

Systemic Antibiotics for the Treatment of Skin and Soft Tissue Abscesses: A Systematic Review and Meta-Analysis

Michael Gottlieb, MD*; Joshua M. DeMott, PharmD, MSc; Marilyn Hallock, MD, MS; Gary D. Peksa, PharmD

*Corresponding Author. E-mail: michaelgottliebmd@gmail.com, Twitter: @MGottliebMD.

Study objective: The addition of antibiotics to standard incision and drainage is controversial, with earlier studies demonstrating no significant benefit. However, 2 large, multicenter trials have recently been published that have challenged the previous literature. The goal of this review was to determine whether systemic antibiotics for abscesses after incision and drainage improve cure rates.

Methods: PubMed, the Cumulative Index of Nursing and Allied Health Literature, Scopus, the Cochrane Database of Systematic Reviews, the Cochrane Central Register of Controlled Trials, and bibliographies of selected articles were assessed for all randomized controlled trials comparing adjuvant antibiotics with placebo in the treatment of drained abscesses, with an outcome of treatment failure assessed within 21 days. Data were dual extracted into a predefined worksheet and quality analysis was performed with the Cochrane Risk of Bias tool.

Results: Four studies (n=2,406 participants) were identified. There were 89 treatment failures (7.7%) in the antibiotic group and 150 (16.1%) in the placebo group. The calculated risk difference was 7.4% (95% confidence interval [CI] 2.8% to 12.1%), with an odds ratio for clinical cure of 2.32 (95% CI 1.75 to 3.08) in favor of the antibiotic group. There was also a decreased incidence of new lesions in the antibiotic group (risk difference -10.0%, 95% CI -12.8% to -7.2%; odds ratio 0.32, 95% CI 0.23 to 0.44), with a minimally increased risk of minor adverse events (risk difference 4.4%, 95% CI 1.0% to 7.8%; odds ratio 1.29, 95% CI 1.06 to 1.58).

Conclusion: The use of systemic antibiotics for skin and soft tissue abscesses after incision and drainage resulted in an increased rate of clinical cure. Providers should consider the use of antibiotics while balancing the risk of adverse events. [Ann Emerg Med. 2018;■:1-9.]

Please see page XX for the Editor's Capsule Summary of this article.

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INTRODUCTION

Background

Skin and soft tissue infections are a common presentation to both the emergency department (ED) and outpatient clinics, comprising more than 6 million visits each year in the United States.^{1,2} Abscesses represent nearly half of all cases and the overall incidence is increasing annually.²⁻⁵

Although the standard clinical management of skin and soft tissue abscesses includes incision and drainage, the adjunctive use of systemic antibiotics remains controversial.⁶ Recommendations by the Infectious Diseases Society of America for the treatment of methicillin-resistant *Staphylococcus aureus* (MRSA) infections in adults and children state that for simple abscesses, incision and drainage alone is likely to be adequate, adding that adjunctive antibiotics may be

beneficial in select patients.⁷ This was based on early studies demonstrating no statistically significant difference in outcomes with antibiotic therapy.⁸⁻¹¹ However, previous literature was limited by small sample sizes and antibiotic selection. Since then, 2 large randomized controlled trials have been published, demonstrating improved cure rates when antibiotics were added to standard therapy.^{12,13}

Goals of This Investigation

With increasing MRSA prevalence and several new studies, it is important to reevaluate the effectiveness of adjunctive antibiotics. The purpose of this systematic review and meta-analysis was to determine the effectiveness of systemic antibiotics for the treatment of skin and soft tissue abscesses after incision and drainage. Secondary outcomes included differences in rates of recurrence and adverse events.

Editor's Capsule Summary*What is already known on this topic*

Skin abscesses in many parts of the world are predominantly caused by methicillin-resistant *Staphylococcus aureus*. The primary treatment of a skin abscess is incision and drainage.

What question this study addressed

Do methicillin-resistant *S aureus*-active antibiotics improve clinical outcomes among patients with a drained skin abscess?

What this study adds to our knowledge

Meta-analysis of 4 randomized placebo-controlled trials involving 2,406 participants found that methicillin-resistant *S aureus*-active antibiotics were associated with a significantly increased primary lesion cure rate (risk difference 7.4 percentage points) and reduced new lesion development rate (10.0 percentage points), with an increased rate of minor adverse events (4.4 percentage points).

How this is relevant to clinical practice

Antibiotics for drained skin abscesses incrementally improve patient outcomes, with a low risk of adverse events. Studies do not inform associated rates of rare serious adverse effects or antibiotic-preventable invasive infections.

MATERIALS AND METHODS

Our study conforms to the Preferred Reporting Items for Systematic Reviews and Meta-analyses guidelines for systematic reviews and was performed in accordance with best practice guidelines.¹⁴ In conjunction with a medical librarian, we conducted a search of PubMed, the Cumulative Index of Nursing and Allied Health Literature, Scopus, the Cochrane Database of Systematic Reviews, and the Cochrane Central Register of Controlled Trials to include citations from inception to November 10, 2017. Details of the search strategy are included in [Appendix E1](#), available online at <http://www.annemergmed.com>. We reviewed the bibliographies of identified studies and review articles for potential missed articles. We also consulted with topic experts to help identify any further relevant studies.

Inclusion criteria consisted of all randomized controlled trials comparing systemic antibiotics with activity against MRSA versus placebo in the treatment of skin and soft tissue abscesses after incision and drainage. The primary outcome was treatment failure, as defined by the original

study, which must have included a specific assessment of the wound within 21 days. Secondary outcomes included recurrence rate for new abscesses, overall adverse events rates, and rates of diarrhea.

Exclusion criteria included case reports, case series, retrospective studies, nonrandomized prospective studies, and studies published in abstract format only. There were no language restrictions. Two investigators (G.D.P. and J.M.D.) independently assessed studies for eligibility based on the above criteria. All abstracts meeting initial criteria were reviewed as full articles. Studies determined to meet the eligibility criteria on full-text review by both extractors were included in the final data analysis. Any discrepancies were resolved by consensus.

Data Collection and Processing

Two investigators (M.G. and G.D.P.) independently extracted data from the included studies. The investigators underwent initial training and extracted data into a predesigned data collection form. The following information was abstracted: last name of the first author, publication year, study country, study population size, study location (eg, ED, ICU), study inclusion criteria, study exclusion criteria, mean age of study patients, sex of study patients, antibiotic selection and time course, definition of clinical cure rate as per the original study, clinical cure rates for both treatment arms, rate of new abscess development, adverse event rates for both treatment arms, and any other outcomes assessed by the studies. All adverse events, as defined by the original study, were included. A subgroup analysis specifically assessing cases of diarrhea was also performed. Studies were independently assessed for quality by 2 investigators (M.G. and M.H.) using the Cochrane Risk of Bias tool.¹⁵ Any discrepancies were resolved by consensus.

Primary Data Analysis

The effect of dichotomous variables was measured by both risk difference and odds ratio with 95% confidence intervals (CIs). Two-sided $P < .05$ was considered statistically significant. For absolute risk difference results, we used percentages to represent percentage points. All cases were analyzed with the Mantel-Haenszel method. χ^2 and I^2 statistics were used to assess heterogeneity of included studies, with $P < .1$ or I^2 greater than 50% considered significant for heterogeneity.¹⁶ In cases in which significant heterogeneity existed, pooled data were analyzed with a random-effects model. In the absence of significant heterogeneity, a fixed-effects model was used. A funnel plot and Egger's test were used to assess for publication bias.¹⁷ Statistical analyses were performed with RevMan (version

5.3; Nordic Cochrane Centre, Copenhagen, Denmark), and StataMP (version 13.0; StataCorp, College Station, TX) was used to assess publication bias.

RESULTS

A total of 2,772 references were identified. PubMed yielded 1,710 studies, Scopus identified 532 studies, the Cumulative Index of Nursing and Allied Health Literature found 320 studies, the Cochrane Central Register of Controlled Trials identified 203, and the Cochrane Database of Systematic Reviews yielded 7 studies. After removal of duplicates, 2,366 abstracts were reviewed, with 15 selected for full-text review (Figure 1). No additional articles were identified through bibliographic review. Four studies, comprising 2,406 patients, were selected for the final analysis.

Characteristics of Study Subjects

All 4 studies were conducted in the United States and involved a total of 16 clinical sites.¹⁰⁻¹³ Three studies were performed in the ED setting,¹⁰⁻¹² and one study involved a

mix of outpatient and ED patients.¹³ Two studies used ultrasonography to assist with abscess identification and management.^{11,12} The median patient age ranged from 4 to 44 years and 57.2% were male patients. Overall, the MRSA prevalence was 49.0% and the methicillin-sensitive *S aureus* prevalence was 16.3%. The remaining cases were caused by either other bacteria or negative-result wound cultures. Three studies used trimethoprim-sulfamethoxazole¹⁰⁻¹² and one study randomized patients to either trimethoprim-sulfamethoxazole or clindamycin.¹³ Table 1 provides a summary of the characteristics of each trial. Table E1 (available online at <http://www.annemergmed.com>) provides the full inclusion and exclusion criteria for each study. One study defined treatment failure by clinical signs and symptoms,¹² whereas the other 3 studies included both clinical signs and symptoms and the need for further intervention (eg, repeated incision and drainage, change in antibiotics, hospital admission) in their primary outcome definition.^{10,11,13} Table E2 (available online at <http://www.annemergmed.com>) provides full definitions of the primary

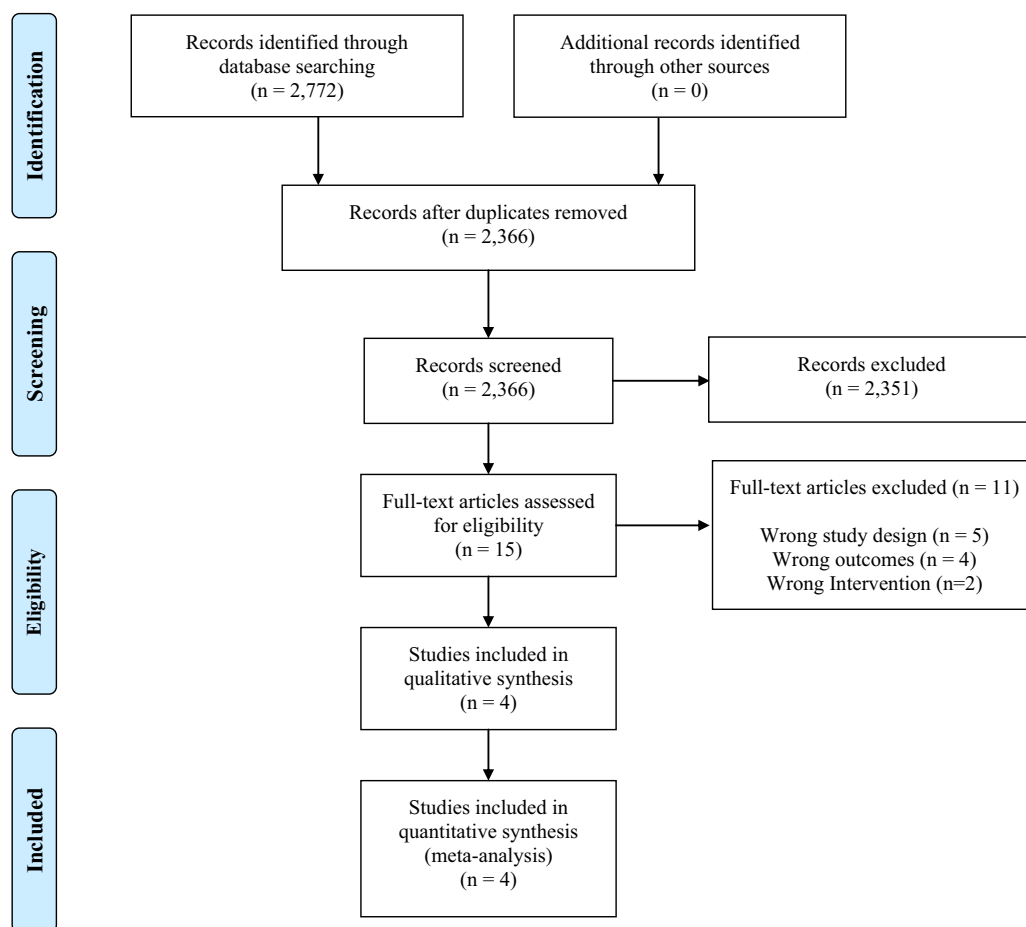


Figure 1. Preferred Reporting Items for Systematic Reviews and Meta-analyses flow diagram.

Table 1. Characteristics of the included studies.

Study	Study Population	Study Location	Median Age (IQR), Years	No. of Male Patients (%)	Antibiotic
Schmitz, 2010 ¹⁰	212	ED	27 (21–38)	140 (66.0)	TMP-SMX 320–1,600 mg PO twice daily for 7 days
Duong, 2010 ¹¹	161	ED	4 (1–12)	62 (41.6)	TMP-SMX 5–6 mg of TMP/kg PO twice daily for 10 days
Talan, 2016 ¹²	1,247	ED	35 (26–48)	726 (58.2)	TMP-SMX 320–1,600 mg PO twice daily for 7 days
Daum, 2017 ¹³	786	Outpatient clinic or ED	25.5*	448 (57.0)	Adult patients Clindamycin 300 mg PO 3 times daily for 10 days TMP-SMX 160–800 mg PO twice daily for 10 days Pediatric patients Clindamycin 8–10 mg/kg PO 3 times daily for 10 days TMP-SMX 4–5 mg of TMP/kg PO twice daily for 10 days

IQR, Interquartile ratio; TMP-SMX, trimethoprim-sulfamethoxazole; PO, per os.

*Mean age.

outcome of treatment failure for each study. All 4 trials were at overall low risk of bias according to the Cochrane Risk of Bias tool (Table 2). The study by Duong et al¹¹ was considered to be at unclear risk of bias for outcome assessment because the authors did not explicitly state whether the outcome assessors were blinded.¹¹ No studies were sponsored by pharmaceutical companies.

Overall, there were 89 treatment failures (7.7%) in the antibiotic group and 150 (16.1%) in the placebo group. The calculated risk difference was 7.4% (95% CI 2.8% to 12.1%; $P=.002$) in favor of the antibiotic group, with a number needed to treat of 14 (Figure 2). The odds ratio for clinical cure was 2.32 (95% CI 1.75 to 3.08; $P<.001$) in favor of the antibiotic group. There was no statistical heterogeneity, with $I^2=0\%$ ($P=.45$). Overall loss to follow-up across all 6 studies was 6.1%. In the assessment of publication bias, a funnel plot depicted no evidence of publication bias (Figure 3). Egger's test for small-study effects also indicated no significant bias existed ($P=.42$).

New lesions at a different site were identified in 68 patients (6.2%) in the antibiotic group and 134 (15.3%) in the placebo group at 10 to 30 days. The calculated risk difference was -10.0% (95% CI -12.8% to -7.2% ; $P<.001$) in favor of fewer new lesions in the antibiotic group, with a number needed to treat of 10 (Figure 4). The odds ratio was 0.32 (95% CI 0.23 to 0.44; $P<.001$) in

favor of fewer new lesions. Development of new lesions at a different site at 49 to 63 days was assessed by Talan et al,¹² who found a statistically significant difference between the antibiotic group and placebo group (10.9% versus 19.1%; risk difference -8.2% ; 95% CI -12.5% to -3.8%). In contrast, although the study used a different study population (ie, mostly children younger than 5 years and with diaper area lesions as opposed to mostly adults with extremity abscesses), Duong et al¹¹ reassessed groups at 90 days and found similar rates of new lesions between both groups (28.3% versus 28.8%; risk difference -0.5% ; 95% CI -18.5% to 17.3%).

There were 327 adverse events (24.8%) in the antibiotic group and 233 (22.2%) in the placebo group, resulting in a calculated risk difference of 4.4% (95% CI 1.0% to 7.8%; $P=.01$), with a number needed to harm of 23 and an odds ratio of 1.29 (95% CI 1.06 to 1.58; $P=.01$) (Figure 5). However, the majority of the adverse events were mild, consisting of gastrointestinal symptoms, mild rashes, and generalized systemic symptoms (eg, drowsiness, headache). A subgroup analysis specifically assessing for the adverse effect of diarrhea identified 155 cases (11.8%) in the antibiotic group and 118 (11.2%) in the placebo group, resulting in a calculated risk difference of 0.8% (95% CI -1.7% to 3.4%; $P=.52$) and an odds ratio of 1.09 (95% CI 0.84 to 1.41; $P=.53$) (Figure 6). There were 2 cases of

Table 2. Risk of bias for included studies.

Study	Random Sequence Generation	Allocation Concealment	Blinding of Participants and Personnel	Blinding of Outcome Assessment	Incomplete Outcome Data	Selective Reporting	Other Bias
Schmitz, 2010 ¹⁰	L	L	L	L	L	L	L
Duong, 2010 ¹¹	L	L	L	U	L	L	L
Talan, 2016 ¹²	L	L	L	L	L	L	L
Daum, 2017 ¹³	L	L	L	L	L	L	L

L, Low risk of bias; U, unclear risk of bias.

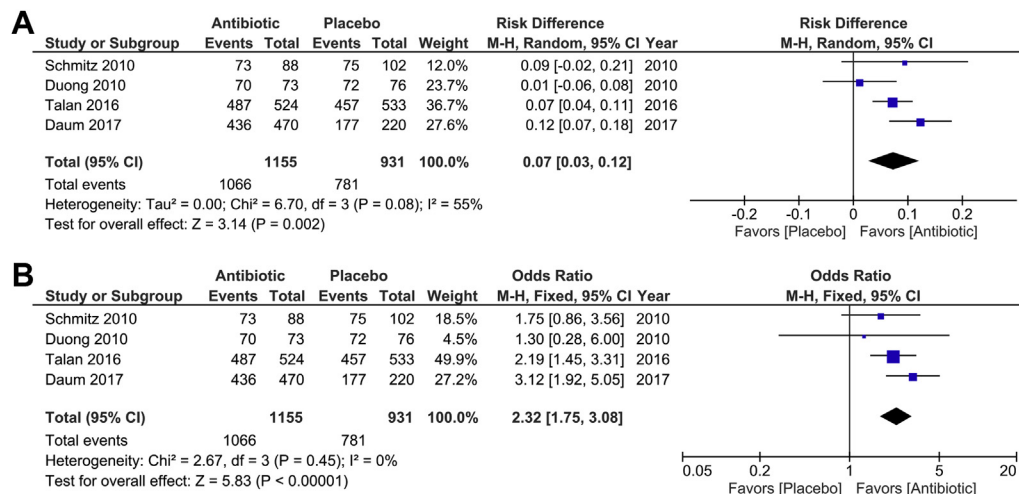


Figure 2. Forest diagram of risk difference (A) and odds ratio (B) demonstrating an increased clinical cure rate in the antibiotic group compared with the placebo group.

hypersensitivity reactions to the antibiotics.^{10,13} Schmitz et al¹⁰ described one mild allergic reaction, whereas Daum et al¹³ described a case of fever, rash, thrombocytopenia, and hepatitis that may have been related to trimethoprim-sulfamethoxazole and resolved without sequelae. There were no other serious or potentially life-threatening reactions identified.

LIMITATIONS

It is important to consider several limitations with respect to this review. First, the studies used 2 different antibiotics (ie, trimethoprim-sulfamethoxazole and clindamycin). However, the clinical cure rates were similar between both treatment groups.¹³ This was also observed in another recent trial comparing clindamycin with

trimethoprim-sulfamethoxazole for the treatment of skin abscesses, which found no difference in the rates of clinical cure.¹⁸ However, clindamycin was found to be associated with a reduced rate of recurrent infections in the study by Daum et al.¹³ This is consistent with results from another recent trial demonstrating reduced recurrence rates in patients treated with clindamycin compared with trimethoprim-sulfamethoxazole.¹⁹ Therefore, it is possible that clindamycin is more effective for reducing recurrence rates despite clinical cure rates similar to those of trimethoprim-sulfamethoxazole.

Additionally, the studies varied in their definition of clinical cure. Three studies used a follow-up period ranging from 7 to 10 days, whereas Talan et al¹² assessed patients at 14 to 21 days.¹² One study defined treatment failure by clinical signs and symptoms,¹² whereas the other 3 studies included both clinical signs and symptoms and the need for further intervention (eg, repeated incision and drainage, change in antibiotics, hospital admission) in their primary outcome definition.^{10,11,13} However, in the largest trial, Talan et al¹² also found that antibiotics were associated with significantly improved rates of clinical cure, using a composite outcome defined as the need for a new antibiotic or a new drainage procedure, with a risk difference of 12.2% (95% CI 7.2% to 17.1%) and number needed to treat of 8.

Finally, only 2 studies specifically standardized the incision and drainage procedure,^{12,13} whereas the remainder relied on the clinician's standard technique.⁸⁻¹¹ It is possible that inadequate drainage caused by improper technique confounded the results, although it is unlikely because this is a common procedure and both studies with a standardized drainage procedure significantly favored the

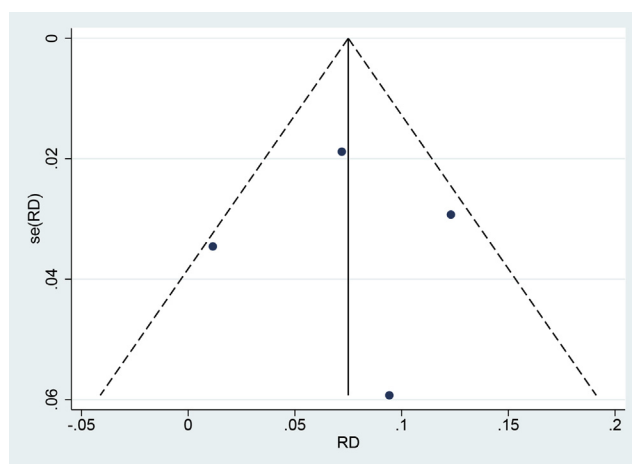


Figure 3. Funnel plot of the included studies comparing the antibiotic and placebo groups. RD, Risk difference.

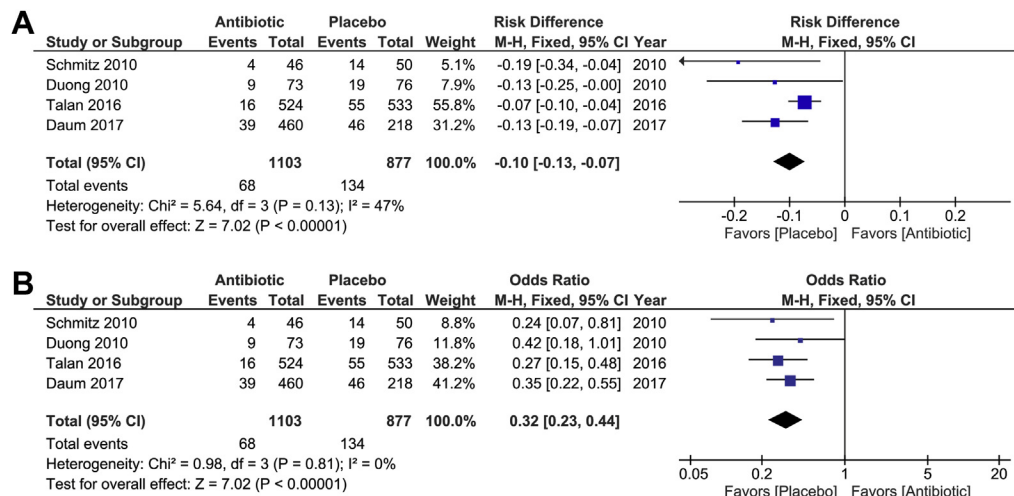


Figure 4. Forest diagram of risk difference (A) and odds ratio (B) demonstrating an increased number of new infections at 10 to 30 days in the placebo group compared with the antibiotic group.

antibiotic group. Additionally, Talan et al¹² used ultrasonography to evaluate the extent of the abscess, which may have helped to further ensure complete drainage, and this trial also found an antibiotic benefit.

DISCUSSION

This systematic review and meta-analysis of 4 studies ($n=2,406$ participants) demonstrated that the use of systemic antibiotics after incision and drainage of cutaneous abscesses resulted in a significantly improved rate of clinical cure compared with placebo. This review has several strengths, including the use of a standardized protocol with dual abstraction; the use of a formal literature search facilitated by an experienced medical librarian; independent dual data extraction into a

predefined, piloted, data extraction form; and inclusion of a large patient population. Additionally, the studies were at overall low risk of bias.

Two previous systematic reviews assessed the effect of systemic antibiotics on the treatment of skin and soft tissue abscesses.^{20,21} Singer and Thode²⁰ included all randomized, controlled trials through 2012 and identified 4 trials of 589 total patients, noting no significant difference between groups in their review. Our study provides an updated review of this study and includes several additional databases, identifying 2 new studies, resulting in a 4-fold increase in the number of patients. As a result of the new data, there is now a statistically and clinically significant difference demonstrating an increased cure rate in the antibiotic group. Fahimi et al²¹ included

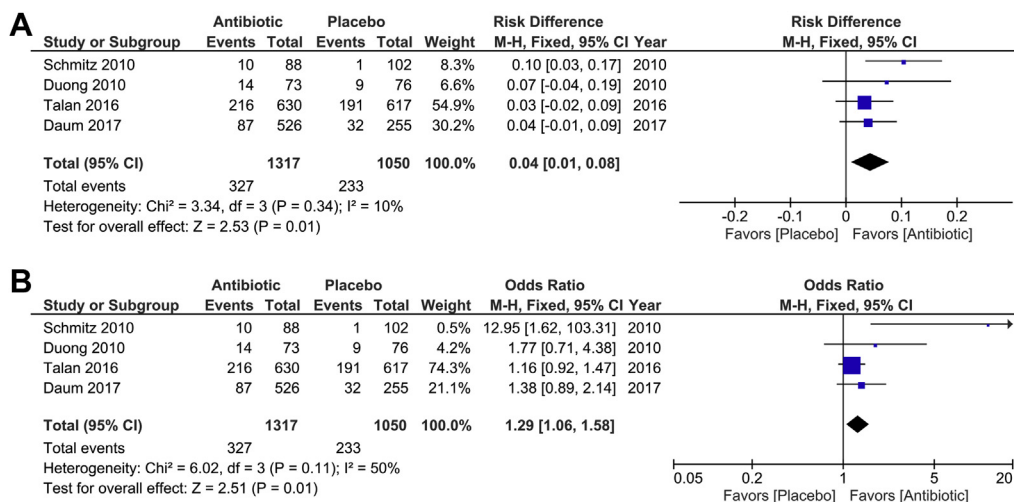


Figure 5. Forest diagram of risk difference (A) and odds ratio (B) demonstrating an increased rate of adverse events in the antibiotic group compared with the placebo group.

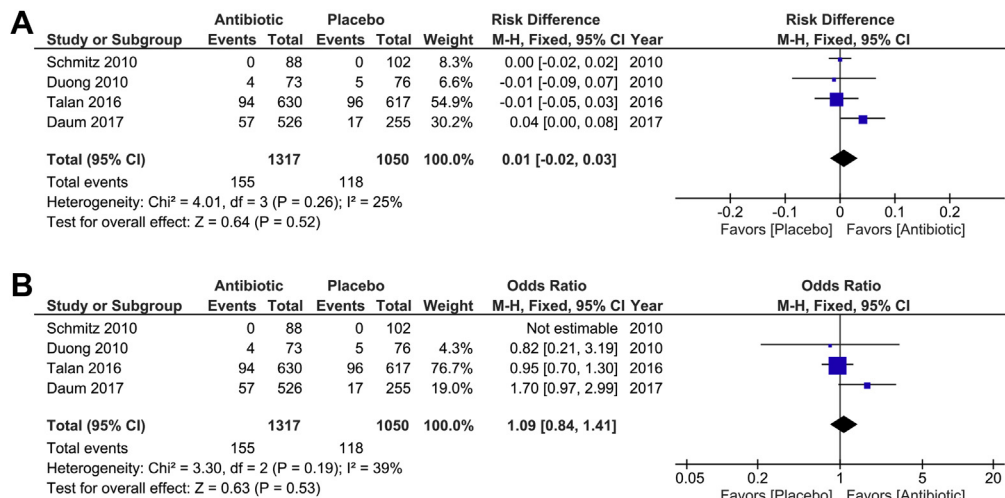


Figure 6. Forest diagram of risk difference (A) and odds ratio (B) demonstrating no difference in the rates of diarrhea between the antibiotic and placebo groups.

retrospective, prospective observational, and randomized controlled trials through 2013.²¹ This group also did not identify a statistically significant difference in outcomes. However, as noted above, 2 recent large trials have been published, significantly increasing the available evidence. Additionally, the inclusion of retrospective and observational studies can be less reliable because of numerous confounders and missing data. Therefore, we believe that our decision to focus on only randomized, controlled trials provides stronger and more reliable data for analysis. To our knowledge, our review is also the first to evaluate rates of new abscess formation and adverse events, which are important considerations when one is deciding whether to initiate antibiotic therapy.

Although the overall cure rate for abscesses after incision and drainage was high in both groups, antibiotics were associated with a near 2-fold improvement in cure rates and a number needed to treat of 14. As a result, antibiotics have the potential to reduce the number of return visits and the need for painful repeated incision and drainage. Additionally, patients who improve may return to work sooner, potentially leading to lower socioeconomic costs for both the patient and health care system in general. The studies by Daum et al¹³ and Talan et al¹² found an improved rate of clinical cure in the antibiotics group among patients with *S aureus*, but no difference was observed with lesions that yielded no growth or other organisms. This is consistent with results of a recent subgroup analysis demonstrating that history of MRSA and a culture with a positive MRSA result were associated with greater cure rates when agents active against MRSA were used.²²

A decreased incidence of new lesions at different sites was identified in the first 2 months. Although no significant difference was noted beyond this period in the study by Duong et al,¹¹ this study was smaller and used a unique population of very young children with diaper area lesions. Although the mechanism is not clear, this may be because the antibiotics decreased the overall MRSA colonization of the patient or improved cure rates reduced the likelihood of autoinoculation of new sites. Additionally, Talan et al¹² found a decreased rate of infections among household contacts in the antibiotic group, which is consistent with another recent study demonstrating that patients receiving adjunctive antibiotics with MRSA activity had lower rates of ongoing *S aureus* colonization.¹⁹ Although further studies are needed on these secondary outcomes, these are important patient-centered outcomes to consider in the decision of whether to initiate antibiotics.

Despite these advantages, one must also consider the possible risks with increased antibiotic use. The use of antibiotics can lead to a number of adverse events, just as the use of other medications can. Although the overall rates were relatively similar between both groups, there was a minimally increased rate of adverse events in the antibiotic group, with a number needed to harm of 23. However, the majority of events were mild and self-resolving in the included studies. Antibiotic use has also been associated with the development of iatrogenic infections (eg, *Clostridium difficile*) and may cause allergic reactions and anaphylaxis in some patients.²³ There were no cases of *C difficile* or severe allergic reactions identified in any of the above trials, and there was only one potentially severe

reaction noted among all of the included patients. However, the studies were not adequately powered to assess for these events. The 2 largest studies performed active surveillance for *C difficile*, but did not identify a significant difference.^{11,12} Finally, increased antibiotic use may lead to antibiotic resistance, resulting in less effective antibiotics for the population at large when used for other infections.^{24,25}

Overall, the data support the value of systemic antibiotics for the treatment of skin and soft tissue infections after incision and drainage, with an improved overall cure rate and reduced rate of subsequent lesions, and with a minimal increase in the rate of adverse events. This article provides overall data, as well as the risk differences and number needed to harm or treat, to allow providers to engage in shared decisionmaking with patients in regard to the risks and benefits.

Future studies should assess which patient factors are associated with a greater benefit from adjuvant antibiotics, as well as involvement of patients with shared decisionmaking models. Additionally, studies should determine whether the use of antibiotics is associated with a difference in the prevention of severe, deep-space infections.

The use of systemic antibiotics for skin and soft tissue abscesses after incision and drainage resulted in an increased rate of clinical cure. Providers should consider the use of antibiotics while balancing the risk of adverse events.

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Author affiliations: From the Department of Emergency Medicine, Rush University Medical Center, Chicago, IL.

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All authors attest to meeting the four [ICMJE.org](http://www.icmje.org) authorship criteria: (1) Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work; AND (2) Drafting the work or revising it critically for important intellectual content; AND (3) Final approval of the version to be published; AND (4) Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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