       | Tertiary        | Lower 4         | 4                       |
| Chen 2009a | Fujian  | January 2006   | December 2008   | 1                 | Retrospective    | Unclear              | Orthopedic    | Yes               | Urban       | Tertiary        | Higher 2        | 2                       |
| Chen 2009b | Guangdong | January 2002  | December 2006   | 1                 | Prospective      | Unclear              | Neurosurgery  | No                | Urban       | Tertiary        | Higher 2        | 2                       |
| Chen 2010 | Beijing  | January 2006   | December 2008   | 1                 | Retrospective    | 214                   | Multiple      | Yes               | Urban       | Tertiary        | Higher 3        | 3                       |
| Chen 2012 | Fujian   | January 2007   | December 2010   | 1                 | Ambispective     | 105                   | Multiple      | No                | Rural       | Non-tertiary   | Higher 3        | 3                       |
| Cui 2008  | Henan    | January 2007   | December 2007   | 1                 | Retrospective    | 1001                  | Multiple      | No                | Urban       | Non-tertiary   | Lower 2         | 2                       |
| Dai 2012  | Zhejiang | February 2009  | May 2011        | 1                 | Retrospective    | 50                     | Abdominal     | No                | Urban       | Tertiary        | Higher 3        | 3                       |
| Deng 2010 | Sichuan  | Unclear        | Unclear         | 10                | Cross-sectional  | 26                     | Multiple      | Yes               | Urban       | Non-tertiary   | Lower 3         | 3                       |
| Ding 2010 | Liaoning | January 2000   | December 2009   | 1                 | Retrospective    | 145                   | Multiple      | No                | Urban       | Non-tertiary   | Higher 3        | 3                       |
| Dong 2007 | Zhejiang | January 2006   | December 2006   | 1                 | Monitoring       | Unclear              | Multiple      | No                | Urban       | Tertiary        | Higher 3        | 3                       |
| Duan 2008 | Hubei    | January 2002   | December 2007   | 1                 | Retrospective    | 18                     | Multiple      | Yes               | Rural       | Non-tertiary   | Lower 4         | 4                       |
| Fan 2008  | Hubei    | January 2004   | December 2007   | 1                 | Retrospective    | 221                   | Abdominal     | Yes               | Urban       | Tertiary        | Lower 4         | 4                       |
| Fan 2010  | Zhejiang | January 2003   | December 2008   | 1                 | Retrospective    | 36                     | Orthopedic    | No                | Urban       | Non-tertiary   | Higher 2        | 2                       |
| Gu 2009   | Xinjiang | January 2002   | December 2006   | 1                 | Retrospective    | 76                     | Gynecologic   | No                | Urban       | Non-tertiary   | Lower 0         | 0                       |
| Hao 2012  | Hebei    | October 2010   | December 2011   | 1                 | Unclear          | 61                     | Orthopedic    | Yes               | Urban       | Tertiary        | Lower 4         | 4                       |
| He 2012   | Jiangxi  | January 2009   | December 2011   | 1                 | Monitoring       | 41                     | Multiple      | No                | Urban       | Tertiary        | Lower 5         | 5                       |
| Huang 2012 | Liaoning | June 2008      | October 2010    | 1                 | Retrospective    | 19                     | Abdominal     | No                | Urban       | Non-tertiary   | Higher 4        | 4                       |
| Jiang 2009 | Guangdong | January 2003  | December 2007   | 1                 | Retrospective    | 332                   | Orthopedic    | No                | Urban       | Tertiary        | Higher 2        | 2                       |
| Jiang 2012 | Beijing | January 2009   | December 2010   | 1                 | Monitoring       | 62                     | Gynecologic   | No                | Rural       | Non-tertiary   | Higher 6        | 6                       |
| Li 2008   | Henan    | December 2004  | December 2007   | 1                 | Retrospective    | 36                     | Gynecologic   | No                | Rural       | Non-tertiary   | Lower 2         | 2                       |
| Li 2009a  | Sichuan  | April 2008     | August 2008     | 1                 | Unclear          | 26                     | Multiple      | No                | Urban       | Tertiary        | Lower 3         | 3                       |

(Continued)
Table 1. (Continued)

| Study ID | Province | Start         | Finishing          | Number of centers | Study type    | Number of SSIs patients | Surgery type* | Relevance to MRSA | Region | Hospital level | Economy Score for risk of bias |
|----------|----------|---------------|--------------------|-------------------|---------------|--------------------------|---------------|-------------------|--------|----------------|-------------------------------|
| Li 2009b [53] | Liaoning | January 2006  | December 2008      | 1                 | Retrospective | 15                       | Gynecologic   | No                | Urban  | Non-tertiary     | Higher 2                       |
| Li 2009c [54] | Henan    | January 2007  | December 2008      | 1                 | Retrospective | 133                      | Orthopedic    | No                | Urban  | Tertiary        | Lower 4                        |
| Li 2010a [55] | Hubei    | January 2005  | December 2008      | 1                 | Retrospective | 241                      | Multiple      | Yes               | Urban  | Non-tertiary     | Higher 3                       |
| Li 2010b [56] | Hunan    | January 2007  | December 2009      | Unclear           | Retrospective | 106                      | Multiple      | No                | Rural  | Non-tertiary     | Lower 3                        |
| Li 2010c [57] | Hebei    | September 2007 | September 2009     | 1                 | Retrospective | 139                      | Orthopedic    | Yes               | Urban  | Tertiary        | Lower 1                        |
| Li 2011a [58] | Guangxi  | January 2007  | June 2010          | 1                 | Unclear       | 118                      | Multiple      | Yes               | Rural  | Non-tertiary     | Lower 4                        |
| Li 2011b [59] | Jiangsu  | Unclear       | Unclear            | Unclear           | Unclear       | 20                       | Gynecologic   | No                | Urban  | Non-tertiary     | Higher 2                       |
| Li 2012 [60] | Xinjiang | November 2009 | November 2011      | 1                 | Retrospective | 32                       | Gynecologic   | No                | Urban  | Tertiary        | Lower 4                        |
| Lin 2007 [61] | Zhejiang | January 2004  | June 2004          | 1                 | Unclear       | 411                      | Multiple      | No                | Rural  | Non-tertiary     | Higher 3                       |
| Lin 2008 [62] | Guangdong | January 2004  | December 2007      | 1                 | Ambispective  | 18                       | Orthopedic    | No                | Urban  | Non-tertiary     | Higher 4                       |
| Lin 2009 [63] | Fujian   | January 2007  | December 2008      | 1                 | Retrospective | 31                       | Abdominal     | No                | Urban  | Tertiary        | Higher 3                       |
| Ling 2011 [64] | Zhejiang | January 2007  | December 2009      | 1                 | Monitoring    | 224                      | Orthopedic    | Yes               | Urban  | Non-tertiary     | Higher 4                       |
| Liu 2008 [65] | Guangdong | January 2005  | May 2007           | 1                 | Ambispective  | 113                      | Abdominal     | No                | Urban  | Non-tertiary     | Higher 4                       |
| Liu 2010 [66] | Henan    | January 2006  | June 2009          | 1                 | Ambispective  | 274                      | Multiple      | No                | Urban  | Tertiary        | Lower 4                        |
| Liu 2011 [67] | Tianjin  | January 2005  | December 2008      | 1                 | Ambispective  | 119                      | Orthopedic    | No                | Urban  | Tertiary        | Higher 3                       |
| Liu 2012a [68] | Jiangxi  | January 2010  | February 2012      | 1                 | Unclear       | 196                      | Thoracic      | Yes               | Urban  | Tertiary        | Lower 2                        |
| Liu 2012b [69] | Henan    | March 2010    | March 2011         | 1                 | Retrospective | 128                      | Abdominal     | No                | Rural  | Non-tertiary     | Lower 3                        |
| Liu 2012c [70] | Hubei    | January 2008  | December 2010      | 1                 | Retrospective | 213                      | Multiple      | Yes               | Rural  | Non-tertiary     | Lower 3                        |
| Lv 2007 [71] | Zhejiang | January 2003  | May 2006           | 1                 | Retrospective | 139                      | Multiple      | No                | Urban  | Non-tertiary     | Higher 4                       |
| Lv 2012 [72] | Zhejiang | January 2006  | June 2011          | 1                 | Retrospective | 26                       | Abdominal     | No                | Urban  | Tertiary        | Higher 3                       |
| Mao 2011 [73] | Zhejiang | June 2008     | September 2010     | 1                 | Retrospective | 285                      | Orthopedic    | Yes               | Urban  | Tertiary        | Higher 3                       |
| Pang 2007 [74] | Sichuan  | January 2001  | December 2004      | 1                 | Retrospective | 64                       | Multiple      | No                | Rural  | Non-tertiary     | Lower 4                        |
| Peng 2008 [75] | Hubei    | January 2004  | December 2007      | 1                 | Unclear       | 78                       | Multiple      | Yes               | Rural  | Non-tertiary     | Lower 1                        |

(Continued)
| Study ID     | Province   | Start            | Finishing       | Number of centers | Study type       | Number of SSIs patients | Surgery type* | Relevance to MRSA | Region | Hospital level | Economy | Score for risk of bias |
|--------------|------------|------------------|-----------------|------------------|------------------|-------------------------|--------------|-------------------|--------|----------------|---------|----------------------|
| Peng 2012a   | Hubei      | January 2009     | December 2010   | 1                | Retrospective    | 254                     | Multiple     | Yes               | Urban  | Tertiary       | Lower   | 3                    |
| Peng 2012b   | Hubei      | January 2008     | May 2011        | 1                | Retrospective    | 169                     | Multiple     | Yes               | Urban  | Tertiary       | Lower   | 3                    |
| Qian 2011    | Zhejiang   | January 2000     | December 2009   | 1                | Retrospective    | 135                     | Gynecologic  | Yes               | Urban  | Non-tertiary   | Higher  | 3                    |
| Qu 2008      | Zhejiang   | January 2006     | December 2007   | 1                | Retrospective    | 75                      | Multiple     | Yes               | Urban  | Non-tertiary   | Higher  | 3                    |
| Qu 2011      | Zhejiang   | January 2006     | January 2011    | 1                | Retrospective    | 113                     | Multiple     | No                | Rural  | Non-tertiary   | Lower   | 4                    |
| Ren 2009     | Ningxia    | January 2007     | August 2007     | 1                | Retrospective    | 23                      | Multiple     | Yes               | Rural  | Non-tertiary   | Lower   | 2                    |
| Ruan 2011    | Zhejiang   | January 2007     | December 2009   | 1                | Retrospective    | 67                      | Abdominal    | No                | Rural  | Non-tertiary   | Higher  | 4                    |
| Sheng 2012   | Zhejiang   | January 2006     | December 2011   | 1                | Retrospective    | 41                      | Orthopedic   | No                | Rural  | Tertiary       | Higher  | 2                    |
| Shi 2011     | Henan      | January 2006     | December 2009   | 1                | Prospective      | 325                     | Multiple     | Yes               | Urban  | Tertiary       | Lower   | 5                    |
| Sun 2008     | Shandong   | March 2000       | May 2005        | 1                | Unclear          | 29                      | Ophthalmology| No                | Urban  | Tertiary       | Higher  | 2                    |
| Sun 2012     | Hubei      | January 2009     | December 2010   | 1                | Retrospective    | 221                     | Multiple     | Yes               | Urban  | Tertiary       | Lower   | 2                    |
| Tang 2009    | Hebei      | January 2005     | December 2005   | Unclear          | Unclear          | 300                     | Thoracic     | No                | Urban  | Tertiary       | Lower   | 2                    |
| Tang 2012    | Guangdong  | January 2008     | December 2011   | 1                | Retrospective    | 65                      | Unclear      | No                | Urban  | Tertiary       | Higher  | 3                    |
| Tao 2011     | Hubei      | January 2007     | December 2009   | 1                | Ambispective     | 20                      | Neurosurgery | No                | Urban  | Tertiary       | Lower   | 3                    |
| Tian 2011    | Hubei      | January 2008     | December 2009   | 1                | Retrospective    | Unclear                | Unclear      | Yes               | Urban  | Tertiary       | Lower   | 3                    |
| Wan 2009     | Hunan      | January 2005     | December 2008   | 3                | Unclear          | 185                     | Multiple     | No                | Rural  | Non-tertiary   | Lower   | 3                    |
| Wang 2007a   | Beijing    | January 2001     | December 2005   | 1                | Retrospective    | 48                      | Abdominal    | Yes               | Urban  | Tertiary       | Higher  | 2                    |
| Wang 2007b   | Hubei      | Unclear          | Unclear         | Unclear          | Unclear          | Unclear                | Unclear      | Unclear          | Yes    | Urban          | Lower   | 1                    |
| Wang 2008    | Hebei      | January 2005     | December 2007   | 1                | Unclear          | Unclear                | Unclear      | Unclear          | No     | Urban          | Tertiary | Lower   | 2                     |
| Wang 2012    | Zhejiang   | June 2003        | June 2011       | 1                | Retrospective    | 223                     | Abdominal    | No                | Urban  | Tertiary       | Higher  | 4                    |
| Wei 2010     | Guangdong  | January 2008     | December 2008   | 1                | Monitoring       | 53                      | Gynecologic  | No                | Urban  | Tertiary       | Higher  | 7                    |
| Xiang 2012   | Zhejiang   | March 2008       | September 2009   | 1                | Retrospective    | 47                      | Orthopedic   | No                | Rural  | Non-tertiary   | Higher  | 3                    |
| Xie 2007     | Zhejiang   | January 2003     | December 2005   | 1                | Prospective      | 211                     | Multiple     | Yes               | Urban  | Tertiary       | Higher  | 4                    |
| Study ID | Province | Start          | Finishing     | Number of centers | Study type | Number of SSIs | Surgery type* | Relevance to MRSA | Region | Hospital level | Economy Score for risk of bias |
|----------|----------|----------------|---------------|-------------------|------------|----------------|---------------|--------------------|--------|----------------|--------------------------------|
| Xie 2008 [99] | Hubei    | January 2004   | December 2006 | 1                 | Retrospective | 128            | Multiple      | Yes                | Urban  | Tertiary       | Lower 4                          |
| Xie 2010 [100] | Hubei    | November 2007  | November 2008 | 10                | Cross-sectional | 80            | Multiple      | No                 | Urban  | Tertiary       | Lower 5                          |
| Xie 2012 [101] | Sichuan  | January 2005   | October 2011  | 1                 | Retrospective | 426           | Unclear       | Yes                | Urban  | Tertiary       | Lower 2                          |
| Xi 2012 [102]   | Heilongjiang | January 2011   | December 2011 | 1                 | Retrospective | 29            | Multiple      | No                 | Urban  | Tertiary       | Lower 4                          |
| Xu 2007 [103]   | Beijing  | August 1997    | September 2006| 1                 | Retrospective | Unclear       | Neurosurgery  | No                 | Urban  | Tertiary       | Higher 2                         |
| Xu 2010 [104]   | Guangxi  | Unclear        | Unclear       | Unclear           | Prospective | 124           | Orthopedic    | No                 | Urban  | Tertiary       | Lower 4                          |
| Xu 2011 [105]   | Guangdong| November 2007  | November 2010 | 1                 | Retrospective | 31            | Unclear       | No                 | Urban  | Non-tertiary   | Higher 3                         |
| Yan 2008 [106]  | Guangdong| January 2003   | September 2006| 1                 | Unclear      | 311           | Multiple      | No                 | Urban  | Tertiary       | Higher 4                         |
| Yang 2009a [107]| Sichuan  | January 2006   | December 2007 | 1                 | Retrospective | Unclear       | Multiple      | No                 | Rural  | Non-tertiary   | Lower 3                          |
| Yang 2009b [108]| Sichuan  | January 2007   | December 2007 | 1                 | Ambispective | 46            | Unclear       | No                 | Urban  | Non-tertiary   | Lower 4                          |
| Yao 2011 [109]  | Zhejiang | January 2005   | December 2010 | 1                 | Retrospective | 51            | Abdominal     | No                 | Urban  | Non-tertiary   | Higher 4                         |
| You 2011 [110]  | Fujian   | January 2001   | June 2009     | 1                 | Retrospective | 50            | Thoracic      | No                 | Urban  | Non-tertiary   | Higher 3                         |
| Yu 2012 [111]   | Zhejiang | January 2009   | July 2011     | Unclear           | Retrospective | 398           | Multiple      | Yes                | Urban  | Non-tertiary   | Higher 3                         |
| Yue 2009 [112]  | Henan    | June 2005      | June 2008     | 1                 | Retrospective | 21            | Gynecologic   | No                 | Rural  | Non-tertiary   | Lower 3                          |
| Zeng 2012 [113]| Hubei    | January 2007   | December 2010 | Unclear           | Retrospective | 108           | Gynecologic   | Yes                | Rural  | Non-tertiary   | Lower 2                          |
| Zhang 2007 [114]| Henan    | January 2004   | December 2005 | 1                 | Unclear      | 91            | Orthopedic    | No                 | Urban  | Tertiary       | Lower 3                          |
| Zhang 2008 [115]| Hubei    | January 2004   | December 2005 | 1                 | Unclear      | 145           | Multiple      | No                 | Urban  | Tertiary       | Lower 2                          |
| Zhang 2009a [116]| Sichuan  | January 2009   | June 2011     | 1                 | Retrospective | 142           | Unclear       | No                 | Urban  | Non-tertiary   | Lower 3                          |
| Zhang 2009b [117]| Hubei    | January 2006   | December 2008 | 1                 | Retrospective | Unclear       | Multiple      | Yes                | Urban  | Tertiary       | Lower 1                          |
| Zhang 2010 [118]| Hunan    | January 2008   | December 2008 | 1                 | Retrospective | 47            | Abdominal     | No                 | Rural  | Non-tertiary   | Lower 4                          |
| Zhang 2011a [119]| Sichuan  | January 2006   | December 2008 | 1                 | Retrospective | 160           | Multiple      | No                 | Urban  | Non-tertiary   | Lower 4                          |
| Zhang 2011b [120]| Zhejiang| January 2007   | December 2009 | 1                 | Retrospective | 87            | Abdominal     | No                 | Urban  | Tertiary       | Higher 2                         |
| Zhang 2011c [121]| Hainan   | March 2007     | March 2009    | 1                 | Retrospective | 30            | Multiple      | No                 | Urban  | Tertiary       | Lower 3                          |
| Study ID    | Province   | Start          | Finishing       | Number of centers | Study type       | Number of SSIs patients | Surgery type* | Relevance to MRSA | Region    | Hospital level | Economy Score | Score for risk of bias |
|------------|------------|----------------|----------------|-------------------|-----------------|-------------------------|---------------|-------------------|-----------|----------------|----------------|------------------------|
| Zhang 2012 | Gansu      | January 2008   | December 2009  | Unclear           | Ambispective    | 252                     | Multiple      | Yes               | Urban    | Tertiary       | Lower          | 5                       |
| Zhao 2011a | Guizhou    | January 2008   | December 2010  | 1                 | Retrospective   | 72                      | Multiple      | No                | Urban    | Tertiary       | Lower          | 3                       |
| Zhao 2011b | Shandong   | January 2008   | December 2010  | 1                 | Retrospective   | 227                     | Multiple      | Yes               | Urban    | Tertiary       | Higher         | 4                       |
| Zheng 2007 | Zhejiang   | January 2005   | December 2005  | 1                 | Retrospective   | Unclear               | Urologic      | Yes               | Urban    | Tertiary       | Higher         | 2                       |
| Zheng 2011a| Hubei      | January 2008   | December 2009  | Unclear           | Unclear         | 148                     | Unclear       | Yes               | Urban    | Tertiary       | Lower          | 4                       |
| Zheng 2011b| Hubei      | January 2008   | December 2009  | 1                 | Retrospective   | 87                      | Abdominal     | Yes               | Urban    | Non-tertiary   | Lower          | 5                       |
| Zheng 2011c| Zhejiang   | January 2005   | December 2010  | 1                 | Cross-sectional | 41                      | Multiple      | No                | Urban    | Tertiary       | Higher         | 4                       |
| Zhou 2007  | Hainan     | January 2001   | December 2005  | 1                 | Retrospective   | 38                      | Gynecologic   | No                | Urban    | Tertiary       | Lower          | 2                       |
| Zhou 2008  | Hainan     | January 2001   | December 2005  | 1                 | Retrospective   | 18                      | Gynecologic   | No                | Urban    | Non-tertiary   | Lower          | 3                       |
| Zhou 2011a | Hubei      | January 2005   | December 2009  | 1                 | Retrospective   | 1172                    | Multiple      | Yes               | Urban    | Tertiary       | Lower          | 5                       |
| Zhou 2011b | Beijing    | October 2009   | September 2011 | 1                 | Prospective     | 24                      | Thoracic      | Yes               | Urban    | Tertiary       | Higher         | 3                       |
| Zhu 2007   | Hubei      | January 2002   | December 2006  | 1                 | Retrospective   | 138                     | Abdominal     | No                | Urban    | Tertiary       | Lower          | 3                       |
| Zhu 2008a  | Guizhou    | January 2006   | January 2008   | 1                 | Retrospective   | 63                      | Orthopedic    | No                | Urban    | Non-tertiary   | Lower          | 4                       |
| Zhu 2008b  | Jiangxi    | January 2000   | December 2006  | 1                 | Retrospective   | Unclear               | Multiple      | Yes               | Urban    | Tertiary       | Lower          | 4                       |
| Zhu 2010   | Guangdong  | December 2009  | March 2010     | 1                 | Unclear         | 20                      | Gynecologic   | No                | Urban    | Tertiary       | Higher         | 3                       |

* In this column multiple surgeries refer to the different kinds of surgeries involved in the study which cannot be discriminated or classified into a specific type of surgery.

doi:10.1371/journal.pone.0116079.t001

Proportions of S. aureus and MRSA among SSIs in China
Table 2. Distribution of *S. aureus* and MRSA isolates in the included studies.

| Characteristics      | S. aureus | MRSA |   |   |
|----------------------|-----------|------|---|---|
|                      | Number of studies | Number of S. aureus | Number of detected isolates | Number of studies | Number of MRSA | Number of S. aureus |
| Publication year     | 2007      | 13   | 351 | 2,441 | 4 | 43 | 95 |
|                      | 2008      | 16   | 380 | 1,636 | 6 | 84 | 198 |
|                      | 2009      | 16   | 285 | 1,806 | 3 | 40 | 123 |
|                      | 2010      | 14   | 200 | 1,257 | 4 | 42 | 92  |
|                      | 2011      | 24   | 714 | 3,613 | 11| 221| 539 |
|                      | 2012      | 23   | 582 | 2,855 | 10| 194| 455 |
| Surgery type         | Orthopedic | 16  | 362 | 2,022 | 5  | 35 | 143 |
|                      | Abdominal  | 15  | 161 | 1,163 | 3  | 35 | 64  |
|                      | Gynecologic | 13  | 88  | 471  | 2  | 10 | 25  |
|                      | Thoracic   | 4   | 88  | 196  | 2  | 19 | 73  |
|                      | Others*    | 49  | 1,556 | 8,754 | 23 | 445 | 1,003 |
|                      | Unclear    | 8   | 257 | 1,029 | 3  | 80 | 194 |
| Study design         | Retrospective | 67  | 1,794 | 10,169 | 26 | 520 | 1,204 |
|                      | Prospective | 10  | 139 | 781  | 4  | 34 | 95  |
|                      | Ambispective | 9   | 117 | 764  | 1  | 11 | 29  |
|                      | Cross-sectional | 3  | 38  | 133  | 1  | 1  | 2   |
|                      | Unclear    | 17  | 424 | 1,761 | 6  | 58 | 172 |
| Regions              | Urban      | 85  | 2,111 | 11,603 | 31 | 563 | 1,344 |
|                      | Rural      | 20  | 378 | 1,925 | 6  | 55 | 135 |
|                      | Unclear    | 1   | 23  | 80   | 1  | 6  | 23  |
| Hospitals            | Tertiary   | 63  | 1,740 | 9,581 | 25 | 499 | 1,168 |
|                      | Non-tertiary | 42  | 749 | 3,947 | 12 | 119 | 311 |
|                      | Unclear    | 1   | 23  | 80   | 1  | 6  | 23  |
| Economic Condition   | Higher     | 45  | 852 | 5,734 | 12 | 152 | 384 |
|                      | Lower      | 60  | 1,637 | 7,794 | 26 | 466 | 1,095 |
|                      | Unclear    | 1   | 23  | 80   | 1  | 6  | 23  |
| Study Quality        | Higher     | 39  | 1,000 | 5,313 | 14 | 271 | 665 |
|                      | Lower      | 67  | 1,512 | 8,295 | 24 | 353 | 837 |
|                      | Unclear    | 1   | 23  | 80   | 1  | 6  | 23  |
| Sample Size**        | >20 isolates | 95  | 2,464 | 13,435 | 26 | 561 | 1,392 |
|                      | ≤20 isolates | 11  | 48  | 173  | 12 | 63 | 110 |
| Total                | 106        | 2,512 | 13,608 | 38 | 624 | 1,502 |

* Others refer to: 1) multiple surgeries involved in the study which cannot be classified into a specific type of surgery or 2) a specific type of surgery, rather than orthopedic, abdominal, gynecologic, or thoracic surgeries, which was reported in a small number of studies.

** Sample size refers to isolates of all identified bacteria for the proportion of *S.aureus*, isolates of all identified *S.aureus* for the proportion of MRSA, and isolates of MRSA for the proportion of antibiotic resistance.

doi:10.1371/journal.pone.0116079.t002
All the MRSA were sensitive to vancomycin (522/522) while only one isolate was resistant to linezolid (1/94). 79.9% (95%CI 67.4–88.4%; I² = 0%) and 92.0% (95%CI 80.2–97.0%; I² = 0%) of MRSA, respectively pooled from four and five studies, were resistant to clindamycin and erythromycin (Fig. S and Fig. T in S1 File).

Meta-regression for the proportion of *S. aureus* isolates

97 studies without any missing data were included for meta-regression to identify related potential factors for heterogeneity with statistical significance. As we found a significant correlation coefficient between levels of hospital and region (coefficient = 0.570, P-value < 0.001), provincial economic condition and region (coefficient = -0.198, P-value = 0.052), the region variable was therefore excluded out of the pre-defined independent factors for the meta-regression (Table 4).

The meta-regression (residual I² = 83.3%, adjusted R² = 17.6%, P-value < 0.001 in the test for the goodness of model fit) showed that compared with thoracic, *S. aureus* proportion was significantly lower in abdominal (OR = 0.224, 95%CI 0.105–0.477, P-value < 0.001), gynecologic (OR = 0.254, 95%CI 0.114–0.565, P-value < 0.001) and orthopedic (OR = 0.352, 95%CI 0.171–0.726, P-value = 0.005) surgeries. Studies with relatively large sample size (>20 isolates) were likely to conclude lower proportions of *S. aureus* (OR = 0.582, 95%CI 0.344–0.985, P-value = 0.044).

Discussion

Proportions of *S. aureus*

The overall proportion of *S. aureus* isolates (19.1%) was consistent with the reported proportion of 18.5% in the US in 2003 [21], but was significantly higher than both estimated in the China Nosocomial Infection Surveillance System (12.7% between 1999 and 2001, 13.5% between 1999 and 2005) [11, 12]. This difference between our review and the Chinese
Figure 3. Overall proportion of S. aureus in patients with SSIs.

doi:10.1371/journal.pone.0116079.g003
surveillance system could not be attributed to the change over time because of insignificant difference between the studies starting before 2007 and those starting after 2007 by subgroup analysis. However, the following reasons may result in such difference. First, the surveillance result derived from only 79 of 134 surveillance hospitals (58.9%), which may reduce the representativeness of the practical situation in China. Nevertheless, 106 studies in our review involved more than 125 hospitals distributed in 21 different provinces or municipalities,
including tertiary and non-tertiary hospitals, urban and rural areas, which may be more representative of the real national status. Second, the sample size of bacteria isolates from the surveillance system (only 3,812 in total) was substantially less than that included in our review (13,608). Pooling data from 106 studies with a larger sample size may provide a more reliable estimate for national situation.

In addition, our finding can provide further useful information which was not available from the Chinese surveillance system, such as the stratified proportions by the surgery type, economics condition, hospital level and province. As shown in the subgroup analysis, *S. aureus* proportions varied between different surgery types—highest for thoracic surgeries (41.1%) whereas lowest for abdominal surgeries (13.8%). Meta-regression suggested the similar result.

### Table 3. Summary of the pooled results of proportions of *S. aureus* and MRSA isolates.

| Subgroup          | Proportions of *S. aureus* isolates | Proportions of MRSA isolates |
|-------------------|-------------------------------------|------------------------------|
|                   | Studies | Sample Size** | Estimate (%) | 95% CI (%) | I² (%) | Studies | Sample Size** | Estimate (%) | 95% CI (%) | I² (%) |
| Surgery type      |         |               |              |            |        |         |               |              |            |        |
| Orthopedic        | 16      | 2,022         | 20.4         | 15.3–26.7  | 87.8   | 5       | 143          | 26.6         | 15.3–42.2  | 56.9   |
| Abdominal         | 15      | 1,281         | 20.1         | 10.3–18.4  | 70.0   | 3       | 64           | 55.0         | 21.4–84.5  | 74.1   |
| Gynecologic       | 13      | 471           | 20.1         | 15.6–25.6  | 33.0   | 2       | 25           | 41.0         | 23.5–61.1  | 0      |
| Thoracic          | 4       | 196           | 41.1         | 26.3–57.7  | 74.4   | 2       | 73           | 39.1         | 3.8–91.2   | 94.0   |
| Others*           | 50      | 8,609         | 18.2         | 15.9–20.7  | 85.6   | 23      | 1,003        | 44.6         | 39.5–49.7  | 51.5   |
| Unclear           | 8       | 1,029         | 24.7         | 20.1–30.0  | 60.2   | 3       | 194          | 41.3         | 34.4–48.6  | 3.0    |
| Economic condition|         |               |              |            |        |         |               |              |            |        |
| Higher            | 45      | 5,777         | 16.6         | 13.9–19.7  | 84.2   | 12      | 384          | 39.4         | 28.6–51.2  | 73.4   |
| Lower             | 60      | 7,751         | 20.7         | 18.5–23.2  | 81.8   | 25      | 1,095        | 42.8         | 37.5–48.3  | 59.4   |
| Unclear           | 1       | 80            | 28.8         | 19.9–39.6  | -      | 1       | 23           | 26.1         | 12.2–47.2  | -      |
| Region            |         |               |              |            |        |         |               |              |            |        |
| Urban             | 85      | 11,678        | 18.5         | 15.9–21.0  | 88.2   | 12      | 311          | 39.0         | 30.0–48.7  | 52.2   |
| Rural             | 20      | 1,850         | 20.9         | 17.4–25.0  | 69.4   | 6       | 135          | 44.9         | 29.2–61.7  | 60.7   |
| Unclear           | 1       | 80            | 28.8         | 19.9–39.6  | -      | 1       | 23           | 26.1         | 12.2–47.2  | -      |
| Hospital Level    |         |               |              |            |        |         |               |              |            |        |
| Tertiary          | 63      | 9,613         | 18.3         | 15.9–21.0  | 88.2   | 25      | 1,168        | 42.7         | 36.9–48.7  | 69.1   |
| Non-tertiary      | 42      | 3,915         | 20.0         | 17.5–22.6  | 68.8   | 12      | 311          | 39.0         | 30.0–48.7  | 52.2   |
| Unclear           | 1       | 80            | 28.8         | 19.9–39.6  | -      | 1       | 23           | 26.1         | 12.2–47.2  | -      |
| Quality           |         |               |              |            |        |         |               |              |            |        |
| Higher            | 39      | 5,225         | 17.9         | 15.5–20.6  | 78.5   | 14      | 665          | 40.1         | 32.6–48.0  | 65.6   |
| Lower             | 67      | 8,383         | 19.9         | 17.4–22.8  | 86.3   | 24      | 837          | 42.1         | 35.7–48.9  | 65.3   |
| Study Design      |         |               |              |            |        |         |               |              |            |        |
| Retrospective     | 67      | 10,169        | 16.6         | 16.9–20.5  | 75.6   | 26      | 1,204        | 42.4         | 37.2–47.7  | 62.2   |
| Non-retrospective** | 22    | 1,678         | 17.9         | 13.1–23.8  | 84.4   | 6       | 126          | 41.3         | 26.3–58.0  | 59.4   |
| Unclear           | 17      | 1,669         | 21.6         | 14.9–30.2  | 92.1   | 6       | 172          | 41.0         | 22.9–61.9  | 75.5   |
| Sample size***    |         |               |              |            |        |         |               |              |            |        |
| >20 isolates      | 95      | 13,435        | 18.6         | 16.7–20.5  | 85.2   | 26      | 1,392        | 39.8         | 35.0–44.8  | 68.2   |
| ≤20 isolates      | 11      | 173           | 28.1         | 19.8–38.1  | 38.7   | 12      | 110          | 53.6         | 36.1–70.3  | 53.1   |
| Start time        |         |               |              |            |        |         |               |              |            |        |
| Before 2007       | 55      | 8,696         | 18.8         | 16.4–21.4  | 85.2   | 17      | 821          | 41.0         | 33.4–49.0  | 72.2   |
| Since 2007        | 47      | 4,642         | 20.0         | 16.1–22.3  | 83.2   | 19      | 638          | 42.3         | 35.6–49.2  | 60.1   |
| Unclear           | 4       | 270           | 25.5         | 20.6–31.1  | 0.1    | 2       | 43           | 32.6         | 20.3–47.8  | 0.0    |
| Total             | 106     | 13,608        | 19.1         | 17.2–21.0  | 84.1   | 38      | 1,502        | 41.3         | 36.5–46.3  | 64.6   |

* Others refer to: 1) multiple surgeries involved in the study which cannot be classified into a specific type of surgery or 2) a specific type of surgery, rather than orthopedic, abdominal, gynecologic, or thoracic surgeries, which was reported in a small number of studies.

** Non-retrospective design comprises prospective, cross-sectional, ambispective study and surveillance.

*** Sample size in the proportions of *S. aureus* isolates refers to the number of all the detected bacteria isolates; in the proportions of MRSA it refers to the number of all *S. aureus* isolates.

doi:10.1371/journal.pone.0116079.t003
that patients undergoing thoracic surgeries were much more vulnerable to SSIs by *S. aureus*, compared with patients with any other involved surgery type. This result was consistent with the guideline for prevention of SSIs, which concluded that *S. aureus* was the dominant pathogen causing SSIs following thoracic surgeries [8], indicating that *S. aureus* should be highly suspected in the case of SSIs after thoracic surgeries. On the contrary, with other influencing factors adjusted, patients with abdominal surgeries were less likely to suffer from SSIs by *S. aureus*. Priority may not be given to *S. aureus* in the SSIs after this surgery type because gram-negative bacilli, rather than *S. aureus*, tend to be predominant in the gastrointestinal tract usually involved in abdominal surgeries [22, 23]. Impoverished regions, non-tertiary hospitals, and some provinces or municipalities such as Ningxia, Tianjin and Jiangxi, may also require more attention paid to *S. aureus* SSIs.

**Proportions of MRSA**

Our estimate focused on SSIs and thus may close the gap of the surveillance system in China which merely reported the MRSA proportion of 79.9% (3,177/3,975) in all kinds of hospital infections instead of in SSIs [12]. Comparison between the results indicated that the proportion of MRSA in SSIs may be lower than the average level among a diversity of hospital infections. Besides, our review concluded a significantly lower proportion than that reported in a recent multi-center study with a smaller sample size in the US [24]. However, the status quo necessitates further improvement since MRSA accounted for more than 40% of *S. aureus* in our review.

Variation in the MRSA proportions was found between different surgery types: highest in abdominal surgeries (55.0%) and lowest in orthopedics surgeries (26.6%). While a recent study showed cases with MRSA SSIs accounted for 30.4% in those with *S. aureus* SSIs in the US [22], the high MRSA proportion (55.0%) following abdominal surgeries in our study provided an alarming picture that, despite *S. aureus* being subordinate pathogen in SSIs after abdominal surgeries, physicians still have to be highly cautious about MRSA in SSIs. On the contrary, orthopedic surgeries saw the lowest proportion of MRSA SSIs (26.6%) in spite of its high proportion of *S. aureus*. A study also concluded that the proportion of MRSA was the lowest in orthopedic surgeries among all the surgical procedures, although the proportion (31.9%) they calculated was higher than ours [10]. However, the mechanism seems still unclear and requires further studies to confirm.

**Proportions of antibiotic-resistant MRSA**

Based on our findings, vancomycin and linezolid appeared to be still effective for treating MRSA in SSIs in vitro. Vancomycin therapy is the primary option in the case of limited current therapeutic methods for patients with MRSA infections [25]. In China, the surveillance system suggested that none of MRSA were resistant to vancomycin (0/3,102) between 1999 and 2005 in a variety of nosocomial infections including SSIs [12], which was similar to our result: we identified none of the MRSA isolates resistant to vancomycin (0/522) in SSIs. However, it is necessary to raise the awareness of the resistance of vancomycin since there has been evidence suggesting the observed rise in minimum inhibitory concentrations (MICs) of vancomycin from less than 0.5 μg/mL in 2005 to 1.0 μg/mL in 2010 [26]. Linezolid is the first available oxazolidinone antibiotic, which uniquely inhibits bacterial protein synthesis by preventing formation of 70S initiation complex [27]. Although surveillance data on linezolid was absent, one of 94 MRSA isolates in our findings was resistant to linezolid. But currently no robust clinical evidence can demonstrate whether linezolid or vancomycin is superior in the treatment of MRSA SSIs [28]. Continuous surveillance of drug resistance for both antibiotics in this treatment is necessary and crucial for the clinical practice.
On the other hand, clindamycin and erythromycin, inhibiting protein synthesis by their effect on ribosome function and commonly used in clinical practice for MRSA SSIs [27, 29], may have a doubtful effectiveness. The proportion of MRSA resistant to clindamycin in our findings (79.9%) was also similarly suggested in the surveillance system for nosocomial infections—78.9% (1,137/1,445) [12]. In our review, more than 90.0% MRSA isolates were identified to be resistant to erythromycin, far higher than that in the UK bacteraemia surveillance where erythromycin resistance only occurred in 67% of MRSA [30]. As such, both treatments may not be the first choice when MRSA in SSIs is suspected.
Limitations

There are several limitations in this review. First, methodological quality of the included studies is the main concern for the combined estimates because less than half of the studies are of high quality according to our criteria. However, study quality seems not to be the main heterogeneity source as both subgroup analysis and meta-regression showed that the pooled result from studies of higher quality were consistent with that from those of lower quality. Second, we only included studies published after 2007 so as to understand the current proportion of *S. aureus* and MRSA in SSIs. Considering some studies had started before 2007, we conducted subgroup analysis for studies initiating before and after 2007 to ensure that it was reasonable to combine results from all included studies to provide more precise estimates and facilitate the meta-regression. Third, none of the pre-defined variables can fully explain the variance in proportions of *S. aureus* ($I^2 = 84.1\%$) and MRSA ($I^2 = 64.6\%$) in subgroup analysis and meta-regression, which could result in uncertainty around the pooled proportions. The major obstacle of extensively exploring the potential source of variation is the limited information about the heterogeneity reported in the publication, such as the duration of surveillance, MICs and molecular epidemiology, which may be significantly associated with the heterogeneity but cannot be examined in our review. However, meta-regression did find that some factors with available information, such as the types of surgery and sample sizes, may partly contribute to the heterogeneity across studies. In addition, despite informal comparisons between subgroups by 95% CI rather than the significance test, the problem with multiple comparisons may be raised in the comparisons with no adjustment made with a stricter criterion for the significant difference. Further study may also be required to confirm some pooled results derived from limited number of included studies in our review.

| Table 4. Summary results of meta-regression for the proportion of *S. aureus* isolates. |
|---------------------------------|-----------------|------|------|-----------------|------------------|
| Factor             | Coefficient | SE  | OR  | 95% CI (OR) | P-Value |
|---------------------|-------------|-----|-----|-------------|---------|
| Surgery type        |             |     |     |             |         |
| Thoracic            |             |     |     |             |         |
| Abdominal           | -1.495      | 0.385| 0.224| 0.105       | 0.477   | <0.001 |
| Gynecologic         | -1.370      | 0.408| 0.254| 0.114       | 0.565   | <0.001 |
| Orthopedic          | 1.043       | 0.369| 0.352| 0.171       | 0.726   | 0.005  |
| Others              | -1.281      | 0.351| 0.278| 0.140       | 0.552   | <0.001 |
| Economic condition  |             |     |     |             |         |
| Lower               |             |     |     |             |         |
| Higher              | -0.232      | 0.139| 0.793| 0.604       | 1.041   | 0.095  |
| Hospital level      |             |     |     |             |         |
| Non-tertiary        |             |     |     |             |         |
| Tertiary            | -0.223      | 0.143| 0.800| 0.605       | 1.058   | 0.118  |
| Sample size         |             |     |     |             |         |
| <20 isolates        |             |     |     |             |         |
| ≥20 isolates        | -0.541      | 0.268| 0.582| 0.344       | 0.985   | 0.044  |
| Quality             |             |     |     |             |         |
| Lower               |             |     |     |             |         |
| Higher              | -0.080      | 0.141| 0.923| 0.700       | 1.218   | 0.573  |
| Constant            | -0.513      | 0.443| -    | -           | -       | 0.247  |

doi:10.1371/journal.pone.0116079.t004
Conclusion
In conclusion, the overall proportion of \textit{S. aureus} causing SSIs in mainland China was similar to that in the US, and the proportion of MRSA was possibly lower. The real proportion of \textit{S. aureus} may be higher than that reported from the Chinese surveillance system. Both proportions of \textit{S. aureus} and MRSA tended to depend on types of surgeries. Therefore, clinicians should take into account the types of surgery when taking care of post-operative patients and managing \textit{S. aureus} and MRSA SSIs. Vancomycin and linezolid appeared to be effective for MRSA in SSIs. Further well-designed studies on this topic, including surveillance and primary prospective studies, are required to provide further reliable evidence.

Supporting Information
S1 Fig. Risk of bias for each included study.
(TIF)
S1 File. Subgroup analyses.
(DOCX)
S1 PRISMA Checklist.
(DOCX)
S1 Table. Search strategies and results.
(DOCX)
S2 Table. Quality assessment of the included studies.
(DOCX)
S3 Table. Distribution of MRSA isolates resistant to specific antibiotics.
(DOCX)

Author Contributions
Conceived and designed the experiments: ZY LH SZ. Performed the experiments: ZY JW WW Yuelun Zhang Yuan Zhang XN. Analyzed the data: ZY JW. Contributed reagents/materials/analysis tools: ZY JW WW Yuelun Zhang Yuan Zhang XN. Wrote the paper: ZY JW LH SZ.

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