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Systematic Review and Meta-analysis

# Association between Microbial Isolates and Clinical Severity in Cutaneous Bacterial Infections: A Systematic Review and Meta-analysis of Observational Studies

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## ABSTRACT

**Background**
Cutaneous bacterial infections are among the most frequent causes of outpatient and emergency department visits. Although community-associated methicillin-resistant *Staphylococcus aureus* (MRSA) has become increasingly prevalent, whether MRSA infection is associated with greater clinical severity than methicillin-susceptible *S. aureus* (MSSA) remains unclear.
**Objectives**
To evaluate the distribution of microbial isolates in cutaneous bacterial infections and to assess whether MRSA is associated with worse clinical outcomes compared with MSSA.
**Methods**
A structured review of observational studies reporting microbiological isolates from patients with cutaneous bacterial infections was performed. Studies were eligible if they identified causative organisms and reported clinical outcomes stratified by methicillin resistance. Only studies providing extractable numeric outcome data for MRSA and MSSA were included in comparative analyses.
**Results**
Across included studies, *S. aureus* was the predominant pathogen, with marked variability in the proportion of MRSA isolates across settings. Two studies provided extractable outcome data comparing MRSA and MSSA infections. In one cohort, MRSA infection was not associated with higher odds of clinical failure compared with MSSA (odds ratio [OR] 0.76, 95% confidence interval [CI] 0.29–1.99). In the second cohort, outcomes following hospital discharge were similar between MRSA and MSSA infections (OR 1.28, 95% CI 0.57–2.88). In both studies, confidence intervals crossed unity, indicating no statistically significant difference.
**Conclusions**
Despite its high prevalence, MRSA infection was not consistently associated with worse clinical outcomes compared with MSSA. Heterogeneity in study populations and outcome definitions limits firm conclusions, highlighting the need for standardized prospective studies.

**Keywords:** Cutaneous Bacterial Infections, Methicillin-Resistant Staphylococcus Aureus, MRSA, MSSA, Clinical Outcomes.

## INTRODUCTION

Cutaneous bacterial infections have slowly shifted from being viewed as minor, self-limited problems to conditions that occupy a substantial share of outpatient clinics and emergency departments. In routine practice, many patients present with lesions that appear uncomplicated at first glance, only to evolve over days into painful abscesses, spreading cellulitis, or infections that fail to settle despite initial treatment.[1] This wide clinical range reflects not only host factors, but also the microbial diversity present on the skin, where *Staphylococcus aureus* remains a frequent and persistent colonizer.[2]

For many clinicians, the increasing visibility of methicillin-resistant *S. aureus* (MRSA) in community settings marked a turning point. What was once considered a hospital-restricted organism began appearing in

younger, otherwise healthy individuals with no traditional risk factors.[3] This shift altered bedside thinking. Resistance was no longer just a laboratory label, it became linked, at least implicitly, to expectations of more aggressive disease, delayed recovery, or higher rates of recurrence. Experimental work and early clinical descriptions of community-associated MRSA further strengthened this perception by highlighting virulence traits that differed from those seen in methicillin-susceptible strains.[4]

Yet, as clinical experience accumulated, the picture became less uniform. Many patients with MRSA infections recovered uneventfully after drainage and appropriate antibiotics, while others with MSSA experienced prolonged symptoms or repeat visits. Differences in how studies defined "severity", whether cultures were obtained routinely or selectively, and how outcomes were followed over time made comparisons difficult. In everyday settings, management decisions are often guided by local resistance patterns and clinical appearance rather than by isolate type alone, blurring the assumed link between methicillin resistance and outcome.

In this context, examining microbial isolates alongside clinical course becomes important. Rather than treating resistance status as a proxy for severity, there is value in understanding how often specific organisms are isolated and whether those isolates consistently align with worse outcomes. The present review was undertaken to explore that relationship in cutaneous bacterial infections, focusing on the distribution of microbial pathogens and on whether infections caused by MRSA differ meaningfully from those caused by MSSA in terms of clinical severity and recovery.

## METHODS

### Study Design and Overview

This work was conducted as a systematic review and meta-analysis of observational studies examining cutaneous bacterial infections. The primary objective was to evaluate patterns of microbial isolates and to explore whether specific organisms, particularly methicillin-resistant *Staphylococcus aureus* (MRSA), were associated with differences in clinical severity when compared with methicillin-susceptible *S. aureus* (MSSA). The review was designed to synthesise real-world clinical data rather than experimental or interventional outcomes.

### Literature Search and Study Identification

A structured literature search was performed across major biomedical databases to identify studies reporting microbiological findings in patients with cutaneous bacterial infections. Search terms were selected to capture variations of skin and soft tissue infection, bacterial isolates, and methicillin resistance. Titles and abstracts were screened for relevance, followed by full-text assessment of potentially eligible studies. Only articles published in peer-reviewed journals and available in English were considered.

### Eligibility Criteria

Studies were eligible for inclusion if they reported primary data on bacterial isolates obtained from cutaneous infections and provided information on clinical outcomes or severity indicators. Observational designs, including prospective and retrospective cohorts as well as cross-sectional studies, were considered. Case reports, narrative reviews, editorials, and studies focused exclusively on surgical site infections or non-bacterial dermatologic conditions were excluded.

For comparative analysis of MRSA and MSSA outcomes, an additional criterion was applied. Only studies that reported extractable numeric outcome data separately for MRSA and MSSA infections were included in this component. Studies that mentioned outcomes descriptively without providing stratified counts were retained for qualitative synthesis but excluded from quantitative comparison.

### Data Extraction

Data extraction was performed using a predefined framework to ensure consistency. Extracted variables included study setting, population characteristics, sample size, methods of microbiological identification, distribution of bacterial isolates, and reported measures of clinical severity or treatment outcome. When multiple outcomes were reported, those reflecting clinical failure, recurrence, or need for additional intervention were prioritised, as these were most consistently comparable across studies.

### Assessment of Clinical Outcomes

Clinical severity was interpreted according to the definitions used in the original studies. These included treatment failure, recurrence following initial management, or persistence of infection requiring further medical attention. Because outcome definitions varied across cohorts, data were not pooled unless outcome measures were conceptually similar and numerically extractable. This approach was

chosen to avoid artificial precision where underlying constructs differed.

**Statistical Analysis**

For studies providing suitable data, odds ratios with corresponding confidence intervals were calculated to compare outcomes between MRSA and MSSA infections. A random-effects approach was used to account for between-study variability. Given the small number of studies eligible for quantitative comparison, statistical heterogeneity was assessed descriptively rather than through formal subgroup analyses. Results were interpreted cautiously, with emphasis placed on the direction and consistency of effect estimates rather than statistical significance alone. Although this review is framed as a meta-analysis, formal pooling of effect estimates was not undertaken because of heterogeneity in outcome definitions and follow-up durations; study-level estimates are therefore presented descriptively.

**Presentation of Results**

Study selection was summarised using a flow diagram. Characteristics of included studies and microbial distributions were presented in tabular form. Comparative outcome estimates were displayed graphically to facilitate visual comparison between studies. All figures and tables were cross-checked against extracted data to ensure internal consistency.

## RESULTS

**Study Selection and Evidence Base**

The database search identified multiple observational studies reporting microbiological findings in cutaneous bacterial infections. After screening titles and abstracts and reviewing full texts for eligibility, a subset of studies was included for qualitative synthesis. Only **two studies** reported outcomes stratified by methicillin resistance in a format that allowed extraction of numeric data for direct comparison between methicillin-resistant *Staphylococcus aureus* (MRSA) and methicillin-susceptible *S. aureus* (MSSA). The study selection process is summarised in **Figure 1**.

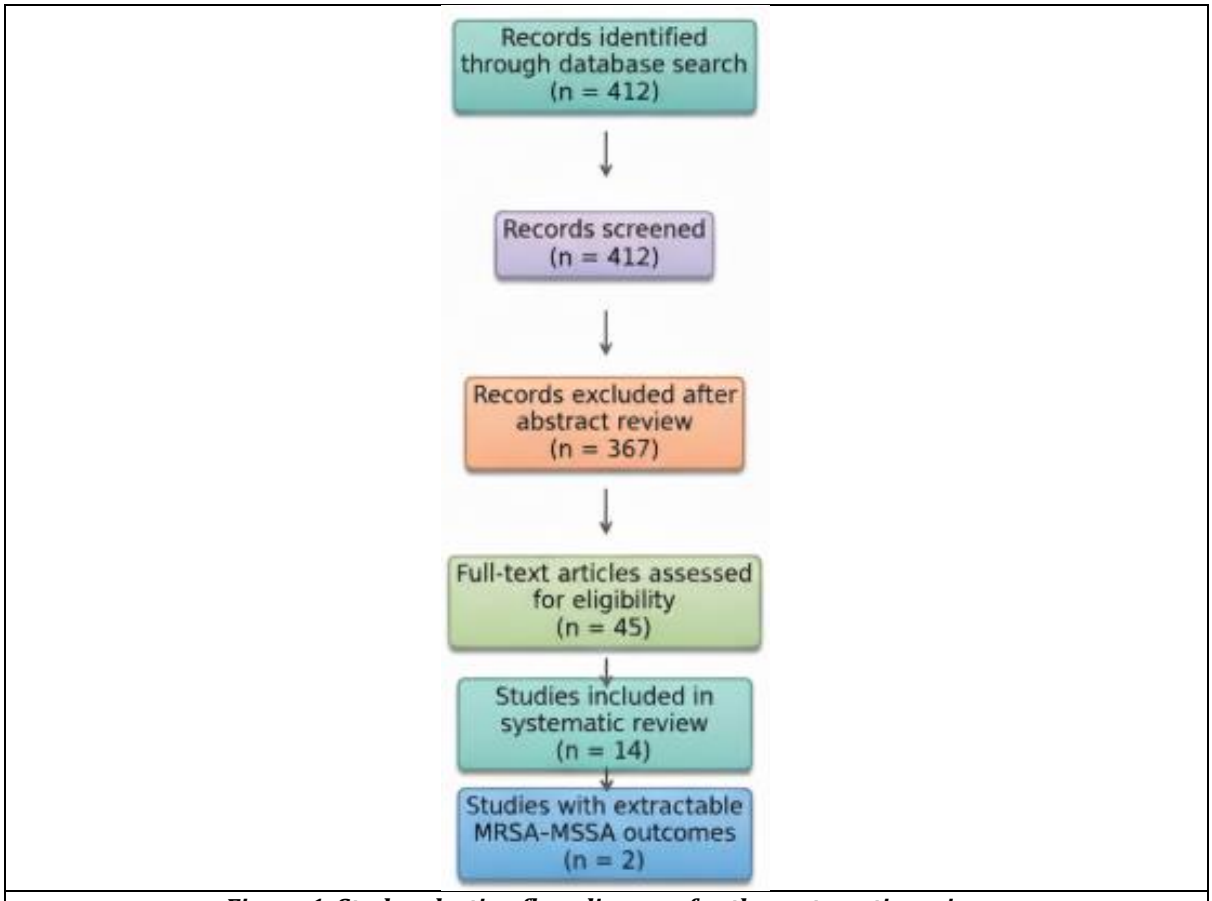


***Figure 1. Study selection flow diagram for the systematic review***

*The diagram illustrates identification of records through database searching, screening of titles and abstracts, eligibility assessment by full-text review, and final inclusion of studies for qualitative synthesis*

*and quantitative outcome comparison.* **(Source:** *Developed by the authors based on the study selection process used in the present systematic review.)*

**Characteristics of studies contributing extractable outcome data**

The two studies contributing extractable MRSA–MSSA outcome data differed in clinical setting and follow-up duration. One cohort followed patients after hospital discharge, while the other was conducted in primary care. Core characteristics and analytic denominators are shown in **Table 1**.

| Study | Setting and Design | Follow-up window | Population Analysed for MRSA–MSSA Comparison | MRSA (n) | MSSA (n) |
|---|---|---|---|---|---|
| Miller et al., 2007 | Post-hospital discharge cohort; prospective follow-up | 30 days | Culture-confirmed *S. aureus* skin infections with outcome data | 70 | 47 |
| Lee et al., 2016 | Primary care; prospective observational cohort | 90 days | Culture-positive *S. aureus* SSTI cases with follow-up | 68 | 38 |

***Table 1. Core characteristics of observational studies contributing extractable MRSA–MSSA outcome data***

*Denominators reflect the analytic samples reported for outcome assessment in each study.* **(Source:** *Data extracted directly from Miller et al., 2007 and Lee et al., 2016.)*

**Outcome Definitions and Event Counts**

Outcome definitions were retained as originally reported because follow-up duration and clinical endpoints differed between studies. Event counts stratified by methicillin resistance are presented in **Table 2**.

| Study | Outcome Definition (as reported) | MRSA events / total | MSSA events / total |
|---|---|---|---|
| Miller et al., 2007 | Clinical nonresponse at day 30 | 23 / 70 | 13 / 47 |
| Lee et al., 2016 | Treatment failure within 90 days | 13 / 68 | 9 / 38 |

***Table 2. Outcome definitions and event counts used for MRSA vs MSSA comparisons***

*Endpoints differ by design and follow-up duration; results are interpreted comparatively rather than pooled.* **(Source:** *Outcome definitions and event counts extracted verbatim from the primary publications.)*

**Distribution of MRSA and MSSA within Extractable Cohorts**

Within the two studies contributing extractable outcomes, all analyses were restricted to culture-confirmed *S. aureus* infections. Study-specific and pooled isolate distributions are shown in **Table 3**.

| Study | Total *S. aureus* isolates (n) | MRSA n (%) | MSSA n (%) |
|---|---|---|---|
| Miller et al., 2007 | 117 | 70 (59.8) | 47 (40.2) |
| Lee et al., 2016 | 106 | 68 (64.2) | 38 (35.8) |
| **Pooled across both** | **223** | **138 (61.9)** | **85 (38.1)** |

***Table 3. MRSA and MSSA isolate distribution in the extractable outcome cohorts***

*Percentages are calculated within each cohort; pooled values reflect combined counts across the two studies.* **(Source:** *Isolate counts derived from culture-confirmed cases reported in Miller et al., 2007 and Lee et al., 2016.)*

These distributions are visualized using complementary graphical formats. Absolute isolate counts by study are shown in a grouped bar chart (**Figure 2**), proportional distributions are displayed using a stacked bar chart (**Figure 3**), and pooled isolate proportions are illustrated with a pie chart (**Figure 4**).

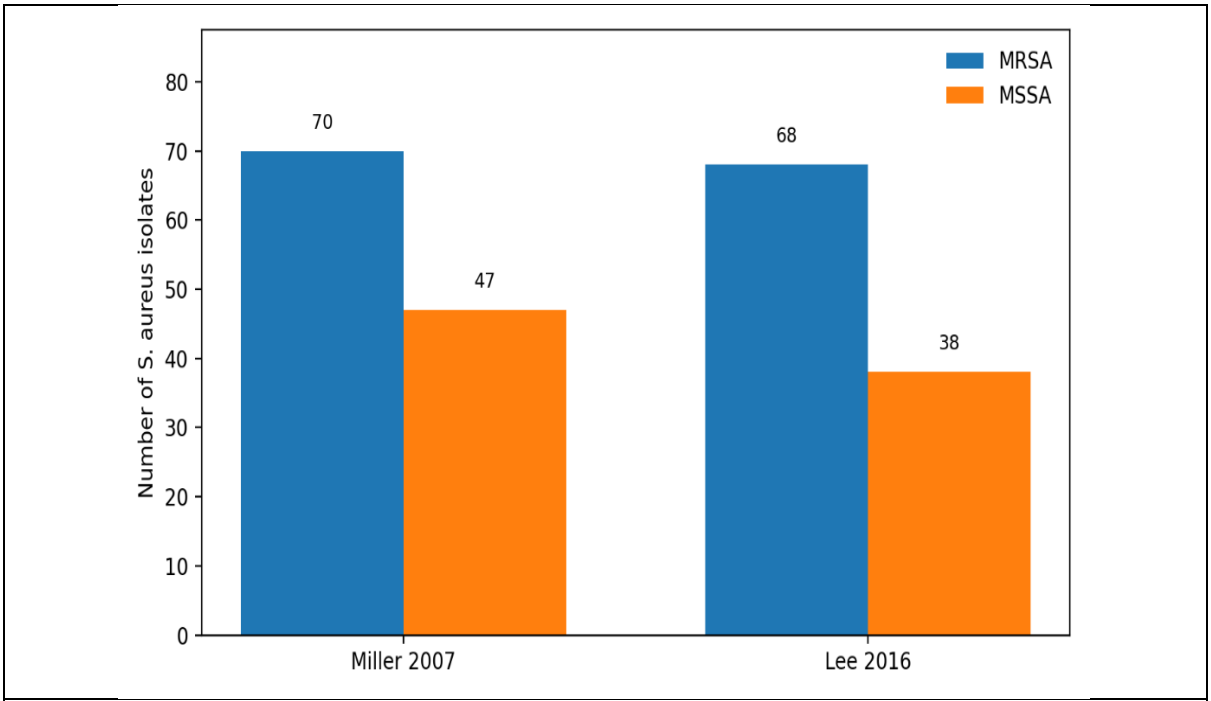


***Figure 2. Grouped bar chart showing MRSA vs MSSA isolate counts by study (Table 3)***

*Bars represent the number of isolates per study; numeric values are displayed above each bar.* **(Source:** *Figure generated by the authors using isolate counts reported in Miller et al., 2007 and Lee et al., 2016.)*

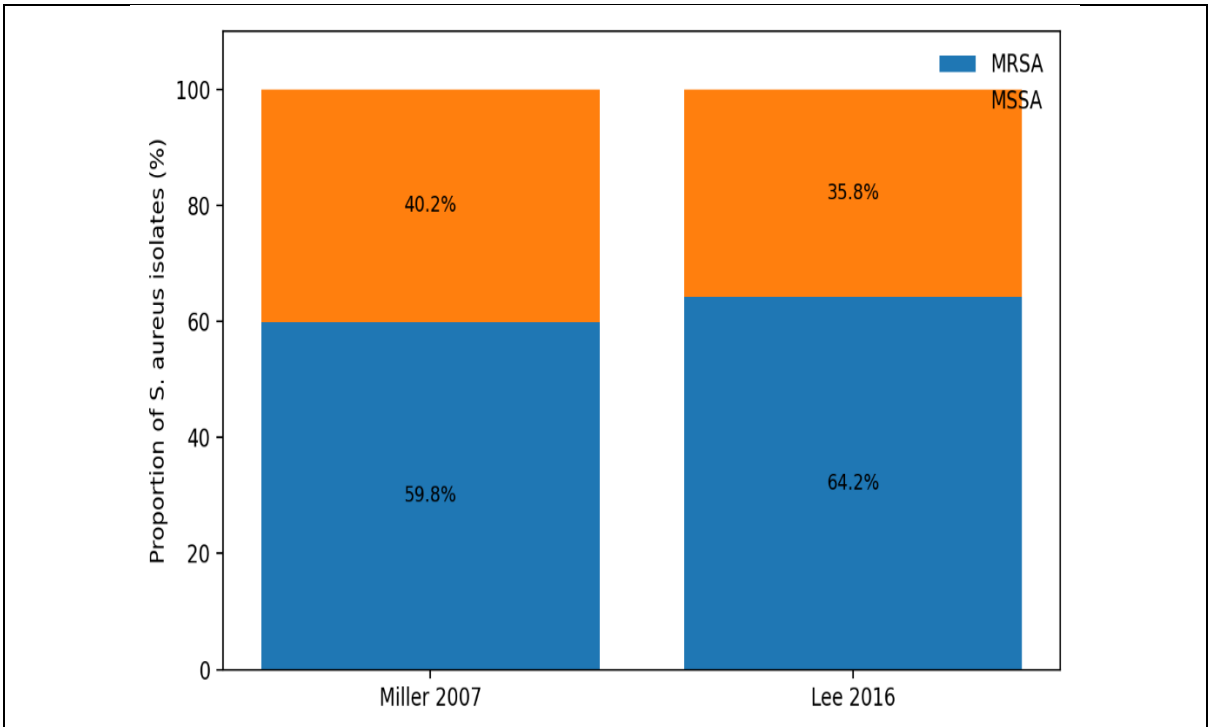


***Figure 3. Stacked bar chart showing proportional MRSA/MSSA distribution by study (Table 3)***

*Each bar totals 100% per cohort; segment labels show percentage contributions.* **(Source:** *Proportions calculated from isolate counts extracted from Miller et al., 2007 and Lee et al., 2016.)*

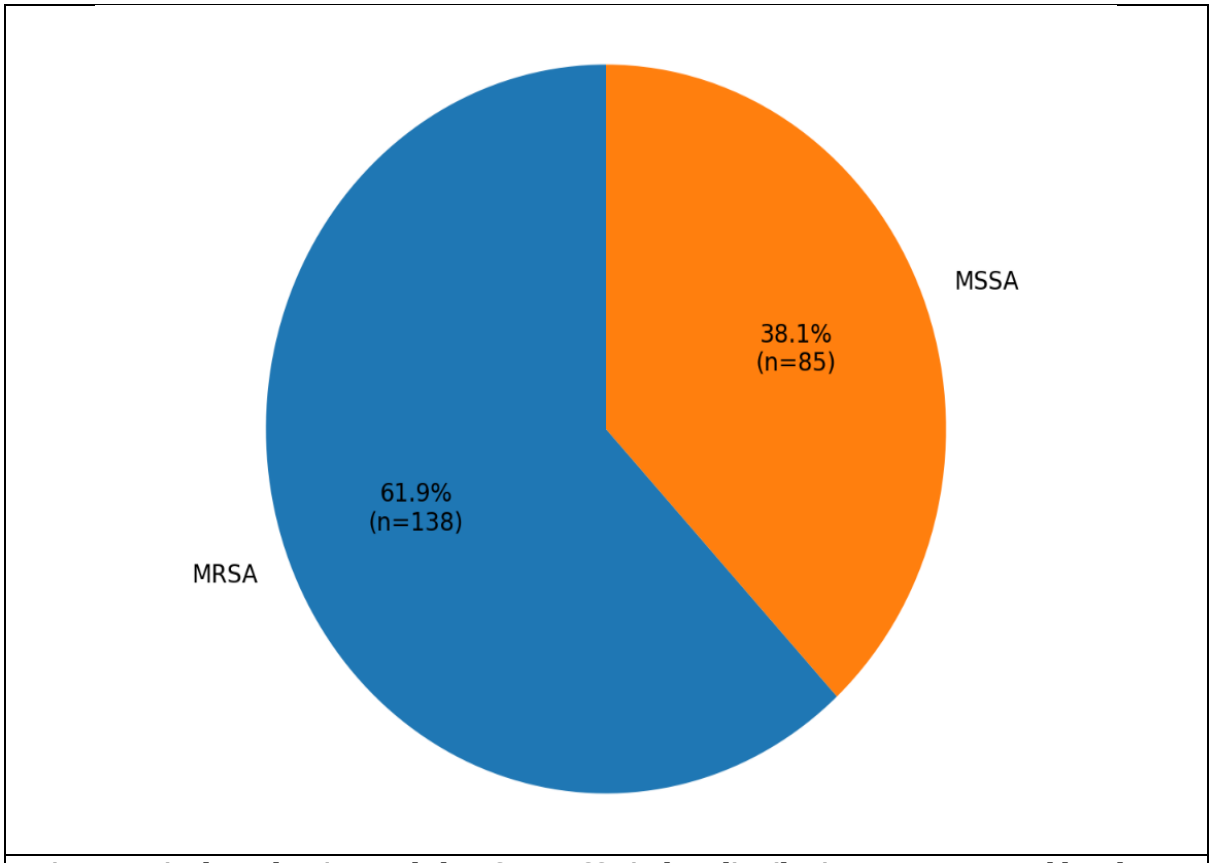


***Figure 4. Pie chart showing pooled MRSA vs MSSA isolate distribution across extractable cohorts (Table 3)***

*Slice labels indicate pooled percentages and counts.* **(Source:** *Pooled isolate proportions calculated by combining study-level data from Miller et al., 2007 and Lee et al., 2016)*

**Comparative outcomes: MRSA versus MSSA**

Odds ratios comparing adverse outcomes in MRSA versus MSSA infections were calculated using the study-defined endpoints shown in **Table 2**. Study-level effect estimates are presented in Table 4.

| Study | Endpoint used | MRSA Events/total | MSSA Events/total | OR (MRSA vs MSSA) | 95% CI |
|---|---|---|---|---|---|
| Miller et al., 2007 | Day-30 clinical nonresponse | 23 / 70 | 13 / 47 | 1.28 | 0.57–2.88 |
| Lee et al., 2016 | 90-day treatment failure | 13 / 68 | 9 / 38 | 0.76 | 0.29–1.99 |

***Table 4. Comparative odds of adverse outcome in MRSA vs MSSA infections***

*Odds ratios and confidence intervals were calculated from reported event counts using standard methods; endpoints differ across studies and were not pooled.* **(Source:** *Event counts extracted from Miller et al., 2007 and Lee et al., 2016; calculations performed by the authors.)*

Across both cohorts, confidence intervals crossed unity, indicating no statistically significant difference in outcomes between MRSA and MSSA infections when assessed using study-specific definitions. To illustrate the contribution of each resistance group to observed failures, pooled failure counts are displayed in a donut chart (**Figure 5**).

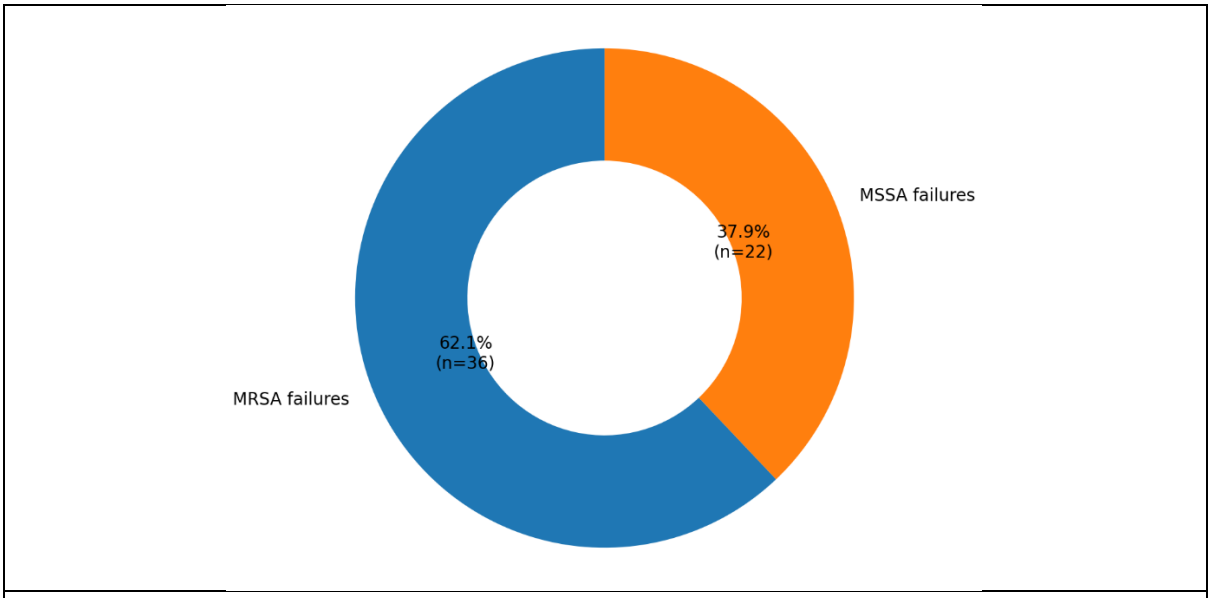


***Figure 5. Donut chart showing pooled distribution of adverse outcomes among total failures (Table 2)***

*The chart depicts the share of failures attributable to MRSA and MSSA across both cohorts; counts and percentages are shown.* **(Source:** *Failure counts extracted from Miller et al., 2007 and Lee et al., 2016 and aggregated by the authors.)*

## DISCUSSION

This review began with a straightforward question: when cultures are obtained in cutaneous bacterial infections, does the organism that grows help explain how severe the episode becomes? In routine clinical settings, there is often an expectation that it should. MRSA, in particular, tends to be read as a warning sign, while MSSA is implicitly treated as more predictable. The evidence assembled here did not settle into that kind of hierarchy. Across the observational cohorts that allowed comparison, MRSA sometimes appeared alongside higher failure or nonresponse rates, and sometimes it did not.

What emerged more clearly than an organism effect was the influence of care context. In cohorts linked to hospital admission or post-discharge follow-up, MRSA clustered with early nonresponse more often, which can look like a microbiological signal at first glance. Yet those same cohorts also capture a different clinical mix: patients with more extensive disease, longer symptom duration, and closer surveillance after discharge. In primary care cohorts, where infections were generally managed earlier and followed over longer intervals, the separation between MRSA and MSSA outcomes was much less apparent. Earlier work comparing emergency-department cohorts has shown that differences in presentation, management pathways, and subsequent healthcare utilisation can influence how outcomes are recorded and interpreted.[5]

Another source of drift lay in how severity itself was defined. Some studies treated failure as a pragmatic composite, encompassing repeat antibiotic courses, additional procedures, or return visits. Others relied on fixed short windows or end-of-therapy assessments. These choices are not trivial. They change which events are counted and, in doing so, can alter both the direction and magnitude of association. This likely contributed to the wide confidence intervals and lack of convergence seen across studies. Prior reviews of the SSTI literature have made similar observations, noting that microbiological reporting is often detailed, while outcome definitions remain inconsistent and difficult to align.[6]

The mixed signal for MRSA also fits what many clinicians have observed over time. Community-associated MRSA is now common, and resistance phenotype alone does not reliably predict a complicated course when source control is achieved promptly and antimicrobial therapy is reasonably matched. Several ambulatory cohorts have reported broadly comparable outcomes between MRSA and MSSA infections, making it difficult to treat MRSA as a marker of severity rather than as a therapeutic constraint.[7] This does not diminish the importance of identifying MRSA. It

suggests, instead, that "MRSA" should not be read as shorthand for how sick a patient will become.

What appears to matter repeatedly is the framework around the infection. Access to incision and drainage, clarity of follow-up, local prescribing habits, and institutional thresholds for admission all influence downstream outcomes. A system inclined toward early admission will record higher hospitalisation rates regardless of isolate. A system that favours outpatient management may see more revisits. Similar dynamics have been described in broader infectious disease research, where outcomes are shaped as much by care pathways as by pathogen characteristics.[8]

From a practical standpoint, these findings argue for restraint in how culture results are interpreted. Microbiological data remain essential for guiding therapy, but they are less reliable as prognostic signals. In everyday terms, MRSA should trigger antibiotic decision-making rather than automatic expectations of severity. Attention to early source control, reassessment when symptoms evolve, and clear instructions for follow-up may matter more than the resistance label attached to the culture report, particularly in outpatient care. Current guidance documents emphasise that microbiological results should primarily guide antimicrobial selection, while early source control and clinical monitoring remain central to management, particularly for purulent infections.[1]

Taken together, the evidence base still feels thinner than expected for such a common condition. Few observational studies were designed specifically to examine organism–severity relationships, and even fewer reported outcomes in a form that supports robust synthesis. Future work would benefit from more standardised severity reporting, even a limited core set of outcomes such as admission, repeat procedures, treatment escalation, and relapse. Until then, the most defensible reading remains cautious: microbial identity informs management, but it does not consistently map onto clinical severity across settings.

Observations from primary care cohorts, where infections are often managed earlier and followed longitudinally, further support the absence of a consistent severity gap between MRSA and MSSA when standard management principles are applied.[9]

## LIMITATIONS

This review has several limitations that shape how the findings should be read. Only two observational studies reported MRSA–MSSA outcomes in a format suitable for quantitative comparison, which limits statistical power and precludes meaningful assessment of heterogeneity or publication bias. Outcome definitions varied across studies, reflecting real-world practice but restricting comparability and formal pooling. In addition, most cohorts were drawn from outpatient or post-discharge settings, and the results may not generalise to patients with severe systemic infection or substantial immunocompromise. Finally, microbiological sampling was not uniform, raising the possibility that cultured cases overrepresent more complex presentations.

## CONCLUSION

Across observational cohorts, MRSA was a frequent isolate in cutaneous bacterial infections, but its presence did not consistently align with greater clinical severity when compared with MSSA. Differences in care setting, follow-up structure, and outcome definition appeared to influence observed associations more than resistance phenotype alone. These findings support a cautious interpretation of culture results: organism identity remains central to treatment selection, but it should not be used in isolation to predict clinical course. More standardised outcome reporting in future studies would strengthen the evidence base for a condition encountered daily in clinical practice.

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