Appendix 1

Evidence Grading (Tabulation of Guidelines and Literature)

Approach

The Workgroup Panel adopted the ADAPTE methodology framework[1] with modifications in the development of the Guideline. Members of the Workgroup Panel aimed to ensure validity, reliability, and applicability of the Guideline for the local setting. The draft document for each surgical procedure was circulated and reviewed by the Workgroup Panel, together with anaesthesia and surgical representatives from the public acute hospitals in Singapore.

Evidence Base and Grading of Recommendation

The primary literature published through December 2020 were 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), 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 greatest credence given to systematic reviews, meta-analyses and randomised controlled double-blinded studies.

The recommended duration of antimicrobial prophylaxis was graded according to the strength of consolidated evidence, applying scoring system of the Singapore Ministry of Health Clinical Practice Guidelines. For the procedures in which antimicrobial prophylaxis is not recommended, the strength of evidence represents the support against prophylaxis. The strength of evidence does not apply to the choice of antimicrobial agent or dosage regimen. Studies supporting the recommended duration were classified as follows:

Table A1: 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, case series
4	Expert opinion

Table A2: 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

BREAST SURGERY

Guidelines

Table A3: Guideline references for surgical prophylaxis recommendations

Reference	Type of Surgery	First line	Alternative for Severe Penicillin Allergy	Duration	Remarks	Level of Evidence (Grade)
ASHP, IDSA, SIS, and SHEA[2]	Plastic surgery and breast procedures (Clean with risk factors or clean-contaminated)	Cefazolin, ampicillin-sulbactam	IV clindamycin or IV vancomycin ± gram-negative cover (aztreonam, gentamicin, fluoroquinolone) if gram-negative infections highly suspected	≤ 24 hours (regardless of presence of indwelling catheters or drains	Antimicrobial prophylaxis does not significantly decrease the risk of infection for clean procedures (including reduction mammoplasty, lumpectomy, mastectomy, axillary node dissection)	Grade C (graded based on the need for prophylaxis)
ASBrS[3]	Breast Surgery	First-generation cephalosporin (unless the patient is allergic or has a history of prior infection with MRSA)	Not stated	≤ 24 hours	1. Indicated for mastectomy, with or without any type of axillary dissection or reconstruction 2. May be used for partial mastectomy for cancer, with or without sentinel lymph node biopsy or axillary dissection 3. May be used for simple surgical excisional biopsy, especially if specific patient or clinical risk factors for SSI are present	Not graded
ASPS[4]	Implant-based reconstruction after mastectomy	Not stated	Not stated	≤ 24 hours (unless a drain is present)	Unless a drain is present, antibiotics should be discontinued within 24 hours of the completion of the procedure. If a drain is present, the role of antibiotics is less clear and should be left to physician judgement	Level 4 (Grade D)

***ASBrS:** The American Society of Breast Surgeons; **ASPS**: American Society of Plastic Surgeons

Literature

Table A4: Literature review of references

Reference	Study Design/Country	Sample Size	Population and Intervention	Outcome	Limitations/Remarks	Level of Evidence	Final Grade
5	Systematic review (Cochrane 2019)	11 RCTs 2,867 patients	Surgery for breast cancer Pre- (within 24 hours prior to surgery) or peri-operative antibiotics (given between commencement of induction of surgery and the patient leaving the recovery room)	Pre-operative prophylactic antibiotics probably reduced the incidence of SSI for patients undergoing breast cancer surgery without reconstruction (pooled risk ratio (RR) 0.67, 95% CI 0.53 to 0.85)	Antibiotic regimens used varied across studies, which encompassed a variety of surgeries. Most studies had a single prophylactic antibiotic dose	1^{+}	A
6	Systematic review (Phillips 2016)	5 clinical studies and 2 systematic reviews	Implant-based breast reconstruction Antibiotic prophylaxis of varying durations	The literature does not support prolonged (>24 hours) post-operative antibiotic use in autologous breast reconstruction. The authors' opinion is that at least 24 hours of antibiotic prophylaxis is warranted following mastectomy with expander or implant-based reconstruction. Level I evidence suggests that 24 hours is not inferior to prolonged antibiotics, and therefore limiting post-operative antibiotic use to 24 hours is recommended Patient-centred antibiotic prophylaxis based on a risk-assessment model may be a more effective alternative	The study states conflicting information from medical literature on duration, and concludes that further studies are needed	1^{-}	B
7	Systematic review and meta-analysis (Wang 2016)	4 cohort studies, 1 RCT	Immediate prosthetic breast reconstruction Prolonged prophylactic antibiotics (>24 hours) vs antibiotics within 24 hours	>24 hours vs 24 hours Surgical-site infections: 14% vs 19% Pooled relative risk of implant loss was 1.17 (95% CI 0.39 to 3.6) with less than 24 hours of antibiotics, not statistically significant	Significant heterogeneity between studies	1-	B
8	Non-inferiority RCT USA (Phillips 2016)	112 patients	Tissue-expander-based immediate breast reconstruction. All received cefazolin (or clindamycin if allergic). Compared 24 hours of IV antibiotic post-operative vs continuing oral antibiotics until all drains removed	SSI: 24 hours (12/62) vs >24 hours (11/50) (19.4% vs 22.0%, p=0.82) Less patients in 24-hour group had implant loss		1^{+}	A

9	Cohort study USA (Drury 2016)	1036 patients	Autologous breast reconstruction Prolonged prophylactic antibiotics (>24 hours) vs antibiotics <24 hours	SSI: Prolonged vs 24 hours (2.92% vs 5.01%, *p*=0.109)	2+	C

Cardiac Surgeries

Guidelines

Table A5: Guideline references for surgical prophylaxis recommendations

Reference	Type of Surgery	First line	Alternative for Severe Penicillin Allergy	Duration	Remarks	Level of Evidence/Grade
ASHP, IDSA, SIS, SHEA[2]	Cardiac surgeries	IV cefazolin or IV cefuroxime If MRSA colonised: IV Vancomycin ± gram-negative cover (aztreonam, aminoglycoside, fluoroquinolone) if high incidence of gram-negative infections	IV clindamycin or IV vancomycin ± gram-negative cover (aztreonam, aminoglycoside, fluoroquinolone) if high incidence of gram-negative infections	≤ 24 hours		A
STS[10,11]	Cardiac surgeries	IV cefazolin 2g MRSA colonised/ high MRSA prevalence/ valve surgery or vascular implants: IV cefazolin + single dose IV vancomycin	IV vancomycin 1-1.5g or 15mg/kg ± single dose IV gentamicin (or other gram-negative cover)	≤ 48 hours		Class IIa, Level B
EACTS[12]	Cardiac Surgeries	IV cefazolin or IV cefuroxime If MRSA colonised: IV Vancomycin	IV clindamycin or IV vancomycin	24-48 hours		Class IIa, Level A
SAAGAR[13]	Coronary artery bypass graft	IV cefazolin 2g If MRSA colonised: IV cefazolin 2g + IV vancomycin 1g (1.5g if weight >80kg)	IV vancomycin 1g (1.5g if weight >80kg) + IV gentamicin 5mg/kg	24 hours		No grading of evidence as this guideline cited other guidelines
	Routine cardiac valve surgery	IV cefazolin 2g + IV vancomycin 1g (1.5g if weight >80kg) (regardless of MRSA status)	IV vancomycin 1g (1.5g if weight >80kg) + IV gentamicin 5mg/kg	24 hours		
	High risk cardiac valve surgery, Transcatheter aortic valve implantation	IV cefazolin 2g + IV vancomycin 1g (1.5g if weight >80kg) ± IV gentamicin 5mg/kg (regardless of MRSA status)	IV vancomycin 1g (1.5g if weight >80kg) + IV gentamicin 5mg/kg	24 hours		

***STS:** Society of Thoracic Surgeons; **EACTS**: European Association of Cardio-Thoracic Surgery; **SAAGAR**: South Australian expert Advisory Group on Antimicrobial Resistance

Literature

Table A6: Literature review of references

Reference	Study Design/Country	Sample Size	Population and Intervention	Outcome	Limitations/Remarks	Level of Evidence	Final Grade
14	Meta-analysis (North America, Europe, Australia)	12 RCTs 7,893 patients	Open heart cardiac surgery Any antibiotic prophylactic regimen: Compared <24 hours vs ≥24 hours	Sternal SSIs: prophylaxis ≥24 hours reduced SSI rates by 38% (RR 1.38, 95% CI 1.13–1.69, p=0.002)	Antibiotic regimens used varied across studies	1^{+}	
15	RCT (Spain)	838 patients	Elective cardiac valve surgery, coronary surgery, or both by means of mean sternotomy IV cefazolin 2g once vs 2g then 1g q8h for 24 hours	SSI: 35 (8.3%) in single dose group vs 15 (3.6%) in 24-hour group But no difference in mortality or length of hospital stay was observed	Supports prophylaxis for 24 hours	1^{+}	
16	RCT (Taiwan)	231 patients	Coronary artery bypass graft surgery IV cefazolin 1g q8h x 1 day vs 3 days	SSI: no difference	No sample size calculation, likely underpowered study	1^{-}	
17	RCT (Switzerland)	53 patients	High risk cardiac surgery (requiring inotropes and IABP post-operatively) IV cefazolin for 24 hours then: Ticarcillin-clavulanic acid + vancomycin until removal of IABP vs none	Mortality, infections (SSI, pneumonia, sepsis): no difference	No sample size calculation, likely underpowered study	1^{-}	
18	RCT (North America)	Not available	Cardiac surgery with cardiopulmonary bypass IV cephalothin 1g once vs once plus 20 doses	Major and minor infections, deaths, or floral changes: no differences A longer duration of prophylaxis was associated with a change in the species of organisms causing major infection	The study from 1972 may be outdated; only the abstract was available	1^{-}	
19	Prospective cohort study (North America)	2,641 patients	Coronary artery bypass graft surgery Antibiotic prophylaxis <48 hours vs >48 hours compared	Prophylaxis >48 hours was not associated with decreased SSI but was associated with	Variability in antibiotic prophylaxis regimen; included	2^{+}	

				antibiotic resistance (adjusted OR 1.6, 95% CI 1.1-2.6)	possible confounders in analysis. Supports prophylaxis for up to 48 hours	
20	Retrospective cohort study (North America)	79,058 patients	Cardiac, orthopaedic total joint replacement, colorectal, and vascular procedures Duration of prophylaxis <24 hours vs 24-48 hours vs 48-72 hours vs ≥72 hours were compared	SSI was not associated with duration of prophylaxis Increased risk of acute kidney injury and *C. difficile* infection with prophylaxis >48 hours	Predominantly male population	2^+
21	Retrospective cohort study (Germany)	1,096 patients	Cardiac surgery IV cefuroxime 1.5g q8h x 32 hours vs 56 hours were compared	SSI: no difference	No sample size calculation was provided, likely underpowered study	2^-
22	Prospective cohort study (North America)	5,158 patients	Cardiac surgery No intervention but prophylaxis 0-24 hours vs 24-48 hours vs >48 hours were compared	Prophylaxis >48 hours was associated with major infection risk (Hazard ratio 1.92; 95% CI 1.28-2.88) and *C. difficile* colitis risk (Hazard ratio 6.31, 95% CI 2.86-14.0) No difference between 0-24 hours and 24-48 hours	Potential confounders as study were not randomised; Supports prophylaxis for up to 48 hours	2^-
					FINAL GRADE	**A**

***IABP**: Intra-aortic balloon pump

Note: So far, no good quality study has compared the outcomes between 24 vs 48 hours prophylaxis duration. The guidelines should be reviewed when new studies published: e.g. van Oostveen RB, et al. Prevention of infections in cardiac surgery study (PICS): study protocol for a pragmatic cluster-randomised factorial crossover pilot trial. Trial. 2018;19:688.

Thoracic Procedures

Guidelines

Table A7: Guideline references for surgical prophylaxis recommendations

Reference	Type of Surgery	First line	Alternative for Severe Penicillin Allergy	Duration	Remarks	Level of evidence/Grade
ASHP, IDSA, SIS, SHEA[2]	Thoracic	IV cefazolin or IV ampicillin-sulbactam	IV clindamycin or IV vancomycin ± gram-negative cover (aztreonam, aminoglycoside, fluoroquinolone) if high incidence of gram-negative infections	Single dose		C (for video-assisted thoracoscopic surgery), A (for other thoracic procedures)
SAAGAR[13]	Thoracic	IV cefazolin 2g ± IV metronidazole 500mg	IV vancomycin 1g (1.5g if weight >80kg) ± IV metronidazole 500mg	Single dose to 24 hours		No grading of evidence provided

***SAAGAR**: South Australian expert Advisory Group on Antimicrobial Resistance

Literature

Table A-8: Literature review of references

Reference	Study Design/Country	Sample Size	Population and Intervention	Outcome	Limitations/Remarks	Level of Evidence	Final Grade
[23]	RCT (United Kingdom)	208 patients	Elective thoracotomy and lung resection IV cefazolin single dose vs 48 hours	SSI: none in single dose group vs 2 in 48-hour group (95% CI: -0.008 to 0.048) Chest infection: 8 in each group Empyema: 3 in each group	Likely underpowered study	1^-	
[24]	RCT (France)	303 patients	Lung resection IV cefuroxime peri-operative vs 48 hours	Infection rate (SSI, pneumonia, bronchopneumonia, empyema): 65% in short duration vs 46% in long duration (p=0.005) Empyema: 6% in short duration vs 1% in long duration (p=0.03)	Infection rate higher compared to other published studies Potential bias identified, e.g. some patients in short duration group, who developed empyema, also had broncho-pleural fistula, suggesting the outcome was	1^-	

					likely related to surgical technique rather than antibiotic duration	
25	RCT (Spain)	127 patients	Thoracic surgery IV cefazolin 1g once vs placebo	SSI: 1.5% in cefazolin vs 14% in placebo group (p<0.01) Post-operative empyema: no difference	No sample size calculation, likely an underpowered study. Study did not compare the difference in prophylaxis duration. This study supports single dose prophylaxis	1^-
26	RCT (Turkey)	102 patients	Elective thoracotomy IV cefuroxime vs cefepime for 24 hours	Infection rate (pneumonia, bronchopneumonia, empyema): 14.0% in cefuroxime vs 26.7% in cefepime group (p=0.12)	Study compared the difference in antibiotic agent and not the difference in prophylaxis duration. This study supports 24-hour duration of prophylaxis	1^-
27	Prospective cohort study (Germany)	60 patients	Lobectomy and segmentectomy IV ampicillin-sulbactam single dose vs 24 hours	SSI: 3 in single dose group vs 2 in 24-hour group (no p-value reported) Empyema: none Bronchitis/pneumonia: 10 in single dose group vs 7 in 24-hour group (no p-value reported)	Likely underpowered study	1^-
28	Prospective cohort study (France)	445 patients	Thoracotomy (lobectomy or pneumectomy for non-infectious disease) Cefamandole x 48 hours during phase 1 of study vs amoxicillin-clavulanic acid x 16 hours post-operative during phase 2 of study	Post-operative pneumonia: 45% reduction with amoxicillin-clavulanic acid (p=0.0027)	Potential confounders: type of antibiotic use, difference in time period. Study appears to support duration <24 hours	2^-
29	Prospective cohort study (Italy)	346 patients	Video-assisted thoracoscopic surgery (wedge resection, pleural biopsy or biopsy of mediastinal mass) At least 90% of the patients received single dose prophylaxis	SSI: 1.7% (low)	No comparison on duration of prophylaxis but majority received single dose and overall infection rate was low	2^-

30	Retrospective cohort study (Japan)	1,855 patients	Surgical lung cancer resection No intervention but studied the effect of change in antibiotic prophylaxis from physician's choice to cefazolin 1g before and after surgery	Change in antibiotic prophylaxis did not change post-operative pneumonia incidence	Study appears to support single dose before and after surgery	2^-
31	Retrospective cohort study (Japan)	477 patients	Radical lobectomy for lung cancer IV cefazolin 1g before surgery then 1g q12h x 72 hours vs no further doses post-operatively	Short duration antibiotic was associated with post-operative pneumonia (OR 6.82, $p<0.001$)	No sample size calculation. Multiple confounders present despite propensity matching done (e.g. long duration prophylaxis group had shorter surgery time)	2^-
					FINAL GRADE	**B**

Vascular Procedures

Guidelines

Table A9: Guideline references for surgical prophylaxis recommendations

Reference	Type of Surgery	First line	Alternative for Severe Penicillin Allergy	Duration	Remarks	Level of Evidence/Grade
ASHP, IDSA, SIS, and SHEA[2]	Vascular	IV cefazolin	IV clindamycin or IV vancomycin ± gram-negative cover (aztreonam, aminoglycoside, fluoroquinolone) if procedure involves abdominal aorta/groin incision to cover GI flora	≤ 24 hours		A
SAAGAR[13]	Vascular	IV cefazolin 2g	IV vancomycin 1g (1.5g if weight >80kg)	Single dose to 24 hours		No grading of evidence provided
SIR, CIRSE, CAIR [32]	Arterial endografts	IV cefazolin 1-2g	IV vancomycin	Single dose		Class IIb, Level B (SAP not recommended) non-randomised study
ESVS[33]	Vascular access creation	Antibiotic with *S. aureus* coverage (e.g. cephalosporin)	No recommendation	Single dose		Class I, Level A

***SAAGAR**: South Australian expert Advisory Group on Antimicrobial Resistance**; SIR:** Society of Interventional Radiology; **CIRSE**: Cardiovascular and Interventional Radiological Society of Europe; **CAIR**: Canadian Association for Interventional Radiology; **ESVS**: European Society for Vascular Surgery; **GI:** gastrointestinal

Literature

Table A10: Literature review of references

Reference	Study Design/Country	Sample Size	Population and Intervention	Outcome	Limitations/Remarks	Level of Evidence	Final Grade
34	Meta-analysis (Sweden, Australia, United Kingdom)	342 patients	Lower limb reconstruction, open arterial surgery amoxicillin-clavulanic acid or ticarcillin-clavulanic acid or cefuroxime	SSIs: prophylaxis >24 hours did not reduce SSI rate (RR 1.28, 95% CI: 0.82-1.98)	Heterogeneity across studies e.g. variability in antibiotic regimens used; some studies included patients with pre-existing cellulitis, wet gangrene or recent antibiotic therapy	1^-	
35	RCT (North America)	408 patients	Arteriovenous graft creation Single dose IV vancomycin	Graft infection: 2 patients (1%) in vancomycin vs 12 (6%) in no prophylaxis group (p=0.006)	Study did not compare duration of prophylaxis. Supports single dose pre-operative prophylaxis	1^-	
36	RCT (North America)	710 patients	Aortic or infrainguinal arterial procedures IV cefamandole for 24 hours vs IV cefazolin for 24 hours	SSIs: no difference	Study did not compare duration of prophylaxis. Supports 24 hours prophylaxis	1^-	
37	RCT (North America)	559 patients	Aortic and lower extremity peripheral vascular surgery IV cefuroxime for 24 hours vs IV cefazolin for 24 hours	SSIs: no difference	Study did not compare duration of prophylaxis. Supports 24 hours prophylaxis	1^-	
38	RCT (Sweden)	211 patients	Peripheral vascular surgery (vascular reconstructive surgery of lower limbs, acute femoral embolectomy or thrombectomy) No prophylaxis vs IV cefuroxime for 24 hours vs IV cefuroxime for 3 days	SSIs: 16.7% in placebo vs 3.8% in 24 hours (p<0.05 vs placebo) cefuroxime vs 4.3% in 3 days cefuroxime (p<0.05 vs placebo) Graft infection: no difference; overall rate is low (n=1, 1% - occurred in placebo group)	Included in meta-analysis above (reference 67) No sample size calculation was provided. Likely underpowered study. 24-hour duration is sufficient for prophylaxis	1^-	

39	RCT (Australia)	302 patients	Vascular surgery IV ticarcillin-clavulanic acid single dose vs multiple doses (maximum 5 days; average 14.3 doses)	SSIs: 18% in single dose vs 10% in multiple-dose (RR 2.00, 95% CI-1.02 to 3.92)	Ticarcillin-clavulanic acid is not a routine antibiotic prophylaxis agent. Its short half-life likely contributed to poorer outcomes in single dose group	1^-
40	Retrospective cohort study (North America)	304 patients	Arteriovenous fistula or graft creation Single dose pre-operative cefazolin or vancomycin vs none	SSIs: no difference Overall SSI rate is low (n=2, 0.68%)	Likely underpowered study. Antibiotic group had more patients with diabetes mellitus Suggests antibiotic prophylaxis may not be necessary	2^-
					FINAL GRADE	**B**

Angioplasty or Stent Insertion

Guidelines

Table A11: Guideline references for surgical prophylaxis recommendations

Reference	Type of Surgery	First line	Alternative for Severe Penicillin Allergy	Duration	Remarks	Level of Evidence/Grade
ASHP, IDSA, SIS, SHEA[2]	Angioplasty or stent insertion	No recommendation. If prophylaxis desired, use the same prophylaxis as vascular procedures				A
SAAGAR[13]	Angioplasty or stent insertion	Prophylaxis not recommended				No grading of evidence provided
SIR, CIRSE, CAIR[32]	Angioplasty or stent insertion	Prophylaxis usually not recommended				Class III, Level B-non-randomised study for angioplasty, Class III, Level C-limited data for stent insertion

***SAAGAR**: South Australian expert Advisory Group on Antimicrobial Resistance; **SIR:** Society of Interventional Radiology; **CIRSE**: Cardiovascular and Interventional Radiological Society of Europe; **CAIR**: Canadian Association for Interventional Radiology

Literature

Table A12: Literature review of references

Reference	Study Design/Country	Sample Size	Population and Intervention	Outcome	Limitations/Remarks	Level of Evidence	Final Grade
41	Case control study (North America)	3,473 patients 4,217 procedures	PTCA No intervention as this is observational study	27 out of 4,217 PTCA (0.64%) had bacteraemia post-procedure	No analysis on role of prophylactic antibiotics. Since incidence of post-procedure bacteraemia is low, antibiotic prophylaxis may not be necessary	3	
42	Case control study (Spain)	22,006 patients	Invasive non-surgical cardiologic procedures, PTCA, cardiac catheterisation, electrophysiologic studies No intervention as this was an observational study	68 out of 22,006 patients (0.3%) had bacteraemia post-procedure	No analysis on the role of prophylactic antibiotics was done Since incidence of post-procedure bacteraemia is low, antibiotic prophylaxis may not be necessary	3	
43	Case report and systematic review (Netherlands)	77 patients with stent infection	Non-coronary and coronary bare metal stent placement No intervention as this was an observational study (13% received antibiotic prophylaxis, 40% no prophylaxis, 47% unknown)	Identified possible risk factors that may require prophylaxis; however, this study was unable to analyse the role of prophylactic antibiotics	No analysis on the role of prophylactic antibiotics was done	4	
44	Case report and systematic review (North America)	35 patients with stent infection	Non-coronary and coronary bare metal stent placement No intervention as this was an observational study (1 received antibiotic prophylaxis, 12 no prophylaxis, 22 unknown)	Identified possible risk factors for stent infection. However, this study was unable to analyse the role of prophylactic antibiotics	No analysis on the role of prophylactic antibiotics was done	4	
						FINAL GRADE	**D**

*__PTCA__: Percutaneous Transluminal Coronary Angioplasty

GASTROINTESTINAL PROCEDURES

Guidelines

Table A13: Guideline references for surgical prophylaxis recommendations

Reference	Type of Surgery	First line	Alternative for Severe Penicillin Allergy	Duration	Remarks	Level of Evidence/ Grade
ASHP, IDSA, SIS, and SHEA[2]	Appendectomy	Cephalosporin with anaerobic activity (cefoxitin or cefotetan) or First-generation cephalosporin (cefazolin) plus metronidazole	Clindamycin plus gentamicin, aztreonam, or fluoroquinolone or Metronidazole plus gentamicin or fluoroquinolone (ciprofloxacin or levofloxacin)	Single dose	Referenced Mui et al[45] and a cohort study	-
ASHP, IDSA, SIS, and SHEA[2]	Gastroduodenal and oesophageal	Cefazolin	Clindamycin or vancomycin plus gentamicin, aztreonam, or fluoroquinolone	Single dose	Referenced Bates et al[46], Mohri et al[47]	-
ASHP, IDSA, SIS, and SHEA[2]	Small bowel	Cephalosporin with anaerobic activity (cefoxitin or cefotetan) or First-generation cephalosporin (cefazolin) plus metronidazole	Clindamycin plus gentamicin, aztreonam, or fluoroquinolone or Metronidazole plus gentamicin or fluoroquinolone (ciprofloxacin or levofloxacin)	No post-operative dosing	Based on inferring effectiveness from other clean-contaminated procedures. No specific RCTs for small bowel surgery	-
ASHP, IDSA, SIS, and SHEA[2]	Colorectal	Second-generation cephalosporin with both aerobic and anaerobic activities (cefoxitin or cefotetan) or	Clindamycin plus aminoglycoside, aztreonam, or fluoroquinolone or Metronidazole plus aminoglycoside or fluoroquinolone	Single dose		-

		Cefazolin plus metronidazole				
ASHP, IDSA, SIS, and SHEA[2]	Hernioplasty Herniorrhaphy	First-generation cephalosporin	Clindamycin or Vancomycin	Single dose	Based on Yin et al[48] and 2012 version of Orelio et al[49]	-
CDC[50]	Clean and clean-contaminated	-	-	No additional prophylactic antimicrobial agent doses after the surgical incision is closed (1A – strong recommendation; high-quality evidence) 21 RCTs, n=14,285. Cardiac, thoracic, vascular, ear, nose and throat, gynaecologic, orthopaedic, and general surgical procedures. No benefit of continuing antimicrobial prophylaxis after the wound is closed in the operating room: OR: 1.19 (0.94-1.50); I^2=25%	Risk of Bias of the RCTs: High (7), moderate (9), low (5). No point deducted in GRADE table for study quality because <50% of studies were rated as high risk	Category IA – strong recommendation; high-quality evidence
ERAS Society[51]	Elective colorectal surgery	IV cephalosporin in combination with metronidazole	-	Single dose	Referenced Nelson et al[52]	Strong recommendation, high-quality of evidence
SAAGAR[13]	Gastroduodenal and oesophageal	Cefazolin High risk of MRSA: add vancomycin	Gentamicin plus vancomycin	Single dose	No primary literature	-
SAAGAR[13]	Herniorrhaphy	Not recommended	Not recommended	NA	No primary literature. References quoted are ASHP[2], Berríos-Torres et al[50] and Therapeutic Guidelines[53]	-

***ERAS**: Enhanced Recovery After Surgery; **SAAGAR**: South Australian expert Advisory Group on Antimicrobial Resistance

Literature

Table A14: Literature review of references

Reference	Study Design/Country	Sample Size	Population and Intervention	Outcome	Limitations / Remarks	Level of Evidence	Final Grade
50	Meta-analysis of RCTs (International)	14,285	Cardiac, thoracic, vascular, ear, nose and throat, gynaecologic, orthopaedic, and general surgical procedures No post-operative antibiotics vs ≤24 hours	SSI: OR 1.19 (0.94-1.50); I^2=25%	No benefit of continuing antimicrobial prophylaxis after the wound is closed in the operating room Risk of Bias of the RCTs: High (7), moderate (9), low (5). No point deducted in GRADE table for study quality because <50% of studies rated as high risk	High quality (as per guideline grading system)	Category IA – strong recommendation (as per guideline grading system)
45	RCT (Hong Kong)	269	Acute appendicitis undergoing open appendectomy Single pre-operative dose vs three doses (pre-operative dose plus two additional doses) *or* 5-day course	*Three doses* SSI: OR 1.01; 95% CI 0.34-3.26 *5-day course* SSI: OR 0.89; 95% CI 0.46-7.79	May be underpowered - target 88 per group; 5-day group had 83 Risk of bias: Selection (moderate: sealed envelopes but how assigned not described), Performance (low), Detection (moderate/high: blinding of assessors not described), Attrition (low), Reporting (low)	1+	A
46	RCT (United Kingdom)	900	At-risk abdominal surgery which included all appendicectomies, laparotomy for intestinal obstruction, and all open gastric, oesophageal, colonic or biliary surgery Single dose (on induction) vs three doses (on induction plus two additional doses)	Wound infection: 10.7% vs 10.9% (95% CI -4.25% - 3.9%) 30-day mortality (septic or sepsis-related): 3.1% vs 1.6%; 95% CI -0.4% - 3% (more elderly patients, more emergency operations)	Met the target number for each group but the outcome measure was not clearly defined Only 114/900 in upper GI 16/449 in single dose and 7/451 in 3-dose received more doses than protocol. Deep sepsis & patients requiring interval antibiotics seemed like important outcomes, but was not elaborated on. Authors only reported as having no difference	1+	B

					Risk of bias: Selection (low), Performance (low), Detection (high: a component of patient-reported outcome), Attrition (low), Reporting (high) Extrapolation was done as majority of the studies were not for gastroduodenal surgeries		
47	RCT (Japan)	486	Elective gastric cancer surgery Single- vs multiple-dose	SSI: 9.5% vs 8.6%; difference 0.9; 95%CI -4.3% - 5.9% (met non-inferiority target of -7%)	A total of 4 were lost to follow-up Risk of bias: Selection (low), Performance (moderate: participants unblinded after randomisation but assessors are), Detection (low), Attrition (low), Reporting (low)	1+	A
54	RCT (Japan)	325	Elective gastric cancer surgery Single- vs multiple-dose	SSI: 9.1% vs 6.2%; difference -2.9; 95%CI -5.9% - 0.0% (met non-inferiority target of -8%)	Met target sample size Risk of bias: Selection (low), Performance (moderate: unclear if personnel are blinded), Detection (moderate: unclear if assessors are blinded), Attrition (low), Reporting (low)	1+	A
52	Meta-analysis of RCTs (International)	2005	Elective and emergency colorectal surgery. Single pre-operative vs multiple doses	SSI: RR 1.21; 95% CI 0.82-1.80	-	1++	A
55	Network meta-analysis of RCTs (International)	3562	Elective colorectal surgery. MBP + oral antibiotics vs MBP	SSI: OR 0.71; 95% equal-tail credible interval 0.57-0.88	Varied regimens of MBP and antibiotics were used among these studies, and may have contributed to lower consistency of the results reported Extrapolated evidence based on regimen of majority of studies	1++	B

48	Meta-analysis of RCTs (International)	3318	Open inguinal hernia repair; mesh repair Antibiotic prophylaxis vs no antibiotics or placebo	SSI: OR 0.61; 95% CI 0.40-0.92; I^2=0%	Based on abstracted data but not individual patient data n=9 studies. All had reporting bias as per authors Extrapolated as studies did not compare single vs multiple doses	1-	B
49	Meta-analysis of RCT (International)	6443	*Hernioplasty* Open elective inguinal or femoral hernia repair; mesh-type based Antibiotic prophylaxis vs no antibiotics or placebo	SSI: RR 0.61; 95% CI 0.48-0.78	RCTs judged to be of low to moderate quality (GRADE level) Extrapolated as studies did not compare single vs multiple doses All RCTs used single doses	1++	B
		1865	*Herniorrhaphy* Open elective inguinal or femoral hernia repair; suture-based Antibiotic prophylaxis vs no antibiotics or placebo	SSI: RR 0.86; 95% CI 0.56-1.33	RCTs judged to be of very low quality (GRADE level)	1++	A
56	RCT (Isreal)	35	Umbilical (n=19) and incisional (n=16) hernia repair Antibiotic prophylaxis (single dose given pre-operatively) vs no antibiotics	SSI: *Total* OR 0.08; 95% CI 0.008-0.72 *Incisional* OR 0.06; 95% CI 0-1.36 *Umbilical* OR 0.19; 95% CI 0.02-2.14	Only 23% (n=8) repaired with mesh; 6 out of 8 received antibiotics; patients with mesh repair higher in prophylaxis group SSI rate for mesh repair group not reported separately Risk of bias: Selection (high: lack of proper randomisation - "assigned alternatively"), Performance (high: not blinded), Detection (high: not blinded), Attrition (low), Reporting (low)	1-	B
57	Retrospective pre-post intervention study (USA)	65	Laparoscopic ventral hernia repair; mesh repair	Seroma formation: 30% (6/20) vs 33% (15/45) (p=0.74)	Single centre Limited description of baseline demographics.	2-	C

	Single IV pre-operative dose (first 20 patients) vs single IV pre-operative plus additional 7 days PO antibiotic (next 45 patients)	Seroma-related cellulitis: 100% (6/6) vs 40% (6/15) (*p*=0.001) Mesh infection: 33% (2/6) vs 0% (0/6) (*p*=0.54)	Outcome measure very specific to seroma-related complications. Mesh infection rates not significant.

***GI**: Gastrointestinal

Biliary Tract Surgery

Guidelines

Table A15: Guideline references for surgical prophylaxis recommendations

Guideline	Procedure	First line	Alternative	Duration	Level of Evidence/Grade
ASHP, IDSA, SIS, and SHEA[2]	Biliary tract (open)	Cefazolin, cefoxitin, cefotetan, ceftriaxone, ampicillin-sulbactam	Clindamycin or vancomycin + aminoglycoside or aztreonam or fluoroquinolone Metronidazole + aminoglycoside or fluoroquinolone	Single dose	NA
	Biliary tract (lap, low risk)	None	None	NA	A
	Biliary tract (lap, high risk)*	Cefazolin, cefoxitin, cefotetan, ceftriaxone, ampicillin-sulbactam	Clindamycin or vancomycin + aminoglycoside or aztreonam or fluoroquinolone Metronidazole + aminoglycoside or fluoroquinolone	Single dose	NA

*Risk factors include performance of emergency procedures, diabetes mellitus, anticipated procedure duration exceeding 120 minutes, risk of intra-operative gallbladder rupture, age of >70 years, open cholecystectomy, risk of conversion of laparoscopic to open cholecystectomy, American Society of Anesthesiologists (ASA) classification of ≥3, episode of biliary colic within 30 days before the procedure, re-intervention in less than a month for noninfectious complications of prior biliary operation, acute cholecystitis, jaundice, pregnancy, and immunosuppression. Because some of these risk factors cannot be determined before the surgical intervention, it may be reasonable to give a single dose of antimicrobial prophylaxis to all patients undergoing laparoscopic cholecystectomy.

Literature

Table A16: Literature review of references

Reference	Study Design/Country	Sample Size	Population and Intervention	Outcome	Limitations / Remarks	Level of Evidence	Overall grade
58	Randomised, controlled, double-blind multi-centre (Netherlands)	1004	High-risk biliary tract surgery Single vs multiple doses of cefuroxime	Post-operative wound infection no difference. NS		1+	
59	Prospective, double blind (USA)	81	High risk biliary surgery	Wound infection: none in both groups	Included patients with recent cholecystitis,	1-	

			Ceftriaxone one dose vs Cefazolin pre-operative and 3 post-operative dose		common duct stones, duct obstructions and age >70 years (high risk group)		
60	Prospective, double-blind, randomised, placebo-controlled (United Kingdom)	295	Elective cholecystectomy (high risk) Single 1.5g cefuroxime or total 4 doses cefazolin	Bacteriologic success 95.5% (cefuroxime) vs 98.2% (cefazolin). NS. Clinical success: 91.4% vs 94.9%, NS		1+	
61	Systematic review (RCTs)	4 RCTs (n=953)	Acute calculous cholecystitis undergoing emergency cholecystectomy Comparing extended post-operative vs no post-operative antibiotics	Post-operative infectious complications OR 0.94, *p*=0.79. SSI OR 1.13, *p*=0.72; post-operative morbidity OR 0.93, *p*=0.7	Comparable baseline characteristics	1+	
					FINAL GRADE	**1+**	**A**

*__NS__: Non-significant

Hepatectomy

Note: Meta-analysis suggests no antibiotic for minor hepatectomy. For hepatectomy involving biliary or intestinal manipulation, two studies below showed no difference in outcomes comparing 2 days vs longer duration. Antibiotic prophylaxis of up to 24 hours is recommended in this guideline.

Table A17: Literature review of references

Reference	Study Design/Country	Sample Size	Population and Intervention	Outcome	Limitations / Remarks	Level of Evidence	Overall grade
113	Network meta-analysis (countries in Asia) Hirokawa 2013 Sugawara 2016 Togo 2007 Wu 1998 Zhou 2015	5 RCTs (n=701)	Hepatectomy Comparing pre-operative, post-operative (≤ 2 days), post-operative (> 2 days) antibiotics	No antibiotic has the highest possibility of best clinical effects on SSI; remote-site and global infection. Pair-wise meta-analysis showed that additional or long-duration applications had no clinical benefits	Supports no antibiotics	1+	
62	Prospective, randomised (Japan)	180	Hepatectomy without reconstruction of biliary or intestinal tract Flomoxef: 2 days vs 5 days	Infection: 7.9% (2-day) vs 6.6% (5-day). NS	Author noted that if systemic inflammatory response syndrome (SIRS) was positive on post-operative day 2, it	1-	

					may be safer to continue antibiotics		
63	Prospective, randomised (Japan)	86	Complicated major hepatectomy with extrahepatic bile duct resection 2 days vs 4 days antibiotic (antibiotic choice based on pre-operative cultures)	Infectious complications: 30.2% (2-day) vs 32.6% (4 day)	Similar baseline and microbiological characteristics between groups	1-	
64	Prospective, randomised, placebo-controlled (China)	120	Elective hepatectomy Cefuroxime IV or placebo single dose pre-operative	Post-operative infection: 23.3% (single dose) vs 20% (placebo), *p*=0.658. SSI: 13.3% vs 15%, NS. Remote site infection NS	Supports no antibiotics	1-	
65	Prospective, randomised, controlled trial (Japan)	241	Liver resection Flomoxef No post-operative antibiotic vs 3-day course of antibiotics	Infections 21.3% vs 25.5% *p*=0.606. Systemic inflammatory response syndrome (SIRS) 11.7% vs 17% *p*=0.406. Infectious complications 7.5% vs 17%, *p*=0.073. SSI 10.6% vs 13.8% *p*=0.657, remote site infection 2.1% vs 8.5% *p*=0.1	Excluded patients with multiple co-morbidities Supports single dose	1+	
					FINAL GRADE	**1+**	**A**

*__NS__: Non-significant

Whipple's Procedure (Pancreaticoduodenectomy)

Guideline

Table A18: Guideline references for surgical prophylaxis recommendations

Guideline	Procedure	First line	Alternative	Duration	Level of Evidence/ Grade
ASHP, IDSA, SIS, and SHEA[2]	Pancreaticoduodenectomy	Cefazolin	Clindamycin or vancomycin + aminoglycoside or aztreonam or fluoroquinolone	Single dose	NA

Literature

Table A19: Literature review of references

Reference	Study Design/Country	Sample Size	Population and Intervention	Outcome	Limitations / Remarks	Level of Evidence	Overall grade
66	Prospective cohort review (Japan)	254	Pancreaticoduodenectomy Non-PBD vs internal-PBD vs external-PBD Antibiotics peri-operative and 2-3 days. Cefazolin for non-PBD; cefozopran (internal-PBD); depends on pre-micro culture (external-PBD)	Overall morbidity and abdominal infection (13%, 17%, 14%) complication and wound infection (2%, 1%, 2%) similar and did not reach statistical significance	Only susceptibility to peri-operative antibiotic of biliary organism classified as resistant was significant independent risk factor for abdominal infectious complications	2+	C
67	Retrospective cohort study (France)	175	Pancreaticoduodenectomy in patients with periampullary malignancy (excluded patients with percutaneous transhepatic biliary drainage) Cefoxitin for low risk group; Piperacillin-tazobactam and gentamicin for high risk group Duration: if culture-negative, stopped on POD2. If culture- positive, continued until POD5	Infection complication was higher in low risk group (46.1%) vs high risk group (29.3%), p=0.018. No difference in SSI, infection complication mainly driven by pneumonia, bacteraemia and UTI	The authors proposed 5-day course of antibiotics in high-risk patients	2+	
68	Retrospective review (USA)	122	Pancreaticoduodenectomy Propensity score matching comparing 72 hours vs 24 hours	SSI: 2.7% (72 hours) vs 16% (24 hours), p=0.04		2+	
69	Controlled before and after study (France)	122	Pancreaticoduodenectomy Cefazolin single dose vs piperacillin-tazobactam until bile culture available. If culture negative, antibiotic ceased. If culture positive, continue until POD5, streamline according to culture	Piperacillin-tazobactam group was associated with reduction in deep abdominal abscess (36% vs 10% p=0.008), respiratory tract infection (15% vs 3% p=0.02), bacteraemia (41% vs 6%, p<0.001) and shorter LOS		2-	
70	Pre-post intervention study (USA)	Pre (n=111) Post (n=216)	Pre: cefazolin Post: ceftriaxone and metronidazole Duration: Single dose up to 24 hours	Overall SSI was reduced from 26.4% to 14.8%, p=0.01. Organ/space SSI 15.3% vs 8.6%,		2-	

				p=0.03. Superficial and deep SSI: no difference *C. difficile* was seen to be higher in cefazolin group (8.1% vs 1.9%, statistically significant)			
[71]	Systematic review of the impact of intra-operative bacterobilia on patient outcome after pancreaticoduodenectomy	28 studies	Pancreatoduodenectomy	Pre-operative biliary drainage was significantly associated with bacterobilia (RR 3.27, 95%CI 2.4-4.4). SSIs significantly increased in cases with bacterobilia (RR 2.84, 95% CI 2.17-3.73). Post-operative fistula, morbidity and mortality were not significantly influenced			
					FINAL GRADE	**2+**	**C**

***PBD:** Percutaneous biliary drainage; **POD**: Post-operative day; **LOS:** Length of stay

Endoscopic Retrograde Cholangio-Pancreatography (ERCP)

Guideline

Table A20: Guideline references for surgical prophylaxis recommendations

Guideline	First line	Alternative	Duration	Remarks	Level of Evidence/ Grade
ASGE Standard of Practice Committee (2015)[72]	None If required: to cover enteric gram-negative, enterococci	None	NA	Prophylaxis is not required when obstructive biliary tract disease is not suspected or complete biliary drainage is expected Antibiotic prophylaxis is recommended for those who had liver transplantation; known or suspected biliary obstruction, possible incomplete biliary drainage	High quality evidence for the first group (further research is very unlikely to change the confidence in the estimate of effect) Moderate quality for the second group
ESGE Guidelines 2020[73]	None	None	NA	Recommends antibiotic prophylaxis in the case of anticipated incomplete biliary drainage, for severely immunocompromised, and when performing cholangioscopy	High quality (moderate quality evidence)

***ASGE**: American Society for Gastrointestinal Endoscopy; **ESGE**: European Society of Gastrointestinal Endoscopy

Literature

Table A21: Literature review of references

Reference	Study Design/Country	Sample Size	Population and Intervention	Outcome	Limitations / Remarks	Evidence Level	Overall grade
74	Meta-analysis	5 RCTs	ERCP	RR of antibiotic prophylaxis and bacteraemia was 0.39 (95% CI 0.12-1.29). RR for sepsis and cholangitis was 0.91 (95% CI 0.39-2.15)	Routine use cannot be recommended	1+	A
75	Cochrane Review until Mar 2010	9 RCTs (n=1573)	Elective ERCP without evidence of acute or chronic cholecystitis, or acute or chronic cholangitis or severe acute pancreatitis	Fixed-effect of the meta-analysis favored the use of antibiotic in preventing cholangitis (RR 0.54, 95% CI 0.33-0.91), septicemia (RR0.35, 0.11-1.11), bacteraemia (RR 0.5, 0.33-0.78), and pancreatitis (RR 0.54, 0.29-1.0) In random-effect analysis, only the effect on bacteraemia remained significant Overall mortality was not reduced (RR 1.33, 0.32-5.44)	Majority of trials had risk of bias Authors concluded that prophylactic antibiotic seems to prevent cholangitis and septicemia. In the subgroup of patients with uncomplicated ERCP, the effect of antibiotic less evident	1+	
76	Meta-analysis	7 trials (n=1389)	Patients undergoing ERCP	Post ERCP cholangitis: 5.8% vs 3.4% (antibiotic group), RR 0.58, 0.22-1.55, NS)	Antibiotics cannot significantly prevent ERCP induced cholangitis in unselected patients and should not be routinely recommended. More trials are required in those with incomplete biliary drainage	1+	
					FINAL GRADE	**1+**	**A**

***NS**: Non-significant

Caesarean Section

Guidelines

Table A22: Guideline references for surgical prophylaxis recommendations

Reference	Year	Type of Surgery	First line	Alternative for Severe Penicillin Allergy	Duration	Remarks	Level of Evidence/ Grade	Grading System
ASHP, IDSA, SIS, and SHEA[2]	2013 [Jan 1999 to Jun 2010]	C-section	IV Cefazolin 2g, 3g for pts weighing ≥120kg	IV clindamycin 900mg WITH IV aminoglycosides (gentamicin 5 mg/kg, single dose)	Single dose	The use of single-dose prophylaxis is supported by ACOG and AAP for procedures lasting less than 2 hours	A	**Agency for Healthcare Research and Quality, and ASHP, IDSA, SIS, and SHEA** **Category A (Levels I–III)** - Level I (evidence from large, well-conducted, randomised, controlled clinical trials or a meta-analysis) - Level II (evidence from small, well-conducted, randomised, controlled clinical trials) - Level III (evidence from well-conducted cohort studies) The strength of evidence represents only support for or against prophylaxis and does not apply to the antimicrobial agent, dose, or dosage regimen
ACOG[77]	2018 [Jan 1990 to Apr 2018]	C-section	First-generation cephalosporin, IV Cefazolin:	IV clindamycin 900mg WITH IV gentamicin 5mg/kg/dose	Single dose	For cesarean delivery prophylaxis, a single dose is recommended. A meta-analysis of 16 studies showed no difference in single-dose vs	A	**U.S. Preventive Services Task Force** Based on the highest level of evidence found in the data

			1g for <80kg, 2g if 80- 120kg, 3g if ≥120kg			multi-dose therapy for uncomplicated cesarean deliveries (Pinto-Lopes et al[78]) Addition of IV azithromycin to a standard antibiotic prophylaxis regimen may be considered for women undergoing a non-elective caesarean delivery (Tita et al[79]). No RCT to recommend this in electives		**Level A:** Recommendations are based on good and consistent scientific evidence
						For women with a history of a significant penicillin or cephalosporin allergy (anaphylaxis, angioedema, respiratory distress, or urticaria), a single-dose combination of clindamycin with an aminoglycoside is a reasonable alternative though limited data to support this. No references quoted	B	**Level B:** The following recommendations are based on limited or inconsistent scientific evidence
NICE[80]	2011 (Updated 2019)	C-section	NA	NA	Single dose, before skin incision	Offer women prophylactic antibiotics at C-section to reduce the risk of post-operative infections. Choose antibiotics effective against endometritis, urinary tract and wound infections, which occur in about 8% of women who have had a C-section. Avoid the use amoxicillin-clavulanic acid	No grading	NA
ANZOG[81]	2012	C-section	IV cefazolin 1g for <80kg, 2g if ≥80kg	IV clindamycin 600mg	Single dose	Studies showed that single-dose antibiotic prophylaxis was as effective as multiple doses of antibiotic. Referenced only this RCT by McGregor et	I	**NHMRC Levels of Evidence** Level I: A systematic review of level II studies

						al[82], and a systematic review (Tita et al[83]) of antibiotic prophylaxis timing at cesarean delivery		(Level II: A RCT)
SOGC[84]	2010 [Jan 1978 to Jun 2009]	C-section	First-generation cephalosporin	IV clindamycin 600mg or IV erythromycin 500mg	Single dose, 15 – 60 minutes prior to skin incision	References did not compare single vs multiple doses of antibiotics, mainly need for and timing of antibiotic (Chelmow et al[85], Costantine et al[86]). RCT showing superiority of cefazolin prior skin incision vs at cord clamping for preventing post C-section infectious morbidity (Sullivan et al[87])	I-A	**Canadian Task Force on Preventive Health Care** **Level I:** Evidence obtained from at least one RCT **Class A:** Opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees
						Additional dose may be considered if blood loss exceeds 1500ml or at 4 hours if the procedure lasts more than 4 hours (i.e. up to 2 half-lives of the drug) Gordon[88] - review on antibiotic prophylaxis	III-L	**Level III:** Opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees **Class L:** There is insufficient evidence (in quantity or quality) to make a recommendation; however, other factors may influence decision-making

*__ACOG__: American College of Obstetricians and Gynecologists; **AAP**: American Academy of Pediatrics; **ANZOG**: Royal Australian and New Zealand College of Obstetricians and Gynaecologists; **NHMRC**: National Health and Medical Research Council; **SOGC**: Society of Obstetricians and Gynaecologists of Canada

Literature

Table A23: Literature review of references

Reference	Study Design/ Country	Sample Size	Population and Intervention	Outcome	Limitations/ Remarks	Level of Evidence	Final Grade

78	Systematic review (Multiple countries)	2695 (16 RCTs, of which 3 are quasi-RCTs)	C-section, both elective and emergency Intervention: Multiple doses antibiotics (varied dosing regimens) Comparator: Single dose antibiotics (varied regimens)	Composite post-partum infectious morbidity (endometritis, wound infection, UTI and other causes of febrile morbidity of probably infectious origin): RR 0.95 (95% CI: 0.75 – 1.20) Urinary tract infection: RR 0.65 (95% CI: 0.34 – 1.24)	Quality of evidence is rated as very low, with low to unclear risk of bias. A trend towards a decreased risk of UTI was noted when using a multiple doses regimen but was not significant	1-	B
89	Systematic review (Multiple countries)	15000 (95 RCTs, quasi-RCTs)	C-section, both elective and emergency Intervention: Antibiotics (varied dosing regimen) Comparator: None Duration: Varied (ranges from single dose to 7 days)	Wound infection: RR 0.40 (95% CI: 0.35 – 0.46) for all, RR: 0.62 (95% CI: 0.47 – 0.82) for elective C-section Endometritis: RR 0.38 (95% CI: 0.34 – 0.42) for all, RR: 0.38 (95% CI: 0.24 – 0.61) for elective C-section Serious infectious complications: RR 0.31 (95% CI: 0.20 – 0.49) for all, RR: 1.01 (95% I: 0.04 to 24.21) for elective C-section	Varied antibiotic regimens, made no mention about the duration of antibiotic prophylaxis and impact on outcomes. Included studies dating back to 1980s, with high rates of endometritis, which may no longer be representative of the current surgical technique of C-section	1-	B
90	RCT (USA)	403	Obese women (BMI ≥30) underwent C-section Intervention: IV cefazolin 2g prior to surgical incision, then (PO cephalexin 500mg TDS PLUS PO metronidazole 500mg TDS) x 48 hours Comparator: cefazolin 2g prior to surgical incision	SSI: RR 0.41 (95% CI: 0.22 - 0.77); 6.4% (Intervention) vs 15.4 % (Comparator), (difference, 9.0%, 95% CI: 2.9 – 15.0%)	Baseline rate of infection was high at 15.4% (with single dose IV cefazolin). NNT to prevent 1 SSI in all obese women undergoing C-section was 12 (95% CI: 6.7 – 33.8) Included as this explains the rationale for remark: “Continuation of antimicrobial prophylaxis for patients with major risk factors for surgical infections, e.g. obesity (BMI≥30) may be considered”	1+	A
91	RCT (Austria)	1112	Elective C-section Intervention: IV cefazolin 2g prior to surgical incision	Post-operative infection (wound infection, endometritis, UTI): 4.9% (Intervention), vs 3.8% (Comparator 1) vs, 12.1% (Comparator 2),	Baseline rates of post-operative infection relatively high at 12.1% (without antibiotic prophylaxis). Balanced demographics across all 3 arms – age, BMI (approximate mean	1+	B

			Comparator: (1) IV cefazolin 2g after cord clamping (2) Placebo (sodium chloride 0.9%) prior to surgical incision	*p*<0.05 Antibiotic prophylaxis: OR 0.31 (95% CI: 0.19 – 0.50)	of 28), gestational diabetes mellitus (approximately 9-10%), and use of immunosuppression. Does not compare the use of single vs multiple doses of antibiotic prophylaxis, but supports evidence for antibiotic prophylaxis (as a single dose) in a high baseline post-operative infection risk setting		
92	Randomised controlled, non-inferiority trial (Africa)	176	C-section (elective and emergency) Intervention: Single dose of IV ampicillin 1g AND IV metronidazole 500mg Comparator: Day 1: IV ampicillin 1g AND IV metronidazole 500mg, followed by IV ampicillin 500mg and IV metronidazole 500mg for 2 more doses (8 hours apart) Day 2-5: PO amoxicillin 500mg TDS with PO metronidazole 400mg TDS	Wound infection: 6.7% (Intervention) vs 10.3% (Comparator), difference 3.60; 95% CI: -4.65 – 11.85)	Reported length of hospital stay at 7 days is long (LOS for elective C-section locally is shorter at 2 – 3 days). Only 1 is an elective procedure, the rest are emergency C-section; high percentage in intervention group had ruptured membranes before C-section – 70.8% vs 59.8%. Dose of IV ampicillin used lower than usual (vs those used for maternal Group B Streptococcus (GBS) prophylaxis), body weight of population studied generally lean at 50 – 60kg, compared with the local (Singapore) population	1+	B
93	Quai-randomised trial (Pakistan)	100	Elective C-section Intervention: IV cefotaxime 1g pre-operation Comparator: 3 doses IV cefotaxime 1g, given 12 hours apart, followed by PO cefuroxime for 5 days	Febrile morbidity (wound hematoma, superficial wound infection, deep wound infection, chest infection, UTI): 20.0% (Intervention) vs 20.0% (Comparator), OR 1.0	High rate of febrile morbidity at 20% even with antibiotics, reported length of hospital stay at 6 days is long (LOS for elective C-section locally is shorter at 2 – 3 days)	2+	C
94	Quai-randomised trial (Nepal)	100	Elective C-section Intervention: Single dose of IV cefazolin AND IV metronidazole Comparator: IV cefazolin AND IV metronidazole for 7 days	Febrile morbidity: 4.0% (Intervention) vs 6.0% (Comparator), *p*=1.00	Similar BMI between both groups (approximate mean of 27 - 28). 22% in intervention arm, vs 34% in comparator arm are obese (BMI >30) but did not develop post-operative wound infection. Definition of febrile morbidity was	2+	C

					not clearly defined, and there was no mention of antibiotic doses given		
95	Quasi-randomised trial (Sri Lanka)	369	C-section (both elective and emergency) Intervention: Single dose of IV cefuroxime 1.5g and IV metronidazole 500mg after cord clamping Comparator: IV cefuroxime 750mg q8h and IV metronidazole q8h for up to 24 hours, then PO cefuroxime 750mg q8h AND PO metronidazole 400mg q8h for 7 days	Post-operative infection (fever, wound infection, endometritis, UTI or serious infection such as bacteraemia, septic shock, septic thrombophlebitis, necrotising fasciitis and death): 1.8% (Intervention) vs 3.2% (Comparator), rate ratio 0.3 [95% CI 0.065-1.63) p =0.284]. NS: febrile morbidity (p=0.28), wound infections (p=0.123), perinatal outcome (p>0.05) and median duration of hospital stay (p=0.329) in both arms	Non-blinded trial 1/3 were emergency C-section, generally similar baseline demographics. Median LOS at 3 – 4 days, similar to the local (Singapore) context	1-	B
96	Quasi-randomised trial (Palestine)	313	C-section Intervention: Single pre-operative dose IV cefazolin 1g Comparator: multiple post-operative doses of antibiotics (1g cefazolin, gentamicin 80mg, metronidazole 500mg TDS till discharge)	Readmission due to wound infection: 2% (Intervention) vs 1% (Comparator), p=0.375 Nil endometritis, UTI, or febrile morbidities in both groups	Non-blinded trial. Attempted randomisation by "manual-blocks formation based on the rolling of a die". Mean LOS was 39.62 hours (I) AND 40.48 hours. Well-conducted case control/ cohort study with low risk of bias	2+	C
97	Quasi-randomised trial (Africa)	500	Emergency C-section Intervention: Single pre-operative dose IV gentamicin 3mg/kg AND metronidazole 500mg Comparator: IV gentamicin 3mg/kg AND metronidazole 500mg q8h for 24 hours	SSI: 4.8% (Intervention) vs 6.4% (Comparator), difference 1.6% (95% CI -2.4 – 5.6%)	2/3 high BMI, approximately half: operation time >1 hour but NS difference in both groups. A higher proportion in multiple dose group had ruptured membranes	1+	B
					FINAL GRADE	**1-**	**B**

***LOS:** Length of stay; **NNT:** Number needed to treat; **NS**: Non-significant

Normal Vaginal Delivery

Guidelines

Table A24: Guideline references for surgical prophylaxis recommendations

Reference	Year	Type of Surgery	First line	Alternative for Severe Penicillin Allergy	Duration	Remarks	Level of Evidence/ Grade	Grading System
SOGC[84]	2010	Operative vaginal delivery	Not recommended	Not recommended	NA	NA Based on Liabsuetrakul et al. Cochrane 2014 (1 trial- Heitmann JA, Southern Medical Journal 1989); has been updated in 2020[98] (2 trials, added ANODE trial)	Level II-1C	Canadian Task Force on Preventative Health Care II-1: Evidence from well-designed controlled trials without randomisation C. The existing evidence is conflicting and does not allow a recommendation for or against the use of the clinical preventive action; however, other factors may influence decision-making
		Third or fourth-degree perineal lacerations	IV cefotetan 1g or IV cefoxitin 1g	NA	Single dose	NA Ref: Buppasiri et al. Cochrane 2005 (updated in 2014[99]), but quotes only 1 trial: Duggal M et al[100]	I-B	Canadian Task Force on Preventative Health Care I: Evidence obtained from at least one properly randomised controlled trial B. There is fair evidence to recommend the clinical preventive action
ACOG[101]	2020	Operative vaginal delivery	Not recommended	Not recommended	NA	Findings from ANODE trial may not be generalisable to USA. As 89% of women received an episiotomy, mostly mediolateral (routine in the UK), hence does not recommend routine prophylaxis before delivery. May consider antibiotics in the presence of third- or fourth-degree laceration	No grading (Level I, Knight et al[102])	U.S. Preventive Services Task Force Level I: Evidence obtained from at least one properly designed RCT

						(also based on Duggal et al[100])		
RCOG[103]	2020	Assisted vaginal delivery	IV amoxicillin-clavulanic acid 1.2g	NA	Single dose	Lack of evidence for the role of antibiotics at normal birth (Heitmann and Benrubi[104]) ANODE[102] trial provided evidence of benefit of prophylactic antibiotic administration after assisted vaginal birth, with few observed adverse events in relation to the intervention	Level 1++, Grade A	Level 1++ High-quality meta-analyses, systematic reviews of RCTs or randomised Grade A: At least one meta-analysis, systematic reviews or RCT rated as 1++, and directly applicable to the target population; or a systematic review of RCTs or a body of evidence consisting principally of studies rated as 1+, directly applicable to the target population and demonstrating overall consistency of results
ANZOG[105]	2020	Instrumental vaginal birth	IV amoxicillin-clavulanic acid 1.2g	IV cefazolin 2g or IV clindamycin 600mg	Single dose	NA	Evidence based, Level A	NHMRC Levels of Evidence Level A: Body of evidence can be trusted to guide practice
SOGC[106]	2019	Assisted vaginal birth	Not recommended	Not recommended	NA	Consider single dose IV antibiotic after obstetrical anal sphincter injury repair	No grading (Liabsuetrakul et al[98] - Cochrane review 2014 which was updated in 2020)	Canadian Task Force on Preventative Health Care
WHO[107]	2015	Uncomplicated vaginal birth	Not recommended	Not recommended	NA	NA	Strong recommendation, very low-quality evidence	Grading of Recommendations, Assessment Development and Evaluation (GRADE)
		Operative vaginal birth	Not recommended	Not recommended	NA	NA	Conditional recommendation, very low-quality evidence	
		Third- or fourth-degree perineal lacerations	Recommended	Recommended	NA	Insufficient evidence to determine clinical benefits of routine administration of prophylactic antibiotics in women with third- or fourth-degree perineal tear post-partum. However, indirect evidence of benefit	Strong recommendation, very low-quality evidence	

	exists for potentially contaminated wounds (considering the bacterial flora in the rectum).

***SOGC**: Society of Obstetricians and Gynaecologists of Canada**; ANODE**: Prophylactic ANtibiotics for the prevention of infection following Operative Delivery; **ACOG**: American College of Obstetricians and Gynecologists; **RCOG**: Royal College of Obstetricians and Gynaecologists; **ANZOG**: Royal Australian and New Zealand College of Obstetricians and Gynaecologists; **NHMRC**: National Health and Medical Research Council; **WHO:** World Health Organization

Literature

Table A25: Literature review of references

Reference	Study Design/ Country	Sample Size	Population and Intervention	Outcome	Limitations/Remarks	Level of Evidence	Final Grade

98	Systematic review (Multiple countries)	3813 (2 RCTs)	Operative vaginal delivery (vacuum or forceps delivery) Intervention: Antibiotics (IV amoxicillin-clavulanic acid 1.2g or 2g IV cefotetan immediately after cord clamping) Comparator: Placebo Duration: Single dose	Superficial perineal wound infection: RR: 0.53 (95% CI: 0.40 – 0.69) Deep perineal wound infection: RR: 0.46 (95% CI: 0.31 – 0.69) Reduction of wound breakdown: RR: 0.52 (95% CI: 0.43 – 0.63) Organ or space perineal wound infection: RR: 0.11 (95% CI: 0.01 – 2.05) Endometritis: RR: 0.32 (95% CI: -0.23 – 0.41)	Evidence was mainly derived from a single multicenter study conducted in a high-income setting (referenced ANODE trial[102]). The evidence of antibiotic prophylaxis on endometritis, organ or space perineal wound infection, maternal adverse reactions and LOS remain unclear	1+	B
108	Systematic review (Multiple countries)	1779 (1 RCT, 2 quasi-RCTs)	Normal (uncomplicated) vaginal birth Intervention: Antibiotics (IV amoxicillin-clavulanic acid 1.2g or 2g IV cefotetan immediately after) Comparator: Placebo Duration: Single dose	Endometritis: RR 0.28 (95% CI: 0.09 to 0.83) Urinary tract infection: RR 0.25 (95% CI: 0.05 – 1.19) Wound infection after episiotomy: RR: 0.78 (95% CI: 0.31 – 1.96)	Relatively low incidence of puerperal endometritis and UTI were reported. Infection prevention and control measures remain important	1-	B
102	Prospective RCT (United Kingdom)	3420	Operative vaginal delivery (vacuum or forceps delivery) Intervention: IV Amoxicillin-clavulanic acid 1.2g Comparator: Placebo Duration: Single dose	Confirmed or suspected maternal infection within 6 weeks of delivery: 11.0% (Intervention) vs 19.0% (Comparator), RR: 0.58 (95% CI: 0.49 – 0.69)	High baseline rate (>10%) of infections/ complications observed after operative vaginal delivery. Use of a composite primary outcome (including new prescription of antibiotics for confirmed or suspected infection)	1++	A
109	Prospective RCT (France)	121	Normal (uncomplicated) vaginal birth	Endometritis rates: 0.66% (Intervention) vs 2.38% (Comparator) (p=0.013, 95% CI 0.36-3.08).	Overall rates were low. Similar in demographics, but not blinded. High risk of bias, small numbers	1-	B

			Intervention: Antibiotics (IV Amoxicillin-clavulanic acid 1.2g) Comparator: No treatment Duration: Single dose, 1 hour after birth	NS difference in hospitalisation duration			
104	Prospective RCT (USA)	393	Operative vaginal delivery (vacuum or forceps delivery) Intervention: IV Cefotetan 2g Comparator: No treatment Duration: Single dose	Endomyometritis: none in intervention group vs 7 with endometritis (no antibiotic) (RR 0.07, 95% CI 0.00–1.21)	Baseline demographics were similar, NS difference in proportion with fourth-degree laceration (approximately 40% delivered by forceps, the other 60% by vacuum extraction). Baseline rate of endometritis: 3.47% (high) without prophylaxis vs normal vaginal delivery 0.83%. Patients were randomised by "randomisation table"	1-	B
100	Randomised control trial (USA)	146	Third- or fourth-degree perineal lacerations Intervention: IV Ccefotetan or IV cefoxitin 1g, or IV clindamycin 900mg (if penicillin allergy) Comparator: Placebo Duration: Single dose	Perineal wound complications (wound disruption and purulent discharge) at two-week: 8.20% (intervention) vs 24.10% (comparator), RR: 0.34 (95% CI: 0.12 – 0.96)	Study has a high loss of follow-up (27.2% lost to follow-up at 2 weeks post-partum check-up); the study terminated early as it was unable to achieve the desired enrolment number	1+	B
110	Systematic review (Brazil)	73 (1 quasi-RCT)	Episiotomy repair after vaginal birth Intervention: PO Chloramphenicol 500mg QDS for 72 hours after episiotomy repair Comparator: No treatment	Episiotomy wound dehiscence with infection: RR: 0.13 (95% CI: 0.01 – 2.28) Episiotomy wound dehiscence without infection: RR: 0.82 (95% CI: 0.29 – 2.34) No cases of other puerperal infections (e.g. endometritis) were reported	Only 1 quasi-RCT was included with small numbers (n=73), high risk of selection bias (non-random sequence generation and allocation concealment according to protocol number) and wide CIs	2-	C

111	Quasi-Randomised control trial (Brazil)	73	Episiotomy repair after vaginal birth Intervention: PO Chloramphenicol 500mg QDS for 72 hours after episiotomy repair Comparator: No treatment	NS difference in episiotomy wound dehiscence with and without infection, no cases of other puerperal infections reported	Assessment at day 10 post-partum. One trial - Bonet et al[110] [High risk of selection bias (non-random sequence generation and allocation concealment according to protocol number), no double-blinding]	2-	C
112	Quasi-Randomised control trial (India)	300	Episiotomy repair after vaginal birth Intervention: PO cefixime 200mg BD and PO metronidazole 400mg TDS for 5 days after episiotomy repair Comparator: No treatment	Presence of infection at 5 days post-partum 0.7% (Intervention) vs 2.0% (Comparator), *p*=0.622	Nil comparison of baseline characteristics. Outcomes were assessed only at 5 days post-partum, which may be too early to draw conclusions	2-	C
				Operative vaginal delivery	FINAL GRADE	1+	A
				Third- or fourth-degree perineal lacerations	FINAL GRADE	1+	B
				Episiotomy repair	FINAL GRADE	2-	C
				OVERALL	**FINAL GRADE**	**1-**	**B**

***ANODE**: Prophylactic ANtibiotics for the prevention of infection following Operative Delivery**; LOS:** Length of stay; **NS**: Non-significant

Hysterectomy

Guidelines

Table A26: Guideline references for surgical prophylaxis recommendations

Reference	Year	Type of Surgery	First line	Alternative for Severe Penicillin Allergy	Duration	Remarks	Level of Evidence/ Grade	Grading System
ASHP, IDSA, SIS, and SHEA[2]	2013	Hysterectomy (vaginal or abdominal)	IV cefazolin or IV cefotetan or IV cefoxitin or IV ampicillin-sulbactam	[(IV clindamycin or IV vancomycin) WITH (IV aztreonam or IV fluoroquinolone)] or [IV metronidazole WITH (IV aminoglycosides or IV fuoroquinolones)]	Single dose	Limited trials involving Single dose cefazolin was used, mainly for vaginal hysterectomy. Single doses of cefotetan, ceftizoxime, or cefotaxime appeared to be as effective as multiple doses of cefoxitin. The studies were done mainly in the 1980-1990s	A	**Agency for Healthcare Research and Quality, and ASHP, IDSA, SIS, and SHEA** **Category A (levels I–III)** - Level I (evidence from large, well-conducted, randomised, controlled clinical trials or a meta-analysis) - Level II (evidence from small, well-conducted, randomised, controlled clinical trials) - Level III (evidence from well-conducted cohort studies)
ANZOG[81]	2012	Hysterectomy	IV metronidazole 500mg WITH IV cefazolin 1g (2g if weight ≥80kg)	(IV clindamycin 600mg WITH IV gentamicin) or IV cefoxitin 2g	Single dose	Multiple doses were not found to be more effective than a single dose prior to incision. Based on Chang et al[113]. Single dose cefazolin was as effective as multiple doses in laparoscopic-assisted vaginal hysterectomy. Screen and treat patients for bacterial vaginosis prior to undergoing hysterectomy. Antibiotic prophylaxis should	Level I	**NHMRC Levels of Evidence** Level I: A systematic review of level II studies (RCTs)

						include an antibiotic with an anaerobic spectrum		
ACOG[114]	2018	Hysterectomy, including supracervical (vaginal, abdominal, laparoscopic, robotic)	IV cefazolin 2g (3g if weight ≥120kg)	(IV clindamycin 900mg or IV Metronidazole 500mg) PLUS (IV Gentamicin 5mg/kg or IV Aztreonam 2g)	Single dose	Single dose cefazolin is recommended, based on ASHP[2]. Studies were mainly based on need for antibiotic prophylaxis (Mittendorf et al[115] meta-analysis on antibiotic prophylaxis for abdominal hysterectomy, Ayeleke et al[116] elective hysterectomy) Screening for bacterial vaginosis in women undergoing hysterectomy can be considered	Level A	**U.S. Preventive Services Task Force** Level A: Recommendations are based on good and consistent scientific evidence
SOGC[117]	2012	Vaginal and abdominal hysterectomy Laparoscopic hysterectomy Laparoscopy not entering the uterus and/or vagina	First- or second-generation cephalosporin (IV)	IV clindamycin or IV erythromycin or IV metronidazole	Single dose	Considered Class II (clean-contaminated) **Vaginal:** Review by Duff et al[118], 20 studies, supports use of antibiotic prophylaxis. **Abdominal:** -3 meta-analyses (Tanos et al[119], Mittendorf et al[115], Wttewaall-Evelaar[120]. **RCT:** Chongsomchai et al[121], single dose vs placebo, Eckenhausen and Jonker[122], single dose cefuroxime/ metronidazole vs 24 hours) **Laparoscopic:** clean contaminated procedure, similar rates of SSI vs vaginal hysterectomy Chang et al[113] (single dose cefazolin as effective as multiple doses).	• Level I-A • Level III-B • Level I-E	**Canadian Task Force on Preventive Health Care** **Level I:** Evidence obtained from at least one properly RCT **Level III:** Opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees **Class A:** Opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees **Class B:** There is fair evidence to recommend the clinical preventive action

						Johnson et al. Cochrane 2006: laparoscopic procedures lower SSI rates vs abdominal hysterectomy (updated in 2015[123]). **Not entering uterus and/or vagina:** clean procedure. RCT: Kocak et al[124], laparoscopy (non-hysterectomy) found no difference in SSIs in those who received 1 dose cefazolin vs without		**Class E:** There is good evidence to recommend against the clinical preventive action
SOGC[125]	2019	Hysterectomy for benign gynaecologic conditions	First-generation cephalosporin	NA	Single dose	Additional doses should be administered if an open procedure exceeds 3 hours or if blood loss is greater than 1500ml For need for single dose antibiotics, this guideline references the SOGC Guidelines (Van Eyk et al[117]: The SOGC recommends a first-generation cephalosporin as a single dose given 15 to 60 minutes prior to the first incision)	Strong, High	**Grading of Recommendations, Assessment, Development, and Evaluation (GRADE)** Strong: Highly confident of the balance between desirable and undesirable consequences (i.e., desirable consequences outweigh the undesirable consequences; or undesirable consequences outweigh the desirable consequences) High (++++): Very confident that the true effect lies close to that of the estimate of the effect
ERAS Society[126]	2019 [1966 – 2018]	Hysterectomy	First-generation cephalosporin	NA	Single dose	Antibiotic prophylaxis should be adjusted according to the planned procedure, with the addition of anaerobic cover in the setting of pelvic cancer surgery or bowel surgery. (Ref: Re-dosing should be performed as indicated based on duration of surgical case and blood loss)	Strong, High	**Grading of Recommendations, Assessment, Development, and Evaluation (GRADE)** Strong recommendations: The panel is confident that the desirable effects of adherence to a recommendation outweigh the undesirable effects

					Ref: ASHP[2]		Recommendations are based on quality of evidence (high, moderate, low) but also on the balance between desirable and undesirable effects, and on values and preferences of practitioners. Thus, strong recommendations may be reached from low-quality data and vice versa

*__ANZOG__: Royal Australian and New Zealand College of Obstetricians and Gynaecologists; **NHMRC:** National Health and Medical Research Council; **ACOG:** American College of Obstetricians and Gynecologists; **SOGC**: Society of Obstetricians and Gynaecologists of Canada; **ERAS:** Enhanced Recovery After Surgery

Literature

Table A27: Literature review of references

Reference	Study Design/ Country	Sample Size	Population and Intervention	Outcome	Limitations/ Remarks	Level of Evidence	Final Grade
127	Systematic review (Multiple countries)	13 RCTs	Intervention: Cefazolin Comparator: other first-choice antimicrobials with anti-anaerobic activity	SSI risk higher with cefazolin vs cefoxitin or cefotetan (RR 1.7; 95% CI, 1.04–2.77; *p*=0.03)	Most studies included non-standardised dosing and duration, had indeterminate or high risk of bias, did not include patients with gynecological malignancies, and/or were older RCTs not reflective of current clinical practices. Did not comment on single vs multiple doses of antibiotic	1-	B
116	Systematic review (Multiple countries)	6079 (37 RCTs)	Elective hysterectomy (vaginal and abdominal, benign gynaecological conditions) Intervention: Antibiotic (varied) Comparator: None	Vaginal hysterectomy Post-operative infections: RR 0.28 (95% CI: 0.19 – 0.40) Abdominal hysterectomy Post-operative infections: RR 0.16 (95% CI: 0.06 – 0.38)	Unclear evidence on which dose regimen or route is safest or most effective. Studies included had very low to moderate quality of evidence with risk of bias such as poor reporting of randomisation, small sample sizes, low event rates, inadequate reporting of adverse effects	1-	B

					Did not comment on single vs multiple dose antibiotic. Studies/ RCTs mostly in the 1980s		
128	Observational prospective cohort study (Finland)	5279	Hysterectomy (abdominal, laparascopic, and vaginal) Intervention(s): A) IV cefuroxime 1.5g at induction B) IV metronidazole 500mg at induction C) Combination of IV cefuroxime with IV metronidazole	Total infections: cefuroxime OR 0.29 (95% CI: 0.22 – 0.39); metronidazole OR 0.95 (95% CI: 0.72 – 1.24)	Lack of randomisation, possible bias (single drug may have been chosen for the less challenging cases)	2-	D
129	Retrospective observational study (China)	1783	Minimally invasive endometrial staging Intervention: IV cefazolin 1g q6h PLUS IV metronidazole 500mg q8h Comparator: IV cefoxitin 2g q8h Duration: 24 hours	SSI: 3.6% (Intervention) vs 5.7% (Comparator) Higher incidence of SSI in cefoxitin vs cefazolin/ metronidazole: OR 2.213 (95% CI: 1.193 – 4.107)	No available records of bacterial vaginosis in this study (known that bacterial vaginosis may increase the incidence of vaginal cuff infections)	2-	D
130	Retrospective observational study (Taiwan)	139	Radical hysterectomy or staging operation for gynaecologic cancers Intervention: Cefazedone for 1 day Comparator: Cefazedone for >1 day	SSI: 6.4% (Intervention) vs 8.3% (Comparator)	Metronidazole was added in 3 cases (5.0%) in "Comparator" group	2-	D
131	Retrospective cohort study (USA)	18,255	Abdominal, vaginal, laparoscopic, or robotic hysterectomy for benign or malignant indications Intervention(s): 1) IV cefazolin 2) Second-generation cephalosporin 3) IV cefazolin and IV metronidazole (combination)	Unadjusted SSI rate: 1.8% (cefazolin), 2.1% (second-generation cephalosporin), 1.4% (combination) SSI higher in cefazolin group (Adjusted OR, 2.30; 95% CI 1.06-4.99) and second-generation cephalosporin (Adjusted OR 2.31, 95% CI 1.21-4.41) vs combination	Lack of randomisation, possible bias in antibiotic selection	2-	D
113	Retrospective cohort study	319	Laparoscopic-assisted vaginal hysterectomy	Prophylactic effect similar in single dose cefazolin group vs	Select population with similar baseline demographics	2+	C

	(Taiwan)		Intervention: 1g IV cefazolin, single dose Comparator: Multiple doses of IV Cefazolin	multiple doses (range 2-4 doses), 94.6% vs 93.9%, NS difference between operative site infection and UTI			
122	Open study (Netherlands)	159	Abdominal hysterectomy Intervention: IV cefuroxime, IV Metronidazole single dose Comparator: IV cefuroxime, IV Metronidazole 24 hours	Post-operative wound infections, UTI similar in both groups (2/84 vs 1/75, 3/84 vs 4/75, NS). No significant differences in other parameters, e.g.: pyrexia and LOS	Lack of randomisation, information on demographics. possible bias in antibiotic selection	2-	D
132	Retrospective observational study (Japan)	Benign indication: 131 Malignant indication: 93	Open hysterectomy for benign indication (without lymphadenectomy) a for malignant indication (with lymphadenectomy) For benign indication Intervention (post-optimisation): IV cefazolin x 1 dose, 30-60 minutes pre-skin incision Comparator (pre-optimisation): IV cefazolin, up to 1 day For malignant indication Intervention (post-optimisation): IV cefmetazole x 24 hours Comparator (pre-optimisation): IV cefmetazole, up to 1 day	For benign indication SSI: 0.0% (Intervention), vs 4.7% (Comparator) For malignant indication SSI: 9.5% (Intervention), vs 7.8% (Comparator)	Real-world study of pre- and post-guidelines implementation in Japan, but small sample size. Similar demographics between both groups (benign and malignant indications), approximately 30% of those with malignant indication were abdominal radical hysterectomy. Showed no change in SSI post-national guidelines optimisation of antibiotics use (intervention arm). Cefmetazole use or malignant indications (hysterectomy with lympadenectomy, abdominal radical hysterectomy) included anaerobic cover	2+	C
					FINAL GRADE	**2-**	**C**

***LOS:** Length of stay; **NS**: Non-significant

Hysteroscopy

Guidelines

Table A28: Guideline references for surgical prophylaxis recommendations

Reference	Year	Type of Surgery	First line	Alternative for Severe Penicillin Allergy	Duration	Remarks	Level of Evidence/ Grade	Grading System
ANZOG[81]	2012	Hysterosalpingography or hysterosocopy or chromotubation for patients with dilated tubes or a history of PID or tubal damage	PO doxycycline 100g BD for 5 days PLUS IV metronidazole 500mg single dose	PO azithromycin 1g single dose	5 days (doxycycline); Single dose (metronidazole, azithromycin)	Reported rate of infection after HSG: 1.4 – 3.4%, lower when fallopian tubes were not dilated	IV	**NHMRC Level of Evidence** **Level IV:** A case series with either post-test outcomes or pre-test/post-test outcomes
		Hysterosalpingography or hysterosocopy or chromotubation with no history of PID and normal tubes on visualisation	NA	NA	NA		IV	
ACOG[114]	2018	Hysterosocopy	Not recommended	Not recommended	NA	Infectious complications after hysteroscopic surgery are uncommon (approx. 1–2%). A systematic review (4 RCTS), one RCT, no difference in post-operative infection after hysteroscopy between women who received antibiotic prophylaxis and those who received a placebo	Level I to II-3, Level B	**U.S. Preventive Services Task Force** **Level I:** Evidence obtained from at least one properly designed RCT. **Level II-3:** Evidence obtained from multiple time series with or without the intervention. Dramatic results in uncontrolled experiments also could be regarded as this type of evidence**.** **Level B:** Recommendations are based on limited or inconsistent scientific evidence

SOGC[117]	2012	Hysteroscopy	Not recommended	Not recommended	NA	Case series by Baggish et al[133] suggests that infection risk is low (< 1%). References Kasius et al[134] - A pseudo-randomised study of 266 women who underwent office hysteroscopy, and received PO amoxicillin-clavulanic acid and doxycycline 2 hours pre-procedure, with no difference in infection; Bhattacharya et al[135] - A randomised trial of amoxicillin-clavulanic acid vs placebo for hysteroscopic ablation (n=116) found a significant difference in the occurrence of bacteraemia (16% vs 2%); however, isolated organisms of dubious clinical significant	Level II-2D	**Canadian Task Force on Preventive Health Care** **II-2:** Evidence from well–designed cohort (prospective or retrospective) or case–control studies, preferably from more than one centre or research group **D.** There is fair evidence to recommend against the clinical preventive action

*__ANZOG__: Royal Australian and New Zealand College of Obstetricians and Gynaecologists; **NHMRC**: National Health and Medical Research Council; **ACOG:** American College of Obstetricians and Gynecologists**;** **SOGC:** Society of Obstetricians and Gynaecologists of Canada

Literature

Table A29: Literature review of references

Reference	Study Design/ Country	Sample Size	Population and Intervention	Outcome	Limitations/ Remarks	Level of Evidence	Final Grade
136	Meta-analysis (Multiple countries)	2327, 5 RCTs	Hysteroscopic procedures, various indications Intervention: Antibiotic prophylaxis (1106) vs none (698) vs placebo (523)	Pooled incidence of events was very low. Fever, 3.79% vs 1.8%, OR 2.17 (95% CI 0.80-5.88), infection 0.52% vs 0.58%, OR 1.66, (95% CI 0.43-6.5) Incidence of serious infections requiring treatment was very low at 0.2% (pre-treated, none in control groups)	Indications and techniques of hysteroscopies, definition and timing of prophylaxis are heterogenous, no event for some outcomes	1-	B

137	Meta-analysis (Multiple countries)	2221	Hysteroscopic procedures, various indications Intervention: Antibiotic prophylaxis vs none	Infection rate between the antibiotic prophylaxis group and control group: NS difference (OR: 0.50, 95% CI: 0.987–1.008)	As above, all were European studies, with inadequate raw data for analysis	1-	B
138	RCT (Italy)	180	Hysteroscopic procedures, various indications Intervention: IV cefazolin 2g vs no antibiotic pre-operatively	NS difference between post-operative fever 2.4% (Intervention) vs 2.3% (Comparator), infectious complications including endometritis, PID (none)	Various indications for hysteroscopy including endometrial hyperplasia, myomas, and endometrial polyps	1-	B
139	RCT (Italy)	1046	Hysteroscopy for intrauterine lesions Intervention: IM cefazolin 1g Comparator: placebo, pre-operative	Post-surgical infection after 5 days: 1.0% (Intervention) vs 1.15% (Comparator), NS	Various indications for hysteroscopy in the office/ clinic setting, for endometrial polypectomy, uterine septa, submucosal myomas and intrauterine adhesions	1+	B
140	RCT (Greece)	364	Diagnostic hysteroscopy Intervention: antibiotic prophylaxis vs no antibiotics (pre-operative)	No difference in post-procedural infection, 0.57% (Intervention) vs 0.53% (Comparator)	Various indications for diagnostic hysteroscopy such as, menometrorrhgia, post-menopausal vaginal bleeding, thickened endometrium, or as routine examination prior to 1st in-vitro fertilisation (IVF) or intracytoplasmic sperm injection (ICSI), over 8 years	1-	B
134	Quasi-Randomised control trial (Netherlands)	631	Diagnostic hysteroscopy for infertility candidates (prior to 1st IVF or ICSI) Intervention: PO augmentin 625mg and doxycycline 200mg 2 hours pre-procedure Comparator: none	No difference in post-procedural infection, 1 in antibiotic group (0.4%)	Low risk of infectious complication at 0.4%. No randomisation	2-	C
135	RCT	116	Hysteroscopic surgery (TCRE or ELA)	No difference in bacteraemia (16% vs 2%, 95% CI 0.05-0.25) and women	Majority of organisms were of dubious clinical significance;	1-	B

	(United Kingdom)	Intervention: IV Augmentin 1.2g at induction Comparator: Placebo Duration: once	treated for presumed infection (11.4% vs 9%)	contamination could not be excluded in 7 of 10 cases, and none of the women were seriously ill. No objective measures for presumed infection			
					FINAL GRADE	**1-**	**B**

***IVF:** in-vitro fertilization; **ICSI:** intracytoplasmic sperm injection; **TCRE:** transcervical resection of the endometrium; **ELA**: laser ablation of the endometrium; **NS**: Non-significant

Hysterosalphingography (HSG)

Guidelines

Table A30: Guideline references for surgical prophylaxis recommendations

Reference	Year	Type of Surgery	First line	Alternative for Severe Penicillin Allergy	Duration	Remarks	Level of Evidence/ Grade	Grading System
ANZOG[81]	2012	Hysterosalpingography or hysterosocopy or chromotubation for patients with dilated tubes or a history of PID or tubal damage	PO doxycycline 100g BD for 5 days PLUS IV metronidazole 500mg single dose	PO azithromycin 1g single dose	5 days (doxycycline); Single dose (metronidazole, azithromycin)	Reported rate of infection after HSG: 1.4 – 3.4%, lower when fallopian tubes are not dilated	IV	**NHMRC Level of Evidence** **Level IV:** A case series with either post-test outcomes or pretest/post-test outcomes
		Hysterosalpingography or hysterosocopy or chromotubation with no history of PID and normal tubes on visualisation	NA	NA	NA		IV	
ACOG[114]	2018	Hysterosalpingography	NA	NA	NA	If a history of PID or abnormal tubes is noted on HSG, PO doxycycline 100mg BD for 5 days can be considered to reduce	Level II-2	**U.S. Preventive Services Task Force** **II-2** Evidence obtained from well-designed cohort or

						the incidence of post-procedural PID		case–control analytic studies, preferably from more than one centre or research group
SOGC[117]	2012	Hysterosalpingography	PO doxycycline 100g BD for 5 days (in the presence of dilated tubes)	NA	5 days (doxycycline)	Screen for STI, and treat if necessary. Antibiotics prophylaxis should be given to patients at high risk (determined by history and/or as indicated by the presence of tubal obstruction at time of HSG)	Level II-3B	**Canadian Task Force on Preventative Health Care** **II-3:** Evidence obtained from comparisons between times or places with or without the intervention. Dramatic results in uncontrolled experiments (such as the results of treatment with penicillin in the 1940s) could also be included in this category **B:** There is fair evidence to recommend the clinical preventive action

*__ANZOG__: Royal Australian and New Zealand College of Obstetricians and Gynaecologists; **NHMRC**: National Health and Medical Research Council; **ACOG**: American College of Obstetricians and Gynecologists; **SOGC**: Society of Obstetricians and Gynaecologists of Canada; **STI:** Sexually transmitted infection

Literature

Table A31: Literature review of references

Reference	Study Design/ Country	Sample Size	Population and Intervention	Outcome	Limitations/ Remarks	Level of Evidence	Final Grade	Reference
141	Retrospective observational (case-control) (USA)	604	Group 1: 278 Group 2: 326	Hysterosalpingography with a history of tubal dilatation, or dilated tubes at time of HSG PO doxycycline 100mg BD for 5 days	PID in women with dilated tubes: 0% (doxycycline) vs 11.4% (without doxycycline), $p<0.02$	NA	2-	C

	FINAL GRADE	**2-**	**C**

Endometrial Biopsy, Cervical Tissue Excision, Cervical Cone Procedures

Guidelines

Table A32: Guideline references for surgical prophylaxis recommendations

Reference	Year	Type of Surgery	First line	Alternative for Severe Penicillin Allergy	Duration	Remarks	Level of Evidence/ Grade	Grading System
ANZOG[81]	2012	Endometrial biopsy	Not indicated	Not indicated	NA	NA	Level IV	**NHMRC Level of Evidence** Level IV: A case series with either post-test outcomes or pretest/post-test outcomes
ACOG[114]	2018	Endometrial biopsy	Not recommended	Not recommended	NA	Considered clean-contaminated procedures. Although, even without antimicrobial prophylaxis, the risk of infection complicating these procedures is very low. No estimates of infectious complications of endometrial biopsy was found in the review, the incidence is presumed to be negligible	NA (unclear grading)	**U.S. Preventive Services Task Force**
		Cervical tissue excision procedures (LEEP, biopsy, endocervical curettage)	Not recommended	Not recommended	NA	Two randomised trials of antibiotics prophylaxis undergoing LEEP with prolonged antibiotics were included, with significant limitations including prolonged duration of antibiotics and	NA (unclear grading)	**U.S. Preventive Services Task Force**

					surrogate outcomes (vaginal discharge, vaginal discharge). A Cochrane review, which included an additional study, showed no evidence of reduction in infection with antibiotic prophylaxis		
SOGC[117]	2012	Endometrial biopsy	None recommended	None recommended	There were no studies that assessed the use of prophylactic antibiotics given before an endometrial biopsy procedure. Insufficient evidence to support the use of antibiotic prophylaxis for an endometrial biopsy	Level III-L	**Canadian Task Force on Preventative Health Care** Level III: Opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees Grade; L: There is insufficient evidence (in quantity or quality) to make a recommendation; however, other factors may influence decision-making

***ANZOG**: Royal Australian and New Zealand College of Obstetricians and Gynaecologists; **NHMRC**: National Health and Medical Research Council; **ACOG**: American College of Obstetricians and Gynecologists; **LEEP**: loop electrosurgical excision procedure; **SOGC**: Society of Obstetricians and Gynaecologists of Canada

Literature

Table A33: Literature review of references

Reference	Study Design/ Country	Sample Size	Population and Intervention	Outcome	Limitations/ Remarks	Level of Evidence	Final Grade
142	Systematic review (NA)	NA	Transcervical intrauterine procedures	NA	No trials were eligible for inclusion in the systematic review, no conclusions regarding the use of prophylactic antibiotics in	4	GPP

					transcervical intrauterine procedures. A few RCTs have been conducted since for hysteroscopic procedures		
143	Systematic review (Multiple countries)	708 (3 RCTs)	Excisional treatment to cervix (for cervical intraepithelial neoplasia) Intervention: Prophylactic antibiotics (oral or pessary), 1 trial with PO ofloxacin 400mg once daily for 5 days; 2 trials with antimicrobial pessaries (1 for 5 days, 1 for 14 days) Comparator: Placebo (oral antibiotics); No treatment (pessaries)	Incidence of prolonged vaginal discharge: 13.3% (Intervention) vs 10.3% (Comparator), RR 1.29 (95% CI: 0.72 – 2.31) No difference in incidence of fever, lower abdominal pain, unscheduled medical consultation, or additional self-medication	2 trials with antimicrobial pessary, only one with oral antibiotics (ofloxacin for 5 days). Only 1 trial (oral antibiotics) reported the outcome of prolonged vaginal discharge (presumed cervicitis), other outcomes reported were possible "surrogate" outcomes of infection (such as fever, abdominal pain), but unknown whether symptoms were due to infection (no microbiological cultures taken, self-reported symptoms). But no direct comparison of the incidence of cervicitis, endometritis, and PID	1-	B
144	Prospective, randomised, placebo controlled RCT (United Kingdom)	348	LEEP Intervention: Ofloxacin 400mg Comparator: Placebo Duration: once daily for 5 consecutive days	Post-operative vaginal loss (vaginal discharge, bleeding): 15% (Intervention) vs 11% (Comparator), *p*=0.39	Assessment was done via pictorial chart, with self-reported outcomes. Did not reach final sample size	1-	B
145	Prospective observational cohort study (Bulgaria)	92 (only 72 had follow-up outcome data)	Diagnostic and therapeutic curettage (49 were emergency, 23 had an endometrial biopsy) Intervention: PO doxycycline 200mg after procedure, then 100mg BD for 3 days	No signs of infection in all patients with endometrial biopsy; 6 patients (8.3%) of patients with emergency curettage had signs of infection and PO doxycycline	Unable to access article (in Bulgarian). There was no comparator arm, all patients received PO doxycycline, and continued use for 6 days was at physicians' discretion	2-	D

			No comparator arm	was continued for 6 days			
146	Prospective observational cohort study (Greece)	67	Endometrial curettage for metrorrhagia Intervention: PO doxycycline 200mg once daily for 1 week Comparator: No treatment	PID: 4 patients, 9% (Intervention), vs 3 patients, 9% (Comparator), NS	Unable to access article	2-	D
147	Prospective observational cohort study (Indonesia)	60	Curettage for indications for diagnostic and therapeutic indications Intervention: Group A: IV cefazolin 2g single dose, then PO amoxicillin 500mg TDS x 3 doses Comparator: Group B: IV cefazolin 2g single dose only Group C: PO amoxicillin 500mg TDS x 3 doses post-procedure only	Similar occurrence of PID symptoms (high leukocyte counts, high ESR, abdominal pain, fever, vaginal discharge and bleeding) between groups, except pain (p=0.03)	Selection bias, no mention of randomisation process. Most common reason for curettage was for abortion (65 – 70%). Small sample size, did not evaluate the need for no antibiotics but of different antibiotics regimens	2-	D
					FINAL GRADE	**2-**	**C**

* **LEEP**: loop electrosurgical excision procedure; **ESR**: erythrocyte sedimentation rate; **NS**: Non-significant

Intra-Uterine Device (IUD) Insertion

Guidelines

Table A34: Guideline references for surgical prophylaxis recommendations

Reference	Year	Type of Surgery	First line	Alternative for Severe Penicillin Allergy	Duration	Remarks	Level of Evidence/ Grade	Grading System
ANZOG[81]	2012	IUD insertion	Not recommended	Not recommended	NA	A 2001 meta-analysis of four randomised trials (Grimes et al[148]) found no evidence that antibiotic prophylaxis reduced the risk of PID. Antibiotic prophylaxis at time of IUD insertion does not impact on the risk of future actinomycosis	Level 1	**NHMRC Level of Evidence** Level I: A systematic review of level II studies
ACOG[114]	2018	IUD insertion	Not recommended	Not recommended	NA	Considered as clean-contaminated procedures, although even without antimicrobial prophylaxis, the risk of infection complicating these procedures is very low Main reference: ACOG 2017 Practice Bulletin No. 186: Long-Acting Reversible Contraception: Implants and Intrauterine Devices[149]	Level III, Level A	**U.S. Preventive Services Task Force** Level III: Opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees. Level A: Recommendations are based on good and consistent scientific evidence
ACOG[149]	2017	IUD insertion	Not recommended	Not recommended	NA	The 1999 Cochrane meta-analysis (Grimes et al. Cochrane 1999, updated 2001[148]) showed that antibiotics prophylaxis at the time of IUD insertion did not reduced risk of PID, or reduce the likelihood of IUD removal within the 1st 3 months. Risk of IUD-related infection occurs within first few weeks to months after insertion, suggesting that bacterial contamination of endometrial cavity at time of insertion was the cause of infection.	Level III, Level A	**U.S. Preventive Services Task Force** Level III: Opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees. Level A: Recommendations are based on good and consistent scientific evidence

						Absolute risk of developing PID is less than 0.5%		
SOGC[117]	2012	IUD insertion	Not recommended	Not recommended	NA	Consider screening for STI in high-risk populations	Level I-E	**Canadian Task Force on Preventative Health Care** **Level I:** Evidence obtained from at least one properly randomised controlled trial **Level E:** There is good evidence to recommend against clinical preventive action
SOGC[150]	2016 [Jan 1994 to Jan 2015]	IUD insertion	Not recommended	Not recommended	NA	Perform STI testing in women at high risk. If tested positive for chlamydia and/or gonorrhea, treat post-insertion, IUD can remain in-situ	Level I-B	**Canadian Task Force on Preventative Health Care** **Level I:** Evidence obtained from at least one properly randomised controlled trial **Level B:** There is fair evidence to recommend clinical preventive action

*__ANZOG__: Royal Australian and New Zealand College of Obstetricians and Gynaecologists; **NHMRC**: National Health and Medical Research Council; **ACOG**: American College of Obstetricians and Gynecologists; **SOGC**: Society of Obstetricians and Gynaecologists of Canada; **STI**: Sexually transmitted infection

Literature

Table A35: Literature review of references

Reference	Study Design/ Country	Sample Size	Population and Intervention	Outcome	Limitations/ Remarks	Level of Evidence	Final Grade
[148]	Meta-analysis (Multiple countries)	4119 (6 RCTs)	IUD insertion Antibiotics (either PO doxycycline 200mg before IUD insertion; 200mg before insertion followed by daily for two days; or PO azithromycin 500mg before insertion) vs placebo	PID: OR 0.89 (95% CI: 0.53 – 1.51) Removal of IUD within 90 days: OR 1.05 (95% CI: 0.68 – 1.63) Antibiotic prophylaxis confers little benefit, low risk of IUD-associated infection, with or without use of prophylaxis	Higher prevalence of STI among women enrolled in the African studies. But low overall prevalence of cervical infection with *Neisseria gonorrhoeae* at 3% (in Kenyan trial), and 1% (Nigerian trial)	1+	B

151	RCT (USA)	1985	Copper IUD insertion in women with a low self-reported risk of STIs Intervention: PO azithromycin 500mg Comparator: Placebo Duration: Single dose 1 hour prior IUD insertion	IUD removal (for reasons other than partial expulsion): 3.8% (Intervention) vs 3.4% (Comparator), RR 1.1, 95% CI 0.7-1.8), no difference in rate of unscheduled visits	Low STI risk in this population (screened for STI prior). Reasonable follow-up period of 90 days	1+	B
152	RCT (Nigeria)	1813	IUCD insertion Intervention: PO doxycycline 200mg Comparator: Placebo Duration: Single dose 1 hour prior IUD insertion	PID: 1.3% (Intervention) vs 1.9% (Comparator), RR 0.69, 95% CI 0.32-1.47. IUCD-related visits statistically significant: RR 0.69; 95% CI 0.52 to 0.91)	Ladipo et al[153] attempted to replicate this and found no difference in both outcomes	1+	B
					FINAL GRADE	**1+**	**A**

*__STI__: Sexually transmitted infection; __IUCD__: Intrauterine contraceptive device

Clean Orthopaedic, Non-Spinal Procedure with No Implantation

Guidelines

Table A36: Guideline references for surgical prophylaxis recommendations

Reference	Type of Surgery	First line	Alternative for Severe Penicillin Allergy	Duration	Remarks	Level of Evidence/Grade
ASHP, IDSA, SIS, and SHEA[2]	Clean orthopaedic surgery not involving implantation of foreign materials	Not recommended	Not recommended	NA		1+/C
SIGN[154]	Orthopaedic surgery without implants	Not recommended	Not recommended	NA		4/D
SAAGAR[13]	Arthroscopic and other clean procedures not involving foreign material	Not recommended	Not recommended	NA		No grading of evidence as this guideline cited other guidelines

***SIGN:** Scottish Intercollegiate Guidelines Network; **SAAGAR**: South Australian expert Advisory Group on Antimicrobial Resistance

Literature

Table A37: Literature review of references

Reference	Study Design/ Country	Sample Size	Population and Intervention	Outcome	Limitations/ Remarks	Level of Evidence	Final Grade
155	Randomised placebo controlled trial (USA)	715 patients	General orthopaedic procedures (fractures, osteoarthritis, internal knee derangements) Cefamandole vs placebo Cefamandole given 1 dose pre-operative and 4 doses post-operative till 24 hours	SSI: 1.6% vs 4.2% (NS)	Old study: Oct 1976 to Sep 1976 There was a significant reduction in post-operative infection in the prophylaxis group. There was a significant reduction when operation time was >120 minutes	1+	
						FINAL GRADE	**B**

***NS**: Non-significant

Clean Orthopaedic Surgery with Implants

Guidelines

Table A38: Guideline references for surgical prophylaxis recommendations

Reference	Type of Surgery	First line	Alternative for Severe Penicillin Allergy	Duration	Remarks	Level of Evidence/Grade
ASHP, IDSA, SIS, and SHEA[2]	Clean orthopaedic surgery with implants	Cefazolin	Vancomycin Clindamycin	24 hours		1+/A
SIGN[154]	Arthroplasty	NA	NA	24 hours		2++/B
SAAGAR[13]	Orthopaedic surgery with and without joint replacement	Cefazolin If MRSA colonised: IV cefazolin + IV vancomycin	IV vancomycin	24 hours		No grading of evidence as this guideline cited other guidelines
CDC[50]	Fracture surgery and prosthetic joint arthroplasty	No recommended antibiotic choice	No recommended antibiotic choice	24 hours		1+/A

***SIGN:** Scottish Intercollegiate Guidelines Network; **SAAGAR**: South Australian expert Advisory Group on Antimicrobial Resistance

Literature

Table A39: Literature review of references

Reference	Study Design/ Country	Sample Size	Population and Intervention	Outcome	Limitations/ Remarks	Level of Evidence	Final Grade
156	Randomised placebo controlled trial (Unknown)	312 patients	Hip fracture surgery Cefazolin 4 doses vs 1 dose vs placebo	SSI: 1.6% vs 2.4% vs 3.7%, NS	Full text not available	1+	
157	Randomised placebo controlled trial (Sweden)	121 patients	Trochanteric hip fracture surgery Cefuroxime x 24 hours vs cefuroxime x 24 hours + PO cefalexin x 6 days	SSI: 7.6% vs 10.7%, NS	Sep 1982 to May 1984 - Authors concluded that there is no need for prophylaxis to be extended beyond 72 hours	1++	
158	Meta-analysis (USA)	14 RCTs 9691 patients	Orthopaedic procedures where implants are utilised	SSI: 2.0% vs 2.0%, p=0.74	Authors concluded that quality of evidence was low	1++	

			Single dose vs multiple doses of peri-operative antibiotics		14 RCTs: 7 arthroplasty surgeries, 1 spine surgery, 6 general orthopaedic procedures (2 hip fractures) There were 4 studies with high bias	
159	Retrospective cohort study (USA)	2181 patients	Primary total knee and hip arthroplasty surgery Antibiotic prophylaxis ≤24 hours vs additional oral antibiotic prophylaxis x 7 days	High-risk patients without extended antibiotic prophylaxis were 4.9 (p=0.009) and 4.0 (p=0.037) times more likely to develop prosthetic joint infections after total knee arthroplasty and total hip arthroplasty	2011 to 2016 - Authors concluded that high- risk patients should receive oral antibiotics for 7 days to reduce infection	2++
160	Case-control study (USA)	418 patients	Revision total hip placement surgery Antibiotic prophylaxis ≤24 hours vs >24 hours	SSI: 2.4% vs 4.8%, NS	Retrospective review of cases between 2000 to 2015: No benefit was noted with extending antibiotic prophylaxis	2++
161	Randomised double-blinded case-control study (USA)	160 patients	ORIF of closed extremity fractures Post-operative 23 hours Cefazolin prophylaxis (1g q8h, 2 doses) vs Placebo	SSI: NS Patients treated with cefazolin prophylaxis were less likely to develop SSI either superficial or deep infection (5 SSI in treatment vs 10 in prophylaxis, NS)	Patients with diabetes mellitus and risk score ≥2 more likely to develop SSI (smoking, ≥65 years old, diabetes mellitus, BMI ≥35, surgery >3 hours, urinary catheter)	2+
162	Retrospective cohort study (USA)	20682 patients	Total knee or hip arthroplasty Antibiotic prophylaxis (cefazolin or vancomycin) single dose vs multiple doses (24 hours)	SSI: 0.6% vs 0.88%, NS	There was a trend towards a lower prosthetic joint infection risk among patients who received a single dose. Patients who received multiple doses of antibiotics demonstrated a trend toward higher rates of acute kidney	2+

					injury compared with a single dose. *C. difficile* infections were infrequent in both groups		
163	Retrospective cohort study (Hong Kong)	887 patients	Total knee or hip arthroplasty Cefazolin x 1 peri-operative dose vs Cefuroxime x 3 doses (1 peri-operative and 2 post-operative doses)	SSI: Hip: 1.1% vs 1.1%, *p*=1.00 Knee: 1.0% vs 1.6%, *p*=0.63	887 patients with 1367 arthroplasties were included. The overall deep wound infection rate in the cefuroxime group was 1.4% and 1.0% in the cefazolin group (Fisher's exact test, *p*=0.72). The overall superficial wound infection rates of the cefuroxime group and the cefazolin group were 2.8% and 1.6% (Fisher's exact test, *p*=0.26) respectively	2++	
164	Systematic review (United Kingdom)	23 studies 8447 patients	Closed fracture fixation No antibiotic prophylaxis vs single dose vs multiple dose antibiotic prophylaxis	SSI: Deep infection: 2.4% vs 2.0%, *p*=0.91 Superficial infection: 6.2% vs 10.7%, *p*=0.37	Antibiotics are effective in reducing the incidence of infection. Single dose antibiotic prophylaxis significantly reduced deep surgical site infection, superficial SSI, urinary infections, and respiratory tract infections. Multiple dose prophylaxis had an effect of similar size on deep surgical site infection, but significant effects on urinary and respiratory infections were not confirmed	1++	
						FINAL GRADE	**A**

***ORIF**: Open reduction and internal fixation; **NS**: Non-significant

Spine Procedures with/without Implantation

Guidelines

Table A40: Guideline references for surgical prophylaxis recommendations

Reference	Type of Surgery	First line	Alternative for Severe Penicillin Allergy	Duration	Remarks	Level of Evidence/ Grade

ASHP, IDSA, SIS, SHEA[2]	Spinal Procedures with and without Instrumentation	Cefazolin	Vancomycin Clindamycin	24 hours	1+/A
SAAGAR[13]	Spinal Procedures	Cefazolin If MRSA colonised: IV cefazolin + IV vancomycin	IV Vancomycin	24 hours	No grading of evidence as this guideline cited other guidelines
NASS[165]	Spine Surgery	No recommended antibiotic choice	No recommended antibiotic choice	Single dose	1+/B

***SAAGAR**: South Australian expert Advisory Group on Antimicrobial Resistance; **NASS**: North American Spine Society

Literature

Table A41: Literature review of references

Reference	Study Design/ Country	Sample Size	Population and Intervention	Outcome	Limitations/ Remarks	Level of Evidence	Final Grade
166	Systematic review and Meta-analysis (USA)	5 studies 2824 patients	Spinal surgery Pre-operative antimicrobial prophylaxis vs extended antimicrobial prophylaxis (indefinite)	SSI: 1.28% vs 1.38% (NS)		1++	
167	Randomised case-control study (Canada)	552 patients	Posterior thoracolumbar spinal surgery managed with a closed-suction drain Post-operative antibiotic prophylaxis x 24 hours vs 24 hours after drain removal	SSI: 6.0% vs 5.2%, p=0.714	A complicated infection developed in 17 (6.0%) of 282 patients in the 24-hour group and in 14 (5.2%) of 270 patients in the 72-hour group; the rates did not differ between antibiotic groups (p=0.714) The superficial infection rate was 9.6% (27 of 282) among patients in the 24-hour group and 8.1% (22 of 270) among patients in the 72-hour group (p=0.654)	1++	

168	Randomised double-blinded case-control study (USA)	314 patients	Multilevel thoracolumbar spinal surgery, followed by use of post-operative drain Antibiotic duration x 24 hours vs duration that drain was in place	SSI: 12.4% (24 hours) vs 13.2% (drain-duration), *p*=0.48	There were NS differences between the 24 hours and drain-duration groups with respect to demographic characteristics (except for the ASA classification), operative time, type of surgery, drain output, or length of hospital stay. Authors commented that a much larger sample size could have led to a decreased rate of infection in the 24 hours arm	2+
169	RCT (USA)	233 patients	Instrumented lumbar spinal fusion surgery Cefazolin x single dose pre-operatively vs cefazolin x 3 days + PO cefalexin x 7 days post-operatively (total 10 days)	SSI: 4.3% (single dose) vs 1.7% (10 days), NS	Study limitations were its small sample size	1-
170	Retrospective cohort study (Korea)	548 patients	Spinal surgery Antibiotics x 48 hours vs 72 hours	SSI: 1.4% (48 hours) vs 0.4% (72 hours), *p*=0.325	A subgroup analysis was performed for cases with instrumented fusion. NS differences were noted between both groups in this subgroup analysis (*p*=1.0) Study limitations were its small sample size	2+
171	Retrospective cohort study (Hong Kong)	226 patients	Posterior spinal fusion surgery Cefazolin prophylaxis x 2 post-operative doses vs continued cefazolin antibiotic prophylaxis till drain removal	SSI: 1.9% (2 doses) vs 1.4% (antibiotics till drain removal), *p*=1.0	It was also noted that shorter antibiotic prophylaxis did not negatively affect wound healing. Study limitations were small sample size and likely underpowered study. Groups were compared across 2 time periods	2+
172	Prospective cohort study (Poland)	5208 patients	Spine surgery (instrumented) Single dose antibiotic prophylaxis vs 72 hours antibiotic prophylaxis	SSI: 5.3% (single-dose) vs 2.2% (72 hours prophylaxis), *p*<0.01	Both groups were compared in 2 different time periods, whereby there could have been other factors that may have affected the results e.g. new non-pharmacological interventions. Different antibiotics	2+

		were also used and not clearly documented	
		FINAL GRADE	**A**

*__NS__: Non-significant; **ASA**: American Society of Anesthesiologists

Clean Head and Neck Procedures

Guidelines

Table A42: Guideline references for surgical prophylaxis recommendations

Reference	Type of Surgery	Fist line	Alternative for Severe Penicillin Allergy	Duration	Remarks	Level of Evidence/ Grade
ASHP, IDSA, SIS, and SHEA[2]	Head and neck – clean	None	None	NA	Thyroidectomy, lymph node excision	B
	Head and neck – clean with placement of prosthesis	Cefazolin, cefuroxime	Clindamycin*	24 hours		C

*The addition of an aminoglycoside to clindamycin may be appropriate when there is an increased likelihood of gram-negative contamination of the surgical site.

Literature

Table A- 43: Literature review of references

Reference	Study Design/ Country	Sample Size	Population intervention	Outcome	Limitations/Remarks	Level of Evidence	Final grade
173	Randomised, double-blinded (Italy)	500	Thyroid procedure Prophylaxis vs none	SSI 0.8% (prophylaxis) vs 0.4% (none). NS	Excluded patients with diabetes mellitus, immunocompromised, patients with secondary surgeries, >80 years old	1+	
174	Systematic review	6 studies (n=4428)	Thyroidectomy Parathyroid surgery (RCT, non-RCT)	SSI 0.6% (case) vs 0.4% (control). NS	No evidence of heterogeneity (Q statistic=8.36)	1+	
175	Retrospective cohort (Israel)	464	Parotidectomy Comparing those with peri-operative antibiotic (cefazolin or clindamycin) vs none	Wound infection rates: *p*=0.168. Multivariate analysis showed female gender, neck dissection and drain output > 50ml/24hours were predictive of post-operative wound infection		2+	
						FINAL GRADE	**1+ (Grade A)**

Neck Dissection							
176	Retrospective cohort	192	Uncontaminated neck dissection	Wound infection – 10% (no antibiotic), 3.3% (antibiotics). NS	Low power beta greater than 0.2	2-	
177	Prospective series	57 (antibiotic group) vs 51 (no antibiotic)	Clean neck dissection Unasyn 24 hours vs no peri-operative antibiotic	Wound infection 1/57 (1.7%) in study group and 7/51 (13.3%) in control group, *p*=0.02	Baseline high infection rate Small sample size	1-	
178	Retrospective chart review	273 procedures	Uncontaminated neck dissections Group 1 – no antibiotic Group 2 – intra-operative Group 3 – Intra-operative and post-operative antibiotic	Wound infection only occurred in Group 2 and 3. 4/157 (Group 2) vs 5/75 (Group 3) (*p*=0.11). Wound infection associated with operative time and with radical or extended neck dissection	Conclusion: Antibiotic prophylaxis may be required in extended lymphadenectomy procedures	2+	
					FINAL GRADE	**2+**	**Grade C**

*__NS__: Non-significant

Clean-Contaminated Head and Neck

Guidelines

Table A44: Guideline references for surgical prophylaxis recommendations

Guideline	Type of Surgery	Fist line	Alternative for Severe Penicillin Allergy	Duration	Remarks	Level of Evidence/ Grade
ASHP, IDSA, SIS, and SHEA[2]	Clean-contaminated cancer surgery	Cefazolin/cefuroxime + metronidazole Ampicillin-sulbactam	Clindamycin**	24 hours		A
	Other clean-contaminated procedures (except tonsillectomy and FESS)	Cefazolin/cefuroxime + metronidazole Ampicillin-sulbactam	Clindamycin**	24 hours	Parotidectomy, submandibular gland excision, adenoidectomy, rhinoplasty,	B

					mandibular fracture repair		

*** FESS:** Functional endoscopic sinus surgery

**The addition of an aminoglycoside to clindamycin may be appropriate when there is an increased likelihood of gram-negative contamination of the surgical site.

Literature

Table A45: Literature review of references

Reference	Study Design/ Country	Sample Size	Population and Intervention	Outcome	Limitations/ Remarks	Level of Evidence	Final Grade
179	Systematic review and meta-analysis (only RCT)	4 RCTs (n=340)	Clean-contaminated head and neck surgery	Pooled relative risk of wound infection 0.98 (95% CI 0.58-1.61, NS) comparing 1 day vs 5 days	1 day vs 5 days no difference	1++	
180	Systematic review and meta-analysis (RCTs, observational studies)	15 studies compared duration	Clean-contaminated head and neck surgery	Treatment for more than 48 hours did not reduce wound infection. Increased infection with clindamycin treated patients OR 2.73	>48 hours no benefit	1+	
181	Systematic review and meta-analysis (3 retrospective, 2 prospective)	5 studies (n=861)	Clean-contaminated head and neck with microvascular free flap reconstruction (short course 24-48 hours vs long course)	SSI were higher in ≤24 hours (RR 1.56, 95% CI 1.13-2.14). Post hoc multivariate analysis based on individual level data from 697 patients showed that risk of SSI 24 hours vs > 24 hours was not significant after adjusting for antibiotic type (RR 1.09, CI 0.78-1.55). Those who received clindamycin had higher SSIs	Risks of SSI NS between 1-2 days vs longer after adjusting for antibiotic type	1-	
182	Prospective, randomised trial (USA)	181 Antibiotic (n=81) No-Antibiotic (n=100)	Open mandibular fractures with ORIF 2.4 MU PenG +/- metronidazole, cefazolin or clindamycin with (5-7 days) or without post-operative antibiotic	Infection: 8/81 vs 14/100, (*p*=0.399)	High drop-out rate 20-30% No difference between with or without post-operative antibiotic	1-	

183	Prospective, randomised, double-blind (Taiwan)	53	Clean-contaminated head and neck IV clindamycin 24 hours vs 72 hours	30-day wound infections were not associated with duration of antibiotics Pre-operative haemoglobin level and surgical reconstruction with free flaps or pectoralis major myocutaneous flaps were independent factors significantly related to wound infection	Excluded diabetes mellitus patients 26 patients had reconstruction surgery including flaps	1-
184	Prospective randomised double blind study (Turkey)	60	Major head and neck surgery Cefotaxime 24 hours vs 7 days	Wound infection: 13% (24 hours) vs 10% (7 days), NS	*Unable to access full article* No difference between 1 day vs 7 days	1-
185	Prospective randomised (Iran)	90	Laryngectomy Cefazolin 2 days vs 5 days	No wound infection in either group. Mucocutaneous fistula 4.4% (2 days) vs 6.7% (5 days) NS		1-
186	Retrospective review (USA)	147	Free tissue reconstruction Short course (≤2 days) or long course (>2 days)	SSI, flap dehiscence, flap loss and LOS – no difference. Those receiving long course has higher rates of pneumonia but lower UTI	No difference between ≤2 and >2 days	2+
187	Retrospective multi-institution analysis (multivariate log regression) (USA)	8836	Clean-contaminated head and neck	Patients on Unasyn had OR 0.28 when used antibiotic on day of surgery +1 day (vs on day of surgery alone). This effect was not seen in the clindamycin group	Favours 2 days as compared to 1 day	2++
188	Retrospective cohort (USA)	150 (75 each arm)	Complicated and non-complicated mandibular fractures 24 hours vs up to 10 days	Infection: 10.6% (extended duration) vs 13.3% (24 hours) p=0.8	No difference: 24 hours vs up to 10 days	2+
189	Retrospective cohort study (USA)	427 96 (24 hours or less) 331 (prolonged)	Free flap reconstruction of head and neck defects Unasyn (53.2%), Clindamycin (36%), others (10.3%)	Clindamycin associated with post-operative infection OR 6.71, p=0.004; not the duration of antibiotic		2++
					FINAL GRADE	**1+ (A)**

Oncologic Head And Neck						
190	Prospective, randomised trial (Italy)	162 (81 on each arm)	Oncologic head and neck Clindamycin-cefonicid (1 day vs 3 days)	20-day wound infection: 2.5% (1 day) vs 3.7% (3 days), NS. Pre-operative radiotherapy associated with greater severity of infection and higher risk of late wound complications	No difference comparing 1 vs 3 days	1+
191	Prospective randomised (USA)	74	Head and neck cancer surgery with free-flap reconstruction Clindamycin (3 doses) vs (15 doses)	Wound infection: 11% (3 doses) vs 10% (15 doses), NS	No difference comparing 1 vs 5 days	1-
192	Prospective, quasi-randomised (Germany)	75 (25 in each arm)	Major oncologic head and neck Group 1: 5 day Group 2: Peri-operative Group 3: Peri-operative + local antiseptic care	SSI: Group 1 (1/25), Group 2 (9/25), Group 3 (9/25), p=0.01	Suggest prolonged course (5 day has lower SSI compared to peri-operative only)	1-
193	Retrospective review	100 procedures (61 free flap, 39 local flap reconstructions)	Oropharyngeal reconstruction after oncologic resection. 48 hours vs long course (>48 hours)	Duration of antibiotic is not associated with recipient-site complications. Clindamycin was associated with complications		2-
					FINAL GRADE	**2+ (C)**

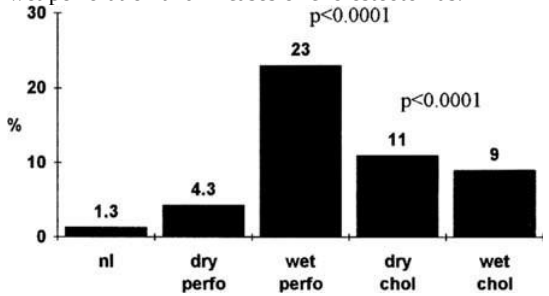
*__ORIF__: Open reduction and internal fixation; **NS**: Non-significant; **LOS**: Length of stay

Otologic procedures

Clean procedures include tympanostomy tubes, tympanoplasty, staphedectomy and mastoidectomy.
Clean-contaminated procedures include cholesteotoma or drainage involved.

Literature

Table A46: Literature review of references

Reference	Study Design/ Country	Sample Size	Population and Intervention	Outcome	Limitations/Remarks	Level of Evidence	Final Grade
194	Cochrane review (through 2002) Randomised and quasi-randomised	11 studies	Clean and clean-contaminated ear surgery	No difference between prophylaxis group (peri-operative antibiotic) vs control group (no antibiotic) for post-operative infection, graft failure, draining of outer ear and adverse drug reaction	Combined both clean and clean-contaminated	1+	
195	Prospective randomised controlled, double-blind (India)	78	Tympanoplasty with cortical mastoidectomy Group 1: Peri-operative Group 2: 8 days more	Wound infection rate – NS Graft success rate – NS LOS longer in Group 2 Higher GI adverse drug reaction in Group 2		1-	
196	Prospective, double-blind, randomised, placebo-controlled (Belgium)	750	Ear surgery Cefuroxime 1 day vs placebo	Infection rate: 3.1% (cefuroxime) vs 4.7% (placebo), NS. All infections occurred in the tympanoplasty group. *p*<0.005	Extrapolation Risk of infection was higher in pre-operative state of wet perforation and in cases of cholesteotomas.  The authors recommend that antibiotics, when given as in the present study design, may decrease the incidence of early post-operative infections by factor 3 (which is statistically significant) in draining ears and cholesteatomas	1+	

197	Retrospective chart review (USA)	195	Tympanoplasty +/- mastoidectomy for cholesteotoma Clindamycin and ceftazidime or gentamicin	SSI: 11% (no antibiotic) vs 1% (pre-operative antibiotic), *p*=0.02	Clean-contaminated (extrapolation as no direct duration comparison)	2+	
						FINAL GRADE	**Clean: 1+(A)** **Clean-contaminated: 1-(B)**

*__NS__: Non-significant; **LOS**: Length of stay; **GI**: Gastrointestinal

Tonsillectomy

Guidelines

Table A47: Guideline references for surgical prophylaxis recommendations

Guideline	Type of Surgery	Fist line	Severe Penicillin Allergy	Duration	Remarks	Level of Evidence/ Grade
ASHP, IDSA, SIS, and SHEA[2]	Other clean-contaminated procedures (**except tonsillectomy** and FESS)	Cefazolin/cefuroxime + metronidazole Ampicillin-sulbactam	Clindamycin**	24 hours	Parotidectomy, submandibular gland excision, adenoidectomy, rhinoplasty, mandibular fracture repair	B

*** FESS**: Functional endoscopic sinus surgery

**The addition of an aminoglycoside to clindamycin may be appropriate when there is an increased likelihood of gram-negative contamination of the surgical site.

Literature

Table A48: Literature review of references

Reference	Study Design/ Country	Sample Size	Population and Intervention	Outcome	Limitations/ Remarks	Level of Evidence	Final Grade
198	Systematic review (only RCTs included)	5 trials	Tonsillectomy	Fever RR 0.62 (0.45-0.85); duration of halitosis -1.94 (-3.57, -0.3), time taken to resume normal activity -0.63 (-1.12, -0.14). No effect on pain score -0.01 or the need for analgaesia. RR for antibiotic adverse drug event was 2.45 (0.45, 13.31)		1+	

199	Systematic review (RCTs)	10 trials (n=1035)	Tonsillectomy	Most did not find significant reduction in pain with antibiotics. Not associated with reduction in hemorrhage. Secondary outcome: Antibiotic reduced the proportion of patients with fever (RR 0.63, 0.46-0.85, *p*=0.002)		1+	
					FINAL GRADE	**1+**	**A**

Septorhinoplasty

Literature

Table A49: Literature review of references

Reference	Study Design/ Country	Sample Size	Population and Intervention	Outcome	Limitations/Remarks	Level of Evidence	Final Grade
200	Prospective, randomised, single-blind study (Australia)	200	Septorhinoplasty (simple) Single shot IV Augmentin vs 7-day regimen	Local wound infection (3%) in 7-day group; none (single dose), NS Side effects: 29% vs 2% (*p*=0.03)	Excluded patients with significant comorbidities (cardiovascular, diabetes mellitus, infections, malignancy, immunodeficiencies) Nasal packing only 24 hours	1+	
201	Prospective, randomised, single-blinded (United Kingdom)	164	Complex septorhinoplasty Augmentin 1 day vs 7-day	10th day post-operative infection: 7% (1-day) vs 11% (7-day). NS 80% were minor	*full article not available*	1-	
202	Systematic review (up to Feb 2018)	5 RCTs n=589	Rhinoplasty Post-operative vs pre-operative and peri-operative or placebo	Infectious complications – no difference Pooled RR 0.92 (*p*=0.86)	Low internal risk of bias Moderate heterogeneity in terms of surgical techniques	1+	
203	Systematic review (all study types)	6 studies n=990	Nasal packing for epistaxis or septoplasty	Purulent drainage was 11.2% (no antibiotic) vs 9.9% (with antibiotic), NS. None developed toxic shock syndrome	Only 3 of the studies were prospective RCTs Study number may be too small	1-	
					FINAL GRADE: Simple	**1-**	**B**

	FINAL GRADE: Complex	**1-**	**B**

*__NS__: Non-significant

Note: Two older RCTs (1980, 1977) showed no benefits of antibiotics for septorhinoplasty with nasal packing (n=504). Another RCT (n=100) found that 7-day course reduce infection as compared to placebo in complex rhinoplasty. (1988) – extrapolation done using these older studies.
For simple septorhinoplasty, extrapolations done based on 1+ studies. The only study that addressed this was by Lange JL (Level of evidence 1-).

Endoscopic sinus surgery (clean-contaminated)

Note: Given the lack of studies comparing intra-operative antibiotic vs no antibiotics, one dose of antibiotic is recommended to be given intra-operatively.

Guidelines

Table A50: Guideline references for surgical prophylaxis recommendations

Guideline	Type of Surgery	Fist line	Alternative for Severe Penicillin Allergy	Duration	Remarks	Level of Evidence/ Grade
ASHP, IDSA, SIS, and SHEA[2]	Other clean-contaminated procedures (**except** tonsillectomy and **FESS**)	Cefazolin/cefuroxime + metronidazole Ampicillin-sulbactam	Clindamycin**	24 hours	Parotidectomy, submandibular gland excision, adenoidectomy, rhinoplasty, mandibular fracture repair	B

*** FESS**: Functional endoscopic sinus surgery

**The addition of an aminoglycoside to clindamycin may be appropriate when there is an increased likelihood of gram-negative contamination of the surgical site.

Literature

Table A- 51: Literature review of references

Reference	Study Design/ Country	Sample Size	Population and Intervention	Outcome	Limitations/Remarks	Level of Evidence	Final Grade
204	Systematic review and meta-analysis (Through May 2011)	4 studies (all RCTs)	Endoscopic sinus surgery	Antibiotic prophylaxis associated with NS reduction of infection (RR 0.76, 95% 0.64-1.09), symptom scores -0.04 (-0.46-0.38)	Heterogeneity was significant only for the outcomes of change of symptoms	1+	

205	Randomised, double-blind, placebo (China)	97	FESS for chronic sinusitis Group 1: on Traditional Chinese Medicine Group 2: amoxicillin 4 weeks Group 3: placebo	NS difference in subjective and objective outcomes	Did not state clearly if antibiotic was given intra-operative. Patients were given antibiotic pre-surgery but instructed to stop 1 week before surgery	1-	
206	Prospective, randomised, double-blind, placebo-controlled (Romania)	75	Endoscopic sinus surgery Augmentin 2 weeks vs placebo	5^{th} day nasal obstruction and drainage better in antibiotic group. Endoscopic score was statistically significantly different. Use of antibiotic was able to improve outcome in early blood crust healing phase, nasal obstruction and drainage	Favours antibiotic use for early stage outcome improvements Did not state if antibiotic was given intra-operative	1-	
207	Randomised, double-blind, placebo-controlled, non-inferiority trial (USA)	77	Endoscopic sinus surgery Cefazolin was given intra-operative for both groups, then amoxicillin-clavulanic acid 1 week vs placebo	Placebo was non-inferior to antibiotic in terms of - SNOT-22 score - LK score Post-operative infection rates (2.6% vs 2.4%, NS). Diarrhoea was significantly higher in the antibiotic group (24.3% vs 2.5%, *p*=0.02)		1-	
					FINAL GRADE**	**1-**	**Grade B**

* **FESS**: Functional endoscopic sinus surgery; **NS:** Non-significant; **SNOT-22**: Sino-nasal outcome test; **LK:** Lund-Kennedy

**Note: Extrapolation was made based on one 1+ study and mainly 1- studies.

NEUROSURGERY

Guidelines

Table A52: Guideline references for surgical prophylaxis recommendations

Reference	Type of Surgery	First line	Severe Penicillin Allergy	Duration	Remarks	Level of Evidence/ Grade
ASHP, IDSA, SIS, and SHEA[2]	Clean wounds e.g. Elective craniotomy, EVD, ICP monitors	IV cefazolin 2g (3g if > 120kg) MRSA colonised IV vancomycin 15mg/kg	IV vancomycin 15mg/kg or IV clindamycin 600mg-900mg	Single dose*		A
	Clean wounds with foreign body or instrumentation e.g. CSF shunting procedures	IV cefazolin 2g (3g if > 120kg) MRSA colonised IV vancomycin 15mg/kg	IV vancomycin 15mg/kg or IV clindamycin 600mg-900mg	Single dose*		A
IDSA[208]	Clean wounds e.g. Elective craniotomy, EVD	NA	NA	Single dose*		Strong, moderate
	Clean wounds with foreign body or instrumentation e.g. CSF shunting procedures	NA	NA	Single dose*		Strong, moderate
Neurocritical Care Society[209]	Clean wounds EVD	NA	NA	Single dose*	Prolonged prophylactic antibiotic until EVD removed may increase the risk of resistant organisms and *C. difficile* diarrhea. Most studies of ventriculostomy-related infections are prospective or retrospective large case series, only 3 RCT exist	Conditional recommendation; low quality

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

Elective Craniotomy

Table A53: Literature review of references

Reference	Study Design/ Country	Sample Size	Population and Intervention	Outcome	Limitations/Remarks	Level of Evidence	Final Grade
210	Systematic review and meta-analysis	7 studies (1 RCT, 6 case series) (n=1655)	6 craniotomies, 1 ICP monitor. Comparing the efficacy of peri-operative antibiotic (no antibiotic, penicillin family antibiotics, first-generation cephalosporins vs fluoroquinolones, lincosamides, vancomycin, third-generation cehalosporins), single vs combination antibiotics	Lincosamides, glycopeptides, third-generation cephalosporins, other combinations of antibiotics or penicillin family antibiotics alone offer better coverage against SSI than first-generation cephalosporins	The inclusion of only 1 RCT and 6 case series can present bias. High heterogeneity in the pooled studies. Included Gliadel wafer implantation (1 case, ampicillin), primary brain tumor (2 cases, ampicillin and cefazolin) associated with high risk of post-surgical infection	1-	
211	Systematic review and meta-analysis	5 RCT (n=2209)	4 studies included craniotomy and shunt procedure, 3 studies include bur-hole and spinal surgery, 2 studies included transphenoidal. Comparing the efficacy of third-generation cephalosporin with peri-operative conventional regimens (vancomycin plus gentamicin, trimethoprim-sulfamethoxazole, ampicillin-sulbactam,	The pooled OR for SSI with third-generation cephalosporin was 0.94 (95% CI, 0.59-1.52; *p*=0.81) Single dose conventional antibiotic regimen is much favourable as third-generation cephalosporin failed to show superiority in reduction of SSI	This study may not have included all the conventional antibiotics as comparators during cranial surgeries in view of the strict inclusion criteria (third-generation cephalosporin). Hence, unable to infer a specific conventional antibiotic regimen that provides the best coverage from infections	1++	

			cefazolin). End point of the RCTs was the occurrence of SSI				
212	Meta-analysis	6 prospective randomised trials (n=1729)	Craniotomies with or without a prophylactic antibiotic. Protocol specified single dose allowed additional dose if the operation lasted longer than a prescribed time Primary end point was a random effects OR meta-analysis for meningitis after craniotomy	The pooled OR for meningitis with antibiotic treatment was 0.43 (95% CI 0.20-0.92; *p*=0.03) showing a significant benefit from antibiotics Subgroup analyses showed no detectable difference in antibiotic efficacy with or without gram-negative coverage	Excluded patients with implanted shunts or hardware, transphenoidal surgeries and patients who are undergoing re-operation Bias in interpretation or selective reporting due to differences in the definitions of meningitis used in individual studies	1++	
						FINAL GRADE	**1+ (Grade A)**

External Ventricular Drain (EVD), ICP Monitors

Table A54: Literature review of references

Reference	Study Design/ Country	Sample Size	Population and Intervention	Outcome	Limitations/Remarks	Level of Evidence	Final Grade
213	Prospective performance analysis (USA)	866	Patients who underwent intraventricular catheterisation. Patients in period 1 received 1g q8h IV cefazolin until EVD removed. Patients in period 2 only received peri-operative antibiotic up to 24 hours prior to antibiotic coated EVD placement	Overall incidence of ventriculitis was 0.92%. Rates of ventriculitis did not differ significantly between period 1 and period 2 (1.1% vs 0.4%, *p*=0.22) Single dose antibiotic following placement of antibiotic coated EVD did not result into more incidence of catheter-related ventriculitis	Results may not be generalisable. A low rates of ventriculitis raised the possibility of study is not sufficiently powered to see a difference	2+	

214	Systematic review and meta-analysis	3 RCT and 7 observational studies	Patients who received prolonged prophylactic antibiotic and antibiotic coated EVD as a preventive measures for VRI	Pooled analysis showed a protective effect of SAP and antibiotic coated EVD for VRI (RR:0.32; 95% CI: 0.18-0.56)	Moderate heterogeneity in the pooled studies. The definitions of ventriculitis were variable, the type and dose of antimicrobials were different. Pooled analysis effect was likely contributed by the majority of the retrospective studies that were prone to bias. Mixture of placebo vs SAP and peri-operative antibiotic vs SAP makes the impact on peri-operative vs SAP difficult to interpret. Study by Poon et al. demonstrated that SAP caused more drug resistant virulent pathogens and higher mortality rate. SAP use is not recommended	1-
215	Retrospective cohort (USA)	345	EVD ≥3 days. 209 patients received prophylactic antibiotic for the duration of the EVD vs 99 patients who received peri-operative antibiotic	Overall rate of ventriculitis was 3.9%. The infection rate for prophylactic group (3.8%) vs peri-operative group (4.0%) Prophylactic antibiotic did not significantly reduce the rate of ventriculitis in patients with EVD and they may select for resistant organisms	With the baseline of overall rate of ventriculitis (4%), the sample size is inadequate to achieve power (80%) to observe differences in the infection rate for both arms	2+
216	Retrospective cohort (USA)	279	Patients with ICP monitor who received narrow spectrum antibiotic, cefazolin or vancomycin or no antibiotic (n=119), broad spectrum antibiotic, ceftriaxone or ciprofloxacin (n=160) as prophylaxis	Overall CNS infection occurrence was 3.2%. Narrow spectrum or no prophylaxis was 1.7% vs broad spectrum antibiotic (4.4%) (*p*=NS) but associated with a shift to resistant gram-negative pathogens	This study was non-randomised and retrospective.	2++

[217]	Retrospective cohort (USA)	30	Patients with severe closed-head injury who placed on ICP monitoring. 14 patients were initiated with cefazolin 1g q8h or nafcillin 1g q6h immediately before ICP placement and was continued for the duration of ICP monitoring vs 16 patients without ICP and prophylactic antibiotic	Patients with prophylactic antibiotic demonstrated statistically higher septic morbidity rates (78.6% vs 31.3%) and statistically higher pneumonia rates (57.1% vs 18.8%) compared with patients who did not. No patients developed CNS infection	Prolonged duration of prophylactic antibiotic use is unnecessary, if given at all, should be limited to the up to 24 hours prior to ICP monitor placement	2+
					FINAL GRADE	**2++ (Grade B)**

*__VRI:__ ventriculostomy-related infections; **CNS:** Central Nervous System; **NS**: Non-significant

Cerebrospinal Fluid (CSF) Shunting

Table A55: Literature review of references

Reference	Study Design/ Country	Sample Size	Population and Intervention	Outcome	Limitations/Remarks	Level of Evidence	Final Grade
218	Randomised prospective trial (Italy)	176 (88 vancomycin, 88 cefazolin single dose)	Patients aged >16 who underwent elective placement of internal and external shunts in a high MRSA prevalence hospital. Primary end point was the rate of shunt infections	Shunt infection in vancomycin group (4%) vs cefazolin group (14%) (p=0.03). Mortality among patients with post-surgical infections was higher in the cefazolin group vs vancomycin (5 vs 0) (p=0.02)	-	1+	
219	Systematic review and meta-analysis	15 RCT (n=1736)	Patients of any age with any type of intracranial ventricular CSF shunt surgical procedure. Comparing the use of prophylactic antibiotics vs placebo/no antibiotic in intracranial shunt procedures. Primary end point was the presence of shunt infection	The use of systemic antibiotic prophylaxis (vs placebo/no antibiotic) was associated with a decrease in shunt infection (OR: 0.52, 95% CI 0.36-0.74) regardless of the type of internal shunt (VA/VP) used Prophylactic antibiotic use up to 24 hours (vs continuous antibiotic) was found to be significant different (OR: 0.53, 95% CI 0.34-0.83; OR: 0.50, 95% CI 0.36-0.74 respectively)	No conclusion could be reached regarding the administration of prophylactic antibiotics for EVD	1++	
220	Prospective, open-label study (Italy)	100	Patients with hydrocephalus underwent VP shunt and received single dose of ceftriaxone prior to surgery	No shunt infection was observed over 4 year follow-up period	Exclusion: patients who received post-operative treatment in other departments or clinics might have missed the events (shunt infection)	2+	
						FINAL GRADE	**1+ (Grade A)**

*__VA__: ventriculoatrial**; VP:** ventriculoperitoneal

Cystourethroscopy

Guidelines

Table A56: Guideline references for surgical prophylaxis recommendations

Reference	Type of Surgery	First line	Alternative for Severe Penicillin Allergy	Duration	Remarks	Level of Evidence/Grade
AUA [221]	Cystourethroscopy	Not required	NA	NA	Small RCT (n=47); recruited patients underwent urethrocystoscopy or urethrocystography with clear urine. Compared antibiotic prophylaxis and no antibiotic None of the patients in either group developed pyuria, bacteriuria or a febrile infection	1^{+}
EAU[222]	Cystourethroscopy	Not required	NA	NA	Cited two systematic reviews (details in *Table A- 57*) that show benefits of antibiotic prophylaxis with high NNT and concluded as below: Given the low absolute risk of post-procedural UTI in well-resourced countries, the high numbers of procedures being performed and the high risk of increasing antimicrobial resistance, the Workgroup Panel consensus strongly recommend not using antibiotic prophylaxis in patients undergoing urethrocystoscopy (flexible or rigid)	1^{+}

***AUA:** American Urological Association; **EAU:** European Association of Urology; **NNT**: Needed number to treat

Literature

Table A57: Literature review of references

Reference	Study Design/ Country	Sample Size	Population and Intervention	Outcome	Limitations/Remarks	Level of Evidence	Final Grade
[223]	Systematic review – meta-analysis (Cochrane) 2019	20 RCTs and 2 quasi-RCTs with 7711 participants	Adults undergoing cystoscopy Antibiotic prophylaxis vs	**Primary outcomes** Systemic UTI RR 1.12 (95% CI 0.38-3.32) from 5 RCTs, 504 participants, low quality evidence Symptomatic UTI RR 0.49 (95% CI 0.28-0.86) from 11 RCTs, 5441 participants, low quality	Most of the evidence reviewed were RCT which were graded as low and very low quality by the investigators; therefore, the	1^{+}	

			placebo or no treatment	evidence. Serious adverse events: no serious adverse events were observed in either intervention group or control group and no effect size could be calculated **Secondary outcomes** Minor adverse events RR 2.82 (0.54-14.80) from 4 RCTs, 630 participants, very low quality evidence Localized UTI RR 1.0 (0.06-15.77) from 1 RCT, 200 participants, very low quality evidence Bacterial resistance RR 1.73 (1.04-2.87) from 2 RCTs 38 participants, very low quality evidence	recommendation is not strong Antibiotic prophylaxis is favourable in the prevention of symptomatic UTI, although it also causes significant bacterial resistance
224	Systematic review and meta-analysis	7 RCTs – 5107 patients undergoing flexible cystoscopy	RCTs compare antibiotic vs placebo or no antibiotic administration	Confirmed bacteriuria on mid-stream urine OR 0.36 (95% CI 0.27-0.48), NNT 15 Asymptomatic bacteriuria OR 0.40 (95% CI 0.29-0.54), NNT 32 Symptomatic bacteriuria OR 0.34 (95% CI 0.25-0.47), NNT 26	High NNT reflects less significant clinical benefit of antibiotic prophylaxis
225	Systematic review and meta-analysis	7 RCTs – 3038 patients (Jan 1998 – Dec 2013)	RCTs compare antibiotic vs placebo or no antibiotic administration	**Primary outcomes** UTI RR 0.53 (0.31-0.90), Absolute RR 1.3% (from 2.8% to 1.5%) NNT 74 (from 5 studies with moderate quality of evidence) **Secondary outcomes** Asymptomatic bacteriuria RR 0.28 (0.20-0.39) from 6 RCTs with moderate quality of evidence	High NNT for prevention of UTI reflects a low clinical benefit of antibiotic prophylaxis
					FINAL GRADE A

*__NNT:__ Number needed to treat

Transurethral Procedures

Guidelines

Table A58: Guideline references for surgical prophylaxis recommendations

Reference	Type of Surgery	First line	Alternative for Severe Penicillin Allergy	Duration	Remarks	Level of Evidence/ Grade
AUA [221]	Transurethral procedures	Cefazolin or cotrimoxazole	Aminoglycosides	Single dose	Cited 1) systematic review (2005) showed any antibiotic prophylaxis (cephalosporins, fluoroquinolones, cotrimoxazole, aminoglycosides etc.) were effective in reducing the incidence of post-operative bacteriuria and fever (duration of antibiotic varied in each trial included in the systematic review) 2) RCTs compared single dose ciprofloxacin and cefazolin and ciprofloxacin vs cefotaxime show no statistical difference in post-operative UTI Lack of large RCTs or systematic reviews to compare the effectiveness of a single-dose to multiple-dose of antibiotic	1^{+}
EAU[222]	Transurethral procedure	Aminopenicillin + beta-lactamase inhibitor or cotrimoxazole or second- /third-generation cephalosporins	Non-penicillins agents in the first line	NA	Cited systematic review (published in 2010) that showed benefit of antibiotic prophylaxis Does not specify type of antibiotic but recommends urologists to give antibiotics according to local susceptibility data for the common uropathogens	1^{+}
SAAGAR[13]	Transurethral procedure	Cefazolin or gentamicin		Single dose	No reference provided	
ASHP/IDSA[2]	Transurethral procedure	Fluoroquinolones or cotrimoxazole or cefazolin	Aminoglycoside with or without clindamycin	Single dose or less than 24 hours	Cited systematic reviews showed benefit of antibiotic prophylaxis for TURP in reducing post-operative infectious complication. Effective antibiotic included aminoglycosides, fluoroquinolones, cotrimoxazole and cephalosporins. Treatment protocols of any duration were effective	1^{+}

***AUA:** American Urological Association; **EAU:** European Association of Urology; **SAAGAR**: South Australian expert Advisory Group on Antimicrobial Resistance; **TURP:** Transurethral resection of the prostate

Literature

Table A59: Literature review of references

Reference	Study Design/ Country	Sample Size	Population and Intervention	Outcome	Limitations/Remarks	Level of Evidence	Final Grade
226	RCT, multicentre	n=203, (Jan 2015 – Dec 2018 in Japan)	Patients with benign prostatic hyperplasia (without pyuria or bacteriuria) underwent transurethral enucleation of the prostate Single dose cefazolin (n=101) vs multiple dose cefazolin (n=102)	**Primary outcome** Rate of genitourinary tract infection: single dose (1.0%) vs multiple dose (2.0%), *p*=1.00 **Secondary outcome** Antibiotic related adverse effect 1 case in the multiple dose group No mention about this outcome in the single dose	Small sample size (did not indicate how sample size was calculated; this may have affected the power of the study)	1^-	
						FINAL GRADE	**B**

Transrectal Procedure

Guidelines

Table A60: Guideline references for surgical prophylaxis recommendations

Reference	Type of Surgery	First line	Alternative for Severe Penicillin Allergy	Duration	Remarks	Level of Evidence/ Grade
AUA [221]	Transrectal procedure	Fluoroquinolones or cephalosoporins (commonly use third-generation) + aminoglycosides	NA	Single dose	Cited 1) RCT (1992-1993, n=537) compared single dose PO ciprofloxacin to placebo. The study showed benefit of PO ciprofloxacin in prevention of bacteriuria and UTI 2) RCT (1996-1998, n=231) compared single dose PO ciprofloxacin + tinidazole vs 3-day dose vs placebo. The study found antibiotic lowers the incidence of UTI post procedure compared to placebo. There was no difference in UTI in the single dose and 3-day group	1^+
EAU[222]	Transrectal procedure	Fluoroquinolones or cephalosporins or fosfomycin or aminoglycosides	NA	NA	Cited 1) RCT (1998-2001, n=192 in China) compared single dose ciprofloxacin + metronidazole vs 3-day dose of ciprofloxacin + metronidazole BD vs	1^+

					placebo. Study showed higher incidence of infection in the placebo group. There was no difference in infection rate in the antibiotic groups 2) RCT (1996-1997, n=110) compared single dose ofloxacin vs single dose cotrimoxazole vs no antibiotic. The study showed higher frequency of bacteriuria in the non-prophylactic group (26.08%) while there was no difference in the antibiotic group 4.76% vs 6.66% (ofloxacin vs cotrimoxazole). There were 3 patients in non-prophylactic group required hospitalisation for pyelonephritis and prostatitis while there was no patient in the antibiotic group required hospitalisation EAU recommended fluoroquinolones but also emphasised on the issue of drug resistance for urologists to consider using targeted therapy or using alternatives such as cephalosporins	
ASHP/IDSA[2]	Transrectal procedure	Fluoroquinolone or cotrimoxazole or cefazolin	Aminoglycoside +/- clindamycin	Single dose or less than 24 hours	Cited RCTs compared single dose and 3-day antibiotic prophylaxis and found no difference in infectious complication between the 2 groups	1^+

***AUA:** American Urological Association; **EAU:** European Association of Urology

Literature

Table A-61: Literature review of references

Reference	Study Design/ Country	Sample Size	Population and Intervention	Outcome	Limitation/Remarks	Level of Evidence	Final Grade
[227]	Systematic review – meta-analysis (Cochrane)	19 RCTs (total 3599 patients) Including studies from 1966 to 2010	Patients underwent transrectal prostate biopsy Antibiotic prophylaxis vs placebo/no treatment Short-course (one day) treatment vs long-course (3 days) treatment Single dose vs multiple dose	**Primary outcomes** Bacteriuria – RR 0.25 (0.15-0.42) – benefit of antibiotic prophylaxis regardless the drug class (quinolones, sulfonamides and other classes) Bacteraemia – RR 0.67 (0.49-0.92) Fever – RR 0.39 (0.23-0.64) UTI – RR 0.37 (0.22-0.62) Sepsis – 0.36 (0.04-3.24) **Secondary outcomes** Mortality – no case of mortality reported Hospitalisation due to infection – RR 0.13 (0.03-0.55)	Several classes of antibiotic were effective while fluoroquinolones were used in the highest number of studies and patients; however, this meta-analysis does not show the difference in outcomes from different antibiotic classes	1^+	

				Adverse effects of antibiotic – RR 1.62 (0.23-11.56) **Short-course vs long-course** Data shows favor long-course for bacteriuria only (RR 2.09, 1.17-3.73) **Single dose vs multiple dose** Data shows favor multiple dose for bacteriuria only (RR 1.98, 1.18-3.33)		
228	Non-RCT (SGH study) – compared prospective intervention with retrospective control	367 vs 374	Patient underwent transrectal ultrasound guided prostate biopsy from Sep 2003 to Aug 2004, who received ciprofloxacin only (n=367), were classified as the control group (ciprofloxacin-only). Patient underwent TRPB from Sep 2004 to Aug 2005 would be added 80mg IM gentamicin to the regimen (n=374) and classified as the intervention group (ciprofloxacin + gentamicin) Ciprofloxacin was given at 500mg BD x 3 days, started 24 hours prior to the procedure Gentamicin was given IM over the gluteal muscle 30 minutes prior to the procedure	**Primary endpoint** Hospitalisation secondary to sepsis – 12 cases in ciprofloxacin-only vs 5 cases in ciprofloxacin+ gentamicin (p=0.0458) **Secondary endpoint** Isolated bacteria and antibiotic susceptibility – 9 cases of ciprofloxacin resistant *E. coli* were isolated in the control group while there was 1 case in the intervention group	The investigators matched samples with underlying conditions and characteristics like diabetes mellitus, age, prostate size and prostate-specific antigen but did not match the history of antibiotic exposure and hospitalisation which potentially affect resistance and clinical infection	2^-
229	Retrospective cohort study (Jan 2011 to Oct 2013)	n=487 (455 for evaluation)	Ciprofloxacin vs alternative regimens – ciprofloxacin + cephalosporin	**Infection related complication** Ciprofloxacin 7.5% vs ciprofloxacin + cephalosporin 1.1% OR 7.29 (1.65-32.37)	Sample size was calculated to achieve the power of test Baseline demographic data were collected and analysed by	2^-

			(cefodoxime) vs ciprofloxacin + additional agent vs IM gentamicin	Ciprofloxacin 7.5% vs ciprofloxacin + additional agent 2.3% (p=0.014) Ciprofloxacin vs gentamicin – OR 0.39 (0.13-1.17, p=0.08) Gentamicin vs any alternative regimen – OR 4.23 (1.5-12.2, p=0.004)	univariate and multivariate analysis to determine the influence of infection; however, there was no mention of distribution of these factors to each group	
230	Systematic review Articles were recruited from 1946 to Nov 2015 All studies were comparing infective outcomes of patients undergoing TRUS-guided biopsy with either fluoroquinolone or culture-based targeted antimicrobial prophylaxis	9 studies	Patients underwent TRUS received either fluoroquinolone or culture-based targeted antimicrobial prophylaxis	**Primary outcome** Post TRUS biopsy infective complication – empiric prophylaxis vs targeted prophylaxis – 4.55% vs 0.72% p<0.001 **Secondary outcome** Baseline prevalence of fluoroquinolone-resistance before TRUS – 505/2219 (22.8%)		2^{++}
231	Systematic review	19 Trials (published in English from 2005 -2015, 10 RCTs, 7 prospective trials and 2 retrospective trials) were reviewed	Clinical trials compared the effect of antibiotic prophylaxis between active treatment (different agents or different duration)	**Post biopsy infectious complication** – 5 RCTs as follow, 1) tosufloxacin vs levofloxacin, 2) single dose IM ceftriaxone vs single dose PO ciprofloxacin vs 3-day PO ciprofloxacin 3) single dose ciprofloxacin vs single dose levofloxacin vs 3-day ciprofloxacin vs 3-day levofloxacin 4) ciprofloxacin vs ciprofloxacin + cephalosporin None of the trials demonstrated any differences in infectious or non-infectious complication rates following TRUS 5) single dose PO ciprofloxacin vs 3-day PO ciprofloxacin vs 3-day PO chloramphenicol vs 3-day PO norfloxacin – significant reduction in the risk of post-biopsy infection favoring ciprofloxacin both as single-dose and 3-day regimen compared to	This systemic review did not include a placebo controlled study. So the results cannot be used solely to determine the effective of using ciprofloxacin as a prophylactic choice especially in the era of high fluoroquinolone-resistant *E. coli* and *K. pneumoniae*. However, it did show that the duration of prophylaxis should be limited to no more than 3 days and ideally to a single dose	1^{-}

				chloramphenicol (p=0.0003) and norfloxacin (p=0.03) Duration of prophylaxis – none of the studies were able to show a benefit of continuing prophylaxis for more than a single dose (5 studies) or a 3-day regimen (1 study)		
232	Observational prospective study (2 phases of 5 years between 2001 and 2010)	300 vs 897	First phase (Group 1, 2001 to 2005) - 300 patients were given ciprofloxacin 500 mg BD 1 day prior to the procedure, on the day of biopsy and 2 days after biopsy Second phase (Group 2, 2006 to 2010) - 897 patients were given additional IV amikacin 500 mg 30 minutes prior to biopsy (added to ciprofloxacin regimen)	**Septicemia** Group 1 vs Group 2 – 24/300 (8%) vs 15/897 (1.7%) (p<0.001) There was an increase in the incidence of post-procedural septicemia in Group 1, while the incidence was steady in the Group 2 In 39 cases of septicemia, ciprofloxacin resistant *E.coli* is responsible for 33 cases	Ciprofloxacin-resistant pathogens (*E. coli*, *K. pneumoniae* and *E. faecalis*) are a major concern of post-procedural infection	2^-
					FINAL GRADE	**A**

***SGH:** Singapore General Hospital; **TRUS:** Transrectal ultrasonography

Transperineal Procedures

Guidelines

Table A62: Guideline references for surgical prophylaxis recommendations

Reference	Type of Surgery	First line	Alternative for Severe Penicillin Allergy	Duration	Remarks	Level of Evidence/Grade
AUA [221]	Transperineal procedure (prostate brachytherapy)	Cefazolin	Clindamycin	Single dose	Cited RCT (conducted in 1998 to 2001) in which patients underwent prostate brachytherapy and were randomised to receive peri-operative antibiotic (n=258), either cefazolin or ciprofloxacin	1^+

				or no antibiotic prophylaxis (n=259). The author did not provide details on dose and duration. 1/258 (0.4%) in the antibiotic group developed epididymitis while 4/259 (1.5%) in no prophylaxis group developed epididymitis The number of cases was too small for statistical analysis regarding antibiotic use		

***AUA:** American Urological Association

Literature

Table A63: Literature review of references

Reference	Study Design/ Country	Sample Size	Population and Intervention	Outcome	Limitations/Remarks	Level of Evidence	Final Grade
233	Retrospective case review	n=485	Patients underwent a transperineal prostate biopsy between 2014 to 2016. Cefazolin (1g twice daily for 1 day at induction and 4 hours later) was used for antimicrobial prophylaxis	**Infectious complications up to post-operative day 30** The rate of an infectious complications was 0.82% (4/485)	The rate of post-operative infection was very low. This was not an RCT so it is not certain that antibiotic prophylaxis is truly needed	2^{-}	
234	Multicenter cohort study (retrospective chart review) conducted in Japan between Jan 2009 to Dec 2010	n=826	Patients who underwent transperineal ^{125} brachytherapy and were evaluated for the relationships between various antimicrobial prophylaxis protocols and the incidence of post-implant infection	**Peri-operative infection up to post-operative day 30** 6/826 (0.73%) had infection received antibiotic prophylaxis for 1 or more days (4 patients received 1-day regimen of second-generation cephem). None of the patients who received single dose antibiotic prophylaxis (first-generation cephem, penicillin with beta-lactamase inhibitor and quinolone) had infection	The rate of peri-operative infection was very low. This was a chart review therefore it cannot be used to recommend antibiotic prophylaxis. However, the benefit of using antibiotic prophylaxis is questionable	2^{-}	
235	Pooled prospective databases (from Sep 2009 to 2011) on transperineal prostate biopsy from multiple centres in Melbourne,	244 patients were reviewed	**Case review**: Patients underwent transperineal biopsy. All patients received antibiotic prophylaxis – type of antibiotic as follows:	**Case review**: 245 transperineal biopsies were taken from 244 patients – no patient was re-admitted for infective complications. Ten patients (4%) developed acute urinary retention and 3 (1%) patients had clot retention	Due to very low rate of infection, the author suggested antibiotic prophylaxis is probably not required for transperineal biopsy	2^{++}	

	and systematic literature review from PubMed and Embase		cephalosporin alone (6%), cephalosporin + gentamicin (16%), cephalosporin + quinolone + gentamicin (45%), Quinolone alone (25%), Not specified (8%) **Systematic review**: from PubMed and Embase from 2003 to the time of study conducted (using search terms: transperineal, prostate biopsy, fever, infection, sepsis, septicemia and complications)	**Systematic review**: There were 4 studies that did not use antibiotic prophylaxis. There were 5/6609 (0.076%) patients re-admitted to hospital for sepsis	The author did not mention on the type of studies included in the systematic review. It is difficult to determine biases	
236	Retrospective review	242 cases of transperineal prostate biopsy by Precision Point transperineal access system	212/242 cases (88%) received no antibiotic prophylaxis. 30/242 (12%) cases received IM ceftriaxone or PO ciprofloxacin based on their individual risk factors	No report of sepsis (0/242, 0.0%) and 1 report of late onset perianal abscess in the group of no antibiotic prophylaxis (1/212, 0.5%)	3	
					FINAL GRADE	**C**

Percutaneous Renal Surgery

Guidelines

Table A64: Guideline references for surgical prophylaxis recommendations

Reference	Type of Surgery	First line	Alternative for Severe Penicillin Allergy	Duration	Remarks	Level of Evidence/ Grade

AUA [221]	Percutaneous renal surgery	First- /Second- generation cephalosporins or aminoglycoside + metronidazole or clindamycin		Single dose	Cited retrospective review of 126 cases of percutaneous extraction of renal stones 107 patients had sterile urine pre-operatively and did not receive antibiotic prophylaxis. Of these patients, 37 (35%) had a post-operative bacteriuria. 11% had fever. 19 patients had UTI pre-operatively and were treated with antibiotic started at least 24 hours pre-operatively and continued for a minimum of 3 weeks. The author concluded that the risk of clinical infection was low, and suggested to perform careful bacteriological screening and to treat the infection appropriately. Short-term antibiotic prophylaxis should be appropriate	4
EAU[222]	Percutaneous renal surgery	Cotrimoxazole or second- /third- generation cephalosporins or aminopenicillin + beta-lactamase inhibitor		NA	Cited systematic review and meta-analysis of RCTs, showed moderate level of evidence that antibiotic prophylaxis was associated with reduction in the risk of post-procedural UTI 2 RCTs with overall low risk of bias found no difference in SIRS and urosepsis rates between ampicillin-sulbactam and cefuroxime. Another study found no difference in rate of infectious complications between single dose ceftriaxone vs ceftriaxone plus subsequent PO third-generation cephalosporin – concluded that a single dose of effective antibiotic should be sufficient	1^-
SAAGAR[13]	Percutaneous renal surgery	Cefazolin + gentamicin (+metronidazole if risk of entering GI tract is present)	Vancomycin + gentamicin	Single dose	No reference was provided, but recommendations in the Australian guideline was assessed to be reasonable. The chances of entering the GI tract secondary to this procedure was deemed to be very rare	4
ASHP/IDSA[2]	Percutaneous renal surgery	Cefazolin + metronidazole or cefoxitin	Fluoroquinolone or aminoglycoside + metronidazole or clindamycin	Single dose or less than 24 hours	Cited a small RCT which recruited 81 patients with large stones, who underwent PCNL. Patients were randomised to receive single-dose ofloxacin or short-course ofloxacin until removal of the nephrostomy catheter There was no difference in infectious complication between the two groups	1^+

***AUA:** American Urological Association; **EAU:** European Association of Urology; **SIRS**: Systemic inflammatory response syndrome; **SAAGAR:** South Australian expert Advisory Group on Antimicrobial Resistance; **GI**: Gastrointestinal

Literature

Table A65: Literature review of references

Reference	Study Design/ Country	Sample Size	Population and Intervention	Outcome	Limitations/Remarks	Level of Evidence	Final Grade
[237]	RCT	n=86	Low risk patients (negative pre-operative urine cultures and without urinary drains) underwent PCNL Nitrofurantoin 100mg twice daily for 7 days preceding surgery vs no antibiotic All patients received peri-operative doses of ampicillin + gentamicin	**Primary outcome:** Sepsis 12% vs 14% (p=1.0) No benefit of giving one week of pre-operative oral antibiotic in low risk patients. Peri-operative antibiotic appears sufficient	Randomised trial distributed confounding factors equally to both groups	1^{+}	
						FINAL GRADE	**A**

Ureteroscopy

Guidelines

Table A66: Guideline references for surgical prophylaxis recommendations

Reference	Type of Surgery	First line	Alternative for Severe Penicillin Allergy	Duration	Remarks	Level of Evidence/ Grade
AUA [221]	Ureteroscopy	Cotrimoxazole or first-/second- generation cephalosporin		Single dose	RCT, n=113, Patients underwent ureteroscopy Intervention: PO levofloxacin 250 mg 60 minutes prior to the procedure (n=57) Comparator: no antibiotic (n=56) **Post-operative symptomatic UTI –** no report in both groups **Post-operative bacteriuria –** without prophylaxis vs prophylaxis – 12.5% vs 1.8%, *p*=0.026 Antibiotic showed benefit in prevention of post-operative bacteriuria and single dose is sufficient	1^+
EAU[222]	Ureteroscopy	Cotrimoxazole or second-/ third- generation cephalosporins or aminopenicillin + beta-lactamase inhibitor		NA	Cited single systematic review and two meta-analysis of RCTs showed low-grade evidence that antibiotic prophylaxis reduced risk of bacteriuria but not clinical UTI	1^+
SAAGAR[13]	Ureteroscopy	Gentamicin or cefazolin		Single dose	No reference provided	4
ASHP/IDSA[2]	Ureteroscopy	Cefazolin + metronidazole	Fluoroquinolone or aminoglycoside	Single dose or less than 24 hours	Cited an RCT of 113 patients who underwent ureteroscopy (received single dose PO levofloxacin or no prophylaxis) and found rate of post-operative bacteriuria of 1.8% and 12.5% respectively *p*=0.0026	1^+

***AUA:** American Urological Association; **EAU:** European Association of Urology; **SAAGAR:** South Australian expert Advisory Group on Antimicrobial Resistance

Literature

Table A67: Literature review of references

Reference	Study Design/ Country	Sample Size	Population and Intervention	Outcome	Limitations/Remarks	Level of Evidence	Final Grade
237	Retrospective review (at the University of British Columbia, Canada and Massachusetts General Hospital, USA), included patients from Feb 2009 to Aug 2011	n=81	All patients with renal calculi received single dose of antibiotic (cefazolin, cotrimoxazole or quinolone) prior to ureteroscopic stone treatment. 42 patients received only pre-operative antibiotic (Group 1) and 39 patients received both pre-operative and post-operative antibiotics at the surgeon's discretion (Group 2)	**Post-operative UTI (total 8 patients (9.9%)** Group1 vs Group 2 – 2 vs 6, *p*=0.1457	Retrospective review cannot control biases	2^{-}	
238	Systematic review and meta-analysis the last search was conducted on 23 Jan 2017	11 studies (5 RCTs + 1 prospective comparative study + 5 retrospective comparative studies) in a total of 4591 patients	Comparative studies investigating the efficacy of different antibiotic prophylaxis in ureteroscopic lithotripsy in patients without pre-operative infection Antibiotic prophylaxis vs no antibiotic Single dose of PO vs IV antibiotic Timing of dosing (single dose), ≤1 hour vs >1 hour	**Outcomes: Post-operative infections** **Post-operative UTI** Antibiotic vs no antibiotic: OR 0.82 (95% CI 0.40-1.67) ≤1 hour vs >1 hour: OR 0.93 (95% CI 0.20-4.34) PO vs IV: OR 1.00 (95% CI 0.26-3.88) Single dose vs multiple dose: OR 0.98 (95% CI 0.06-16.12) **Post-operative fever** Antibiotic vs no antibiotic: OR 1.75 (95% CI 1.22-2.50) **Pyuria** Antibiotic (single dose) vs no antibiotic: OR 0.42 (95% CI 0.25-0.69)	Included RCTs with high quality and low risk of biases and non-RCTs of high quality	1^{++}	

	Single dose vs multiple dose	≤1 hour vs >1 hour: OR 0.81 (95% CI 0.41-1.59) PO vs IV: OR 1.24 (95% CI 0.63-2.43) Single dose vs multiple dose: OR 0.44 (95% CI 0.08-2.54) **Post-operative bacteriuria** Antibiotic (single dose) vs no antibiotic: OR 0.25 (95% CI 0.11-0.58) ≤1 hour vs >1 hour: OR 2.97 (95% CI 0.35-25.35) PO vs IV: OR 0.34 (95% CI 0.04-2.87) Single dose vs multiple dose: OR 5.11 (95% CI 0.24-109.17)		
			FINAL GRADE	**A**

Open/Laparoscopic Surgery

Guidelines

Table A68: Guideline references for surgical prophylaxis recommendations

Reference	Type of Surgery	First line	Alternative for Severe Penicillin Allergy	Duration	Remarks	Level of Evidence/ Grade
AUA [221]	Open/laparoscopic surgery	cefazolin		Single dose	Extrapolated from systematic review of general surgery and obstetrics and gynaecology surgery antibiotic prophylaxis Cited retrospective review (2006) cases of radical retropubic prostatectomy which compared the incidence of surgical site infection and remote site infection between 1-day and 4-day antibiotic regimen for surgical prophylaxis. The studies found no difference in the outcomes between the two groups	2^- and 4
SAAGAR[13]	Open/laparoscopic surgery (urinary tract entered)	Cefazolin + gentamicin	Vancomycin + gentamicin (+metronidazole when there is risk of entry into the GI tract lumen)	Single dose	No reference provided	4

ASHP/IDSA[2]	Open/laparoscopic surgery	cefazolin	Fluoroquinolone or aminoglycoside with or without clindamycin	Single dose or less than 24 hours	Mentioned that there was no clinical trial in this type of surgery but extrapolated results from other major intra-abdominal procedures	4

***AUA:** American Urological Association; **SAAGAR:** South Australian expert Advisory Group on Antimicrobial Resistance; **GI**: Gastrointestinal

Literature

Table A69: Literature review of references

Reference	Study Design/ Country	Sample Size	Population and Intervention	Outcome	Limitations/Remarks	Level of Evidence	Final Grade
239	Prospective registry database review (between Jan 2010 and Oct 2015)	n=229	All patients underwent laparoscopic robot-assisted radical prostatectomy Group1 (n=60): antibiotic prophylaxis according to AUA guideline (single dose cephalosporin; cefamezine 2g + aminoglycoside; gentamicin 240 mg) and continued with PO ofloxacin 200mg or ciprofloxacin 250 mg twice daily until urethral catheter removal vs Group2 (n=169): pre-operative antibiotic (according to AUA guideline) only	**Rate of CAUTI –** 8.3% vs 8.9%, *p*=0.89 **LOS –** 5.8 vs 4.5 days, *p*<0.001	The number of subjects who received a single dose of antibiotic were more than 2 times the subjects received prolong antibiotic. The results favoured giving a single dose of antibiotic prophylaxis	2^+	
						FINAL GRADE	**B**

* **CAUTI:** Catheter-associated urinary tract; **LOS:** Length of stay; **AUA:** American Urological Association

Urinary Diversion

Guidelines

Table A70: Guideline references for surgical prophylaxis recommendations

Reference	Type of Surgery	First line	Alternative for Severe Penicillin Allergy	Duration	Remarks	Level of Evidence/

						Grade
AUA [221]	Urinary diversion	Cefazolin + metronidazole	Clindamycin + aminoglycoside	Single dose	Extrapolated from GI surgery antibiotic prophylaxis (colorectal surgery and appendicectomy) Systematic review and meta-analysis	4
ASHP/IDSA[2]	Urinary diversion	Cefazolin + metronidazole	Fluoroquinolone or aminoglycoside +/- clindamycin or metronidazole	Single dose or less than 24 hours	Cited study (in Japan) which compared prospective intervention using 1 day antibiotic prophylaxis (piperacillin, n=38) to retrospective review using 3 days or more antibiotic prophylaxis (n=46). Patients' demographics were matched. All possible post-operative complications within 30 days were measured. There were no differences in the occurrence rate of infections listed below: Total SSI (18.1% vs 20.5%) Superficial incisional SSI (12.1% vs 13.6%) Deep incisional SSI (12.1% vs 13.6&) Space SSI (12.1% vs 11.4%) Post-operative ileus (18.2% vs 11.4%) Febrile UTI (15.2% vs 15.9%) Pneumonia (3.0% vs 4.3%)	2^-

***AUA:** American Urological Association; **GI:** gastrointestinal

Literature

Table A71: Literature review of references

Reference	Study Design/ Country	Sample Size	Population and Intervention	Outcome	Limitations/Remarks	Level of Evidence	Final Grade
[240]	Chart review (in 3 centres, University Medical Centre Regensburg Germany, Laval University Quebec Canada and general hospital of Bolsano Italy) between 2009 and 2015	n=217	Patients with urothelial bladder cancer underwent open radical cystectomy and created urinary diversion either incontinent (ileal, colon conduit or ureterocutaneostomy) or continent (neobladder or continent cutaneous reservoir) Risk factors of infections were recorded Urine samples were collected for antimicrobial susceptibility prior to	**Primary outcome** In-hospital incidence of UTI after radical cystectomy within 30 days – 42 patients (19.4%) **Identification of risk factors of UTI** (using binary univariable and multivariable logistic regression analysis) Continent diversion was associated with the occurrence of UTI (OR = 5.027, 95% CI 2.119-11.923)	This was not an RCT, therefore it could not be used for determining the antibiotic of choice and duration. However, the multivariate logistic regression analysis did not show an association of duration of antibiotic with the occurrence of UTI There was no RCT/systematic review/meta-analysis based on a search of articles up until Dec 2020 using Medline (PubMed)	2^-	

	the procedure. Patients with positive urine culture were treated accordingly at least 24 hours prior to the procedure. Patients with negative urine culture were given antibiotic at the induction of anaesthesia and continued according to the respective institution guidelines The most frequent used antibiotic prophylaxis was a combination of metronidazole (98.2%) and cephalosporin (89.9%) Median duration of antibiotic - 7 days (IQR 5-14) – 56 patients (25.8%) received antibiotic for only 24 hours	The duration of antibiotic prophylaxis was not a protective factor against UTI	
			FINAL GRADE B

Other Procedures

Table A72: Guideline references for surgical prophylaxis recommendations

Reference	Type of Surgery	First line	Alternative for Severe Penicillin Allergy	Duration	Remarks	Level of Evidence/ Grade
AUA [221]	Implanted prosthesis	Aminoglycoside + first- /second-generation cephalosporin	Aminoglycoside + vancomycin	Single dose	Extrapolated from orthopaedic surgery (hip fracture surgery) and obstetric-gynecologic surgery (Mesh Inguinal Hernioplasty) – systematic review and meta-analysis	4
SAAGAR[13]	Implanted prosthesis	Cefazolin + gentamicin	Vancomycin + gentamicin	Single dose	No reference provided	4
ASHP/IDSA[2]	Implanted prosthesis	Cefazolin + aminoglycoside	Clindamycin or vancomycin +/- aminoglycoside or aztreonam	Single dose or less than 24 hours	No reference provided	4
EAU[222]	Urodynamic study	Not required			Cited Cochrane review (search date of Dec 2009) and 2 later RCTs: the meta-analysis found no benefit of antibiotic prophylaxis vs placebo in terms of clinical UTI (RR 0.73, 95% CI 0.52-1.03). The antibiotic reduced the rate of post-procedural bacteriuria (RR 0.35, 95% CI 0.22-0.56) The 2 RCTs did not report the incidence of clinical UTI and had conflicting findings in terms of the risk of bacteriuria	1^+
ASHP/IDSA[2]	Urodynamic study	Cefazolin	Fluoroquinolone or aminoglycoside with or without clindamycin	Single dose or less than 24 hours	Cited meta-analysis of 8 RCTs (methodologically poor, searched up to Jan 2007) with 995 patients who underwent urodynamic study. The study found a decrease in bacteriuria with antibiotic prophylaxis (OR 0.39; 95 CI 0.24-0.61), NNT was 13. The antibiotic use was different in type, dose and duration. There were reports of 1 mild allergy and 1 anaphylaxis in the treatment group	1^-
EAU[222]	Shockwave lithotripsy	Not required		NA	For patients without bacteriuria undergoing ESWL, EAU cited a systematic review and meta-analysis (2012), the Canadian guidelines (2015) and 1 RCT The systematic review and meta-analysis found no evidence of benefit in terms of reducing the rate of post-procedural fever or bacteriuria	1^+

					One trial in 2017 with 274 patients with a severe risk of bias found no difference in the rate of bacteriuria and no reduction in fever For patients with bacteriuria or deemed at high risk of complication, one RCT compared the use of ofloxacin or trimethoprim-sulphamethoxazole for 3 days prior and 4 days subsequent to ESWL in 56 patients. They found no difference in the rate of clinical UTI at 7 days and no difference in post-ESWL bacteriuria	
AUA [221]	Shockwave lithotripsy	Not required antibiotic unless there are risk factors			Cited the same systematic review (2012) as EAU	1^+
EAU[222]	Shockwave lithotripsy	Not required unless with high risk of infection (large stone burden, associated pyuria, history of pyelonephritis and adjunctive procedure including stent, nephrostomy insertion, PCNL or ureteroscopy)			Conducted a systematic review (8 studies included for meta-analysis) – the incidence of UTI and fever were f4.2% and 3.4% respectively. Antibiotic prophylaxis was not associated with a significant difference in the risk of post-procedural UTI (RR 0.76, 95% CI 0.39-1.48)	1^+
ASHP/IDSA[2]	Shockwave lithotripsy	Cefazolin	Fluoroquinolone or aminoglycoside	Single dose or less than 24 hours	Cited meta-analysis of 8 RCTs and 6 clinical case series. The overall rate of UTI in the RCTs ranged from 0-7.7% with antimicrobial prophylaxis and from 0%-28% in the control group (RR 0.45, 95% CI 0.22-0.91)	1^-

***AUA:** American Urological Association; **SAAGAR**: South Australian expert Advisory Group on Antimicrobial Resistance; **EAU**: European Association of Urology; **NNT:** Number needed to treat; **ESWL:** Extracorporeal shock wave lithotripsy

Note: ASHP guidelines do not specify antimicrobial prophylaxis to specific procedures but did recommend antimicrobial prophylaxis to procedures that are considered clean and clean-contaminated.

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