

National surgical antibiotic prophylaxis guideline in Singapore

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ABSTRACT

Introduction: Institutional surgical antibiotic prophylaxis (SAP) guidelines are in place at all public hospitals in Singapore, but variations exist and adherence to guidelines is not tracked consistently. A national point prevalence survey carried out in 2020 showed that about 60% of surgical prophylactic antibiotics were administered for more than 24 hours. This guideline aims to align best practices nationally and provides a framework for audit and surveillance.

Method: This guideline was developed by the National Antimicrobial Stewardship Expert Panel's National Surgical Antibiotic Prophylaxis Guideline Development Workgroup Panel, which comprises infectious diseases physicians, pharmacists, surgeons and anaesthesiologists. The Workgroup adopted the ADAPTE methodology framework with modifications for the development of the guideline. The recommended duration of antibiotic prophylaxis was graded according to the strength of consolidated evidence based on the scoring system of the Singapore Ministry of Health Clinical Practice Guidelines.

Results: This National SAP Guideline provides evidence-based recommendations for the rational use of antibiotic prophylaxis. These include recommended agents, dose, timing and duration for patients undergoing common surgeries based on surgical disciplines. The Workgroup also provides antibiotic recommendations for special patient population groups (such as patients with β -lactam allergy and patients colonised with methicillin-resistant *Staphylococcus aureus*), as well as for monitoring and surveillance of SAP.

Conclusion: This evidence-based National SAP Guideline for hospitals in Singapore aims to align practices and optimise the use of antibiotics for surgical prophylaxis for the prevention of surgical site infections while reducing adverse events from prolonged durations of SAP.

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CLINICAL IMPACT

What is New

- This is the first surgical antibiotic prophylaxis (SAP) guideline in Singapore that provides evidence-based recommendations for the antibiotic choice, dose, timing and duration for adult patients undergoing elective clean or clean-contaminated surgeries.
- It highlights the evidence that prolonged SAP duration has no benefit, and may be associated with harm.

Clinical Implications

- This guideline aims to align practices and optimise the use of SAP for the prevention of surgical site infections, while also reducing adverse events from prolonged durations of SAP.

INTRODUCTION

Surgical antibiotic prophylaxis (SAP) refers to the administration of antibiotics prior to clean and clean-contaminated surgeries to prevent postoperative surgical site infections (SSIs). An optimal SAP should be highly effective in preventing SSI. An ideal prophylactic antibiotic regimen is: (1) effective against pathogens—generally skin flora—most likely to contaminate the surgical site; (2) appropriately dosed, and timed so that the highest tissue concentration is present upon skin incision; (3) safe; and (4) administered for the shortest effective period to minimise adverse effects, the development of antimicrobial resistance, and costs.¹ Antibiotics should also be re-dosed if surgery is prolonged or there is significant blood loss, to ensure adequate serum and tissue concentrations throughout the entire procedure.

Institutional SAP guidelines are in place at all public hospitals in Singapore but variations exist, and adherence to these guidelines is not reported nationally. Point prevalence surveys on antimicrobial utilisation conducted by Singapore public hospitals in 2020 showed that the prophylactic use of antibiotics for surgeries accounted for 10% of all antimicrobial agents prescribed, and about 60% of these prophylactic antibiotics were administered for more than 24 hours.² This is particularly concerning as various international guidelines state that SAP should be discontinued after skin closure following most procedures. These are

strong recommendations based on moderate- to high-quality clinical evidence.^{1,3,4} Current evidence shows that SAP has no benefit when given beyond 24 hours, and may be associated with harm such as an increased risk of acute kidney injury and *Clostridioides difficile* infections.⁵⁻⁷ Moreover, unnecessarily long durations of SAP do not prevent wound infections, but in fact, may increase the risk of infections with multidrug-resistant organisms due to antibiotic selection pressure.⁸

Appropriate SAP should be regarded as one of the components of an effective policy for the control of healthcare-associated infection (HAI), and also an important aspect of quality, patient safety, and antibiotic stewardship in the hospital. Based on the first national point prevalence survey conducted in public hospitals in Singapore, SSI was the second most common HAI after pneumonia, accounting for 17.3% of HAI.⁹ The establishment of the National SAP Guideline for hospitals in Singapore may reduce the rate of SSI by improving the choice and timing of SAP, while also reducing adverse events from prolonged courses of SAP, thereby promoting patient safety and addressing the problem of antimicrobial resistance.⁸

Thus, the National SAP Guideline provides evidence-based recommendations for the rational use of antibiotic prophylaxis. These include recommended agent(s), dose, timing and duration for patients undergoing more common surgical procedures. This guideline aims to align national best practices and provide a framework for audit and surveillance. The National Antimicrobial Stewardship Expert Panel (NASEP) envisions that this guideline would be an impetus for all institutions to improve the use of SAP for the benefit of patient care and quality.

METHOD

This guideline was developed by the NASEP's National Surgical Antibiotic Prophylaxis Guideline Development Workgroup Panel. The workgroup was led by 2 co-chairs and comprised infectious diseases physicians, infectious diseases and/or antimicrobial stewardship-trained pharmacists, surgeons and anaesthesiologists. The workgroup was divided into subgroups of 9 main surgical disciplines, and literature search was performed and presented by the individual subgroups.

The Workgroup Panel adopted the ADAPTE methodology framework¹⁰ with modifications in the development of the guideline. Members of the Workgroup Panel aimed to ensure the validity, reliability and applicability of the guideline for the Singapore setting. The primary literature published

in the English language through December 2020 was identified by searches of PubMed and the Cochrane Database of Systematic Reviews. Studies from the literature search, together with published international guidelines—such as the American Society of Health-System Pharmacists (ASHP), the Infectious Diseases Society of America (IDSA), the National Institute for Health and Care Excellence (NICE), and the US Centers for Disease Control and Prevention (CDC)—were reviewed in detail. Particular attention was paid to the study design, with the greatest credence given to systematic reviews, meta-analyses and randomised controlled double-blinded studies.

The recommended duration of antibiotic prophylaxis was graded according to the strength of consolidated evidence-based on the scoring system of the Singapore Ministry of Health (MOH) Clinical Practice Guidelines

(Tables 1 and 2). For procedures in which antibiotic prophylaxis is not recommended, the strength of evidence represents the support against prophylaxis. The description of the evidence base can be found in the online Supplementary Appendix 1.

The draft documents for each surgical procedure were collated and edited by the co-chairpersons before being circulated and reviewed by the Workgroup. The completed guideline was formally submitted for review and endorsement by the MOH National Antimicrobial Resistance Control Committee (NARCC) and National Centre for Infectious Diseases (NCID), together with Chapter of Infectious Disease Physicians, College of Anaesthesiologists, and College of Surgeons of the Academy of Medicine, Singapore. Medical practitioners from the private hospitals were also formally engaged for comments. The Workgroup had 6 rounds of

Table 1. Levels of evidence

Level	Type of evidence
1 ⁺⁺	High-quality meta-analyses, systematic reviews of randomised controlled trials (RCTs), or RCTs with a very low risk of bias
1 ⁺	Well-conducted meta-analyses, systematic reviews of RCTs, or RCTs with a low risk of bias
1 ⁻	Meta-analyses, systematic reviews of RCTs, or RCTs with a high risk of bias
2 ⁺⁺	High-quality systematic reviews of case control or cohort studies. High-quality case-control or cohort studies with a very low risk of confounding or bias and a high probability that the relationship is causal
2 ⁺	Well-conducted case control or cohort studies with a low risk of confounding or bias and a moderate probability that the relationship is causal
2 ⁻	Case control or cohort studies with a high risk of confounding or bias and a significant risk that the relationship is not causal
3	Non-analytic studies, e.g. case reports and case series
4	Expert opinion

Table 2. Grades of recommendation

Grade	Recommendation
A	At least one meta-analysis, systematic review of RCTs, or RCT rated as 1 ⁺⁺ and directly applicable to the target population; or A body of evidence consisting principally of studies rated as 1 ⁺ , directly applicable to the target population, and demonstrating overall consistency of results
B	A body of evidence including studies rated as 2 ⁺⁺ , directly applicable to the target population, and demonstrating overall consistency of results; or Extrapolated evidence from studies rated as 1 ⁺⁺ or 1 ⁺
C	A body of evidence including studies rated as 2 ⁺ , directly applicable to the target population and demonstrating overall consistency of results; or Extrapolated evidence from studies rated as 2 ⁺⁺
D	Evidence level 3 or 4; or Extrapolated evidence from studies rated as 2 ⁻
GPP (good practice points)	Recommended best practice based on the clinical experience of the guideline development group

virtual meetings from December 2020 to April 2022 to discuss the comments and make modifications to the guideline (Fig. 1).

The recommendations in this guideline apply to elective clean and clean-contaminated procedures in the adult population. Clean procedures involve an incision in which no inflammation is encountered, without a break in sterile technique, and during which the respiratory, alimentary or genitourinary tracts are not entered; clean-contaminated procedures involve an incision through which the respiratory, alimentary or genitourinary tract is entered under controlled conditions but with no contamination encountered.¹¹

This guideline does not cover the following:

- Treatment of infection in patients undergoing emergency surgery for contaminated or dirty wounds.
- Antibiotic prophylaxis for prevention of infective endocarditis.
- Antibiotic prophylaxis in patients with prosthetic implants undergoing dental surgery or other surgery that may cause bacteraemia.
- Use of antiseptic for prevention of wound infection after elective surgery.
- Administration of topical antibiotics in wounds.

Individual healthcare institutions should consider resistance patterns of organisms and overall SSI rates at

their respective sites when adopting these recommendations. The Workgroup Panel recognises the importance of other non-antimicrobial factors to reduce the risk of SSI, but the discussion of these factors lies outside the scope of this guideline.

This guideline will be of interest to surgeons, infectious diseases physicians, anaesthesiologists, pharmacists, microbiologists, infection control nurses, epidemiologists and public health professionals.

The full guideline is available at <https://www.ncid.sg/Health-Professionals/Documents/NationalSAPGuidelineSingapore.pdf> as a reference to guide practice.

RESULTS

Surgical antibiotic prophylaxis practice points

SAP with the right antibiotic, dose and timing has been found to be of benefit for most clean-contaminated, as well as in certain clean procedures where there are severe consequences of infection (e.g. placement of prosthesis or implant).¹ SAP may not be required in clean, uncomplicated procedures not involving the placement of prostheses or implants. For contaminated or infected wounds, antibiotic treatment is indicated and not considered as surgical prophylaxis.

Antibiotic choice

Most SSI are caused by skin flora or from flora that may be found at the site of the organ being operated

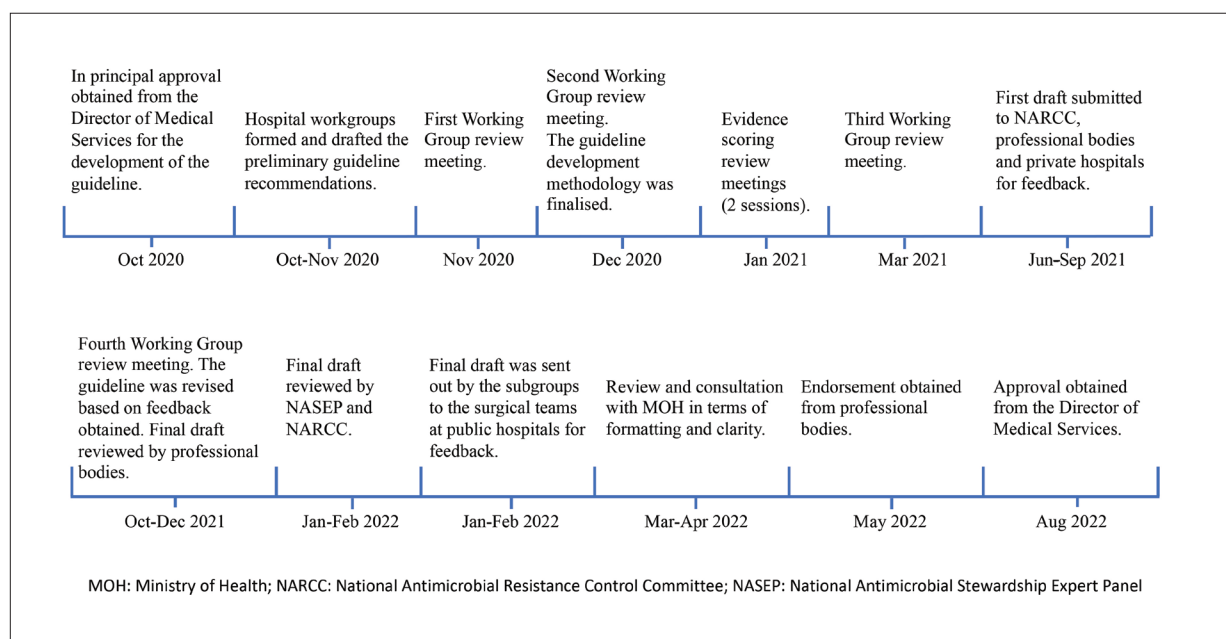


Fig. 1. Timeline of guideline development process highlighting time points at which feedback was solicited and incorporated into guideline development and revision.

on (e.g. Gram-negative and anaerobic bowel flora for surgeries traversing the colon). The antibiotic selected must cover the expected pathogen for the operative site and concentrate in high levels at the site prior to incision. Narrow-spectrum antibiotic agents are preferred. The association of some antibiotic agents (such as third-generation cephalosporins, fluoroquinolones and clindamycin) with the increased risk of *C. difficile* infections, and the development of multidrug-resistant colonisation or infections, should be taken into consideration.^{12,13} The choice of antibiotics should also take into account the resistance patterns at their respective sites. The recommended antibiotic prophylaxis for specific surgical procedures, along with alternatives for patients with severe penicillin allergy, is provided in Table 3.

Administration timing

The ideal antibiotic dose should be given in time to reach and maintain optimal levels in both blood and tissue from the time of incision until the closure of surgical wounds. Therefore, the dose and timing of antibiotic administration are important. The optimal time for administration of most preoperative doses is 30 to 60 minutes before surgical incision. The antibiotic should be infused completely prior to the incision. Specific agents (fluoroquinolones and vancomycin) that require longer infusion time should be administered at least 1 hour before the incision.^{1,14,15} Prospective cohort studies specifically in cardiac surgeries have demonstrated that incomplete infusion of preoperative vancomycin was associated with a higher risk for SSI.^{16,17} For emergency procedures when vancomycin cannot be infused due to limited time, teicoplanin is an effective option. Teicoplanin may be administered over 3 to 5 minutes or as a 30-minute infusion.^{18,19}

Methicillin-resistant *Staphylococcus aureus* (MRSA) risk and antimicrobial coverage

Screening and selective decolonisation of patients positive for MRSA have been shown to prevent SSI.²⁰⁻²⁵ The Workgroup Panel recommends screening and decolonisation for patients who will be undergoing high-risk surgeries (cardiac, orthopaedic and neurosurgery with implant). Decolonisation without screening is not recommended as the widespread use of mupirocin has been shown to promote resistance.²⁰

Vancomycin prophylaxis should be considered for patients with known MRSA colonisation or recent MRSA infection. This is recommended for (but not limited to) patients undergoing high-risk surgeries.¹

As vancomycin is less effective than cefazolin in preventing SSI caused by methicillin-susceptible *Staphylococcus aureus*, the addition of cefazolin to vancomycin should be considered for prophylaxis in MRSA colonised patients.¹ This combination was shown to have lower SSI rates,²⁶⁻²⁹ although some studies showed a slightly higher risk of acute kidney injury.³⁰ The Workgroup Panel recommends the use of this combination in MRSA-colonised patients, who undergo cardiac or orthopaedic (involving implants) procedures.

Antibiotic dosing and re-dosing intervals

The recommended re-dosing intervals for commonly used antibiotics are provided in Table 4.

For aminoglycosides, once-daily dosing is recommended. Gentamicin dosing regimens have been compared for prophylaxis in colorectal surgery. A single gentamicin dose of 5mg/kg was found to be more effective in SSI prevention than multiple doses of 1.5mg/kg given 8-hourly.³¹ A large retrospective cohort study of surgical patients (n=1,590) showed that the use of once-daily gentamicin was safe, with similar nephrotoxicity risk between gentamicin versus control (2.5% vs 1.8%, $P=0.17$).³²

Intraoperative re-dosing is required when:^{1,15,33-36}

- the duration of the procedure exceeds 2 half-lives of the drug, or
- there is excessive intra-operative blood loss (i.e. >1,500mL), or
- there are extensive burns.

Therapeutic drug monitoring for vancomycin and aminoglycosides is not required due to the short duration of prophylaxis. If these antibiotics are continued beyond the recommended duration for surgical prophylaxis, therapeutic drug monitoring should be initiated according to institutional guidelines.

Dosing in obese patients

Obesity has been linked to an increased risk of SSI.^{37,38} These patients may require higher doses to ensure adequate tissue concentrations.

These are the recommended dosing for obese patients:

- For cefazolin, the recommended dose if weight is >120kg is 3g instead of the usual 2g.¹
- For aminoglycoside use in obese patients (actual body weight is 20% above the ideal body weight), the dose is calculated based on the patient's adjusted body weight.^{1,3,39}

Table 3. Recommendations for surgical antibiotic prophylaxis

Types of surgery	First line	Alternative for severe penicillin allergy	Duration	Remarks	Level of evidence (Grade)
Breast surgery					
Breast cancer surgery without oncoplastic/reconstruction surgery	Not recommended For patients with risk factors IV cefazolin 2g	Not recommended For patients with risk factors IV clindamycin 600–900mg or IV vancomycin 15–20mg/kg	Single dose	Risk factors: - Post-neoadjuvant chemotherapy - Immunocompromised individuals	Level 1- (Grade B)
Breast cancer surgery with oncoplastic/reconstruction surgery	IV cefazolin 2g Followed by: 1–2g q8h	IV clindamycin 600–900mg Followed by: 600mg q8h or IV vancomycin 15–20mg/kg Followed by: 15mg/kg q12h	Up to 24 hours		Level 1+ (Grade A)
Breast lump excision biopsy	Not recommended	Not recommended	NA	If prophylactic antibiotic is used, it should not exceed a single dose. Refer to the above choices if prophylactic antibiotic is used	Level 1- (Grade B)
Wire localisation excision biopsy					
Cardiothoracic and vascular surgery					
Cardiac (aortic dissection, CABG, TEVAR, valve repair or replacement, LVAD placement, permanent pacemaker/defibrillator insertion)	IV cefazolin 2g Followed by: 1–2g q8h MRSA colonised IV cefazolin 2g + IV vancomycin 15–20mg/kg Followed by: IV cefazolin 1–2g q8h + IV vancomycin 15mg/kg q12h	IV vancomycin 15–20mg/kg Followed by: 15mg/kg q12h	24–48 hours	IV vancomycin dose of 20mg/kg preoperatively may be preferred to achieve sufficient tissue concentrations at the time of surgery At the onset of bypass: May consider an additional 1–2g of IV cefazolin via cardiopulmonary bypass circuit	Level 1+ (Grade A)
Thoracic (decortication, lobectomy, thymectomy, VATS)	IV cefazolin 2g MRSA colonised IV vancomycin 15–20mg/kg	IV clindamycin 600–900mg or IV vancomycin 15–20mg/kg	Single dose		Level 1- (Grade B)
Vascular (artery or vein repair, AVF or AVG creation, excision, jump graft, aortic stent graft)	IV cefazolin 2g Followed by: 1–2g q8h MRSA colonised IV vancomycin 15–20mg/kg Followed by: 15mg/kg q12h	IV clindamycin 600–900mg Followed by: 600mg q8h or IV vancomycin 15–20mg/kg Followed by: 15mg/kg q12h	Up to 24 hours		Level 1- (Grade B)
Cardiac or vascular (angioplasty, stent insertion)	Not recommended	Not recommended	NA		Level 3 (Grade D)

Table 3. Recommendations for surgical antibiotic prophylaxis (Cont'd)

Types of surgery	First line	Alternative for severe penicillin allergy	Duration	Remarks	Level of evidence (Grade)
Gastrointestinal surgery					
Appendectomy	IV cefazolin 2 g + IV metronidazole 500mg or IV ceftriaxone 2 g + IV metronidazole 500mg or IV amoxicillin-clavulanic acid 1.2 g	IV gentamicin 5mg/kg + IV metronidazole 500mg or IV gentamicin 5mg/kg + IV clindamycin 600–900mg ^c	Single dose		Level 1+ (Grade A)
Gastroduodenal and oesophageal	IV cefazolin 2 g or IV ceftriaxone 2 g or IV amoxicillin-clavulanic acid 1.2 g	IV gentamicin 5mg/kg +/- IV clindamycin 600–900mg	Single dose		Level 1+ (Grade A)
Small bowel	IV cefazolin 2 g + IV metronidazole 500mg or IV ceftriaxone 2 g + IV metronidazole 500mg or IV amoxicillin-clavulanic acid 1.2 g	IV gentamicin 5mg/kg + IV metronidazole 500mg or IV gentamicin 5mg/kg + IV clindamycin 600–900mg ^c	Single dose		Level 1+ (Grade B)
Colorectal	IV cefazolin 2 g + IV metronidazole 500mg or IV ceftriaxone 2 g + IV metronidazole 500mg or IV amoxicillin-clavulanic acid 1.2 g	IV gentamicin 5mg/kg + IV metronidazole 500mg or IV gentamicin 5mg/kg + IV clindamycin 600–900mg ^c	Single dose		Level 1++ (Grade A)
	To be used in conjunction with mechanical bowel preparation (MBP) (if given): PO neomycin sulfate 1g + PO erythromycin base 1g or PO neomycin sulfate 1g + PO metronidazole 1g		Three doses in conjunction with MBP	To be administered over approximately 10 hours the day before operation (e.g. 1 pm to 11 pm) Need for MBP + PO prophylaxis to be decided by individual institutions	Level 1++ (Grade B)
Hernia repair Hernioplasty (i.e. with mesh placement)	IV cefazolin 2 g	IV vancomycin 15mg/kg	Single dose	Recommendations for prophylaxis are mainly derived from studies on inguinal/femoral hernia repairs. Mixed outcomes for other types of hernias and studies were often of poor quality.	Level 1++ (Grade B)
Herniorrhaphy (i.e. no mesh placement)	Not recommended	Not recommended	NA		Level 1++ (Grade A)

Table 3. Recommendations for surgical antibiotic prophylaxis (Cont'd)

Types of surgery	First line	Alternative for severe penicillin allergy	Duration	Remarks	Level of evidence (Grade)
Hepatobiliary surgery					
Biliary tract surgery	IV cefazolin 2g or IV ceftriaxone 2g or IV amoxicillin-clavulanic acid 1.2g	IV clindamycin 600–900mg or IV vancomycin 15–20mg/kg + IV gentamicin 5mg/kg or IV aztreonam 2g	Single dose	It is reasonable to give a single dose of prophylaxis to patient undergoing laparoscopic cholecystectomy although evidence showed that antibiotic is not required for low-risk patients. This is because some of these risk factors cannot be determined prior to surgery.	Level 1+ (Grade A)
Hepatectomy	IV cefazolin 2g Followed by: 1–2g 8h or IV ceftriaxone 2g once	IV clindamycin 600–900mg or IV vancomycin 15–20mg/kg + IV gentamicin 5mg/kg or IV aztreonam 2g	Up to 24 hours	If the procedure is expected to involve the lower gastrointestinal tract, consider adding anaerobic coverage	Level 1+ (Grade A)
General surgery					
Splenectomy or left-sided pancreatic surgery	IV cefazolin 2g	IV vancomycin 15–20mg/kg	Single dose	There is no need to extend the antibiotic duration for patients who are not immunised. Administer the appropriate immunisations	GPP
Whipple's operation (no recent biliary intervention/ stenting)	IV cefazolin 2g Followed by: 1–2g 8h or IV ceftriaxone 2g once or IV amoxicillin-clavulanic acid 1.2g Followed by: 1.2g 8h	IV clindamycin 600–900mg or IV vancomycin 1520mg/kg +/- IV gentamicin 5mg/kg or IV aztreonam 2g	Up to 24 hours	For patients with recent biliary intervention/stenting, there is a higher incidence of bacterobilia with ESBL-producing organisms. Antibiotic should be tailored according to in-house antibiogram or recent bile/ blood cultures from the patient.	Level 2+ (Grade C)
Endoscopic retrograde cholangio-pancreatography (ERCP)	Not recommended except in cases of incomplete biliary drainage or obstructive biliary tract disease IV cefazolin 2g or IV ceftriaxone 2g	Not recommended except in cases of incomplete biliary drainage or obstructive biliary tract disease IV gentamicin 5mg/kg	Single dose	Antibiotic prophylaxis for ERCP was shown to increase the proportion of resistant bacteria ^{49,51}	Level 1+ (Grade A)
Obstetrics and gynaecology					
Caesarean section (C-section) ⁵²	IV cefazolin 2g	IV clindamycin 900mg	Single dose	Continuation of antimicrobial prophylaxis (up to 2 days) may be considered for patients with major risk factors for surgical infections, e.g. obesity (body mass index ≥ 30).	Level 1- (Grade B)

Table 3. Recommendations for surgical antibiotic prophylaxis (Cont'd)

Types of surgery	First line	Alternative for severe penicillin allergy	Duration	Remarks	Level of evidence (Grade)
Normal vaginal delivery (non-operative/instrumental)	Not recommended	Not recommended	NA	Antibiotic prophylaxis may be considered in the setting of a third- or fourth-degree perineal laceration Group B <i>Streptococcus</i> and preterm premature rupture of membranes prophylaxis are excluded in this guideline.	Level 1- (Grade B)
Normal vaginal delivery (operative/instrumental)	IV amoxicillin-clavulanic acid 1.2g	IV clindamycin 900mg	Single dose after delivery	Antibiotic prophylaxis may be considered in the setting of a third- or fourth-degree perineal laceration Group B <i>Streptococcus</i> and preterm premature rupture of membranes prophylaxis are excluded in this guideline.	Level 1- (Grade B)
Hysterectomy Abdominal/vaginal/ laparoscopic	IV cefazolin 2g + IV metronidazole 500mg	IV clindamycin 900mg + IV gentamicin 5mg/kg	Single dose		Level 2- (Grade C)
Hysteroscopy	Not recommended	Not recommended	NA	The risk of infection is very low, antibiotic prophylaxis generally not necessary unless high risk e.g. dilated fallopian tubes, history of pelvic inflammatory disease, tubal damage or abnormal tubal architecture (associated with risk of postoperative pelvic inflammatory disease/endometritis). If evidence of endometritis/infection found at point of procedure, treat accordingly.	Level 1- (Grade B)
Hysterosalpingography	Not recommended	Not recommended	NA	As above.	Level 2- (Grade C)
Endometrial biopsy, cervical tissue excision, cervical cone procedures	Not recommended	Not recommended	NA		Level 2- (Grade C)
Intrauterine device insertion	Not recommended	Not recommended	NA	Consider sexually transmitted infections screens in high-risk populations and advise to complete treatment prior procedure.	Level 1+ (Grade A)

Table 3. Recommendations for surgical antibiotic prophylaxis (Cont'd)

Types of surgery	First line	Alternative for severe penicillin allergy	Duration	Remarks	Level of evidence (Grade)
Orthopaedic/spine surgery					
Clean orthopaedic, non-spinal procedure with no implantation (arthroscopy, tendon repair surgery)	Not recommended For patients with risk factors IV cefazolin 2g MRSA colonised IV cefazolin 2g +/- IV vancomycin 15–20mg/kg	Not recommended For patients with risk factors IV vancomycin 15–20mg/kg or IV clindamycin 600–900mg	Single dose	Risk factors include dermatological conditions, predicted prolonged operative time, malnutrition, immunosuppressant use and poorly controlled diabetes mellitus	Level 1- (Grade B)
Clean orthopaedic surgery with implants	IV cefazolin 2g Followed by: 1–2g q8h	IV vancomycin 15–20mg/kg Followed by: 15mg/kg q12h or IV clindamycin 600–900mg Followed by: 600mg q8h	Up to 24 hours		Level 1++ (Grade A)
Wrist arthroplasty	MRSA colonised IV cefazolin 2g + IV vancomycin 15–20mg/kg Followed by: IV cefazolin 1–2g q8h + IV vancomycin 15mg/kg q12h				
Spine surgery (with and without implants)					
	IV cefazolin 2g Followed by: 1–2g q8h MRSA colonised IV cefazolin 2g + IV vancomycin 15–20mg/kg Followed by: IV cefazolin 1–2g q8h + IV vancomycin 15mg/kg q12h	IV vancomycin 15–20mg/kg Followed by: 15mg/kg q12h or IV clindamycin 600–900mg Followed by: 600mg q8h	Up to 24 hours		Level 1++ (Grade A)
Otorhinolaryngology					
Clean head and neck (thyroidectomy, parotidectomy, salivary gland excisions)	Not recommended	Not recommended	NA		Level 1+ (Grade A)
Clean-contaminated head and neck	IV amoxicillin-clavulanic acid 1.2g q8h or IV cefazolin 2g q8h + IV metronidazole 500mg q8h	IV clindamycin 600–900mg q8h +/- IV gentamicin 5mg/kg once ^a	Up to 24 hours	Prolonged course of oral antibiotics has not been shown to reduce postoperative infections and may increase the risk of complications.	Level 1+ (Grade A)
Neck dissection procedures				For neck dissection: Level 2+ (Grade C)	
Clean otologic procedures	Not recommended	Not recommended	NA		Level 1+ (Grade A)

Table 3. Recommendations for surgical antibiotic prophylaxis (Cont'd)

Types of surgery	First line	Alternative for severe penicillin allergy	Duration	Remarks	Level of evidence (Grade)
Clean-contaminated otologic procedures	IV amoxicillin-clavulanic acid 1.2g q8h or IV cefazolin 2g q8h + IV metronidazole 500mg q8h	IV clindamycin 600–900mg q8h +/- IV gentamicin 5mg/kg once ^a	Up to 24 hours		Level 1- (Grade B)
Tonsillectomy	Not recommended	Not recommended	NA		Level 1+ (Grade A)
Simple septorhinoplasty	Not recommended	Not recommended	NA	Infection rates are very low, especially when nasal packing/splint use ≤48 hours	Level 1- (Grade B)
Complex Septorhinoplasty	IV amoxicillin-clavulanic acid 1.2g q8h or IV cefazolin 2g q8h + IV metronidazole 500mg q8h	IV clindamycin 600–900mg q8h +/- IV gentamicin 5mg/kg once ^a	Up to 24 hours		Level 1- (Grade B)
Endoscopic sinus surgery	IV amoxicillin-clavulanic acid 1.2g or IV cefazolin 2g + IV metronidazole 500mg	IV clindamycin 600–900mg +/- IV gentamicin 5mg/kg ^a	Single dose	Post-operative antibiotics should not be given if there is no mucous seen intra-operatively.	Level 1- (Grade B)
Neurosurgery					
Clean wounds Elective craniotomy, external ventricular drain (EVD), intracranial pressure (ICP) monitors	IV cefazolin 2g <u>MRSA colonised</u> IV vancomycin 15–20mg/kg	IV vancomycin 15–20mg/kg or IV clindamycin 600–900mg	Single dose ^b		Level 1+ (Grade A) For EVD and ICP: Level 2++ (Grade B)
Clean wounds with foreign bodies or instrumentation Cerebrospinal fluid shunting procedures	IV cefazolin 2g <u>MRSA colonised</u> IV vancomycin 15–20mg/kg	IV vancomycin 15–20mg/kg or IV clindamycin 600–900mg	Single dose ^b		Level 1+ (Grade A)
Urological procedures					
Lower urinary tract instrumentation					
Cystourethroscopy -With or without minor manipulation, and without a significant break in mucosal barriers -With a significant break in mucosal barriers/significant manipulation	Not recommended, except in those with risk factors, to manage as transurethral cases (refer to the section on transurethral procedure) To manage as transurethral cases (refer to transurethral section)	Not recommended, except in those with risk factors, to manage as transurethral cases (refer to the section on transurethral procedure)	NA	If urine culture shows no growth prior to the procedure, antimicrobial prophylaxis is not necessary Risk factors: poor functional status/frailty, anatomic anomalies of the urinary tract, chronic steroid use, immunocompromising condition or recent systemic chemotherapy, poorly controlled diabetes mellitus, prior severe urosepsis	Level 1+ (Grade A)

Table 3. Recommendations for surgical antibiotic prophylaxis (Cont'd)

Types of surgery	First line	Alternative for severe penicillin allergy	Duration	Remarks	Level of evidence (Grade)
Transurethral cases and minimally invasive surgical therapy to the prostate	IV/IM gentamicin 3–5mg/kg or IV amoxicillin-clavulanic acid 1.2g or IV ceftriaxone 2g	IV/IM gentamicin 3–5mg/kg or PO ciprofloxacin 500mg/IV 400mg ^a	Single dose		Level 1+ (Grade B)
Transrectal prostate biopsy	PO ciprofloxacin 500 mg + IV/IM gentamicin 3–5mg/kg or IV amoxicillin-clavulanic acid 1.2g/ PO 625mg + IV/IM gentamicin 3–5mg/kg or IV ceftriaxone 2g	PO ciprofloxacin 500 mg + IV/IM gentamicin 3–5mg/kg	Up to 48 hours	For PO ciprofloxacin, dose 1–2 hours before the procedure For PO amoxicillin-clavulanic acid, dose 24 hours before the procedure	Level 1+ (Grade A)
Transperineal procedures e.g. prostate brachytherapy, transperineal prostate biopsy	Not recommended	Not recommended	NA	Prophylaxis may be recommended in patients with risk factors (chronic steroid use, immunocompromising condition or recent systemic chemotherapy, poorly controlled diabetes mellitus), prior severe urosepsis or post-biopsy infection. Antibiotic choice: PO cephalosporins or amoxicillin-clavulanic acid 2 hours before the procedure	Level 2+ (Grade C)
Upper urinary tract instrumentation					
Percutaneous renal surgery, e.g. percutaneous nephrolithotomy	IV cefazolin 2g + IV gentamicin 3–5mg/kg or IV amoxicillin-clavulanic acid 1.2g or IV ceftriaxone 2g	IV gentamicin 3–5mg/kg + IV clindamycin 600–900mg or IV gentamicin 3–5mg/kg + IV vancomycin 15–20mg/kg	Single dose		Level 1+ (Grade A)
Ureteroscopy (including laser lithotripsy)	IV gentamicin 3–5mg/kg or IV amoxicillin-clavulanic acid 1.2g or IV ceftriaxone 2g	IV gentamicin 3–5mg/kg or PO ciprofloxacin 500mg/IV 400mg ^a	Single dose		Level 1+ (Grade A)
Open, laparoscopic or robotic surgery					

Table 3. Recommendations for surgical antibiotic prophylaxis (Cont'd)

Types of surgery	First line	Alternative for severe penicillin allergy	Duration	Remarks	Level of evidence (Grade)
Urethoplasty; reconstruction of anterior urethra, stricture repair, including urethrectomy; controlled entry into the urinary tract e.g. renal surgery, nephrectomy, ureterectomy, pyeloplasty, radical prostatectomy; partial cystectomy	IV cefazolin 2g + IV gentamicin 3–5mg/kg or IV amoxicillin-clavulanic acid 1.2g or IV ceftriaxone 2g	IV gentamicin 3–5mg/kg + IV clindamycin 600–900mg or IV gentamicin 3–5mg/kg + IV vancomycin 15–20mg/kg	Single dose	Consider preoperative urine cultures and treat accordingly For buccal mucosal graft, consider adding anaerobic coverage	Level 2+ (Grade B)
Urinary diversion involving small or large bowel	IV cefazolin 2g + IV gentamicin 3–5mg/kg + IV metronidazole 500mg or IV amoxicillin-clavulanic acid 1.2g or IV ceftriaxone 2g + IV metronidazole 500mg	IV gentamicin 3–5mg/kg + IV metronidazole 500 mg or IV gentamicin 3–5mg/kg + IV clindamycin 600–900mg	Single dose	Metronidazole may be optional for small bowel surgery	Level 2- (Grade C)
Implanted prosthetic devices: AUS, IPP, sacral neuromodulators	IV cefazolin 2g + IV gentamicin 3–5mg/kg or IV amoxicillin-clavulanic acid 1.2g or IV ceftriaxone 2g <u>MRSA colonised</u> IV vancomycin 15–20mg/kg	IV vancomycin 15–20mg/kg + IV aztreonam 2g or IV clindamycin 600–900mg + IV gentamicin 3–5mg/kg	Single dose		Level 4 (GPP)
Others					
Urodynamic study	Not recommended except in those with risk factors (see cystourethroscopy section)	NA	NA	For shockwave lithotripsy, consider antibiotic prophylaxis (single-dose IV gentamicin or IV ceftriaxone) only if high risk of infection e.g. infected stones, recent instrumentation, nephrostomy tubes, positive urine culture, or history of recent urinary tract infection/sepsis	Level 1+ (Grade A)
Penile surgery					
Shockwave lithotripsy					

^a The addition of gentamicin may be appropriate when there is an increased likelihood of Gram-negative contamination of the surgical site.

^b While single-dose prophylaxis is usually sufficient, the duration of prophylaxis for all procedures should be less than 24 hours.

^c Clindamycin resistance has been increasing in *Bacteroides* species. Metronidazole may be preferred if the procedure transverses the lower gastrointestinal tract.

^d Due to the high local resistance of Gram-negative organisms to quinolones, this is only recommended if the organism is shown to be sensitive in the preoperative urine culture.

^e An additional single dose of IV azithromycin 500mg to routine prophylaxis may be considered for a non-elective Caesarean section. However, the extrapolation of benefit to local centres where rates of post-C-section infections are low still remains to be determined.

AUS: Artificial urinary sphincter; AVF: arteriovenous fistula; AVG: arteriovenous graft; CABG: coronary artery bypass grafting; ERCP: endoscopic retrograde cholangio-pancreatography; GPP: good practice points; IPP: intravesical prostatic protrusion; IM: intramuscular; IV: intravenous; LVAD: left ventricular assist device; MRSA: methicillin-resistant *Staphylococcus aureus*; NA: not applicable; PO: per oral (oral administration); TEVAR: thoracic endovascular aortic repair; VATS: video-assisted thoracoscopic surgery

Superscript numbers: Refer to REFERENCES

Table 4. Recommended doses and re-dosing interval

Antibiotic	Adult dose	Re-dosing interval
IV cefazolin	2g (3g if >120kg)	Every 4 hours ^a
IV ceftriaxone	2g	Every 12 hours
IV metronidazole	500mg	Every 8–12 hours
IV clindamycin	600–900mg	Every 4–6 hours
IV vancomycin	15–20mg/kg	Every 8–12 hours ^a
IV/IM gentamicin	3–5mg/kg	NA
IV amoxicillin-clavulanic acid	1.2g	Every 4 hours ^a
IV/PO ciprofloxacin	400mg (IV), 500mg (PO)	Every 8–12 hours ^a
IV aztreonam	2g	Every 4 hours ^a

IM: intramuscular; IV: intravenous; NA: not applicable; PO: per oral (oral administration)

^a Recommended doses and re-dosing intervals are based on normal renal function. Renal dose adjustment may be required.

Source: Bratzler DW, Dellinger EP, Olsen KM, et al. Clinical practice guidelines for antimicrobial prophylaxis in surgery. Am J Health Syst Pharm 2013;70:195-283.

Adjusted body weight = Ideal body weight + 0.4 x (Total body weight - Ideal body weight)

where

Ideal body weight (male) is $50 + 2.3 \times (\text{height in inches} - 60)$

Ideal body weight (female) is $45.5 + 2.3 \times (\text{height in inches} - 60)$

(1 inch = 2.54cm)

- For vancomycin, it should be dosed at 15–20mg/kg of actual body weight, with the first dose capped at 3g per dose.^{1,3,40-43}

Patients with β -lactam allergy

β -lactams, including cephalosporins, are the mainstay of SAP and have the highest efficacy. Studies have shown that patients with reported β -lactam allergy have increased odds of SSI, attributed to the receipt of second-line antibiotics.^{44,45} Thus, patients with a history of β -lactam allergy should have a detailed antibiotic and allergy assessment to determine if a true allergy exists, and to exclude any non-immunological adverse reaction (for example diarrhoea, vomiting and non-specific rash). This can be done in advance for elective surgeries, so patients with no true allergy or a mild allergy to penicillin can be given the first-line SAP.

Patients with severe penicillin allergy should not receive β -lactam for surgical prophylaxis. These include patients with severe immunoglobulin E (IgE)-mediated reactions (anaphylaxis, urticaria, bronchospasm and angioedema), or non-IgE-mediated reactions (Steven-Johnson syndrome, toxic epidermal necrolysis and drug-induced hypersensitivity

syndrome). Alternatives to β -lactam antibiotics are provided in Table 3.

In patients with an uncomplicated non-IgE-mediated allergic reaction to penicillin (i.e. maculopapular rash), cephalosporins (i.e. cefazolin or 3rd generation cephalosporins) can be considered after discussion with the patient and the allergy team (if available). Cefazolin, in particular, has a unique R1 side chain that is distinct from other cephalosporins and β -lactams, and side chain cross-reactivity with penicillin and other beta-lactams is not expected.^{46,47}

Patients receiving therapeutic antibiotics for an active infection before surgery

If the antibiotic used to treat the current infection is deemed appropriate for surgical prophylaxis, an extra dose should be administered within 60 minutes before the surgical incision. If the current antibiotic is insufficient for surgical prophylaxis, the recommended antibiotic prophylaxis for the procedure should be used. The need for re-dosing should be individualised and evaluated on a case-by-case basis.

Patients with prior colonisation or infection with multidrug-resistant pathogens

The causative link between the carriage of multidrug-resistant organisms and the resultant SSI caused by these pathogens has not been established. Whether prophylaxis should be expanded to cover these pathogens depends on many factors, including the host, the pathogen and its antimicrobial susceptibility profile, the procedure, and the proximity of the reservoir of the pathogen to the operative site.¹ These patients should be evaluated on a case-by-case basis.

Consideration for formal infectious diseases consultation

Formal infectious diseases consultation should be considered for the following patients:

- Patients who have contraindications to both the first- and second-line antibiotic prophylaxis regimen (including complex allergy history and impaired renal function).
- Patients with a recent history of colonisation and/or infection with multidrug-resistant organisms and who are undergoing high-risk procedures.

Duration of surgical antibiotic prophylaxis

In clean and clean-contaminated procedures, additional prophylactic antibiotic agents should not be administered after the surgical incision is closed, even in the presence of a drain. This recommendation also applies to patients on systemic corticosteroids or other immunosuppressive therapy.^{1,3} At most, the duration of antibiotic prophylaxis should not exceed 24 hours for most procedures. A recent systematic review of 83 randomised controlled trials across various surgical subspecialties found no additional benefit from extending the duration of prophylaxis as compared to immediate discontinuation. A prespecified subgroup analysis in this study also showed that when best practice standards (defined as the first dose within an hour of incision and appropriate re-dosing) were applied, prolonged antibiotic prophylaxis had no effect on the risk of SSI.⁴⁸ Prolonged SAP beyond 24 hours has been shown to be associated with acute kidney injury and *C. difficile* infections.⁷ This practice may also increase selective pressure favouring the emergence of multidrug-resistant organisms.⁸ The recommended duration of antibiotic prophylaxis for various surgical procedures is provided in Table 3.

Recommendations for monitoring and surveillance

The Workgroup Panel recommends the following indicators for monitoring and audit:

- The choice, dosage, and route of administration of antimicrobial agents are consistent with the national guideline.
- The first dose of prophylaxis is given at the right time in relation to the incision time.
- Re-dosing of antimicrobial agents is consistent with the national guideline.
- The duration of prophylaxis is consistent with the national guideline.

Data on the choice and duration of SAP in public hospitals in Singapore are collected annually through

the Antimicrobial Utilisation-Point Prevalence Survey (AMU-PPS). The above additional process measures may be incorporated into the AMU-PPS to provide useful information to improve antimicrobial stewardship initiatives.

Limitations

Immunocompromised patients and patients colonised with multidrug-resistant organisms may be under-represented in a majority of the studies. Some of these patients who are undergoing high-risk surgeries are recommended for a formal infectious disease consultation prior to surgery. Additional limitations pertaining to the studies in certain surgical specialties were stated in the respective sections under the online Appendix 1. The cost-effectiveness of the recommended antibiotic regimen was also not discussed in this guideline. The majority of the antimicrobial agents recommended are generic formulations and of relatively low price.

CONCLUSION

This is the first national surgical antibiotic prophylaxis guideline in Singapore. It provides evidence-based recommendations for the rational use of antibiotic prophylaxis—including the recommended agent(s), dose, timing and duration for adult patients undergoing elective clean or clean-contaminated surgeries. This guide aims to align best practices nationally and provide a framework for audit and surveillance. Current evidence indicates that SAP has no benefit when given beyond 24 hours, and may be associated with harm. The establishment of the national SAP guideline for hospitals in Singapore may lower the rate of SSI, while also reducing adverse events from the prolonged duration of SAP.

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