

Brief description of patient problem/setting : A 30 year-old immunocompetent female presents to urgent care with a 3-day history of a painful, erythematous, fluctuant lesion on the right upper gluteal region, with progressive swelling and tenderness and minimal spontaneous drainage. She reports a similar lesion on her right abdomen one week prior that self-drained. She denies systemic symptoms including fever or chills. On exam, there is an approximately 3 cm abscess with surrounding erythema and induration. Incision and drainage were performed with expression of purulent material, and a wound culture was obtained. Given her stable clinical status, the clinical question is whether clindamycin or trimethoprim-sulfamethoxazole is the more appropriate adjunctive outpatient antibiotic therapy to reduce the risk of treatment failure and recurrence.

Search Question: In adults with uncomplicated skin and soft tissue infections following incision and drainage, how does clindamycin compared to trimethoprim-sulfamethoxazole affect clinical cure rates, recurrence, and medication-related adverse events?

Question Type: What kind of question is this?

- Prevalence Screening Diagnosis Prognosis **Treatment** **Harms**

Assuming that the highest level of evidence to answer your question will be meta-analysis or systematic review, what other types of study might you include if these are not available (or if there is a much more current study of another type)?

The highest level of evidence would be systematic reviews and meta-analyses of randomized controlled trials comparing clindamycin and trimethoprim-sulfamethoxazole for skin and soft tissue infections. If these are not available or are outdated, randomized controlled trials (RCTs) would be included since they provide the most reliable comparison between treatments and minimize bias. Clinical practice guidelines may also be reviewed to understand current standards of care and how the evidence is applied in practice. Observational studies can be considered for additional information on recurrence rates and adverse events in real-world settings, although they are lower-quality evidence due to potential confounding.

PICO search terms:

P	I	C	O
Skin and soft tissue infection	Clindamycin	trimethoprim-sulfamethoxazole	Cure
SSTI	Cleocin	TMP-SMX	Treatment success

Uncomplicated skin infection	Lincosamide Antibiotics	cotrimoxazole	Recurrence
Cutaneous abscess		Bactrim	Treatment failure
Wound Infection		Septra	Adverse Events

Search Strategy

	Pubmed	Cochrane Library	Google Scholar
Search Terms	(“skin and soft tissue infection” OR SSTI OR abscess OR “wound infection”) AND (clindamycin OR Cleocin) AND (“trimethoprim-sulfamethoxazole” OR TMP-SMX OR cotrimoxazole OR Bactrim OR Septra) AND (“clinical cure” OR recurrence OR “treatment failure” OR “adverse events”)	skin and soft tissue infection AND clindamycin AND trimethoprim-sulfamethoxazole	clindamycin vs TMP-SMX skin infection randomized trial recurrence cure
Filters	Publication date: 2010 - 2026, English language, Humans, MEDLINE indexed	Publication date: January 2015 - January 2026	Results were sorted by relevance and Reviewed articles Publication date within 5 years
Results	About 20	About 7	About 147
Selected	Choose 2 articles	Choose 1 article	none

- Titles and abstracts were then reviewed to identify studies evaluating antihistamine use during breastfeeding, with a focus on breast milk transfer, infant exposure, and potential adverse effects. Studies that did not involve breastfeeding populations, did not evaluate antihistamines, or lacked data on infant safety or lactation outcomes were excluded.
- Priority was given to higher levels of evidence, including systematic reviews, clinical studies, and human lactation studies. Among these, studies with clear outcomes related to

relative infant dose, reported infant adverse effects (such as sedation), and potential impact on milk production were selected.

- Ultimately, three key articles were chosen based on their relevance, study design, and direct applicability to the clinical question, including a systematic review evaluating antihistamine safety in breastfeeding women, a human lactation study quantifying cetirizine transfer into breast milk and infant exposure, and a clinical review providing broader guidance on medication safety during lactation.
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Results found:

Article # 1 : Clindamycin versus Trimethoprim–Sulfamethoxazole for Uncomplicated Skin Infections

Miller, L. G., Daum, R. S., Creech, C. B., Young, D., Downing, M. D., Eells, S. J., Pettibone, S., Hoagland, R. J., & Chambers, H. F. (2015). Clindamycin versus trimethoprim–sulfamethoxazole for uncomplicated skin infections. *New England Journal of Medicine*, 372(12), 1093–1103.

<https://doi.org/10.1056/nejmoa1403789>

Abstract

Background: Skin and skin-structure infections are common in ambulatory settings. However, the efficacy of various antibiotic regimens in the era of community-acquired methicillin-resistant *Staphylococcus aureus* (MRSA) is unclear.

Methods: We enrolled outpatients with uncomplicated skin infections who had cellulitis, abscesses larger than 5 cm in diameter (smaller for younger children), or both. Patients were enrolled at four study sites. All abscesses underwent incision and drainage. Patients were randomly assigned in a 1:1 ratio to receive either clindamycin or trimethoprim–sulfamethoxazole (TMP-SMX) for 10 days. Patients and investigators were unaware of the treatment assignments and microbiologic test results. The primary outcome was clinical cure 7 to 10 days after the end of treatment.

Results: A total of 524 patients were enrolled (264 in the clindamycin group and 260 in the TMP-SMX group), including 155 children (29.6%). One hundred sixty patients (30.5%) had an abscess, 280 (53.4%) had cellulitis, and 82 (15.6%) had mixed infection, defined as at least one abscess lesion and one cellulitis lesion. *S. aureus* was isolated from the lesions of 217 patients (41.4%); the isolates in 167 (77.0%) of these patients were MRSA. The proportion of patients cured was similar in the two treatment groups in the intention-to-treat population (80.3% in the clindamycin group and 77.7% in the TMP-SMX group; difference, –2.6 percentage points; 95% confidence interval [CI], –10.2 to 4.9; P=0.52) and in the populations of patients who could be evaluated (466 patients; 89.5% in the clindamycin group and 88.2% in the TMP-SMX group; difference, –1.2 percentage points; 95% CI, –7.6 to 5.1; P=0.77). Cure rates did not differ significantly between the two treatments in the subgroups of children, adults, and patients with

abscess versus cellulitis. The proportion of patients with adverse events was similar in the two groups.

Conclusion: We found no significant difference between clindamycin and TMP-SMX, with respect to either efficacy or side-effect profile, for the treatment of uncomplicated skin infections, including both cellulitis and abscesses.

- This is a prospective, multicenter, double-blind, randomized controlled trial. This article was chosen because it directly compares clindamycin and TMP-SMX, the two most commonly used outpatient antibiotics for uncomplicated skin infections, especially in the setting of community-acquired MRSA. It closely matches the clinical scenario of a patient presenting with an abscess requiring incision and drainage, where the provider must decide between these two options. It is also one of the first large, well-designed randomized trials to directly compare the safety and effectiveness of these medications, making it highly relevant and widely cited. Overall, it provides strong evidence to guide antibiotic selection in uncomplicated skin and soft tissue infections

Key Findings:

- Both clindamycin and TMP-SMX achieved equivalent cure rates in the intention-to-treat population (80.3% vs 77.7%, difference -2.6 percentage points, $P=0.52$) and in the evaluable population (89.5% vs 88.2%, difference -1.2 percentage points, $P=0.77$), demonstrating clinical equivalence between the two antibiotics for uncomplicated skin infections
- This was the first large, well-designed randomized controlled trial to directly compare clindamycin and TMP-SMX head-to-head for uncomplicated skin and soft tissue infections in the community-associated MRSA era, making it a landmark study that has been widely cited and used to guide clinical practice
- The study enrolled a diverse population including both abscesses (30.5%), cellulitis (53.4%), and mixed infections (15.6%), making results applicable across the spectrum of uncomplicated skin infections commonly seen in outpatient settings
- Cure rates did not differ significantly between clindamycin and TMP-SMX across any subgroup analyzed, including adults vs children, abscess vs cellulitis, and MRSA vs MSSA infections, supporting the conclusion that both antibiotics are appropriate first-line options regardless of infection type or patient age
- MRSA was the predominant pathogen, isolated from 77.0% of all *S. aureus*-positive cultures (167 of 217 patients), confirming that community-associated MRSA is the primary cause of skin infections and supporting empiric use of clindamycin or TMP-SMX which have activity against MRSA
- Clindamycin resistance significantly impacted treatment outcomes: cure rate was only 73.3% among patients infected with clindamycin-resistant *S. aureus* who were treated with clindamycin, compared to 91.7% among those with clindamycin-susceptible

isolates, this highlights the importance of knowing local resistance patterns when selecting empiric therapy

- TMP-SMX demonstrated similar effectiveness to clindamycin even in cellulitis cases, which challenges the traditional teaching that TMP-SMX lacks adequate streptococcal coverage and should not be used for cellulitis.
- Adverse event rates were similar between both groups, including rates of diarrhea and rash, with no cases of *Clostridioides difficile* infection observed in either group, likely reflecting the relatively young, healthy, and low-risk outpatient population studied
- The study used standard outpatient dosing for both antibiotics: clindamycin 300 mg three times daily and TMP-SMX 160 mg/800 mg (one double-strength tablet) twice daily for 10 days, making results directly applicable to typical prescribing practices
- Follow-up was limited to approximately 1 month, which may be insufficient to fully assess recurrence rates, especially for *S. aureus* infections that are known to recur over longer periods.
- The study population consisted of relatively healthy outpatients with uncomplicated infections, so results may not generalize to immunocompromised patients, those with diabetes, or patients with more severe or complex skin and soft tissue infections requiring hospitalization
- The clinical implication is that clindamycin and TMP-SMX can be considered interchangeable first-line options for uncomplicated skin infections, with the choice guided by factors such as local resistance patterns (favoring TMP-SMX in areas with high clindamycin resistance), dosing convenience (favoring TMP-SMX with twice-daily dosing), and concern for recurrence (potentially favoring clindamycin based on subsequent studies)

Article #2: A Randomized Trial of Clindamycin Versus Trimethoprim-sulfamethoxazole for Uncomplicated Wound Infection

Talan, D. A., Lovecchio, F., Abrahamian, F. M., Karras, D. J., Steele, M. T., Rothman, R. E., Krishnadasan, A., Mower, W. R., Hoagland, R., & Moran, G. J. (2016). A randomized trial of clindamycin versus trimethoprim-sulfamethoxazole for uncomplicated wound infection. *Clinical Infectious Diseases*, 62(12), 1505–1513. <https://doi.org/10.1093/cid/ciw177>

Abstract

Background: With the emergence of community-associated methicillin-resistant *Staphylococcus aureus* (MRSA) in the United States, visits for skin infections greatly increased. *Staphylococci* and *streptococci* are considered predominant causes of wound infections. Clindamycin and trimethoprim-sulfamethoxazole (TMP-SMX) are commonly prescribed, but the efficacy of TMP-SMX has been questioned.

Methods: We conducted a randomized, double-blind, superiority trial at 5 US emergency departments. Patients >12 years of age with an uncomplicated wound infection received oral clindamycin 300 mg 4 times daily or TMP-SMX 320 mg/1600 mg twice daily, each for 7 days. We compared the primary outcome, wound infection cure at 7-14 days, and secondary outcomes through 6-8 weeks after treatment, in the per-protocol population.

Results: Subjects had a median age of 40 years (range, 14-76 years); 40.1% of wound specimens grew MRSA, 25.7% methicillin-susceptible *S. aureus*, and 5.0% streptococci. The wound infection was cured at 7-14 days in 187 of 203 (92.1%) clindamycin-treated and 182 of 198 (91.9%) TMP-SMX-treated subjects (difference, 0.2%; 95% confidence interval [CI], -5.8% to 6.2%; P = not significant). The clindamycin group had a significantly lower rate of recurrence at 7-14 days (1.5% vs 6.6%; difference, -5.1%; 95% CI, -9.4% to -0.8%) and through 6-8 weeks following treatment (2.0% vs 7.1%; difference, -5.1%; 95% CI, -9.7% to -0.6%). Other secondary outcomes were statistically similar between groups but tended to favor clindamycin. Adverse event rates were similar.

Conclusions: In settings where MRSA is prevalent, clindamycin and TMP-SMX produce similar cure and adverse event rates among patients with an uncomplicated wound infection. Further study evaluating differential effects of antibiotics on recurrent infection may be warranted.

- This is a prospective, multicenter, double-blind, randomized controlled superiority trial. This is a head-to-head therapeutic comparison trial, which is considered the gold standard for comparing two active treatments. This article was chosen because it directly compares clindamycin and trimethoprim-sulfamethoxazole (TMP-SMX), two of the most commonly prescribed outpatient antibiotics for uncomplicated skin infections. The study focuses on uncomplicated wound infections, including traumatic wounds, surgical wounds, and infected lacerations. While these are not identical to abscesses, they fall within the same spectrum of skin and soft tissue infections and involve overlapping pathogens, making the findings clinically relevant. This is clinically important because TMP-SMX has traditionally been thought to have poor streptococcal coverage, as wound infections were believed to be primarily caused by streptococci. Overall, this study directly addresses the clinical question of which antibiotic to choose for outpatient management of uncomplicated skin & soft tissue infections.

Key Findings:

- Both clindamycin (300 mg four times daily) and TMP-SMX (320 mg/1600 mg twice daily) achieved equivalent initial cure rates of approximately 92% for uncomplicated wound infections (92.1% vs 91.9%, difference 0.2%, P = not significant), demonstrating that both antibiotics are highly effective first-line options for this indication
- Clindamycin was significantly better than TMP-SMX at preventing recurrence at both time points measured: 1.5% vs 6.6% at 7-14 days after treatment (difference -5.1%, 95%

CI -9.4% to -0.8%) and 2.0% vs 7.1% through 6-8 weeks after treatment (difference -5.1%, 95% CI -9.7% to -0.6%)

- MRSA was the predominant pathogen, isolated from 40.1% of wound specimens, with an additional 25.7% growing methicillin-susceptible *S. aureus* (MSSA).
- The study used higher-than-standard doses of both antibiotics: clindamycin was dosed at 300 mg QID (four times daily) rather than the more commonly prescribed 300 mg TID (three times daily), and TMP-SMX was dosed at 320 mg/1600 mg BID (two double-strength tablets twice daily) rather than the standard 160 mg/800 mg BID (one double-strength tablet twice daily).
- The possible mechanism for clindamycin's superior recurrence prevention may relate to its ability to inhibit bacterial toxin production (including Pantone-Valentine leukocidin and other virulence factors) and its potential to reduce nasal colonization with *S. aureus*, which TMP-SMX does not accomplish to the same degree
- Several secondary outcomes, including the need for subsequent surgical procedures, development of new infections at other body sites, and overall treatment failure, showed trends favoring clindamycin over TMP-SMX, although these differences did not reach statistical significance
- Although the 6-8 week follow-up period is longer than many antibiotic trials, *S. aureus* skin infections are known to recur beyond this timeframe, so the long-term durability of recurrence prevention with either antibiotic remains uncertain
- Potential enrollment bias may have affected results, as clinicians may have been less likely to enroll patients they perceived as higher risk or more likely to fail treatment, potentially limiting generalizability to more severe or complicated cases
- The clinical implication is that for patients with uncomplicated wound infections where preventing recurrence is a priority, clindamycin may be the preferred choice over TMP-SMX despite equivalent initial cure rates.

Article #3: A Placebo-Controlled Trial of Antibiotics for Smaller Skin Abscesses

Daum, R. S., Miller, L. G., Immergluck, L., Fritz, S., Creech, C. B., Young, D., Kumar, N., Downing, M., Pettibone, S., Hoagland, R., Eells, S. J., Boyle, M. G., Parker, T. C., & Chambers, H. F. (2017). A placebo-controlled trial of antibiotics for smaller skin abscesses. *New England Journal of Medicine*, 376(26), 2545–2555. <https://doi.org/10.1056/nejmoa1607033>

Abstract

Background: Uncomplicated skin abscesses are common, yet the appropriate management of the condition in the era of community-associated methicillin-resistant *Staphylococcus aureus* (MRSA) is unclear.

Methods: We conducted a multicenter, prospective, double-blind trial involving outpatient adults and children. Patients were stratified according to the presence of a surgically drainable abscess, abscess size, the number of sites of skin infection, and the presence of nonpurulent cellulitis. Participants with a skin abscess 5 cm or smaller in diameter were enrolled. After abscess incision and drainage, participants were randomly assigned to receive clindamycin, trimethoprim–sulfamethoxazole (TMP-SMX), or placebo for 10 days. The primary outcome was clinical cure 7 to 10 days after the end of treatment.

Results: We enrolled 786 participants: 505 (64.2%) were adults and 281 (35.8%) were children. A total of 448 (57.0%) of the participants were male. *S. aureus* was isolated from 527 participants (67.0%), and MRSA was isolated from 388 (49.4%). Ten days after therapy in the intention-to-treat population, the cure rate among participants in the clindamycin group was similar to that in the TMP-SMX group (221 of 266 participants [83.1%] and 215 of 263 participants [81.7%], respectively; $P=0.73$), and the cure rate in each active-treatment group was higher than that in the placebo group (177 of 257 participants [68.9%], $P<0.001$ for both comparisons). The results in the population of patients who could be evaluated were similar. This beneficial effect was restricted to participants with *S. aureus* infection. Among the participants who were initially cured, new infections at 1 month of follow-up were less common in the clindamycin group (15 of 221, 6.8%) than in the TMP-SMX group (29 of 215 [13.5%], $P=0.03$) or the placebo group (22 of 177 [12.4%], $P=0.06$). Adverse events were more frequent with clindamycin (58 of 265 [21.9%]) than with TMP-SMX (29 of 261 [11.1%]) or placebo (32 of 255 [12.5%]); all adverse events resolved without sequelae. One participant who received TMP-SMX had a hypersensitivity reaction.

Conclusion: As compared with incision and drainage alone, clindamycin or TMP-SMX in conjunction with incision and drainage improves short-term outcomes in patients who have a simple abscess. This benefit must be weighed against the known side-effect profile of these antimicrobials.

- This is a prospective, multicenter, double-blind, randomized, placebo-controlled superiority trial and represents a gold standard design for evaluating treatment effectiveness. This article was selected because it directly addresses whether antibiotics provide benefit beyond incision and drainage alone and compares clindamycin to trimethoprim-sulfamethoxazole (TMP-SMX). It is highly applicable to my patient, as it includes individuals with small abscesses (≤ 5 cm) who underwent incision and drainage, closely matching my case. The inclusion of a placebo arm is particularly important, demonstrating that adjunctive antibiotics provide a modest improvement in clinical cure. It also evaluates recurrence and adverse effects, showing similar cure rates between the two antibiotics, lower recurrence with clindamycin, and

Key Findings:

- Both clindamycin and TMP-SMX significantly improved cure rates by 12-13 percentage points compared to incision and drainage (I&D) plus placebo (83.1% and 81.7% vs 68.9%, $P < 0.001$ for both), definitively proving that antibiotics provide clinical benefit beyond I&D alone for small skin abscesses
- The clinical benefit of antibiotics was restricted to participants with *Staphylococcus aureus* infection; among participants whose abscess cultures did NOT grow *S. aureus*, cure rates were identical across all three groups (clindamycin, TMP-SMX, and placebo) with $P = 0.99$ for all comparisons, meaning antibiotics provided no benefit when *S. aureus* was not the causative organism
- Clindamycin was significantly better than TMP-SMX at preventing recurrence or new infections after initial cure: only 6.8% of patients treated with clindamycin developed new infections at 1 month compared to 13.5% with TMP-SMX ($P = 0.03$) and 12.4% with placebo ($P = 0.06$)
- Clindamycin resistance significantly impacted treatment outcomes: among 13 participants infected with clindamycin-resistant *S. aureus* who were treated with clindamycin, the cure rate was only 53.8% (7 of 13), compared to 85.3% (145 of 170) among those with clindamycin-susceptible isolates ($P = 0.01$), participants with resistant isolates treated with clindamycin had cure rates similar to those who received placebo
- The impact of TMP-SMX resistance on treatment outcomes could not be assessed because there were no TMP-SMX-resistant isolates identified in the study population
- Clindamycin had approximately double the adverse event rate compared to TMP-SMX or placebo (21.9% vs 11.1% vs 12.5%), primarily gastrointestinal side effects, but all adverse events resolved without long-term consequences
- Among participants with methicillin-susceptible *S. aureus* (MSSA) infections, clindamycin showed a trend toward higher cure rates than TMP-SMX (89.1% vs 79.6%), though this difference did not reach statistical significance ($P = 0.26$); however, clindamycin was significantly superior to placebo ($P = 0.01$) while TMP-SMX was not ($P = 0.16$)
- The authors speculated that a higher dose of TMP-SMX might have been more effective at preventing recurrent or new infections, potentially closing the gap with clindamycin in recurrence prevention
- The study enrolled a diverse population including both adults (64.2%) and children (35.8%), with a mean age of 25.5 years, making the results generalizable.
- The clinical decision between clindamycin and TMP-SMX involves a trade-off: clindamycin offers better recurrence prevention (especially in children) but has more side effects; TMP-SMX has fewer side effects but higher recurrence rates, the choice should be individualized based on patient factors such as age, history of recurrent infections, and tolerance of gastrointestinal side effects
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What is the clinical “bottom line” derived from these articles in answer to your question?

Across multiple randomized controlled trials, clindamycin and trimethoprim-sulfamethoxazole (TMP-SMX) demonstrated similar clinical cure rates with no statistically significant difference between them, and both provide a modest benefit over incision and drainage alone in reducing treatment failure. Some studies suggest that clindamycin may be associated with lower recurrence rates compared to TMP-SMX. In contrast, TMP-SMX is generally better tolerated, with fewer gastrointestinal adverse effects and more convenient twice-daily dosing, while clindamycin carries a higher risk of gastrointestinal side effects, including *Clostridioides difficile* infection. Overall, both antibiotics are similarly effective for initial clinical cure. However, given this patient’s history of a recent prior abscess, which increases her risk of recurrence, clindamycin may be a reasonable choice to potentially reduce recurrence risk. That said, this must be balanced against its higher adverse effect profile. In this case, I would select clindamycin to prioritize recurrence prevention, while ensuring appropriate patient counseling regarding potential side effects.