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Evidence-to-Recommendation Framework for 2026 ACE Clinical Guideline on bacterial skin and soft tissue infections – diagnosis and antibiotic prescribing

Johanan D Ponniah, Bsc (Hon), Rujia Xu, MPH, BSc (Pharm) (Hon), Ye Sun, PhD, Bsc (Hon), Expert Group for Skin and Soft Tissue Infections ACG*, Valentina Ricci, MSc (Social Epidemiology), BSc (Physio), Phyllis AL Kim, MPH, MBChB

*List of members is acknowledged at the end of the article

Evidence to Practice Division, Agency for Care Effectiveness, Ministry of Health, Singapore

Abstract

This Evidence-to-Recommendation (EtR) framework underpins the ACE Clinical Guideline (ACG) for bacterial skin and soft tissue infections (SSTIs), providing rationale and justifications for its recommendations on diagnosis and antibiotic prescribing in primary and community care. Based on the GRADE framework, five evidence-based recommendations were developed to guide practitioners in making appropriate decisions on the diagnosis, assessment and management of SSTIs, including cellulitis, erysipelas, impetigo, folliculitis, ecthyma, furuncles, carbuncles, and skin abscesses. As SSTIs are a leading indication for use of oral antibiotics in primary care, recommendations focus on principles for prescribing antibiotics for specific bacterial SSTIs, including whether to use antibiotics, and when to prescribe topical, oral or intravenous formulations. The EtR framework consolidates the evidence and considerations that informed the ACG recommendations, including the balance of benefits and risks, certainty of evidence, patient preferences and values, resource and feasibility considerations, and acceptability. The ACG can be found at https://go.gov.sg/acg-ssti.

Introduction

Skin and soft tissue infections (SSTIs) - infections of the skin, subcutaneous tissue, fascia, or muscle – may be caused by bacteria, viruses, fungi, or parasites. In clinical practice, bacterial SSTIs are the most common,[1] with beta-haemolytic streptococci and *Staphylococcus aureus* being the main causative organisms.[1, 2] In Singapore, SSTIs are among the top 10 causes of hospitalisation,[3] and skin conditions were among the leading indications for prescription of oral antibiotics in primary care clinics.[4] This suggests SSTIs have a considerable impact on local patient morbidity and on antimicrobial prescribing, highlighting the need to optimise bacterial SSTI management and strengthen antimicrobial stewardship. Local literature highlighted two key practice gaps: topical antibiotic prescriptions for non-infectious skin conditions, as well as concomitant topical and oral antibiotic use.[4]

The Agency for Care Effectiveness (ACE) therefore developed a guideline to provide guidance on diagnosis, assessment, and antibiotic prescribing for bacterial SSTIs in community care settings, with the aim to improve patient outcomes and strengthen antimicrobial stewardship.

Methods

This guideline was developed based on the ACE methods and processes for ACG development, and following a hybrid de-novo/adaptation process.[5] A systematic search for international guidelines was conducted across databases including Guideline Central, Guidelines International Network (GIN) Library, ECRI Guidelines Trust, PubMed, Epistemonikos, and Trip Medical Databases, supplemented by manual retrieval from relevant specialty associations. English-language guidelines (n = 11) published within the previous five years were prioritised and assessed using the Appraisal of Guidelines for Research & Evaluation II (AGREE-II) tool Domain 3 (Rigour of Development), applying a minimum 60% scaled domain score threshold. Overall, eight high-quality guidelines were selected as main reference

guidelines. Recent systematic reviews and meta-analyses were identified from PubMed and Google Scholar to complement guideline evidence.

A multidisciplinary expert group (EG) comprising two dermatologists, six family medicine physicians, two infectious disease specialists, two paediatricians, two pharmacists, two nurses, one general surgeon and one emergency medicine specialist, was appointed to provide clinical expertise throughout guideline development.

Draft recommendations were formulated using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) Evidence-to-Recommendation framework, incorporating five key domains: balance of benefits and harms; certainty of evidence; values and preferences; resources and feasibility; and acceptability and other considerations. EG members individually rated recommendation appropriateness using the RAND Corporation/University of California, Los Angeles (RAND/UCLA) Appropriateness Method, followed by structured discussions to achieve consensus.

Recommendation 1: Diagnose bacterial SSTIs clinically, based on history taking and physical examination findings.

Strength of recommendation: **Strong** Conditional

Summary: Evidence suggests that the diagnostic performance of clinical examination is comparable to imaging for abscesses.[6] There is a lack of high-quality supporting evidence for the use of cellulitis diagnostic tools (such as biomarkers, imaging assays, and diagnostic decision models).[7, 8] Therefore, a strong recommendation for diagnosing SSTI clinically is made to facilitate timely provision of treatment and to reduce expenditure on low-value investigations. This approach is in line with recent international guidelines on SSTI.[8-10]

Balance of benefits and harms

The overall benefit-harm balance is more favourable for clinical diagnosis compared to diagnostic assays for SSTI. Firstly, the diagnostic performances of clinical examination and diagnostic assays may be similar: A systematic review reported that clinical examination is able to detect abscesses with a sensitivity ranging between 75% to 95% and a specificity ranging between 60% to 84%, which were comparable to the diagnostic performance of point-of-care ultrasound (POCUS; sensitivity ranged from 90% to 98% and specificity ranged from 67% to 88%).[6] This suggests that clinical diagnosis alone is sufficient, and there may be minimal value-add to including imaging for diagnosing abscess. Diagnostic tools for cellulitis (such as biomarkers and imaging) lack strong supporting evidence due to high risk of bias in underlying studies[7] (see “Certainty of evidence” section below). Secondly, given the lack of evidence to support diagnostic assays for SSTI, their use may result in unwarranted delay in providing treatment. Clinical diagnosis is generally sufficient in uncomplicated presentations.[8-10]

In addition to clinical features, signs, and symptoms,[8, 10] the patient’s medical history may also inform the overall diagnosis: for example, the presence of a past skin injury may serve as a potential entry site for pathogens and be suggestive of SSTI.[11]

Certainty of evidence	Values and preferences
The evidence on diagnostic assessment of SSTIs is limited by reduced generalisability as there is a lack of studies assessing clinical examination or diagnostic assays for SSTIs other than cellulitis and abscess. The sensitivity and specificity of clinical examination to detect abscess ranged widely,[6] and this is likely	Patients value medical treatment they can access readily and without unnecessary costs. As the clinical benefit of diagnostic tools is not established, clinical diagnosis of SSTI aligns well with these preferences.

dependent on the experience level of the attending healthcare professional. A systematic review of diagnostic tools for lower-limb cellulitis identified studies that assessed the utility of biochemical markers, imaging, and a diagnostic decision model. However, there was a high risk of bias mainly in the domains of patient selection (e.g. excluding cases more difficult to diagnose) and implementation of the index test (most studies did not include a pre-specified threshold).[7] The evidence is therefore insufficient to support the use of such diagnostic tools for cellulitis.[9]	
Resources and feasibility	**Acceptability and other considerations**
Currently, SSTIs are diagnosed clinically in local primary care. Incorporation of diagnostic tools for SSTIs would therefore require a considerable increase in resources required, which may not be warranted as evidence supporting their use is not established.[7, 8]	No significant concerns identified.
Expert Group deliberation of above factors	
The Expert Group agreed that SSTIs remain a clinical diagnosis. They also acknowledged several feasibility considerations with the use of investigations in current primary care practice. For example, the turnaround time for culture and sensitivity results, combined with the high volume of patients, and unclear clinical pathways for positive cultures and susceptibility tests limits the feasibility of conducting such tests in local primary care. There is also a concern on the accuracy of superficial swabs, especially when there are contiguous wounds. Nonetheless, they raised that further diagnostic tests may be considered in cases of diagnostic uncertainty or for patients with high-risk infections (such as infections on the face).	

Recommendation 2: Assess the severity of infection and risk of complications to determine the management approach, including referral urgency

Strength of recommendation: **Strong** Conditional

Summary: A tiered approach is required for appropriate management of SSTIs, given their heterogeneity in severity, as well as variation in patients' overall risk of complications. Assessing these two domains facilitates personalised treatment selection and prompt referral to tertiary care where warranted. A strong recommendation to assess severity of infection and risk of complications is therefore made. This approach is in line with high-quality international guidelines.[12-14]

Balance of benefits and harms

SSTIs are a heterogenous group of infections, with some more life-threatening in nature: for example, bacterial infection on the face may cause meningitis.[15] Necrotising infections have a high mortality rate, and therefore prompt tertiary care is crucial.[16] In one systematic review, surgical treatment provided more than 6 hours after presentation resulted in a mortality rate of 32%, compared with 19% when surgical intervention was provided within 6 hours (odds ratio (OR): 0.43, 95% confidence interval (CI): 0.26, 0.70).[17] Patients who present as systemically unwell (e.g. with fever, lymphangitis, persistent tachycardia, tachypnea, or hypotension) may also require referral to tertiary care.[9, 12, 13, 18] In addition, patients may differ in risk profile, with some being at higher risk of complications such as individuals with diabetes mellitus, in an immunosuppressed state, or who are frail.[12] It is therefore important to assess patients for such factors and refer them to tertiary care as needed.

It is also important to establish the infection severity, as it determines the modality and choice of treatment – this is in line with approaches of international guidelines on SSTI.[8, 9, 12-14, 18] For example, the National Institute for Health and Care Excellence guidelines on impetigo recommend hydrogen peroxide cream for patients with localised non-bullous impetigo who are not systemically unwell or at high risk of complications. However, for patients with bullous impetigo or who are systemically unwell or at high risk of complications, oral antibiotics are recommended.[13]

Based on international guidelines and references,[8, 9, 12-14, 18-25] as well as expert inputs from the Expert Group, consolidated guidance on differentiating between mild and severe SSTI as well as referral considerations has been included in the ACG.

Certainty of evidence

It is well established that necrotising infections require urgent referral to tertiary care. Estimates of reduced mortality risk with prompt surgical intervention is supported by precise estimates and low risk of publication bias.[17] The proposed tiered treatment approach (based on severity of infection and risk of complications) is also well-supported by high-quality international guidelines.[12-14]

Values and preferences

Given that severe SSTIs can cause significant morbidity and even be life-threatening, patients would value prompt referral to tertiary care where warranted. Assessment of infection severity and overall risk of complications enables a tiered treatment approach. This facilitates individualised care, which is highly valued by patients.[26]

Resources and feasibility

The proposed factors (severity of infection and risk of complications) are already embedded as part of routine SSTI assessment in local primary care. Furthermore, these factors do not require investigative assays and are not projected to incur significant cost. In addition, assessing severity of infection and risk of complications enables a tiered management approach where only patients at greater risk of complications are referred to tertiary care. This reduces

Acceptability and other considerations

No significant concerns identified.

unwarranted referral, thereby reducing cost to patients and the healthcare system.	
Expert Group deliberation of above factors	
The Expert Group agreed with the evidence findings. They highlighted for ease of translation to practice, two levels of infection severity (mild and severe) would be most practicable.	

Recommendation 3:
For patients with impetigo or bacterial folliculitis:
a) Prescribe topical antibiotic monotherapy for localised mild infections.
b) Prescribe oral antibiotic monotherapy for severe infections.

Strength of recommendation 3a: **Strong** Conditional

Strength of recommendation 3b: **Strong** Conditional

Summary: For patients with impetigo, evidence suggests equivalent efficacy between topical and oral antibiotics, though the former may be associated with fewer adverse effects. The more favourable benefit-harm balance of topical antibiotics compared to oral antibiotics creates an impetus to use the former where possible. Therefore, a strong recommendation to prescribe a topical antibiotic for mild impetigo is provided. As self-application of topical antibiotics may not be practicable for widespread or bullous impetigo, a strong recommendation to prescribe oral antibiotics for severe infections is made.

Balance of benefits and harms

Among clinical studies on non-bullous impetigo, three out of four studies reported clinical cure rates of at least 50% among patients who did not receive antibiotics, at day 7 of follow-up. However, clinical cure rates at day 14 ranged from 39% to 60%, indicating that non-bullous impetigo may not self-resolve for many patients.[27] Furthermore, cure/improvement rates among patients with unspecified severity of impetigo assigned to placebo ranged from 0% to 33%,[28] signaling considerable uncertainty in estimates of impetigo self-resolution. Among patients with impetigo, provision of topical compared to oral antibiotics has not shown to have different efficacy in terms of cure rates, and relative safety is variable: topical mupirocin results in lower rates of gastrointestinal adverse effects (5.3%) compared to oral erythromycin (19.3%), but similar diarrhoea rates (2.4%) compared to oral cefalexin (3.9%). Evidence has not established a difference in efficacy of intramuscular (IM) compared to oral antibiotics, although provision of IM benzathine benzylpenicillin was associated with greatly elevated adverse events rate (30.6%) compared to oral co-trimoxazole (1.5%), with an RR of 21.01 (95% CI: 8.53 to 51.27). There is also a lack of evidence that the addition of oral antibiotics to topical antibiotics increases cure rates.[28] Overall, current evidence suggests the benefit-harm balance is most favourable for topical antibiotics, followed by oral antibiotics and then IM antibiotics. Notably, the presence of bullae may indicate that a topical application of antibiotics is potentially inadequate to reach the affected area. In such cases (severe infection), oral antibiotics will be required.[13]

Among antibiotics for impetigo treatment, there is overall a lack of high-quality evidence of differences in efficacy. Topical fusidic acid is associated with lower incidence of skin reactions compared to topical mupirocin, though both rates are low: 1.4% and 4.2% respectively.[28] Evidence on ecthyma is lacking, though international guidelines recommend oral, instead of topical, antibiotics.[14, 18] Refer to Appendix 1 for the rationale underpinning the selection of antibiotics in Supplement 2 of the ACG.

Certainty of evidence	Values and preferences
The efficacy of topical antibiotics for achieving cure or improvement among patients with impetigo is well-established in RCTs with moderate to high certainty of evidence. The equivalence in efficacy between topical and oral antibiotics in impetigo treatment is also well-established in RCTs across several antibiotic agents (mupirocin, fusidic acid, erythromycin,	Clinical cure or improvement would be important outcomes for patients with impetigo, given that untreated impetigo could potentially result in sepsis or bone infections.[10] Patients' preference to avoid adverse effects from medications should also be considered, and this supports the preferential use of topical, over oral, antibiotics where possible given the latter's greater

cefalexin, ampicillin), signaling considerable generalisability of the findings.[13]	propensity to cause gastrointestinal adverse effects.[28]
Resources and feasibility	**Acceptability and other considerations**
Overall, the recommendation promotes reserving oral antibiotics for severe impetigo and discourages concurrent use of topical and oral antibiotics. This would reduce unwarranted, low-value prescribing of oral antibiotics, which in turn reduces cost for patients and the healthcare system.	Applying a topical antibiotic may be challenging if the infection covers a large area.[13] Therefore, for more widespread impetigo (higher severity), adult patients would prefer treatment with an oral antibiotic.
Expert Group deliberation of above factors	
The Expert Group agreed with the evidence findings above. While there was a lack of evidence concerning the use of topical antibiotics for folliculitis, the Expert Group highlighted clinical reasons for using topical antibiotics for mild folliculitis (for example, better accessibility to the affected area and less adverse effects). Therefore, bacterial folliculitis was grouped with impetigo in this recommendation.	

Recommendation 4:
For patients with bacterial furuncles, carbuncles, or skin abscess:
a) Consider surgical intervention based on clinical presentation, and
b) Reserve oral antibiotic monotherapy for severe infections.

Strength of recommendation 4a: Strong **Conditional**

Strength of recommendation 4b: **Strong** Conditional

Summary: A conditional recommendation to provide surgical intervention (e.g. incision and drainage) is made in recognition that this is highly dependent on the individual patient's clinical profile and presentation. Oral antibiotics may be added to source control to reduce treatment failure, hospitalisation, and recurrence. Given that the absolute benefit of oral antibiotics may be low for milder purulent SSTIs, and in line with the antimicrobial stewardship principle of avoiding inappropriate prescription, a strong recommendation is made to reserve adjunctive oral antibiotics for severe infections.

Balance of benefits and harms

International guidelines support incision and drainage as a mainstay treatment of furuncles, carbuncles, and skin abscess. In addition to incision and drainage, antibiotics may be provided depending on the severity of infection.[8, 14, 18] A systematic review comparing loop drainage technique with convention incision and drainage reported a higher treatment failure rate with the latter, though the estimate was imprecise (OR: 1.75, 95% CI: 1.07 to 2.86).[29] Overall, the Expert Group noted that individualised decision-making plays a significant role when considering surgical intervention, as such procedures may not always be feasible.

In uncomplicated abscesses, meta-analysis of RCTs report that provision of oral antibiotics compared to placebo/ standard care results in reduced treatment failure rate (56 vs 93 per 1000 population; 95% CI: 56 fewer to 9 fewer, per 1000 population). Hospitalisation rate was also reduced with provision of oral antibiotics, from 39 to 22 per 1000 population (95% CI: 26 fewer to 2 fewer, per 1000 population). Notably, the risk of treatment failure and hospitalisation remains low overall, even when antibiotics are not provided, suggesting a closer benefit-harm balance for treating uncomplicated abscess with oral antibiotics. However, oral antibiotic treatment provides an additional benefit of reducing abscess recurrence. For example, recurrence within one month is reduced with provision of oral antibiotics, from 129 to 66 per 1000 population (95% CI: 86 fewer to 27 fewer, per 1000 population). Network meta-analysis of RCTs further revealed differences in antibiotic effectiveness: oral trimethoprim–sulfamethoxazole and oral clindamycin may result in fewer treatment failures compared to early and late oral cephalosporins. For example, trimethoprim–sulfamethoxazole resulted in 119 treatment failures per 1000 population compared to 280 treatment failures per 1000 population for early cephalosporins (95% CI: 392 fewer to 7 more, per 1000 population).[30, 31] Refer to Appendix 1 for the rationale underpinning the selection of antibiotics in Supplement 2 of the ACG.

A systematic review of RCTs for folliculitis and furuncles found no evidence of differences in efficacy or adverse effect profile between different oral antibiotics. For example, the clinical cure rate with azithromycin was 631 per 1000 population, almost identical to the rate of 625 per 1000 population with cefaclor (RR: 1.01; 95% CI: 0.72 to 1.40).[32]

Certainty of evidence	Values and preferences

There is a degree of indirectness as evidence on carbuncle treatment was lacking and is inferred from RCT data on abscess, furuncles, and folliculitis treatment. Nonetheless, the benefit of oral antibiotics for abscess treatment is established with mostly moderate certainty of evidence.[30]	While the absolute magnitude of benefit of oral antibiotics for uncomplicated skin abscess treatment in terms of treatment failure and hospitalisation is not substantial, the benefit in reducing recurrence may be highly valued by patients. This is because a qualitative study identified that the fear of infection recurrence had a considerable impact on health-related quality of life among patients with an SSTI.[33]
Resources and feasibility	**Acceptability and other considerations**
Overall, the recommendation promotes reserving oral antibiotics for severe infections. Patients with non-severe infections would still receive symptomatic treatment (e.g. warm compress) and potentially, surgical intervention. This is expected to result in reduced unwarranted, low-value prescription of oral antibiotics, in turn reducing cost for patients and the healthcare system.	Conventional incision and drainage is known to be a highly painful procedure for patients,[29] and hence may have reduced acceptability. Oral antibiotics may cause some gastrointestinal adverse effects and nausea,[30] which may affect its overall acceptability by patients.
Expert Group deliberation of above factors	
The Expert Group agreed that for this group of bacterial SSTIs, antibiotics should be reserved for severe cases. They raised that there are several clinical scenarios where surgical intervention would not be recommended, and hence individualised decision-making plays a substantial role in guiding this intervention. Such clinical scenarios include during the early stages of skin abscess, chronic furunculosis, and immunocompromised individuals with multiple abscesses. Furthermore, not all mild infections warrant surgical intervention and less invasive source control (such as removing any foreign body and cleansing with antiseptics) may suffice. Therefore, the strength of the recommendation for surgical intervention was set as conditional.	

Recommendation 5:
For patients with bacterial cellulitis or erysipelas:
a) Prescribe oral antibiotic monotherapy for mild infections.
b) Reserve intravenous antibiotic monotherapy for severe infections.

Strength of recommendation 5a: **Strong** Conditional

Strength of recommendation 5b: **Strong** Conditional

Summary: Cellulitis and erysipelas are infections that extend into the dermis, requiring antibiotic treatment to prevent further spread to deeper tissues. While evidence suggests oral antibiotics are not statistically inferior to intravenous (IV) antibiotics, this is limited by low certainty of evidence (e.g. due to imprecise effect estimates). Considering also that tissue penetration may be higher for IV compared to oral antibiotics, a strong recommendation has been made to prescribe IV antibiotics for severe infections (while maintaining oral antibiotics as first-line treatment for mild infections). Provision of antibiotic monotherapy is sufficient, as current evidence has established no clinical benefit of dual therapy over monotherapy.

Balance of benefits and harms

International guidelines converge in their recommendations on treatment of cellulitis and erysipelas: oral antibiotics are recommended for mild infections while IV antibiotics are reserved for more severe infections.[9, 12, 14, 18]. Current evidence suggests oral antibiotics are not statistically inferior to IV antibiotics: A systematic review pooled results from three RCTs and reported no statistically significant inferiority in clinical response between oral and IV antibiotics in patients with cellulitis or erysipelas (RR: 1.12; 95% CI: 0.98 to 1.27). There was no conclusive evidence of differences in adverse effect profile as well.[34] However, these results must be interpreted alongside the evidence limitations (see "Certainty of evidence" section below). Furthermore, oral antibiotics may not provide sufficient tissue penetration compared to IV antibiotics.[12] Evidence on intramuscular (IM) antibiotics for this population is limited to a small RCT on erysipelas alone.[35] In contrast, there are five RCTs on IV antibiotics which cover both cellulitis and erysipelas,[34] signalling a more established evidence base. Furthermore, IM antibiotics may be associated with greater risk of adverse effects compared to oral antibiotics.[28] Therefore, IM antibiotics were not assessed to be first-line treatment for cellulitis or erysipelas. There is a lack of high-quality evidence to support a difference in efficacy between specific antibiotic agents for treating cellulitis and erysipelas.[36] Refer to Appendix 1 for the rationale underpinning the selection of antibiotics in Supplement 2 of the ACG.

Dual therapy (concurrent administration of two antibiotics) has no proven clinical benefit over monotherapy in several cellulitis RCTs. For example, pooled results from 2 RCTs comparing a cephalosporin and trimethoprim-sulfamethoxazole (dual therapy) to a cephalosporin with placebo (monotherapy) reported similar clinical cure rates: 78% for the dual therapy arm compared to 72% for the monotherapy arm (RR: 1.09; 95% CI: 0.99 to 1.19).[36] This finding has also been confirmed in a recent 2024 systematic review.[37] Therefore, provision of monotherapy is sufficient for treating cellulitis and erysipelas, and dual therapy is not typically required.

Certainty of evidence	Values and preferences
Owing to the small samples sizes in relevant RCTs, estimates of relative efficacy between oral and IV antibiotics are imprecise.[34, 36] Furthermore, several of the underlying RCTs compared oral antibiotics of one class (e.g. a	Cellulitis and erysipelas are infections that extend into the dermis layer,[38] and if untreated, could spread to deeper muscle tissue or even to the bloodstream.[15] To avoid these adverse

macrolide) to IV antibiotics of another class (e.g. a penicillin), obscuring a fair comparison of antibiotic administration mode.[34] The equivalent effectiveness of dual and monotherapy is better established, with consistent findings across various antibiotic classes and more precise pooled estimates.[36, 37]	outcomes, patients would prefer to take an antibiotic rather than be left untreated. Given the reported similarity in outcomes (clinical effectiveness and adverse effects) between oral and IV antibiotics, there are no significant concerns over patients' values and preferences of outcomes when comparing oral and IV antibiotics.
Resources and feasibility	**Acceptability and other considerations**
Reserving IV antibiotics for more severe infections is a prudent approach as such treatment will require greater cost of medication preparation and administration.	Patients tend to prefer oral, over intravenous, antimicrobial therapy.[39] This recommendation is therefore aligned with patients' acceptability of the interventions, as IV antibiotic treatment is reserved for patients with more severe infections.
Expert Group deliberation of above factors	
The Expert Group agreed with the evidence findings above and affirmed that oral antibiotics would be the first option for mild cellulitis or erysipelas, while IV antibiotics should be provided for more severe infections.	

Implementation/Uptake of recommendations

Successful adoption and implementation of these recommendations can reduce the burden of SSTIs and its associated antimicrobial use. Key areas requiring highlighting to healthcare professionals include the overuse of antimicrobials for non-infectious conditions mimicking bacterial SSTIs, and the unnecessary use of combination antimicrobial therapy for patients with uncomplicated bacterial SSTIs.

Initiating and sustaining practice change requires coordinated action across multiple levels of the healthcare system. Healthcare organisations, institutions, and clinicians can consider the following implementation strategies:

- **Patient education and counselling:** Structured patient education can improve health literacy regarding SSTIs and help manage expectations around antimicrobial therapy. Primary care physicians serve as key educators in promoting appropriate antibiotic use and advancing antimicrobial stewardship at the community level.
- **Education and training**: Continuing medical education programmes and professional development initiatives can reinforce the evidence base and recommendations, with particular emphasis on enhancing clinicians' diagnostic skills and confidence in differentiating bacterial SSTIs from non-infectious conditions. Trainings can also focus on appropriate severity assessment and antibiotic selection principles. Concise, visual summaries of the ACG recommendations can help facilitate such educational and training efforts. To this end, the SSTI ACG includes a visual flowchart to summarise the ACG's recommendations (Appendix 2).
- **Antimicrobial stewardship programmes**: ASPs are currently established in public tertiary care settings to monitor and improve in-hospital antimicrobial use through various measures such as formulary restrictions (e.g., mupirocin restriction for MRSA infections), development of in-house guidelines for SSTIs, antimicrobial utilisation reviews, and promoting stewardship mindsets that prioritise narrow-spectrum antibiotics with appropriate treatment duration. Broader implementation of ASPs and

stewardship principles across all healthcare settings would further preserve antimicrobial effectiveness and minimise resistance development.

- **Public health initiatives**: National public education campaigns can aid to address common misconceptions about SSTIs and antimicrobial therapy, promoting understanding of when antibiotics are necessary and effective.

Conclusion

This EtR framework summarises the evidence base, rationale, and expert deliberations underpinning the recommendations for the SSTI ACG, providing clinicians with the necessary context to interpret and apply the guideline effectively in clinical practice.

The recommendations apply across all care settings and are especially relevant for primary care practitioners. Aligned with Singapore's National Strategic Action Plan on AMR and endorsed by the Communicable Diseases Agency Singapore, these recommendations aim to provide a comprehensive approach to bacterial SSTI diagnosis and antibiotic prescribing. The main goals are to optimise bacterial SSTI management while reducing inappropriate antimicrobial use – this includes the overuse of antibiotics for non-infectious conditions and unnecessary combination therapy for uncomplicated infections.

Successful implementation requires a systematic, multi-level approach encompassing healthcare institutions, organisations, and individual healthcare professionals. Collective adoption of these recommendations across diverse care settings will contribute to coordinated national efforts to preserve antimicrobial effectiveness while maintaining optimal patient care standards.

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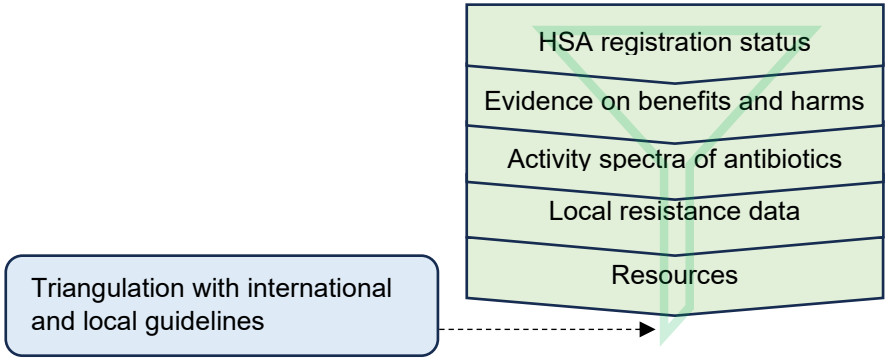
Appendix 1: Rationale for selection of antibiotics in Supplement 2 of the ACG Bacterial skin and soft tissue infections – Diagnosis and antibiotic prescribing



A systematic process was employed to decide on the preferred antibiotics to use from among the wide range of antibiotics that have been developed. Using Health Sciences Authority (HSA) registration status as a starting point, antibiotics were progressively filtered based on evidence on benefits and harms, activity spectra, local resistance data, and consideration on resources. Finally, the list of preferred antibiotics were triangulated against international and local guideline recommendations. Further details on this process are tabulated below. Note that the selection of antibiotics was conducted with outpatient treatment settings as the scope.

HSA registration status
Firstly, only HSA-registered antibiotics indicated for SSTI treatment were considered. This was checked using the Health Sciences Authority website.
Evidence on benefits and harms
Current evidence has found mostly no difference in efficacy between antibiotics for treating SSTIs.[28, 32, 36] One exception is treatment for skin abscess where a network meta-analysis of randomised controlled trials (RCTs) demonstrated that trimethoprim-sulfamethoxazole and clindamycin were more effective than cephalosporins in reducing treatment failure risk. Notably, cephalosporins did not reduce treatment failure risk compared with placebo.[30] Studies on SSTIs tend to report similar rates of adverse events between antibiotic agents.[28, 32] Among topical antibiotics used for patients with impetigo, fusidic acid and mupirocin have the strongest supporting evidence of efficacy as monotherapies.[28] Hence, in Supplement 2 of the ACG these are positioned as preferred treatment options. Gentamicin lacks direct evidence of efficacy compared to placebo, but has indirect evidence of efficacy when compared to neomycin.[28] Therefore, it is positioned as an alternative when fusidic acid and mupirocin are not suitable for patients.
Activity spectra of antibiotics
Beta-haemolytic streptococci and *Staphylococcus aureus* are the main aetiologies for SSTIs.[1, 2] Therefore, empiric treatment should start with antibiotics active against these pathogens. Based on antibacterial spectra collated in the Sanford Guide, a number of penicillins, carbapenems, fluoroquinolones, and cephalosporins displayed activity against both methicillin-sensitive *Staphylococcus aureus* and streptococci.[40] Antibiotics with activity against methicillin-resistant *Staphylococcus aureus* (MRSA) - such as trimethoprim-sulfamethoxazole and vancomycin - were not considered as first-line treatments as it would be more prudent to reserve such options for MRSA infections.

An additional consideration would be the World Health Organization's Access, Watch, and Reserve (AWaRe) principle of prioritising narrow-spectrum antibiotics. Antibiotics with broader spectrum of activity would then be utilised for more severe infections or when resistance to first-line antibiotics is likely.[41] Among oral antibiotics, cefalexin[42] and cloxacillin[43] are noted to be narrow-spectrum antibiotics. Hence, these were prioritised as first-line treatment options while amoxicillin + clavulanic acid is reserved as an alternative-choice antibiotic. Among IV antibiotics considered, carbapenems have a broad antimicrobial spectrum[44] and therefore were not positioned as first-line treatment of bacterial SSTIs.

Local resistance data

The National Skin Centre resistance data was provided to ACE, and based on samples collected between July 2024 and July 2025 (Table A1). The data suggests low levels of resistance to cloxacillin and cefazolin among *S. aureus* samples. These antibiotics have known activity against both *S. aureus* and streptococci.[40] Local MRSA samples remain susceptible to a few antibiotics such as trimethoprim-sulfamethoxazole and vancomycin. Consequently, it may be prudent to reserve such agents for when MRSA is suspected or detected, instead of utilising them as first-line treatment of bacterial SSTIs.

Resources

Having considered all other factors above, the cost of antibiotics was also considered with ACE noting that agents listed on government subsidy lists would be more affordable for patients. This helped to narrow the list of preferred IV antibiotics, with those on government subsidy listing being prioritised as first-line treatment options.

Triangulation with international and local guidelines

International and local guidelines affirmed the use of fusidic acid[13, 45-47] and mupirocin[13, 14, 41, 47, 48] as topical antibiotics. Among oral antibiotics, cefalexin[8, 9, 14, 41, 45-49] and cloxacillin[8, 9, 41, 45, 47, 48] were commonly recommended, while amoxicillin + clavulanic acid was also recommended in selected guidelines.[14, 41, 48] Among IV antibiotics, cefazolin[9, 14, 47, 48, 50] and ceftriaxone[9, 12, 48] were the most commonly-recommended. This corresponded well with the topical, oral and IV antibiotics recommended in Supplement 2 of the ACG.

Table A1. Resistance data from the National Skin Centre (July 2024 – July 2025). For conditions with high risk of mortality and morbidity, it is recommended that 90–95% of isolates be susceptible.[51]

Antibiotic	*S. aureus*	MRSA	Group A Streptococcus	Group A, B, G Streptococcus
Penicillin	0% *(95% CI: 0%, 3%; n=115)*	0% *(95% CI: 0%, 8%; n=35)*	6 samples	100% *(95% CI: 82%, 100%; n=18)*
Ampicillin	0% *(95% CI: 0%, 3%; n=115)*	0% *(95% CI: 0%, 8%; n=35)*	6 samples	100% *(95% CI: 82%, 100%; n=18)*
Cloxacillin	100% *(95% CI: 98%, 100%; n=186)*	0% *(95% CI: 0%, 9%; n=32)*	1 sample	1 sample
Cefazolin	100% *(95% CI: 98%, 100%; n=186)*	0% *(95% CI: 0%, 9%; n=32)*	1 sample	1 sample
Trimethoprim-sulfamethoxazole	94% *(95% CI: 90%, 97%; n=186)*	97% *(95% CI: 85%, 100%; n=35)*	1 sample	1 sample
Clindamycin	90% *(95% CI: 85%, 94%; n=186)*	37% *(95% CI: 22%, 54%; n=35)*	6 samples	72% *(95% CI: 47%, 89%; n=18)*
Gentamicin	0 samples	74% *(95% CI: 57%, 86%; n=34)*	0 samples	0 samples
Vancomycin	0 samples	100% *(95% CI: 90%, 100%; n=34)*	1 sample	5 samples

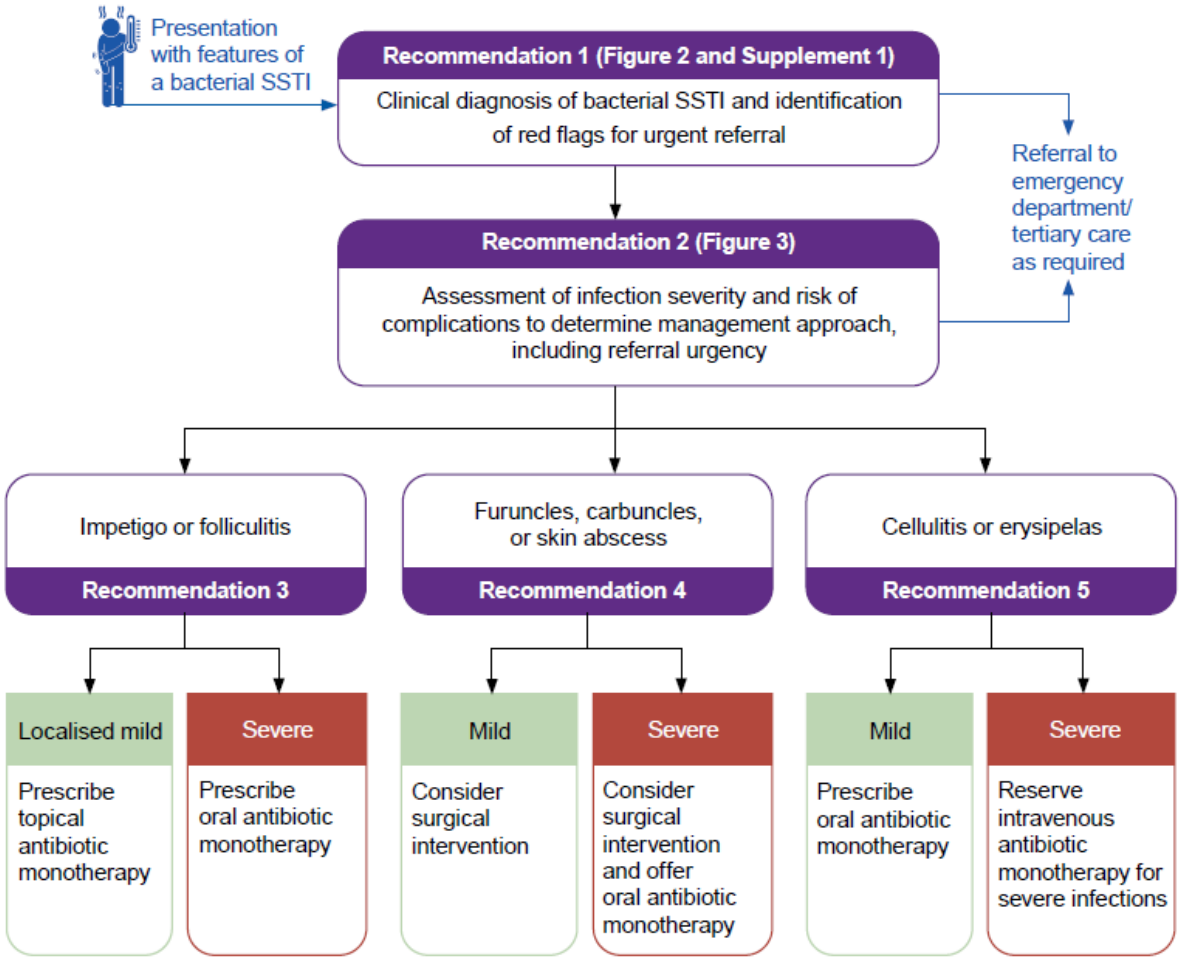
>90% Sensitive	80-90% Sensitive	<80% Sensitive	Too few samples (<10)*

CI: confidence interval; n, total sample size

*There was minimal (sample size <10) or no data for *S. aureus* and Group A, B, G Streptococcus for the following antibiotics: ciprofloxacin, piperacillin–tazobactam, ceftriaxone, cefepime, aztreonam, ertapenem, amikacin, erythromycin, ampicillin–sulbactam, amoxicillin

Appendix 2: Approach to bacterial skin and soft tissue infection (SSTI) management – at a glance.

This flowchart summarises the SSTI ACE Clinical Guidelines' (ACG's) recommendations. Refer to the ACG for figures, supplements, and sections referenced in this flowchart.



For patients presenting with mild infections but who are at high risk of complications (e.g. immunocompromised, presence of diabetes mellitus, or co-existing skin conditions), manage as per severe infection.

See **Supplement 2** for antibiotic options for treating bacterial SSTIs.

Adjunctive supportive treatment can be provided for patients with bacterial SSTIs. See section on *Supportive treatment for bacterial SSTIs* for further details.

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