Cochrane
Library

Cochrane Database of Systematic Reviews

Perioperative antibiotics for preventing post-surgical site infections in solid organ transplant recipients (Protocol)

Chan S, Ng S, Chan HP, Pascoe E, Playford EG, Wong G, Chapman JR, Lim WH, Francis RS, Isbel NM, Campbell SB, Hawley CM, Johnson DW

Chan S, Ng S, Chan HP, Pascoe E, Playford EG, Wong G, Chapman JR, Lim WH, Francis RS, Isbel NM, Campbell SB, Hawley CM, Johnson DW.

Perioperative antibiotics for preventing post-surgical site infections in solid organ transplant recipients.

Cochrane Database of Systematic Reviews 2018, Issue 12. Art. No.: CD013209.

DOI: 10.1002/14651858.CD013209.

www.cochranelibrary.com

TABLE OF CONTENTS

HEADER	1
ABSTRACT	1
BACKGROUND	1
OBJECTIVES	2
METHODS	2
ACKNOWLEDGEMENTS	5
REFERENCES	5
APPENDICES	7
CONTRIBUTIONS OF AUTHORS	11
DECLARATIONS OF INTEREST	11

Perioperative antibiotics for preventing post-surgical site infections in solid organ transplant recipients

Samuel Chan¹, Samantha Ng¹, Hooi P Chan², Elaine Pascoe³, Elliott Geoffrey Playford⁴, Germaine Wong⁵, Jeremy R Chapman⁶, Wai H Lim⁷, Ross S Francis¹, Nicole M Isbel¹, Scott B Campbell¹, Carmel M Hawley¹, David W Johnson¹

¹Department of Nephrology, Princess Alexandra Hospital, Brisbane, Australia. ²General Practice Queensland, Brisbane, Australia. ³Department of Biostatistics, Faculty of Medicine, The University of Queensland, Brisbane, Australia. ⁴Department of Infection Control Management, Princess Alexandra Hospital, Woolloongabba, Australia. ⁵School of Public Health, The University of Sydney, Sydney, Australia. ⁶Department of Nephrology, Westmead Clinical School, Sydney, Australia. ⁷Department of Nephrology, Sir Charles Gardiner Hospital, Perth, Australia

Contact address: Samuel Chan, Department of Nephrology, Princess Alexandra Hospital, Ipswich Road, Woolloongabba, Brisbane, Queensland, 4102, Australia. samuel.chan@uqconnect.edu.au.

Editorial group: Cochrane Kidney and Transplant Group.

Publication status and date: New, published in Issue 12, 2018.

Citation: Chan S, Ng S, Chan HP, Pascoe E, Playford EG, Wong G, Chapman JR, Lim WH, Francis RS, Isbel NM, Campbell SB, Hawley CM, Johnson DW. Perioperative antibiotics for preventing post-surgical site infections in solid organ transplant recipients. *Cochrane Database of Systematic Reviews* 2018, Issue 12. Art. No.: CD013209. DOI: 10.1002/14651858.CD013209.

Copyright © 2018 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

ABSTRACT

This is a protocol for a Cochrane Review (Intervention). The objectives are as follows:

This review aims to look at the benefits and harms of perioperative antibiotics versus placebo or no antibiotics for preventing post-surgical site infections in solid organ transplant recipients.

BACKGROUND

Description of the condition

Infections following solid organ transplantation are a leading cause of morbidity and death (Fishman 2017; Owens 2008). Depending on the organ transplanted and the era at which the transplant took place, surgical site infections (SSI) have been reported to occur in 3% to 53% of patients transplanted (Choi 2013; Guaraldi 2005). A SSI is an infection that occurs after surgery in the part of the body where the surgery took place. This could include simple erythema of the wound, with subsequent treatment, or return to theatre for wound debridement. The highest rates have

been observed in small bowel/multivisceral transplants, where SSI rates can reach over 90% when prosthetic mesh is used, followed by liver, pancreas and kidney transplants (Choi 2013; Guaraldi 2005). SSIs are associated with appreciable morbidity, and have been found to extend the average hospital stay by seven days, increase readmission rates, and increase the cost of hospitalisation by nearly 100% (Hollenbeak 2001; Kirkland 1999). Furthermore, SSIs have been associated with increased risks of graft failure and death in solid organ transplant recipients. Moreover, solid organ transplant recipients are at high risk of developing infections with antibiotic-resistant organisms (Linares 2007; Patel 2008; Safdar 2002). Infections with multidrug-resistant organisms (MDRO) have been associated with increased morbidity and death, par-

ticularly in solid organ transplant recipients (Linares 2007; Patel 2008). It is therefore crucial that strategies are developed to minimise SSIs following transplantation (Everitt 1994; Hellinger 2009; Humar 2001; Loinz 2006; Mattner 2007). The interventions and studies described need to be stratified based on time (era), patient type (organ) and examination of microbiological data.

Description of the intervention

Administration of one or more antibiotics either as a one-off stat dose or extended for several days around the time of the operation may prevent surgical site infections from occurring following solid organ transplantation.

How the intervention might work

Antibiotics have commonly been prescribed prior to surgical procedures to try to mitigate the risk of surgical infections (Anesi 2018; Midtvedt 1998; Soave 2001). The principle is that time-limited administration of antibiotics directed against most likely anticipated organisms in the perioperative period will prevent any resident or introduced micro-organisms from developing an established SSI. Although some transplant centres have used antibiotics prophylactically (Tillegard 1984; Townsend 1980) and some guidelines advocate for pre- or perioperative antibiotic prophylaxis (British Columbia Guidelines 2018; Princess Alexandra Hospital 2015), antibiotic use may be associated with significant harm including antibiotic-associated diarrhoea, antibiotic resistance and increasing costs, and thus warrants further study.

Why it is important to do this review

There is uncertainty regarding the benefits versus harm in using prophylactic antibiotics as a potential strategy for preventing surgical site infections in solid organ transplant recipients (Bratzler 2013; Humar 2005). Specifically, there are no formal recommendations on using perioperative antibiotic prophylaxis in solid organ transplant recipients outside of the Clinical practice guidelines for antimicrobial prophylaxis in surgery by the Infectious Diseases Society of America, American Society of Health-System Pharmacists, Surgical Infection Society, and Society for Healthcare Epidemiology of America (IDSA/ASHP/SIS/SHEA). These provide general prophylactic antibiotic recommendations for solid organ transplant recipients, but do not address the unique circumstances of the transplant population (Bratzler 2013). Indeed, the transplant population is a vulnerable group given their increased risk of cardiovascular morbidity and mortality, and the higher infective risk compared with the general population.

With the high risk of SSIs in solid organ transplant recipients, and a rising incidence of MDROs in solid organ transplant donors

and recipients, it seems logical to progressively broaden and extend perioperative antibiotic prophylaxis. However, the overuse of perioperative antibiotic prophylaxis may lead to a rise in the rates of *Clostridium difficile* colonization and colitis (Jobe 1995; Kreisel 1995; Privitera 1991), increase the rates of antimicrobial resistance (Roberts 1978) and increase adverse drug reactions as well as increase financial costs. Microbial colonisation patterns are also important in determining appropriate strategies. Consideration needs to be given to the amount and type of organism carried by the donor or the recipient at the clinical centre.

Given the complexities of solid organ transplant recipients and the unique risks for SSIs, guidance that is more customised to the solid organ transplant recipient scenario is needed. In the absence of formal guidelines, the aim of this study is to systematically review the evidence of perioperative antibiotics versus placebo or no antibiotics for preventing post-surgical site infections in solid organ transplant recipients.

OBJECTIVES

This review aims to look at the benefits and harms of perioperative antibiotics versus placebo or no antibiotics for preventing post-surgical site infections in solid organ transplant recipients.

METHODS

Criteria for considering studies for this review

Types of studies

All randomised controlled trials (RCTs) and quasi-RCTs (RCTs in which allocation to treatment was obtained by alternation, use of alternate medical records, date of birth or other predictable methods) assessing the safety or efficacy or both of perioperative antibiotics in SSIs in solid organ transplant recipients.

Types of participants

Inclusion criteria

- Adults and children who receive a solid-organ transplant, including combined grafts (e.g. kidney-pancreas).

Exclusion criteria

- Pregnant women

Types of interventions

We will include studies of any antibiotic medication. The following comparisons will be investigated.

- Any antibiotic medication versus placebo or no treatment
- Any antibiotic medication versus any other antibiotic medication
- Low dose versus high dose of the same antibiotic medication
- Short-course versus long-course antibiotic therapy
- Oral versus intravenous administration of the same or different antibiotic medication.

Types of outcome measures

The outcomes selected include the relevant [SONG core outcome sets](#) as specified by the Standardised Outcomes in Nephrology initiative ([SONG 2017](#)).

Primary outcomes

- Incidence of surgical site infection
- Stratification by era of study (multi-drug resistance organisms and technical issues)
- Microbiological data regarding resistance for surgical site infection

Secondary outcomes

- Death (all-causes)
- Incidence of graft loss including death with a functioning graft
- Incidence of graft rejection (classified as clinically suspected and treated, or biopsy proven)
- Antimicrobial resistance
- Wound dehiscence/wound exploration
- Incidence of other infections (e.g. urinary tract infections, pneumonia, bacteraemia)
- Graft health
- Cardiovascular disease
- Cancer
- Life participation
- Biochemical and haematological parameters (e.g. C-reactive protein, white cell count (WCC))
- Adverse reactions to antibiotics
- Length of hospitalisation
- Organ type
- Transplant volume at each centre
- Cost of intervention and side-effects
- Overall hospitalisation costs.

Search methods for identification of studies

Electronic searches

We will search the [Cochrane Kidney and Transplant Register of Studies](#) through contact with the Information Specialist using search terms relevant to this review. The Register contains studies identified from the following sources.

1. Monthly searches of the Cochrane Central Register of Controlled Trials (CENTRAL)
2. Weekly searches of MEDLINE OVID SP
3. Handsearching of kidney-related journals and the proceedings of major kidney and transplant conferences
4. Searching of the current year of EMBASE OVID SP
5. Weekly current awareness alerts for selected kidney journals
6. Searches of the International Clinical Trials Register (ICTRP) Search Portal and ClinicalTrials.gov.

Studies contained in the Register are identified through searches of CENTRAL, MEDLINE, and EMBASE based on the scope of Cochrane Kidney and Transplant. Details of search strategies, as well as a list of handsearched journals, conference proceedings and current awareness alerts, are available in the *Specialised Register* section of information about [Cochrane Kidney and Transplant](#). See [Appendix 1](#) for search terms used in strategies for this review.

Searching other resources

1. Reference lists of review articles, relevant studies and clinical practice guidelines.
2. Letters seeking information about unpublished or incomplete studies to investigators known to be involved in previous studies.

Data collection and analysis

Selection of studies

The search strategy described will be used to obtain titles and abstracts of studies that may be relevant to the review. The titles and abstracts will be screened independently by two authors, who will discard studies that are not applicable; however studies and reviews that might include relevant data or information on studies will be retained initially. Two authors will independently assess retrieved abstracts and, if necessary the full text, of these studies to determine which studies satisfy the inclusion criteria. If there is a disagreement regarding the article validity and inclusion, a tie will be broken by a third author.

Data extraction and management

Data extraction will be carried out independently by two authors using standard data extraction forms. Studies reported in non-English language journals will be translated before assessment. Where more than one publication of one study exists, reports will

be grouped together and the publication with the most complete data will be used in the analyses. Where relevant outcomes are only published in earlier versions these data will be used. Any discrepancy between published versions will be highlighted.

Assessment of risk of bias in included studies

The following items will be independently assessed by two authors using the risk of bias assessment tool (Higgins 2011) (see Appendix 2).

- Was there adequate sequence generation (selection bias)?
- Was allocation adequately concealed (selection bias)?
- Was knowledge of the allocated interventions adequately prevented during the study?
  - Participants and personnel (performance bias)
  - Outcome assessors (detection bias)
- Were incomplete outcome data adequately addressed (attrition bias)?
  - Are reports of the study free of suggestion of selective outcome reporting (reporting bias)?
  - Was the study apparently free of other problems that could put it at a risk of bias?

Measures of treatment effect

For dichotomous outcomes (incidence of surgical site infection, death, graft loss, incidence of other infections, adverse reactions to antimicrobial agents), results will be expressed as risk ratio (RR) with 95% confidence intervals (CI). Where continuous scales of measurement are used to assess the effects of treatment (biochemical parameters such as WCC, length of hospitalisation), the mean difference (MD) will be used, or the standardised mean difference (SMD) if different scales have been used.

Unit of analysis issues

- Cluster RCTs: if cluster studies have been appropriately analysed to account for clustering in the data, direct measures of effect will be extracted if available and used in the meta-analyses using the generic inverse-variance method. If such information is not available, we will use cluster-level data as individual units of analysis, if the necessary data are available.
- Cross-over studies: we will only use data from the first period if these are available.
- Studies with multiple treatment groups: we will try to collapse multiple treatment groups into one where appropriate to enable single pair wise comparison (e.g. collapsing three groups of different doses of antibiotics into one group and include in single pair wise comparison versus placebo) (Higgins 2011).

Dealing with missing data

Any further information required from the original author will be requested by written correspondence (e.g. emailing corresponding author) and any relevant information obtained in this manner will be included in the review. Evaluation of important numerical data such as screened, randomised patients as well as intention-to-treat, as-treated and per-protocol population will be carefully performed. Attrition rates, for example drop-outs, losses to follow-up and withdrawals will be investigated. Issues of missing data and imputation methods (for example, last-observation-carried-forward) will be critically appraised (Higgins 2011).

Assessment of heterogeneity

We will first assess the heterogeneity by visual inspection of the forest plot. We will quantify statistical heterogeneity using the I^2 statistic, which describes the percentage of total variation across studies that is due to heterogeneity rather than sampling error (Higgins 2003). A guide to the interpretation of I^2 values will be as follows.

- 0% to 40%: might not be important
- 30% to 60%: may represent moderate heterogeneity
- 50% to 90%: may represent substantial heterogeneity
- 75% to 100%: considerable heterogeneity.

The importance of the observed value of I^2 depends on the magnitude and direction of treatment effects and the strength of evidence for heterogeneity (e.g. P-value from the χ^2 test, or a confidence interval for I^2) (Higgins 2011).

Assessment of reporting biases

If possible, funnel plots will be used to assess for the potential existence of small study bias (Higgins 2011).

Data synthesis

Data will be pooled using the random-effects model but the fixed-effect model will also be used to ensure robustness of the model chosen and susceptibility to outliers.

Subgroup analysis and investigation of heterogeneity

Subgroup analysis will be used to explore possible sources of heterogeneity (e.g. participants, interventions, study quality). Heterogeneity among participants could be related to age, sex, and time from transplantation to surgical site infection. Heterogeneity in treatments could be related to prior agent(s) used and the agent, dose and duration of therapy. Additionally, heterogeneity could be related to the type of organ transplant (e.g. kidney, liver, lung, pancreas, intestines), as well as the era of transplant (pre-2005 versus post-2005) and the country of origin of the studies.

Heterogeneity among bacterial strains could be related to the following conditions.

- Different antibiotics
- Different doses
- Induction immunosuppression choice (e.g. anti-thymocyte globulin versus basiliximab).

Adverse effects will be tabulated and assessed with descriptive techniques, as they are likely to be different for the various agents used. Where possible, the risk difference with 95% CI will be calculated for each adverse effect, either compared to no treatment or to another agent.

Sensitivity analysis

We will perform sensitivity analyses in order to explore the influence of the following factors on effect size.

- Repeating the analysis excluding unpublished studies
- Repeating the analysis taking account of risk of bias, as specified
- Repeating the analysis excluding any very long or large studies to establish how much they dominate the results
- Repeating the analysis excluding studies using the following filters: diagnostic criteria, language of publication, source of funding (industry versus other), and country.

'Summary of findings' tables

We will present the main results of the review in 'Summary of findings' tables. These tables present key information concerning the quality of the evidence, the magnitude of the effects of the interventions examined, and the sum of the available data for the

main outcomes (Schünemann 2011a). The 'Summary of findings' tables also include an overall grading of the evidence related to each of the main outcomes using the GRADE (Grades of Recommendation, Assessment, Development and Evaluation) approach (GRADE 2008; GRADE 2011). The GRADE approach defines the quality of a body of evidence as the extent to which one can be confident that an estimate of effect or association is close to the true quantity of specific interest. The quality of a body of evidence involves consideration of within-trial risk of bias (methodological quality), directness of evidence, heterogeneity, precision of effect estimates and risk of publication bias (Schünemann 2011b). We plan to present the following outcomes in the 'Summary of findings' tables.

- Incidence of surgical site infection
- Stratification by era of study (multi-drug resistance organisms and technical issues)
- Microbiological data regarding resistance for surgical site infection
- Death (all causes)
- Incidence of graft loss including death with a functioning graft
- Incidence of other infections (e.g. urinary tract infections, pneumonia, bacteraemia)
- Adverse reactions to antibiotics

ACKNOWLEDGEMENTS

The authors would like to thank Cochrane Kidney and Transplant for their support and the referees for their comments and feedback during the preparation of this protocol.

REFERENCES

Additional references

Anesi 2018

Anesi JA, Blumberg EA, Abbo AM. Perioperative antibiotic prophylaxis to prevent surgical site infections in solid organ transplantation. *Transplantation* 2018;**102**(1):21–34. MEDLINE: 28614192

Bratzler 2013

Bratzler DW, Dellinger EP, Olsen KM, Perl TM, Auwaerter PG, Bolon MK, et al. Clinical practice guidelines for antimicrobial prophylaxis in surgery. *Surgical Infections* 2013;**14**(1):73–156. MEDLINE: 23461695

British Columbia Guidelines 2018

British Columbia Guidelines. Clinical guidelines for kidney transplantation 2018. www.transplant.bc.ca/Documents/Health%20Professionals/Clinical%20guidelines/Clinical%20Guidelines%20for%20Kidney%20Transplantation.pdf Accessed 21 November 2018.

Choi 2013

Choi SU, Lee JH, Oh CK, Shin GT, Kim H, Kim SJ, et al. Clinical significance of prophylactic antibiotics in renal transplantation. *Transplantation Proceedings* 2013;**45**(4):1392–5. MEDLINE: 23726580

Evertt 1994

Evertt JE, Wahoff DC, Statz C, Gillingham KJ, Gruessner A, Gruessner RW, et al. Characterization and impact of wound infection after pancreas transplantation. *Archives of Surgery* 1994;**129**(12):1310–6. MEDLINE: 7986162

Fishman 2017

Fishman JA. Infection in organ transplantation. *American Journal of Transplantation* 2017;**17**(4):856–79. MEDLINE: 28117944

GRADE 2008

Guyatt GH, Oxman AD, Vist GE, Kunz R, Falck-Ytter Y, Alonso-Coello P, et al. GRADE: an emerging consensus on

- rating quality of evidence and strength of recommendations. *BMJ* 2008;**336**(7650):924–6. MEDLINE: 18436948
- GRADE 2011**
Guyatt G, Oxman A D, Akl E A, Kunz R, Vist G, Brozek J, et al. GRADE guidelines: 1. Introduction-GRADE evidence profiles and summary of findings tables. *Journal of Clinical Epidemiology* 2011;**64**(4):383–94. MEDLINE: 22818160
- Guaraldi 2005**
Guaraldi C, Cocchi S, Codeluppi M, Di Benedetto F, De Ruvo N, Masetti M, et al. Outcome, incidence and timing of infectious complications in small bowel and multivisceral organ transplantation patients. *Transplantation* 2005;**80**(12):1742–8. MEDLINE: 16378070
- Hellinger 2009**
Hellinger WC, Crook JE, Heckman MG, Diehl NN, Shalev JA, Zubair AC, et al. Surgical site infection after liver transplantation: risk factors and association with graft loss or death. *Transplantation* 2009;**87**(9):1387–93. MEDLINE: 19424041
- Higgins 2003**
Higgins JP, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. *BMJ* 2003;**327**(7414):557–60. MEDLINE: 12958120
- Higgins 2011**
Higgins JP, Green S (editors). *Cochrane Handbook for Systematic Reviews of Interventions* Version 5.1.0 [updated March 2011]. The Cochrane Collaboration, 2011. Available from www.cochrane-handbook.org.
- Hollenbeak 2001**
Hollenbeak CS, Alfrey EJ, Souba WW. The effect of surgical site infections on outcomes and resource utilization after liver transplantation. *Surgery* 2001;**130**(2):388–95. MEDLINE: 11490376
- Humar 2001**
Humar A, Ramcharan T, Denny R, Gillingham KJ, Payne WD, Matas AJ. Are wound complications after a kidney transplant more common with modern immunosuppression?. *Transplantation* 2001;**72**(12):1920–3. MEDLINE: 11773889
- Humar 2005**
Humar A, Matas AJ. Surgical complications after kidney transplantation. *Seminars in Dialysis* 2005;**15**(6):505–10. MEDLINE: 16398714
- Jobe 1995**
Jobe BA, Grasley A, Deveney KE, Deveney CW, Sheppard BC. Clostridium difficile colitis: an increasing hospital-acquired illness. *American Journal of Surgery* 1995;**169**(5):480–3. MEDLINE: 7747823
- Kirkland 1999**
Kirkland KB, Briggs JP, Trivette SL, Wilkinson WE, Sexton DJ. The impact of surgical-site infections in the 1990s: attributable mortality, excess length of hospitalization and extra costs. *Infection Control & Hospital Epidemiology* 1999;**20**(11):725–30. MEDLINE: 10580621
- Kreisel 1995**
Kreisel D, Savel TG, Silver AL, Cunningham JD. Surgical antibiotic prophylaxis and Clostridium difficile toxin positivity. *Archives of Surgery* 1995;**130**(9):989–93. MEDLINE: 7661686
- Linares 2007**
Linares L, Cervera C, Cofan F, Ricart MJ, Esforzado N, Torregrosa V, et al. Epidemiology and outcomes of multiple antibiotic-resistant bacterial infection in renal transplantation. *Transplantation Proceedings* 2007;**39**(7):2222–4. MEDLINE: 17889144
- Loinz 2006**
Loinz C, Kato T, Nishida S, Weppeler D, Levi D, Dowdy L, et al. Bacterial infections after intestine and multivisceral transplantation. The experience of the University of Miami (1994-2001). *Hepato-Gastroenterology* 2006;**53**(68):234–42. MEDLINE: 16608031
- Mattner 2007**
Mattner F, Fischer S, Weissbrodt H, Chaberny IF, Sohr D, Gottlieb J, et al. Post-operative nosocomial infections after lung and heart transplantation. *Journal of Heart & Lung Transplantation* 2007;**26**(3):241–9. MEDLINE: 17346626
- Midtvedt 1998**
Midtvedt K, Hartmann A, Midtvedt T, Brekke IB. Routine perioperative antibiotic prophylaxis in renal transplantation. *Nephrology Dialysis Transplantation* 1998;**13**(7):1637–41. MEDLINE: 9681704
- Owens 2008**
Owens CD, Stoessel K. Surgical site infections: epidemiology, microbiology and prevention. *Journal of Hospital Infection* 2008;**70** Suppl 2:3–10. MEDLINE: 19022115
- Patel 2008**
Patel G, Huprikar S, Factor SH, Jenkins SG, Calfee DP. Outcomes of carbapenem-resistant Klebsiella pneumoniae infection and the impact of antimicrobial and adjunctive therapies. *Infection Control & Hospital Epidemiology* 2008;**29**(12):1099–106. MEDLINE: 18973455
- Princess Alexandra Hospital 2015**
Princess Alexandra Hospital. Princess Alexandra Hospital Renal Transplant Surgical Antibiotic Prophylaxis Guidelines. Version 1; August 2015. www.metrosouth.health.qld.gov.au/sites/default/files/content/pah-renal-transplant.pdf Accessed 21 November 2018.
- Privitera 1991**
Privitera G, Scarpellini P, Ortisi G, Nicastro G, Nicolin R, de Lalla F. Prospective study of Clostridium difficile intestinal colonization and disease following single-dose antibiotic prophylaxis in surgery. *Antimicrobial Agents & Chemotherapy* 1991;**35**(1):208–10. MEDLINE: 2014978
- Roberts 1978**
Robert NJ Jr, Douglas RG Jr. Gentamicin use and Pseudomonas and Serratia resistance: effect of a surgical prophylaxis regimen. *Antimicrobial Agents & Chemotherapy* 1978;**13**(2):214–20. MEDLINE: 348094

Safdar 2002

Safdar N, Maki DG. The commonality of risk factors for nosocomial colonization and infection with antimicrobial-resistant *Staphylococcus aureus*, *Enterococcus*, gram-negative bacilli, *Clostridium difficile*, and *Candida*. *Annals of Internal Medicine* 2002;**136**(11):834–44. MEDLINE: 12044132

Schünemann 2011a

Schünemann HJ, Oxman AD, Higgins JP, Vist GE, Glasziou P, Guyatt GH. Chapter 11: Presenting results and 'Summary of findings' tables. In: Higgins JP, Green S (editors). *Cochrane Handbook for Systematic Reviews of Interventions* Version 5.1.0 [updated March 2011]. The Cochrane Collaboration, 2011. Available from www.cochrane-handbook.org.

Schünemann 2011b

Schünemann HJ, Oxman AD, Higgins JP, Deeks JJ, Glasziou P, Guyatt GH. Chapter 12: Interpreting results and drawing conclusions. In: Higgins JP, Green S (editors). *Cochrane Handbook for Systematic Reviews of Interventions* Version 5.1.0 [updated March 2011].

The Cochrane Collaboration, 2011. Available from www.cochrane-handbook.org.

Soave 2001

Soave R. Prophylaxis strategies for solid-organ transplantation. *Clinical Infectious Diseases* 2001;**33** Suppl 1:S26–31. MEDLINE: 11389519

SONG 2017

SONG Initiative. The SONG Handbook Version 1.0. www.songinitiative.org/reports-and-publications/ 2017.

Tillegard 1984

Tillegard A. Renal transplant wound infection: the value of prophylactic antibiotic treatment. *Scandinavian Journal of Urology & Nephrology* 1984;**18**(3):215–21. MEDLINE: 6387898

Townsend 1980

Townsend TR, Rudolf LE, Westervelt FB Jr, Mandell GL, Wenzel RP. Prophylactic antibiotic therapy with cefamandole and tobramycin for patients undergoing renal transplantation. *Infection Control* 1980;**1**(2):93–6. MEDLINE: 7033157

* Indicates the major publication for the study

APPENDICES

Appendix I. Electronic search strategies

Database	Search terms
CENTRAL	- solid organ transplant*:ti,ab,kw (Word variations have been searched) - kidney transplant*:ti,ab,kw (Word variations have been searched) - pancreas transplant*:ti,ab,kw (Word variations have been searched) - liver transplant*:ti,ab,kw (Word variations have been searched) - heart transplant*:ti,ab,kw (Word variations have been searched) - lung transplant*:ti,ab,kw (Word variations have been searched) - simultaneous pancreas-kidney transplant*:ti,ab,kw (Word variations have been searched) "SPK":ti,ab,kw (Word variations have been searched) {or #1-#8} - MeSH descriptor: [Anti-Bacterial Agents] explode all trees - MeSH descriptor: [Antibiotic Prophylaxis] this term only - antibiotic* or "antibiotic prophylaxis":ti,ab,kw (Word variations have been searched) {or #10-#12} - MeSH descriptor: [Surgical Wound Infection] this term only - surgical site infection*:ti,ab,kw (Word variations have been searched) - surgical wound infection*:ti,ab,kw (Word variations have been searched) ((wound* or site*) and infection*):ti,ab,kw (Word variations have been searched)

(Continued)

	18. {or #14-#17} 19. {and #9, #13, #18}
MEDLINE (OVID)	1. Organ Transplantation/ 2. Kidney Transplantation/ 3. Pancreas Transplantation/ 4. exp Lung Transplantation/ 5. exp Heart Transplantation/ 6. Liver Transplantation/ 7. (pancreas\$ transplant\$ and kidney\$ transplant\$.tw. 8. simultaneous pancreas-kidney transplant\$.tw. 9. spk.tw. 10. lung transplant\$.tw. 11. heart transplant\$.tw. 12. liver transplant\$.tw. 13. solid organ transplant\$.tw. 14. kidney transplant\$.tw. 15. pancreas transplant\$.tw. 16. or/1-15 17. exp Anti-Bacterial Agents/ 18. Antibiotic Prophylaxis/ 19. or/17-18 20. Surgical Wound Infection/ 21. surgical site infection\$.tw. 22. surgical wound infection\$.tw. 23. ((wound\$ or site\$) and infection\$).tw. 24. or/20-23 25. and/16,19,24
EMBASE (OVID)	1. organ transplantation/ 2. exp heart transplantation/ 3. exp kidney transplantation/ 4. exp liver transplantation/ 5. pancreas transplantation/ 6. exp lung transplantation/ 7. kidney pancreas transplantation/ 8. or/1-7 9. exp antibiotic agent/ 10. antibiotic prophylaxis/ 11. or/9-10 12. exp surgical infection/ 13. surgical site infection\$.tw. 14. surgical wound infection\$.tw. 15. ((wound\$ or site\$) and infection\$).tw. 16. or/12-15 17. and/8,11,16

Appendix 2. Risk of bias assessment tool

Potential source of bias	Assessment criteria
Random sequence generation Selection bias (biased allocation to interventions) due to inadequate generation of a randomised sequence	<i>Low risk of bias:</i> Random number table; computer random number generator; coin tossing; shuffling cards or envelopes; throwing dice; drawing of lots; minimisation (minimisation may be implemented without a random element, and this is considered to be equivalent to being random)
	<i>High risk of bias:</i> Sequence generated by odd or even date of birth; date (or day) of admission; sequence generated by hospital or clinic record number; allocation by judgement of the clinician; by preference of the participant; based on the results of a laboratory test or a series of tests; by availability of the intervention
	<i>Unclear:</i> Insufficient information about the sequence generation process to permit judgement
Allocation concealment Selection bias (biased allocation to interventions) due to inadequate concealment of allocations prior to assignment	<i>Low risk of bias:</i> Randomisation method described that would not allow investigator/participant to know or influence intervention group before eligible participant entered in the study (e.g. central allocation, including telephone, web-based, and pharmacy-controlled, randomisation; sequentially numbered drug containers of identical appearance; sequentially numbered, opaque, sealed envelopes)
	<i>High risk of bias:</i> Using an open random allocation schedule (e.g. a list of random numbers); assignment envelopes were used without appropriate safeguards (e.g. if envelopes were unsealed or non-opaque or not sequentially numbered); alternation or rotation; date of birth; case record number; any other explicitly unconcealed procedure
	<i>Unclear:</i> Randomisation stated but no information on method used is available
Blinding of participants and personnel Performance bias due to knowledge of the allocated interventions by participants and personnel during the study	<i>Low risk of bias:</i> No blinding or incomplete blinding, but the review authors judge that the outcome is not likely to be influenced by lack of blinding; blinding of participants and key study personnel ensured, and unlikely that the blinding could have been broken
	<i>High risk of bias:</i> No blinding or incomplete blinding, and the outcome is likely to be influenced by lack of blinding; blinding of key study participants and personnel attempted, but likely that the blinding could have been broken, and the outcome is likely to be influenced by lack of blinding
	<i>Unclear:</i> Insufficient information to permit judgement

(Continued)

Blinding of outcome assessment Detection bias due to knowledge of the allocated interventions by outcome assessors	<i>Low risk of bias:</i> No blinding of outcome assessment, but the review authors judge that the outcome measurement is not likely to be influenced by lack of blinding; blinding of outcome assessment ensured, and unlikely that the blinding could have been broken <i>High risk of bias:</i> No blinding of outcome assessment, and the outcome measurement is likely to be influenced by lack of blinding; blinding of outcome assessment, but likely that the blinding could have been broken, and the outcome measurement is likely to be influenced by lack of blinding <i>Unclear:</i> Insufficient information to permit judgement
Incomplete outcome data Attrition bias due to amount, nature or handling of incomplete outcome data	<i>Low risk of bias:</i> No missing outcome data; reasons for missing outcome data unlikely to be related to true outcome (for survival data, censoring unlikely to be introducing bias); missing outcome data balanced in numbers across intervention groups, with similar reasons for missing data across groups; for dichotomous outcome data, the proportion of missing outcomes compared with observed event risk not enough to have a clinically relevant impact on the intervention effect estimate; for continuous outcome data, plausible effect size (difference in means or standardised difference in means) among missing outcomes not enough to have a clinically relevant impact on observed effect size; missing data have been imputed using appropriate methods <i>High risk of bias:</i> Reason for missing outcome data likely to be related to true outcome, with either imbalance in numbers or reasons for missing data across intervention groups; for dichotomous outcome data, the proportion of missing outcomes compared with observed event risk enough to induce clinically relevant bias in intervention effect estimate; for continuous outcome data, plausible effect size (difference in means or standardized difference in means) among missing outcomes enough to induce clinically relevant bias in observed effect size; 'as-treated' analysis done with substantial departure of the intervention received from that assigned at randomisation; potentially inappropriate application of simple imputation <i>Unclear:</i> Insufficient information to permit judgement
Selective reporting Reporting bias due to selective outcome reporting	<i>Low risk of bias:</i> The study protocol is available and all of the study's pre-specified (primary and secondary) outcomes that are of interest in the review have been reported in the pre-specified way; the study protocol is not available but it is clear that the published reports include all expected outcomes, including those that were pre-specified (convincing text of this nature may be uncommon)

(Continued)

	<i>High risk of bias:</i> Not all of the study's pre-specified primary outcomes have been reported; one or more primary outcomes is reported using measurements, analysis methods or subsets of the data (e.g. sub-scales) that were not pre-specified; one or more reported primary outcomes were not pre-specified (unless clear justification for their reporting is provided, such as an unexpected adverse effect); one or more outcomes of interest in the review are reported incompletely so that they cannot be entered in a meta-analysis; the study report fails to include results for a key outcome that would be expected to have been reported for such a study <i>Unclear:</i> Insufficient information to permit judgement
Other bias Bias due to problems not covered elsewhere in the table	<i>Low risk of bias:</i> The study appears to be free of other sources of bias. <i>High risk of bias:</i> Had a potential source of bias related to the specific study design used; stopped early due to some data-dependent process (including a formal-stopping rule); had extreme baseline imbalance; has been claimed to have been fraudulent; had some other problem <i>Unclear:</i> Insufficient information to assess whether an important risk of bias exists; insufficient rationale or evidence that an identified problem will introduce bias

CONTRIBUTIONS OF AUTHORS

1. Draft the protocol: SC
2. Study selection: SC, SN, HC
3. Extract data from studies: SC, SN, HC
4. Enter data into RevMan: SC, SN, HC
5. Carry out the analysis: SC, SN, HC
6. Interpret the analysis: SC, SN, HC
7. Draft the final review: SC, SN, HC
8. Disagreement resolution: DJ
9. Update the review: SC

DECLARATIONS OF INTEREST

- Samuel Chan: none known
- Samantha Ng: none known
- Hooi P Chan: none known
- E Geoffrey Playford: none known
- Germaine Wong: none known
- Jeremy R Chapman: none known
- Wai H Lim: none known
- Elaine M Pascoe: none known
- Nicole M Isbel: none known
- Ross S Francis: none known
- Scott B Campbell: none known
- Carmel M Hawley: none known
- David W Johnson: none known