Peritoneal dialysis-related infections in patients on peritoneal dialysis and measures designed to prevent them

Denise Campbell

A thesis submitted in fulfilment of the requirements for the degree of Doctor of Philosophy

Faculty of Medicine
University of Sydney

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Declaration

This thesis is submitted to the University of Sydney in fulfilment of the requirements for the degree of Doctor of Philosophy. The work presented in this thesis is, to the best of my knowledge and belief, original except as acknowledged in the text. I hereby declare that I have not submitted this material, either in full or in part, for a degree at this or any other institution.

Signature: .................................................. Date: ..................................................
Author’s contribution

The work presented in this thesis has been carried out by the author under the supervision of Professor Jonathan Craig, School of Public Health, University of Sydney, and the Centre for Kidney Research, Sydney Children’s Hospital Network (Westmead), Associate Professor David Mudge, Department of Nephrology, Princess Alexandra Hospital, and Associate Professor Martin Gallagher, Concord Clinical School, University of Sydney.

The author planned the research, designed the studies, obtained ethics approval, collected, managed and analysed data, interpreted results, drafted and revised the manuscripts for submission to peer-reviewed journals, and wrote and compiled this thesis. For the studies contained in chapter 3 and chapter 5 there was oversight and input from the KHA-CARI Guidelines PD Project Implementation Steering Committee.
Ethical clearance

The study presented in Chapter 3 was approved by the Human Research Ethics Committee at the University of Sydney and the Children’s Hospital at Westmead.

The study presented in Chapter 5 was approved by the Human Research Ethics Committee at the University of Sydney and the Sydney Children’s Hospitals Network at Westmead.

The study presented in Chapter 6 was approved by the Human Research Ethics Committees at the University of Sydney, Monash Health, the Sydney Children’s Hospitals Network at Westmead, Western Sydney Local Health District, and Metro South.
Abstract

Introduction
Some clinical practice guidelines recommend peritoneal dialysis (PD) as the dialysis treatment of choice for adults with residual kidney function and without significant comorbidities. However, PD-related infections (defined as exit-site infections, tunnel infections, and peritonitis) are a serious complication for PD patients. For a PD program to be successful, the prevention of PD-related infections must be a top priority. The most important of these infections is peritonitis.

Although incidence rates of peritonitis have decreased substantially with changes in procedure and the use of improved connection systems, peritonitis remains a major problem with PD. The International Society for Peritoneal Dialysis (ISPD) guidelines published in 2011 suggested that renal units should have a peritonitis rate of <0.36 episodes per patient-year as their benchmark. The current peritonitis rates in Australia (0.41; 95% CI 0.37-0.43 episodes per patient-year) and New Zealand (0.47; 95% CI 0.43-0.52 episodes per patient-year) are higher than this suggested target. Data from various countries show that while mortality directly related to peritonitis is low (less than 4%), peritonitis is a “contributing factor” to death in 16% of deaths on PD. Furthermore, peritonitis can result in peritoneal membrane failure and is a leading cause of technique failure in PD and transfer to hemodialysis.

Peritonitis is also a leading cause of hospitalisation.

To improve outcomes in PD patients, it is important that the prevention of peritonitis be a focus. In addition, the treatment of peritonitis should aim for rapid resolution of inflammation and preservation of peritoneal membrane function. Challenges in the prevention of peritonitis include the fact that peritonitis rates vary greatly between different renal centres and the peritonitis risk appears to vary from patient to patient, as
some patients never get peritonitis but others have frequent episodes. The reasons for the variability are complex and largely unexplained. Studies on preventing PD-related infections are limited both in number and in quality, and practice recommendations are a compilation of expert opinion combined with the available evidence. It is not known how good the uptake of guideline recommendations for the prevention of PD-related infection is in Australia and New Zealand, and what the reasons for their non-uptake might be.

From the patient’s perspective, not much is known about the beliefs, needs and experiences of PD patients in relation to peritonitis. Concern about the risk of peritonitis can lead to fear and anxiety, and the experience of peritonitis can result in immense pain, humiliating events, financial stress, added burden on family members and reluctant admission to hospital. A number of participants were unsure about the symptoms of peritonitis.

The aim of the studies in this thesis is to establish current practice patterns (re antimicrobial prophylaxis) in a selected number of renal units in Australia and New Zealand (ANZ) and to identify barriers to the uptake of relevant guideline recommendations, to establish current practice patterns in relation to antimicrobial prophylaxis in ANZ units more broadly by survey, to assess the evidence base for the antimicrobial agents used to prevent PD-related infections, and to explore patient experiences and beliefs about peritonitis so that the management of these patients and the support they receive can be improved. This is a hybrid thesis with several separate publishable projects presented as chapters. The studies that form this thesis evaluate and summarise the existing literature relating to the prevention of PD-related infections (chapter 2), assess current practice and barriers to antimicrobial prophylaxis at 8 renal units in ANZ (chapter 3), evaluate and summarise the available evidence for the use of antimicrobial agents to prevent peritonitis in PD patients (chapter 4), assess
current practice at ANZ renal units in relation to antimicrobial prophylaxis by survey (chapter 5), and explore patient experiences and beliefs about peritonitis (chapter 6).

Methods and Main Findings

Prevention of peritoneal dialysis-related infections*


Chapter two summarises the evidence relating to the various interventions that have been employed to prevent exit-site infection (ESI), tunnel infection and peritonitis. The strategies include the use of antibiotic prophylaxis at Tenckhoff catheter insertion, the use of oral, nasal and topical antibiotics once the catheter has been implanted, the use of disinfectants at the exit site, modifications of the transfer set used in continuous ambulatory peritoneal dialysis (CAPD), changes to the catheter design, the surgical method used to implant the PD catheter, the type and length of training given to patients, the making of home visits by trained PD nurses, the use of antibiotic prophylaxis in patients undergoing certain invasive procedures and the co-administration of antifungal prophylaxis to PD patients whenever they are given an antibiotic treatment course. The review showed that, overall, there is a lack of RCTs for many interventions and data from less rigorous study designs such as cohort studies are the current best available evidence. In addition, the quality of the available RCTs is variable. The quality of the evidence is strong for some aspects such as the PD connection method and the use of antibiotic to prevent ESI but is weak for other areas such as the method for training patients.
Assessment of current practice and barriers to antimicrobial prophylaxis in peritoneal dialysis patients*

*Campbell DJ, Brown FG, Craig JC, Gallagher MP, Johnson DW, Kirkland GS, Kumar SK, Lim WH, Ranganathan D, Saweirs W, Sud K, Toussaint ND, Walker RG, Williams LA, Yehia M, Mudge DW.


In chapter three, the current practice in relation to antimicrobial prophylaxis in PD patients was assessed at eight renal units located in Australia (7) and New Zealand (1). Barriers and enablers to good practice were also evaluated. This was a prospective study with a focus on adherence to evidence-based guideline recommendations on antimicrobial prophylaxis in PD patients. Current practice was established by asking the PD unit heads to respond to a short survey about practice/protocols/policies and by interviewing the primary PD nurse at each unit, after which a ‘process map’ was constructed. The perceived barriers/enablers to adherence to the relevant guideline recommendations were obtained from the completion of ‘cause and effect’ diagrams by the nephrologist and PD nurse at each unit. Data on PD-related infections were obtained from the Australia and New Zealand Dialysis and Transplant Registry (ANZDATA) for the baseline period 1 January 2011 to 31 December 2011. A number of perceived barriers and enablers were identified. It was also found that the definitions of PD-related infections used by some units varied from those recommended by the International Society for Peritoneal Dialysis (ISPD), particularly with regard to exit-site infection (ESI). PD-related infection rates for the baseline period were found to vary widely. We found wide variation in adherence to guideline...
recommendations between PD units which might contribute to the variation in PD-related infection rates. Although individual patient characteristics may account for some of this variability, inconsistencies in the processes of care to prevent PD-related infection also play a role.

**Antimicrobial agents for preventing peritonitis in peritoneal dialysis patients**

*(Cochrane Review)*

In chapter 4, an update to a Cochrane systematic review was conducted. This review evaluated the effectiveness of antimicrobial agents which have been used to prevent peritonitis in PD patients. We identified 39 trials eligible for inclusion, involving 4374 patients. Twenty more trials (2183 patients) were included than in the original review of 2004. The following antimicrobial interventions were analysed: oral or topical or intraperitoneal antibiotics; nasal antibiotic prophylaxis; pre/peri-operative intravenous antibiotic prophylaxis; topical disinfectants of the exit site; germicidal systems for connection devices; dressing systems for exit sites; silver ring system on catheter; anti-staphylococcal vaccine; and antifungal agents. The primary outcomes assessed were: peritonitis; exit-site infection/tunnel infection; and catheter removal/catheter replacement. Six secondary outcomes were also assessed. We found that of the various interventions, pre/peri-operative intravenous vancomycin compared with no treatment appears to reduce the risk of early peritonitis (but has uncertain effects on the risk of exit-site/tunnel infection) and antifungal prophylaxis with oral nystatin or fluconazole compared with placebo/no treatment appears to reduce the risk of fungal peritonitis after a patient has had an antibiotic course. However, no other antimicrobial interventions had proven efficacy and no intervention reduced the risk of catheter removal or replacement. The findings highlight
the lack of adequately powered and high quality randomised controlled trials (RCTs) to inform decisions about how to prevent peritonitis in PD patients.

**Infection prophylaxis in peritoneal dialysis patients: results from an Australia/New Zealand survey**

Chapter 5 presents the results of a web-based survey of consultant nephrologists who were members of the Australian and New Zealand Society of Nephrology (ANZSN) and was conducted between June and September 2013. Various evidence-based guideline recommendations exist for the prevention of PD-related infections in PD patients and this survey aimed to describe the prophylactic clinical practices used by nephrologists in Australia and New Zealand. An initial email inviting nephrologists to participate and three reminder emails were sent out via the ANZSN office. The survey questions asked about the use of antibiotic and antifungal prophylaxis in PD patients. The ISPD guideline recommendations we focused on state that: prophylactic antibiotics administered at the time of insertion decrease the infection risk; all PD patients should use topical antibiotic either at the catheter exit site or intranasally or both; most episodes of fungal peritonitis are preceded by courses of antibiotics; and fungal prophylaxis during antibiotic therapy may prevent some cases of *Candida* peritonitis in programs that have high rates of fungal peritonitis. The KHA-CARI guideline recommendations are similar. We received 133 responses to the survey, which represents an estimated 39.9% response rate as it was considered there were 333 registered consultant nephrologists in ANZ at the time. We found that most nephrologists (127; 95.5%) prescribed antibiotics at the time of Tenckhoff catheter insertion, 85 (63.9%) routinely screened for nasal *S. aureus* carriage but only 76 (88.4%) reported they treated *S. aureus* carriers with mupirocin ointment. Following Tenckhoff catheter insertion, 79 (59.4%) prescribed mupirocin ointment at the exit site
or intranasally and 93 (69.9%) of nephrologists routinely prescribed a course of oral antifungal agent whenever their PD patients were given a course of antibiotics. The study shows that clinical practice among practising nephrologists in ANZ is variable, with 11.6% of identified nasal S. aureus carriers not being treated, with nearly 40% of patients not receiving antibiotic prophylaxis at the exit site or intranasally, and approximately 30% of patients not being co-prescribed an antifungal agent when they are administered an antibiotic course. This practice variation may contribute to the wide range of PD-related infection rates that is seen between units.

**Patients’ perspectives on the prevention and treatment of peritonitis in peritoneal dialysis: a semi-structured interview study**

Chapter 6 is a qualitative study of patient perspectives on the prevention and treatment of peritonitis in peritoneal dialysis. Semi-structured, face-to-face interviews were conducted with 29 patients from three renal units in Australia who had previous or current experience of PD. The interview transcripts were thematically analysed. Four themes were identified: constant vigilance for prevention (conscious of vulnerability, sharing responsibility with family, demanding attention to detail, ambiguity of detecting infection, ineradicable inhabitation, jeopardising PD success); invading harm (life-threatening, wreaking internal damage, debilitating pain, losing control and dignity); incapacitating lifestyle interference (financial strain, isolation and separation, exacerbating burden on family); and exasperation with hospitalisation (dread of hospital admission, exposure to infection, gruelling follow-up schedule, exposure to harm). The findings suggest that peritonitis is viewed by patients as a threat – one that can affect their health, choice of dialysis modality, and lifestyle. As a consequence, they were motivated to be vigilant when doing an exchange and paid great attention to hygiene. Patients felt a loss of control due to the debilitating symptoms they
experienced, having to be hospitalised and were not sure of the signs of peritonitis. Providing patients with education about the causes and signs of peritonitis and addressing their concerns about lifestyle impact, financial impact, hospitalisation, and peritonitis-related anxieties may improve treatment satisfaction and outcomes for patients on peritoneal dialysis. Based on the findings, patient- and family-centred education and care strategies that may help to inform and support patients on PD are outlined in this chapter.

Conclusion

This thesis outlines what clinical practice in relation to the use of prophylaxis in PD patients is like in ANZ and identifies some barriers to the uptake of relevant guideline recommendations. The evidence base for the use of various antimicrobial agents to prevent PD-related infections has been assessed and only a few interventions can be held to be effective. Studies on the prevention of PD-related infections are limited both in terms of quantity and quality and hence, guideline recommendations are based on a mixture of expert opinion and the available evidence. PD patient beliefs and experiences about peritonitis are also described. Patients are threatened by the prospect of peritonitis and constantly act to minimise the chance of it occurring. An episode of peritonitis leads to patients experiencing a loss of control and impacts on lifestyle and finances, among other things. Patients need to be educated about the causes and signs of peritonitis and to have their concerns about the impacts of a peritonitis episode addressed. These findings have implications for clinical practice and provide a suggestion for future research in this area.
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“The art of teaching is the art of assisting discovery.” Mark van Doren

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units where the patient interviewees for the qualitative study were recruited from.

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Publications arising from this thesis

This thesis is presented for examination as a thesis containing published work. Two of the chapters presented in this thesis have been published in a peer-reviewed journal, one has been submitted to a peer-reviewed journal for which a ‘revise and resubmit’ letter has been received, and two chapters have been submitted to peer-reviewed journals and are awaiting editorial response. The following is a summary of papers arising from this thesis that have been published or are currently submitted for publication:


   [Abstract presented at the 2nd Annual NHMRC Research Translation Faculty Symposium, Sydney, Australia, 2-3 October 2013; Abstract presented at the ANZSN Annual Scientific Meeting 2014, Melbourne, Australia, 25-27 August 2014; Abstract presented at the School of Public Health Conference, Sydney, Australia, 28 September 2015]

3. **Campbell DJ**, Craig JC, Johnson DW, Mudge DW. Assessment of current practice and barriers to antimicrobial prophylaxis in peritoneal dialysis patients. ISPD Asia-Pacific Chapter Newsletter. Fall 2015; Vol 13 Issue 3.
4. Campbell D, Mudge DW, Craig JC, Johnson DW, Tong A, Strippoli GFM, Hodson EM. Antimicrobial agents for preventing peritonitis in peritoneal dialysis patients. Cochrane Database of Systematic Reviews 2015, Issue 10. Art. No.: CD004679. DOI: 10.1002/14651858.CD004679.pub2. (submitted October 2015; has been accepted for publication and is currently In Press).

5. Campbell DJ, Mudge DW, Gallagher MP, Lim WH, Ranganathan D, Saweirs W, Craig JC. Infection prophylaxis in peritoneal dialysis patients: results from an Australia/New Zealand survey. Perit Dial Int (submitted February 2016; has been accepted for publication and is currently In Press).

Chapter 1: Introduction

1.1 Background

Peritoneal dialysis (PD) is a well-established major option for renal replacement therapy in patients with end-stage kidney disease (ESKD). This dialysis modality is often chosen by patients as their initial mode of therapy and is an option for patients wishing or needing to swap from haemodialysis (HD) and after renal transplant failure (1). Some clinical practice guidelines recommend PD as the dialysis treatment of choice for adults with residual kidney function and without significant comorbidities (2). Globally, PD is used to treat ESKD in more than 200,000 patients and represents about 11% of the global dialysis population (3, 4). However, PD-related infections (defined as exit-site infections, tunnel infections, and peritonitis) are a serious complication for PD patients and a barrier to their uptake (5).

One of the most important complications of PD is peritonitis, which creates considerable morbidity and mortality. While mortality directly related to peritonitis is low (less than 4%), peritonitis is a “contributing factor” to death in 16% of deaths on PD (6). Furthermore, peritonitis can result in peritoneal membrane failure, is a leading cause of technique failure, and a leading cause of hospitalisation (7, 8). For all of these reasons, the prevention and treatment of PD-related infections is a clinical priority.

Peritoneal dialysis technique survival in Australia and New Zealand is lower than in other parts of the world but has improved in recent years. Data for the year 2007 found the median time of technique survival in Australia was 1.8 years while in New Zealand it was 2.4 years (9). Data for the 2014 year showed this had increased to 2.7 years for
Australia and 3.0 years for New Zealand (10). In comparison, two countries with high proportions of PD patients, Thailand and Mexico, have median technique survival times of 3.4 and 4.0 years, respectively (9). Registry data for 2014 show that in Australia and New Zealand, infective causes are listed as the reason why 33% and 30% of patients, respectively, experience technique failure and stop using PD as their dialysis modality. Peritonitis is the most common cause of technique failure in Australia and the second most common cause in New Zealand (10). The issue is complicated. For example, the number of patients on PD in each country needs to be considered as clinicians in those countries with policies that promote PD as initial therapy will presumably not always be able to choose the most suitable patients for PD and this will affect patient outcomes.

It is known that peritonitis rates among PD patients vary considerably between renal centres in Australia and New Zealand (11). Peritonitis poses an immediate and direct mortality risk to patients and is a factor over which a renal unit (and associated services) has a substantial degree of influence (12). The protocols and procedures in place at a unit have an influence on the peritonitis rate. Practice patterns vary greatly and many PD units in Australia and New Zealand do not meet the revised ISPD minimum accepted peritonitis rate of <0.36 episodes per patient-year (13). The current peritonitis rates in Australia (0.41; 95% CI 0.37-0.43 episodes per patient-year) and New Zealand (0.47; 95% CI 0.43-0.52 episodes per patient-year) are higher than this suggested target (11).

In many cases, poor peritonitis outcomes reflect significant deviations from practice guidelines. A survey conducted by the Australasian Kidney Trials Network of exit-site care in PD units in Australia and New Zealand found that many units do not adhere to the national guidelines (KHA-CARI guidelines) and that there was an absence of a
uniform, standard practice of exit site care (14). The development of an exit-site infection (ESI) is known to place patients at substantially increased risk of developing peritonitis and the simultaneous occurrence of ESI and peritonitis results in catheter removal in approximately 50% of cases (15).

Challenges in the prevention of peritonitis include the fact that peritonitis rates vary greatly between different renal centres and the peritonitis risk appears to vary from patient to patient (10, 16-19). Some factors such as older age at the start of PD and having diabetes mellitus have been associated with the development of peritonitis and death from peritonitis (20, 21).

The reasons for the variability are complex and largely unexplained. A further challenge is the fact that there are only a limited number of studies with strong evidence to support the use of various interventions. The pre-operative administration of intravenous antibiotic (usually cephalosporin) prior to PD catheter insertion to reduce the risk of early peritonitis (within 4 weeks of insertion) has RCT evidence to support it (22, 23). The obtaining of nose cultures before placement of the catheter and subsequent treatment of anyone who tests positive for *Staphylococcus aureus* nasal carriage, is an opinion-based recommendation and no data on the usefulness of that approach is available (13). There is evidence to support the use of nasal mupirocin prophylaxis, exit-site mupirocin prophylaxis, exit-site gentamicin prophylaxis and the use of antifungal prophylaxis to prevent fungal peritonitis and the ISPD guidelines and KHA-CARI guidelines support these practices (13, 24).

Lastly, the existence of a clinical practice guideline does not guarantee that it will be used in practice. One study investigated guideline use among physicians in the United States and found a wide range of barriers that prevented physicians from adhering to practice guidelines (25).
1.2  **Aims**

The primary aims of the research described in this thesis are:

1. To summarise the current evidence relating to strategies used to prevent the occurrence of PD-related infections (i.e. exit-site infection, tunnel infection, peritonitis).

2. To establish current practice patterns in relation to prevention of PD-related infection at 8 PD units in Australia and New Zealand and to identify perceived barriers and enablers to adherence to relevant guideline recommendations.

3. To summarise and evaluate the current evidence relating to the effectiveness of various antimicrobial agents which have been used to prevent peritonitis in PD patients.

4. To determine and describe the clinical practices currently being used by nephrologists in Australia and New Zealand in relation to key guideline recommendations regarding prophylaxis in PD patients.

5. To explore patient perspectives in relation to the prevention and treatment of peritonitis in peritoneal dialysis.

1.3  **Thesis overview**

The aims and scope of this thesis exclude any discussion of the value of automated peritoneal dialysis (APD) compared with continuous ambulatory peritoneal dialysis (CAPD). No attempt has been made to separate APD from CAPD, either as an intervention or a target for intervention. The key objectives of the projects that make up this thesis are to inform the strategies used with PD patients to prevent PD-related infection and to help create family- and patient- centred care. The projects do this by
assessing the evidence on which various interventions are based, by describing
clinical practice in Australia and New Zealand and identifying evidence-practice
gaps, by identifying barriers which stop guideline recommendations from being
adopted into practice, and by exploring the beliefs, needs and experiences of PD
patients in relation to peritonitis.

Chapter 2 is a narrative review of the current evidence underpinning strategies for the
prevention of PD-related infections in PD patients. The evidence included was drawn
from clinical practice guidelines, systematic reviews and randomised controlled trials
(RCTs). The review summarises the evidence for 9 different categories of intervention
which have been used to reduce the occurrence of peritonitis. The effect of each
intervention on the outcomes of ESI, tunnel infection and peritonitis is reported (when
available).

Chapter 3 is a baseline study of 8 PD units in Australia and New Zealand where the
current practice at each unit was established. The focus was on adherence to guideline
recommendations on antimicrobial prophylaxis in PD patients. A ‘process map’ was
constructed for each unit’s process from meeting with the nephrologist prior to referral
to the surgeon, to the point at which the patient had been trained post catheter insertion
and had commenced independent dialysis. A list of perceived barriers and enablers to
the implementation of relevant guideline recommendations was made for each unit,
following the completion of a ‘cause and effect’ diagram by the nephrologist and PD
nurse at each unit.

Chapter 4 is a systematic review of existing RCTs and pseudo-RCTs of the various
strategies which have been developed to reduce the risk of peritonitis in PD patients.
Nine categories of intervention were assessed with the main ones being the use of
antibiotics, the use of topical disinfectants at the exit site and the use of antifungal
agents. The primary outcomes assessed were peritonitis, exit-site infection/tunnel infection, and catheter removal/catheter replacement. The Cochrane risk of bias tool was used to assess the quality of each included study. The systematic review includes forest plots which show the effect size and the 95% CI around the effect size for the studies which provide evidence for each intervention assessed, and provides a total effect size and 95% CIs.

Chapter 5 is a summary of the survey results obtained from 133 consultant nephrologists who were practising in Australia and New Zealand (ANZ) between June and September 2013. The survey questions asked about the use of antibiotic and antifungal prophylaxis in PD patients and were framed around what the ISPD and KHA-CARI guideline recommendations state.

This chapter describes the prophylactic practices that nephrologists in ANZ report they use and discusses the practice variation that was found.

Chapter 6 is a qualitative in-depth interview study that explores patient perspectives on the prevention and treatment of peritonitis in peritoneal dialysis. The aim was to develop a better understanding of patient beliefs, needs and experiences in relation to peritonitis. Based on the findings, suggestions for clinical practice are made that may help to support patients and their families in general, and more specifically, assist patients during the treatment period for a peritonitis episode.

Chapter 7 concludes this thesis with a summary of the main findings, a discussion of the strengths and potential limitations, and implications for clinical practice, policy making and future research.
1.4 References


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Chapter 2: Prevention of peritoneal dialysis-related infections

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2.1 Abstract
The use of peritoneal dialysis (PD) varies widely from country to country, with the main limitation being infectious complications, particularly peritonitis, which leads to technique failure, hospitalization and increased mortality. A large number of prophylactic strategies have been employed to reduce the occurrence of peritonitis, including the use of oral, nasal and topical antibiotics, disinfection of the exit site, modification of the transfer set used in continuous ambulatory PD exchanges, changes to the design of the PD catheter implanted, the surgical method by which the PD catheter is inserted, the type and length of training given to patients, the occurrence of home visits by trained PD nurses, the use of antibiotic prophylaxis in patients undergoing certain invasive procedures and the administration of antifungal prophylaxis to PD patients whenever they are given an antibiotic treatment course. This review summarizes the existing evidence evaluating these interventions to prevent exit site/tunnel infections and peritonitis.

Keywords: peritoneal dialysis, peritonitis, catheter-related infections, exit site, randomized controlled trial

2.2 Introduction
Peritoneal dialysis (PD)-related infection, including peritonitis, exit-site infection (ESI) and tunnel infection, is a common complication that results in considerable
morbidity and even death in up to 3.5-10.0% of patients [1]. Furthermore, peritonitis is a leading cause of patient transfer to haemodialysis [2] [3], which in turn leads to reduced quality of life for patients [4] and increased costs to the health system [5]. Peritonitis can also lead to loss of residual renal function and reduced dialysis adequacy, deteriorating ultrafiltration and, in some cases, encapsulating peritoneal sclerosis [6].

In this review, we discuss current evidence underpinning strategies for the prevention of PD-related infections, looking primarily at clinical practice guidelines, systematic reviews and randomised controlled trials (RCTs). Preference has been given to the inclusion of results from systematic reviews because explicit methods are used in their conduct, which aim to minimize bias and produce more reliable findings that can be used to inform clinical decision-making.

The searches were conducted in MEDLINE (1946 to November, week 3, 2013) and EMBASE (1980 to 2013 week 50). The Cochrane Library was also searched for relevant systematic reviews using the term ‘peritoneal dialysis’.

### 2.3 Use of prophylactic antibiotics at catheter insertion

A number of randomized trials have examined whether intravenous antibiotic administration prior to or at the time of PD catheter insertion helps to reduce the infections that can occur with PD. The Cochrane systematic review by Strippoli et al [7] included 4 trials (355 patients) which gave various antibiotics at catheter placement versus none and concluded that the use of peri-operative intravenous antibiotic prophylaxis versus no treatment significantly decreased the risk of early peritonitis (relative risk [RR] 0.35, 95% CI 0.15 to 0.80) but not the risk of ESI and
tunnel infection (RR 0.32, 95% CI 0.02 to 4.81). The International Society for Peritoneal Dialysis (ISPD) guidelines published in 2011 suggests that each PD program should consider using vancomycin as prophylaxis at catheter placement but needs to carefully weigh the potential benefit against the risk of vancomycin use promoting the emergence of resistant organisms [8]. The UK guidelines recommend that antibiotic prophylaxis be used peri-operatively but do not stipulate which antibiotic should be used. The Kidney Health Australia – Caring for Australasians with Renal Impairment (KHA-CARI) guidelines also recommend that intravenous antibiotic prophylaxis be used at catheter insertion and suggest that vancomycin, cephalosporins or gentamicin are suitable. The development of vancomycin-resistant enterococci and *Staphylococcus aureus* (including methicillin-resistant *S. aureus*) has caused alarm. Because of concerns about this development, the use of first-generation cephalosporin is common despite it being slightly less effective than vancomycin. To summarize, a single dose of intravenous antibiotic given at the time of catheter insertion has been shown to decrease the risk of early peritonitis [9, 10] (Table 1).

### 2.4 The role of PD catheter design

The systematic review by Strippoli et al [11] assessed eight RCTs (405 patients) which compared the use of straight versus coiled catheters and found no significant difference in the risk of peritonitis (RR 1.14, 95% CI 0.73 to 1.79), peritonitis rate (RR 0.89, 95% CI 0.63 to 1.26), exit site/tunnel infection (RR 1.26, 95% CI 0.91 to 1.73) and exit site/tunnel infection rate (RR 1.04, 95% CI 0.73 to 1.47). More recently, a systematic review by Hagen et al [12] found no statistically significant differences between coiled and
straight catheters (6 studies, 454 patients) with respect to rates of exit site infection
(risk difference [RD] 0.04, 95% CI -0.02 to 0.11; P = 0.22), peritonitis (RD 0.01, 95%
CI -0.05 to 0.06; P = 0.83) or wound/tunnel infection (RD -0.00, 95% CI -0.04 to 0.04;
P = 0.81). Hagen et al also assessed five studies (313 patients) that compared straight
versus Swan neck catheters and found no statistically significant difference between
the two regarding the risk of developing an exit site/tunnel infection (RD 0.04, 95% CI
-0.06 to 0.15; P = 0.42) or peritonitis (RD 0.05, 95% CI -0.06 to 0.16; P = 0.34) (Table
2).

Only one RCT [13] has evaluated whether double-cuff catheters are superior to
single-cuff catheters for the prevention of peritonitis. No significant differences were
observed between the two groups with respect to number of peritonitis episodes (21
versus 24, RD -0.10, 95% CI -0.35 to 0.15; P = 0.44)) or the mean interval between
episodes (23.8 versus 21.6 months).

However, the trial only included 60 patients and had limited statistical power.
The latest ISPD guidelines on PD-related infections state that no particular catheter
has been shown to be better than the standard silicone Tenckhoff catheter for the
prevention of peritonitis [8]. The UK guidelines make a similar statement, saying that
no particular catheter type has been proven to be better than another [9]. Overall, no
one catheter type has been found to be associated with reduced PD-related infection
outcomes.

It should be emphasized that the centre variations in infection rates are greater than the
differences seen between catheter types. For example, two large studies which audited
practice and peritonitis outcomes at a number of PD units, found considerable variation in the peritonitis rates at the different PD units [14, 15]. Both studies could find no single factor that could account for the different peritonitis rates seen at the units.

In summary, the different catheter types are associated with similar PD-related infection outcomes.

2.5 Method and location of PD catheter insertion

Three RCTs comparing laparoscopic versus standard laparotomy PD catheter insertion have reported no significant difference in peritonitis rates after the initial post-surgery period [16][17][18]. The laparoscopic technique, however, had a lower incidence of early exit-site leak, fluid leakage and catheter tip migration. Moreover, a recent meta-analysis by Hagen et al concluded that the laparoscopic insertion technique resulted in higher 1-year catheter survival (OR 3.93, 95% CI 1.80 to 8.57; P = 0.0006) and less frequent catheter migration (OR 0.21, 95% CI 0.07 to 0.63; P = 0.006), although there was no statistically significant difference in the occurrence of peritonitis (OR 0.83, 95% CI 0.48 to 1.42; P = 0.49) or exit site/tunnel infection (OR 0.80, 95% CI 0.47 to 1.37; P = 0.41) [12].

Another method that has been employed involves the burying of the entire PD catheter subcutaneously at the time of insertion, with subsequent exteriorization of the tip of the catheter at a later date (Moncrief-Popovich technique) [19]. A Cochrane systematic review found that burying the catheter did not significantly affect exit-site/tunnel infection rates (RR 1.15, 95% CI 0.39 to 3.42) or peritonitis rates (RR 1.16, 95% CI 0.37 to 3.60) compared with standard insertion techniques [11]
The technique of inserting the PD catheter in a midline versus lateral position has also been investigated. It was theorised that lateral insertion of the catheter might reduce the incidence of leakage and obstruction after insertion [20]. However, the Cochrane systematic review by Strippoli et al [11] found that midline versus lateral insertion of the PD catheter was not associated with a statistically significant difference for the risk of peritonitis (RR 0.65, 95% CI 0.32 to 1.33) or exit-site/tunnel infection (RR 0.56, 95% CI 0.12 to 2.58).

The UK guidelines suggest that the method of PD catheter insertion should depend on the local expertise available at each unit [9]. While none of the different methods of catheter insertion have been found to be associated with a reduction in PD-related infection, the laparoscopic technique was associated with better catheter survival at 1 year and less instances of catheter migration.

2.6 PD patient training

The safe practice of PD requires that a patient be taught how to perform good hand hygiene while carrying out a bag exchange. The aim of this is to reduce the occurrence of touch contamination, which is the commonest cause of peritonitis [21] (Table 3).

There are no RCTs comparing different initial training regimens for PD patients. There are, however, a number of prospective and retrospective observational studies that have looked at the features of training programs for new patients and the characteristics of those doing the training and have assessed these in relation to key patient outcomes. A non-randomized prospective multicentre study was conducted by
Hall et al [22] in which 620 new patients starting PD were trained on the PD technique and diet with an adult learning theory-based course or a conventional training program. Compared with the control group, the adult learning group took significantly longer to train (29 versus 22.6 h, $P < 0.0001$), had comparable peritonitis rates (28.2 versus 36.7 per 1000 patient-months, $P = 0.09783$) and had significantly lower ESI rates (0.22 versus 0.38/patient-year, $P < 0.004$). A retrospective study conducted by Gadola et al over a 28-month period evaluated the practical skills of patients who started PD during this time, following the use of a new multidisciplinary education program. They found that overall peritonitis rates fell significantly (0.28 versus 0.55/patient-year, $P < 0.05$) [23].

A survey of 150 Italian PD centres found that lower peritonitis rates were associated with pre-dialysis education, home visits and retraining, but not with the presence of specialized personnel, the ratio of nurses to patients, or training time [24]. Kavanagh et al also found no link between the peritonitis rate and the nurse-to-patient ratio or the average continuous ambulatory peritoneal dialysis training time [15]. Other studies have reported conflicting results regarding the association between training time and PD-related infections [25-27].

It is also unclear if there is a correlation between home visits and peritonitis rates [25, 28]. Nevertheless, home visits may highlight when retraining is necessary, with one study finding that 23% of the centre’s patients were not following exchange protocol procedures and 11% were non-compliant with the exit-site protocol procedures [29].

Dialysis centre size may have an effect on peritonitis rate, with one survey of paediatric patients reporting a rate of 1 episode/19.9 patient-months for large centres.
and 1 episode/13.5 patient-months for small centres (P < 0.05) [25].

In addition to patient training, the training given to the nurses teaching the patient is important. Although it seems counter-intuitive, one study found that the training nurses with ≥3 years of experience had a more than twofold increased likelihood of subsequent Gram- positive peritonitis in the patients they trained compared with the trainers with less training experience [30]. As explanation, it was suggested that more experienced nurses may be less familiar with the concept of using adult learning principles to train PD patients, nurses with more experience may be providing lower quality care and that nursing knowledge and skills are different to the skills needed to teach. It is also possible that the more experienced nurses were given the more challenging patients to train. There is also a study by Yang et al which found that when nurses with more general medicine experience (≥15 years) trained PD patients, the time to first-episode Gram-positive peritonitis was significantly better than when patients were trained by nurses with less experience [31].

The ISPD guidelines/recommendations published in 2006 [32] state that a nurse should provide PD training whenever possible (opinion based) and that one nurse should train one patient rather than one nurse train a group of patients (opinion). The principles of adult learning should be followed in the training sessions and a new PD trainer should be supervised for at least one patient training course before being considered an independent trainer (opinion). The fact that cognitive skills may be compromised in a CKD patient needs to be understood; their training will require much patience and repetition and a formalised program is needed. The UK guidelines state that education programs for CKD patients starting therapy should be multidisciplinary, multifaceted, tailored to individual needs and based on the
principles of adult learning. Different ways of delivering the education should be available, the information imparted should be relevant to the person and the method, amount and pace of the delivery should be suited to the person’s learning style, capacity and preferences [33].

Although there are no studies on the topic of retraining, the ISPD Nursing Liaison Committee recommends retraining after peritonitis, catheter infection, prolonged hospitalization, or any other disruption to PD [32]. The Committee also recommends periodic retraining should be performed on a regular basis for all patients. The UK guidelines make similar recommendations, stating that patients should be retrained at least annually and more often, if events such as an episode of PD-related infection or major interruption to the patient performing PD occurs [34].

To summarize, an observational study has found that patients taught according to adult learning theory did not experience reduced peritonitis rates compared with the control group, but they did experience significantly lower ESI rates. Other studies found that a multidisciplinary education program, pre-dialysis education and retraining were associated with lower peritonitis rates. It is not clear if the years of experience that the nurse doing the training has affects the patient outcomes, as different studies have yielded different conclusions.

2.7 PD connection methods
The standard connection system that used a ‘spike’ or a luer lock device has largely been replaced by the Y-set or twin-bag systems as spiking was shown many years ago to lead to more frequent peritonitis [8]. A systematic review has shown that peritonitis rates are reduced when disconnect systems (Y-set and twin bag systems) are used rather than conventional spike systems in PD (7 trials, 485
patients, RR 0.64, 95% CI 0.53 to 0.77) [35]. The use of the Y-set compared with the conventional spike system was associated with a significantly lower risk of peritonitis (7 trials, 485 patients, RR 0.64, 95% CI 0.53 to 0.77) and peritonitis rate (8 trials, 7417 patient-months, RR 0.49, 95% CI 0.40 to 0.61) but no difference was found in the incidence of exit-site/tunnel infection (3 trials, 226 patients, RR 1.02, 95% CI 0.72 to 1.46) or rate (2 trials, 2841 patient-months, RR 1.24, 95% CI 0.91 to 1.69). There was no significant difference in the risk of catheter removal (1 trial, 40 patients, RR 0.33, 95% CI 0.04 to 2.94), technique failure (2 trials, 184 patients, RR 0.45, 95% CI 0.19 to 1.05) or the risk of all-cause mortality with the Y-set compared with the standard spike systems (5 trials, 355 patients, RR 1.03, 95% CI 0.48 to 2.21).

The double-bag (twin-bag) system was developed in the 1980s and it was thought that this system would lead to reduced infection rates because there is one fewer connecting procedure [36]. There was a statistically significant difference found with use of the double bag system versus the standard system for the risk of peritonitis (2 trials, 170 patients, RR 0.43, 95% CI 0.29 to 0.62) and the peritonitis rate (2 trials, 2110 patient-months, RR 0.31, 95% CI 0.20 to 0.47). No significant difference was seen for technique failure (1 trial, 80 patients, RR 1.00, 95% CI 0.06 to 15.44), exit-site/tunnel infection (1 trial, 80 patients, RR 0.75, 95% CI 0.18 to 3.14) and all-cause mortality (1 trial, 80 patients, RR 1.00, 95% CI 0.21 to 4.66).

Comparison of the Y-set system with the double bag system [35] found no significant difference between the two for the risk of peritonitis (3 trials, 292 patients, RR 0.59, 95% CI 0.35 to 1.01), peritonitis rate (4 trials, 4319 patient-months, RR 0.90, 95% CI 0.49 to 1.66) and exit-site/tunnel infection rate (2 trials, 2319 patient-months, RR
1.04, 95% CI 0.52 to 2.06). However, the double bag system was associated with a trend towards fewer patients with peritonitis (RR 0.59, 95% CI 0.35 to 1.01, P = 0.05).

Both the UK and the ISPD guidelines recommend that flush-before-fill dialysis delivery systems be used because these reduce the risk of contamination [8, 34]. Use of the disconnect systems has been shown to be associated with a significantly reduced risk of peritonitis but to not alter the occurrence of exit-site/tunnel infection, catheter removal, technique failure and all-cause mortality [37]. There is little difference between the different disconnect systems in terms of PD-related infection outcomes.

### 2.8 Exit-site care to prevent peritonitis

One of the recognized ways for peritonitis to start is via the catheter tunnel in the presence of exit-site colonization and infection, most commonly with *Staphylococcus aureus* and *Pseudomonas aeruginosa* organisms. The cohort study by Luzar et al [38] looked at *S. aureus* nasal carriage and infection in 140 patients starting PD and found that nasal carriage of *S. aureus* was common (45%), carriers had significantly more ESIs than non-carriers, and that the peritonitis episodes caused by *S. aureus* all occurred in carriers. They recommended that nasal cultures be performed before catheter surgery to identify patients at high risk for subsequent *S. aureus* infection.

Subsequent to this, a number of antibiotics were trialled with the aim of preventing ESI and peritonitis. An early RCT used intermittent oral rifampin, which was effective at reducing the catheter-related infection rate but not peritonitis, and was associated with patient withdrawal due to adverse effects [39]. Rifampin has not been
further used to eliminate nasal carriage because it can cause allergic reactions, has
drug interactions and results in the rapid development of resistance [40].

The antibiotic mupirocin was first trialled in the 1990s and has excellent activity
against Gram-positive organisms but does not affect Gram-negative organisms. A
systematic review published in 2010 investigated whether the application of mupirocin
(at the exit site or intranasally) was effective in the prevention of ESI and peritonitis in
PD patients [41]. A total of 14 studies with 1233 enrolled patients and 1217 controls
were included in the review.

Mupirocin was associated with a significantly lower risk of ESI (0.57, 95% CI 0.46-
0.66, P <0.0001) and peritonitis (0.41, 95% CI 0.24-0.54, P <0.0001) due to all
organisms. When only ESI and peritonitis due to S. aureus were considered, a bigger
reduction in risk was seen for both outcomes (0.72, 95% CI 0.60-0.81, P <0.0001;
0.70, 95% CI 0.52-0.81, P <0.00001).

There are no published RCTs that have looked at the effectiveness of applying
mupirocin to the catheter exit site as a routine practice.

Gentamicin antibiotic cream can be applied topically to prevent ESI and is considered
an alternative choice to mupirocin. The main study to support its use is a prospective
RCT of 133 patients which compared the topical application of mupirocin cream (2%)
or gentamicin sulphate cream (0.1%) to the exit site [42]. Application was daily and
follow-up was for a median of 8 months per patient. Use of gentamicin was associated
with a lower catheter infection rate (0.23/yr versus 0.54/year, P = 0.005), a longer time
to first catheter infection (proportion without catheter infection 0.82/year versus
0.65/year, P = 0.03) and a decrease in the peritonitis rate (0.34/year versus 0.52/year, P
The possibility of gentamicin resistance developing is potentially a major problem as gentamicin is used to treat PD-related peritonitis. The study by Pierce et al [43] found a significant increase in episodes of ESI (0.098 versus 0.153/yr, \( P = 0.024 \)) and a decrease in gentamicin susceptibility for Enterobacteriaceae of 12% and for Pseudomonas of 14%, after their unit switched from routinely using mupirocin 2% cream to gentamicin 0.1% cream at the exit site.

There is also the problem of the over-growth of non-susceptible organisms in response to routine gentamicin use. There has been a report of exit-site infection and peritonitis in CAPD patients which was associated with atypical mycobacteria. These patients were using prophylactic application of gentamicin cream at the exit site [44]. Despite these reports, gentamicin is still considered to be an acceptable alternative to mupirocin for prophylactic use at the exit site [45].

A potential alternative agent is medical-grade honey. Honey has long been known to possess antimicrobial properties and is thought to potentially be less likely to lead to the development of drug-resistant microorganisms compared with antibiotics. Medical-grade honey has been shown to be as efficacious as topical mupirocin in the prevention of catheter-associated sepsis in haemodialysis patients but without the problem of antibiotic resistance [46]. An RCT of its use in adult and paediatric PD patients in Australia and New Zealand has been completed, but the findings do not support a role for antibacterial honey in the prevention of PD-associated infections [47]. The intervention involved daily application of honey to the PD catheter exit site in one group and standard prophylactic care in the other group (application of mupirocin intranasally for 5 days each month for the duration of the study in \( S. \textit{aureus} \) carriers only).
A multicentre RCT of mupirocin versus Polysporin Triple (P3) antibiotic ointment (containing bacitracin, gramicidin, and polymyxin B) randomised 201 adult PD patients to apply one or other of the ointments to the exit site with each dressing change [48]. Patients were followed for 18 months or until death or catheter removal. The primary study outcome was a composite endpoint of ESI, tunnel infection or peritonitis. The study found no difference between the two groups in the time to first event (13.2 months for P3, 95% CI 11.9-14.5; 14.0 months for mupirocin, 95% CI 12.7-15.4; P = 0.41). However, a higher rate of fungal ESI was seen in patients using P3 (0.07 versus 0.01, P = 0.02) and there was a corresponding increase in fungal peritonitis (0.04 versus 0.00, P < 0.05). Consequently, the use of P3 over mupirocin as a prophylactic agent cannot be advocated.

A single-centre RCT compared the antibiotic polyhexanide (solution) versus standard care at the exit site (saline solution and povidone-iodine) [49]. Patients were followed for 12 months. Thirty patients were randomised to each group but only 46 completed the 12-month follow-up. Both incident and prevalent patients were enrolled. The primary study outcome was ESI rate. The study found a significant difference between the ESI rate for the polyhexanide group compared with the standard care group (0.117 per year versus 0.328 per year, P = 0.017). The authors suggest polyhexanide is efficient in the prevention of ESI and should be considered a prophylactic agent that can be routinely used at the exit site.

The ISPD guidelines recommend that all PD patients use topical antibiotic either at the catheter exit site or intranasally or both [8]. The UK guidelines also recommend this [34]. The KHA-CARI guidelines are more specific, recommending the use of mupirocin ointment topically (intranasally or at the exit site) [10]. Patients who are
nasal carriers of *S. aureus* have been shown to be at increased risk for ESI and peritonitis [38]. Of the antibiotics/agents that have been trialled to prevent ESI, mupirocin has been found to be the best choice because it significantly reduces ESI and peritonitis without unwelcome effects such as those seen with P3.

### 2.9 Prophylactic nasal antibiotic use

A systematic review found that nasal mupirocin compared with placebo significantly reduced the exit-site and tunnel infection rates and the presence of *S. aureus* nasally but had no significant effect on peritonitis rates [50]. The Mupirocin Study Group ran a large multicentre RCT with 267 PD patients who were identified *S. aureus* nasal carriers randomized to receive intranasal mupirocin (2%) or placebo ointment [51]. Patients applied the nasal ointment twice daily for 5 consecutive days, every 4 weeks. The results did not show any significant difference between the two groups in terms of overall ESIs, but it did show a significant reduction in the number of episodes of ESI due to *S. aureus* in the mupirocin group. The regular use of mupirocin reduced nasal carriage of *S. aureus* to between 10 and 18%, however, the rates of tunnel infection and peritonitis showed no significant difference.

The authors of the MediHoney® trial also performed a systematic review of topical antimicrobial prophylaxis for preventing infections in PD and found nine relevant trials (954 participants). They concluded that the results provide inconclusive evidence for nasal mupirocin, exit-site mupirocin, and exit-site gentamicin prophylaxis.

Studies that looked at the use of nasal mupirocin in identified carriers yielded conflicting results as to whether or not ESI was reduced. Rates of tunnel infection and
peritonitis were unaffected.

2.10 Development of antibiotic resistance to mupirocin

There is concern that the routine use of mupirocin will lead to the emergence of resistant bacteria. The evidence to date suggests minimal development of resistance in the Mupirocin Study Group trial (nasal application), although it has been argued that a follow-up period of only 18 months was insufficient to adequately assess the development of resistance [52]. A study run over 10 years screened for nasal and pericatheter *S. aureus* colonization in PD patients and for nasal colonization in their dialysis partners and treated with mupirocin, if needed. The authors found concerning increases in high-degree mupirocin-resistant *S. aureus* rates (from 0% to 12.9%) [53]. By the end of the study, nearly one-third of patients with *S. aureus* were colonized with mupirocin-resistant strains.

Other studies have reported on the development of resistance to mupirocin when patients were applying the antibiotic to the exit site after cleaning. In one study, patients were assigned to apply either 2% mupirocin ointment or 0.1% gentamicin sulphate cream to the exit site after cleaning, on a daily basis [54]. The study ran for 3 years. The mupirocin group experienced 18 Gram-positive ESIs, with 5 (27.8%) of these being due to *S. aureus* and 3 of these (16.7%) had high-level mupirocin resistance. The gentamicin group had 10 Gram-positive ESIs, with 3 (30%) of these being caused by *S. aureus*, and 1 (10%) of these showed resistance to gentamicin and 1 (10%) had high-level mupirocin resistance. Furthermore, of those 13 patients in the mupirocin group who had a Gram-positive infection not due to *S. aureus*, 8 had high-level mupirocin resistant isolates. Another study assessed the prevalence of carriage
Development of antibiotic resistance to mupirocin

of *S. aureus*, methicillin-resistant *S. aureus* and mupirocin-resistant *S. aureus* in chronic PD patients after the unit had in place for 4 years a policy of prophylactic application of mupirocin to the exit site in its PD patients [55]. Some patients were classed as intermittent mupirocin users (applying it 1-4 times per week) and others were classed as continuous users (applying it 5-7 times per week). *Staphylococcus aureus* was isolated from 26 of 149 (17.4%) patients and of these, 4 (15.4%) patients had isolates that showed high-level mupirocin resistance. The authors noted that all 4 *S. aureus* carriers with mupirocin-resistant strains were applying mupirocin to the exit site 1 to 4 times per week. Lastly, another study determined the prevalence of *S. aureus*, methicillin-resistant *S. aureus*, and mupirocin-resistant *S. aureus* after their PD centre had a policy in place for 7 years re the use of mupirocin ointment at the exit site [56]. This centre allowed patients to use a range of prophylactic measures which included application of mupirocin daily or three times per week or intermittently or to use mupirocin and polysporin alternately. In addition, 4 patients used an antibiotic other than mupirocin, 6 patients did not use any antibiotic and 1 patient used mupirocin in the nares only. The study found that *S. aureus* was isolated from 16 of 147 (10.9%) patients and 4 of these (25%) were resistant to mupirocin with 3 (18.8%) having high-level resistance and 1 (6.3%) having low-level resistance. The authors noted that all 4 *S. aureus* carriers with mupirocin-resistant isolates were applying mupirocin to the exit site regularly (i.e. daily or 3 times per week).

This development raises concerns about the ability to continue using mupirocin in the future to prevent *S. aureus* colonization in PD patients. In PD patients using prophylactic mupirocin, there is the potential for high-level mupirocin-resistant *S.
2.10 Development of antibiotic resistance to mupirocin

*aureus* strains to develop and result in peritonitis due to *S. aureus* and treatment failure because of catheter loss. Antibiotic resistance is a growing problem and has also been seen with the development of vancomycin intermediate-susceptible *S. aureus* which shows reduced responsiveness to vancomycin, which is commonly used to treat methicillin-resistant *S. aureus* infections [57].

2.11 Pre-procedural prophylaxis

Although there are no RCTs in this area, intravenous antibiotic prophylaxis is recommended to prevent early peritonitis in PD patients undergoing invasive gastrointestinal and gynaecological procedures, such as colonoscopy with or without polypectomy, barium enema, laparoscopic cholecystectomy, uterine biopsy and hysteroscopy as these procedures have been shown to sometimes cause peritonitis in PD patients [8]. Peritonitis is thought to occur as a result of transient bacteremia, from the transmural migration of organisms from the gut into the peritoneal cavity and via the gynaecological tract [58]. Oral antibiotic prophylaxis 2 h before extensive dental work is also suggested because transient bacteremia resulting from the dental work can lead to peritonitis [8].

The UK guidelines recommend that invasive procedures are accompanied by antibiotic prophylaxis and emptying the abdomen of dialysis fluid for the period of time that the procedure takes [34].

2.12 Prophylaxis to prevent fungal peritonitis

Fungi account for 1-15 % of PD peritonitis episodes and are associated with significant morbidity and mortality and high rates of permanent hemodialysis transfer [59]. Patients who receive prolonged or repeated antibiotics courses are at increased
risk of developing fungal peritonitis. A number of studies have looked at the use of antifungal prophylaxis but only two of these studies have been RCTs. The first of these by Lo et al [60] randomly allocated PD patients to treatment with oral nystatin tablets (500,000 units four times a day) whenever a course of antibiotics was prescribed or to no co-prescribed antifungal treatment (control). The proportion of patients who did not experience *Candida* peritonitis by the end of 2 years was higher in the group given Nystatin compared with controls (0.974 versus 0.915, *P* <0.05). This finding may be limited because the control arm had a relatively high incidence of *Candida* peritonitis [61] such that the results may not necessarily be generalizable to PD units with lower PD peritonitis rates (Table 4).

A more recent RCT used oral fluconazole as the prophylactic agent and randomised 420 patients with any PD-related infection to receive or not receive fluconazole (200 mg every 48 h) for the period that they were receiving therapeutic antibiotics [62]. Of patients with bacterial peritonitis, those receiving fluconazole during all courses of antibiotics had significantly fewer fungal peritonitis episodes than did controls (3 versus 15, *P* = 0.0051).

The ISPD work group recommends that each PD program should look at their history of fungal peritonitis and decide if an antifungal with antibiotic protocol would be beneficial, particularly for patients taking prolonged or frequent courses of antibiotics [8]. The KHA- CARI guidelines state that oral antifungal prophylaxis should be considered when PD patients are given antibiotics to reduce their risk of developing fungal peritonitis [10].

In summary, two RCTs co-prescribed an antifungal agent to PD patients whenever...
they were administered a course of antibiotics. The control group did not receive the antifungal treatment. The intervention group had significantly fewer episodes of fungal peritonitis than did the control group. This is a prophylactic measure that those caring for PD patients need to consider.

2.13 Summary of the evidence

Overall, there is a lack of RCTs for many interventions and so data from less rigorous study designs such as cohort studies are our current best available evidence. It also means that systematic reviews have few RCTs that can be included in the analysis. In addition, the quality of the RCTs is variable with some having small patient numbers, short follow-up times and an increased risk of bias because of poor or unclear randomization and blinding processes. In summary, the quality of the evidence is strong for some aspects such as the PD connection method and the use of antibiotic to prevent ESI but is weak for other areas such as the method for training patients.

2.14 Conclusion

Intravenous antibiotic administration prior to PD catheter insertion is well proven to prevent the occurrence of early postoperative peritonitis. The elimination of *S. aureus* nasal carriage using topical mupirocin reduces the risk of exit-site/tunnel infections but not peritonitis. The routine application of mupirocin at the exit site is recommended for all PD patients at increased risk for *S. aureus* infection. The daily use of gentamicin cream at the exit site reduces both the catheter-associated infection and peritonitis rates. The prescribing of oral nystatin with an antibiotic course reduces the development of *Candida* peritonitis.
While improvements in connection technology have reduced peritonitis rates in the past decade, PD-related infection remains a serious problem for PD patients. The disconnect systems are better than the standard spike system in terms of preventing peritonitis. No advantage can be found for using different catheter designs, surgical implantation techniques, catheter placement or automated peritoneal dialysis (APD) versus chronic peritoneal dialysis (CPD). Adoption of a team-based, multifaceted approach to continuous quality improvement with regular audit of infection rates and outcomes is considered essential to improving peritonitis rates.

The training of patients is recognized as a modifiable risk factor for PD peritonitis and it is known that the training given to patients varies considerably between different centres.

Patient training and retraining should become a major clinical and research focus for all units striving to improve their peritonitis rates. Future studies should specifically examine the roles of use of pretraining assessment tools, home-based versus centre-based training, group versus single patient training, training programs using adult learning principles versus an alternative approach, and routine (pre-emptive) versus reactive re-training. The training of staff is also important, and active continued learning and retraining is required to achieve good outcomes. In addition, evidence-based national and international guidelines exist in regard to optimal antimicrobial practice and PD units should review their protocols/policies to ensure that they accord with guideline recommendations.
### Table 2.1: Characteristics of included studies – prophylactic use of antibiotic/antibacterial

<table>
<thead>
<tr>
<th>Study author (year)</th>
<th>Study design</th>
<th>Intervention category</th>
<th>Intervention (experimental group)</th>
<th>Intervention (control group)</th>
<th>N</th>
<th>Duration of follow-up (months)</th>
<th>Effect of intervention on ESI</th>
<th>Effect of intervention on tunnel infection</th>
<th>Effect of intervention on peritonitis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Strippoli et al. (2004)</td>
<td>Systematic review</td>
<td>Prophylactic intravenous antibiotics at catheter insertion</td>
<td>Various antibiotics</td>
<td>No antibiotic</td>
<td>355</td>
<td>N/A</td>
<td>No effect</td>
<td>RR: 0.35 (0.15–0.80)</td>
<td>P = 0.013</td>
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<tr>
<td>Zimmerman et al. (1991)</td>
<td>RCT</td>
<td>Prophylactic antibiotic to prevent PD-related infections</td>
<td>Oral rifampin 2× day for 5 days every 3 months</td>
<td>No antibiotic</td>
<td>64</td>
<td>20</td>
<td>Reduced</td>
<td>Rate ratio 0.28 (0.12–0.63)</td>
<td>P &lt; 0.05</td>
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<tr>
<td>Xu et al. (2010)</td>
<td>Systematic review</td>
<td>Prophylactic antibiotic to prevent PD-related infections</td>
<td>Topical application of mupirocin intranasally or at the exit site</td>
<td>No antibiotic</td>
<td>2450</td>
<td>N/A</td>
<td>Reduced</td>
<td>OR: 1.55 (1.05–2.28)</td>
<td>P = 0.024</td>
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<tr>
<td>Bernardini et al. (2005)</td>
<td>RCT</td>
<td>Prophylactic antibiotic to prevent PD-related infections</td>
<td>Topical application of gentamicin at the exit site</td>
<td>No antibiotic</td>
<td>133</td>
<td>8</td>
<td>Reduced</td>
<td>RR: 0.59 (0.46–0.76)</td>
<td>P &lt; 0.0001</td>
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<tr>
<td>Pierce et al. (2012)</td>
<td>Observational</td>
<td>Prophylactic antibiotic to prevent PD-related infections</td>
<td>Topical application of gentamicin at the exit site</td>
<td>No antibiotic</td>
<td>377</td>
<td>30</td>
<td>Reduced</td>
<td>RR: 0.59 (0.46–0.76)</td>
<td>P &lt; 0.0001</td>
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<tr>
<td>McQuillan et al. (2012)</td>
<td>RCT</td>
<td>Prophylactic antibiotic to prevent PD-related infection</td>
<td>Topical application of P to the exit site</td>
<td>No antibiotic</td>
<td>201</td>
<td>18</td>
<td>Reduced</td>
<td>RR: 0.37 versus 0.40 per</td>
<td>P = 0.32</td>
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<tr>
<td>Nones-Moral et al. (2014)</td>
<td>RCT</td>
<td>Prophylactic antibiotic to prevent PD-related infections</td>
<td>Topical application of piperacillin-tazobactam at the exit site</td>
<td>Standard care at the exit site</td>
<td>60</td>
<td>12</td>
<td>Reduced</td>
<td>RR: 0.37 versus 0.40 per</td>
<td>P = 0.39</td>
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<tr>
<td>Johansson et al. (2013)</td>
<td>RCT</td>
<td>Antibacterial honey to prevent PD-related infections</td>
<td>Topical application of antibacterial honey at the exit site</td>
<td>Standard care at the exit site</td>
<td>371</td>
<td>12-24</td>
<td>Equivalent</td>
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<tr>
<td>Strippoli et al. (2004)</td>
<td>Systematic review</td>
<td>Prophylactic nasal antibiotic to prevent PD-related infections</td>
<td>Nasal application of antibiotic</td>
<td>No antibiotic</td>
<td>282</td>
<td>N/A</td>
<td>Reduced</td>
<td>RR: 0.59 (0.40–0.85)</td>
<td>P = 0.74</td>
</tr>
</tbody>
</table>
### Table 2.1: Characteristics of included studies – prophylactic use of antibiotic/antibacterial (continued)

<table>
<thead>
<tr>
<th>Study author (year)</th>
<th>Study design</th>
<th>Intervention category</th>
<th>Intervention (experimental group)</th>
<th>Intervention (control group)</th>
<th>N</th>
<th>Duration of follow-up (months)</th>
<th>Effect of intervention on ESI</th>
<th>Effect of intervention on tunnel infection</th>
<th>Effect of intervention on peritonitis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mupirocin Study Group (1996)</td>
<td>RCT</td>
<td>Prophylactic nasal antibiotic to prevent PD-related infections</td>
<td>Nasal application of mupirocin</td>
<td>No antibiotic (placebo ointment)</td>
<td>267 18</td>
<td>No effect on overall ESI</td>
<td>No effect 1 in 154.4 patient-months versus 1 in 123.6 patient-months</td>
<td>No effect 1 in 18.1 patient-months versus 1 in 19.3 patient-months</td>
<td>Peritonitis rate due to <em>S. aureus</em> 1 in 81.8 patient-months versus 1 in 53.8 patient-months (P = NS)</td>
</tr>
<tr>
<td>Davey et al. (1999)</td>
<td>RCT</td>
<td>Prophylactic nasal antibiotic to prevent PD-related infections</td>
<td>Nasal application of mupirocin</td>
<td>No antibiotic (placebo ointment)</td>
<td>267 18</td>
<td>No effect on overall ESI</td>
<td>No effect 192 versus 217 episodes</td>
<td>No effect on peritonitis due to <em>S. aureus</em> 1 in 81.8 patient-months versus 1 in 53.8 patient-months</td>
<td></td>
</tr>
</tbody>
</table>

N/A, not available; ESI, exit-site infection; G, gentamicin; M, mupirocin.
## 2.10 Development of antibiotic resistance to mupirocin

### Table 2.2: Characteristics of included studies – catheter design, method of insertion and connection method

<table>
<thead>
<tr>
<th>Study author (year)</th>
<th>Study design</th>
<th>Intervention category</th>
<th>Intervention (control group)</th>
<th>N</th>
<th>Duration of follow-up (months)</th>
<th>Effect of intervention on ESI</th>
<th>Effect of intervention on tunnel infection</th>
<th>Effect of intervention on peritonitis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Strippoli et al. (2004)</td>
<td>Systematic review</td>
<td>PD catheter design</td>
<td>Straight catheter</td>
<td>324</td>
<td>N/A</td>
<td>No effect (RR: 1.26 (0.91–1.73))</td>
<td>No effect (RR: 1.26 (0.91–1.73))</td>
<td>P = 0.17</td>
</tr>
<tr>
<td>Hagen et al. (2013)</td>
<td>Systematic review</td>
<td>PD catheter design</td>
<td>Straight catheter</td>
<td>454</td>
<td>N/A</td>
<td>No effect (RD: 0.04 (-0.02 to 0.11))</td>
<td>No effect (RD: 0.04 (-0.04 to 0.04))</td>
<td>P = 0.22</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Straight catheter</td>
<td>313</td>
<td>N/A</td>
<td>No effect (RD: 0.04 (-0.06 to 0.15))</td>
<td>No effect (RD: 0.04 (-0.06 to 0.15))</td>
<td>P = 0.42</td>
</tr>
<tr>
<td>Tsipouliannis et al. (2000)</td>
<td>RCT</td>
<td>Method of PD catheter insertion</td>
<td>Laparoscopic surgery</td>
<td>50</td>
<td>21</td>
<td>Not stated</td>
<td>Not stated</td>
<td>No effect (3/25 versus 5/25 (P &gt; 0.1))</td>
</tr>
<tr>
<td>Gadallah et al. (1999)</td>
<td>RCT</td>
<td>Method of PD catheter insertion</td>
<td>Laparoscopic surgery</td>
<td>148</td>
<td>36</td>
<td>No effect on 'late' ESI (33/76 versus 28/72 (NS))</td>
<td>Not stated</td>
<td>No effect on 'late' peritonitis (11/76 versus 16/72 (NS))</td>
</tr>
<tr>
<td>Wright et al. (1999)</td>
<td>RCT</td>
<td>Method of PD catheter insertion</td>
<td>Laparoscopic surgery</td>
<td>50</td>
<td>285 months (standard = 361 months)</td>
<td>Not stated</td>
<td>Not stated</td>
<td>No effect on 'late' peritonitis (6/21 versus 4/24 (NS))</td>
</tr>
<tr>
<td>Hagen et al. (2013)</td>
<td>Systematic review</td>
<td>Method of PD catheter insertion</td>
<td>Laparoscopic surgery</td>
<td>474 (ESI/tunnel); 541 (peritonitis)</td>
<td>N/A</td>
<td>No effect (OR: 0.80 (0.47–1.37))</td>
<td>No effect (OR: 0.80 (0.47–1.37))</td>
<td>P = 0.41</td>
</tr>
<tr>
<td>Strippoli et al. (2004)</td>
<td>Systematic review</td>
<td>Method of PD catheter insertion</td>
<td>Subcutaneous burial of catheter</td>
<td>233</td>
<td>N/A</td>
<td>No effect (RR: 1.15 (0.39–3.42))</td>
<td>No effect (RR: 1.15 (0.39–3.42))</td>
<td>P = 0.80</td>
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<tr>
<td>Daly et al. (2000)</td>
<td>Systematic review</td>
<td>PD connection method</td>
<td>Y-set or twin-bag disconnect system</td>
<td>485</td>
<td>N/A</td>
<td>No effect (RR: 0.56 (0.12–2.58))</td>
<td>No effect (RR: 0.56 (0.12–2.58))</td>
<td>P = 0.45</td>
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*Continued*
Table 2.2: Characteristics of included studies – catheter design, method of insertion and connection method (continued)

<table>
<thead>
<tr>
<th>Study author (year)</th>
<th>Study design</th>
<th>Intervention category</th>
<th>Intervention (experimental group)</th>
<th>Intervention (control group)</th>
<th>N</th>
<th>Duration of follow-up (months)</th>
<th>Effect of intervention on ESI</th>
<th>Effect of intervention on tunnel infection</th>
<th>Effect of intervention on peritonitis</th>
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<tbody>
<tr>
<td>Bazzato et al. (1984)</td>
<td>Observational</td>
<td>PD connection method</td>
<td>Twin-bag disconnect system</td>
<td>Standard spike connection system</td>
<td>78</td>
<td>11.4</td>
<td>No effect RR: 1.24 (0.91–1.69) P = 0.18</td>
<td>No effect RR: 1.24 (0.91–1.69) P = 0.18</td>
<td>Reduced Peritonitis rate = 1 per 18.8 patient-months Equivalent RR: 0.90 (0.49–1.66) P = 0.73</td>
</tr>
<tr>
<td>Daly et al. (2000)</td>
<td>Systematic review</td>
<td>PD connection method</td>
<td>Y-set system</td>
<td>Twin-bag system</td>
<td>292</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
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<td>2319 patient-months</td>
<td>N/A</td>
<td>Equivalent RR: 1.04 (0.52–2.06) P = 0.91</td>
<td>Equivalent RR: 1.04 (0.52–2.06) P = 0.91</td>
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Table 2.3: Characteristics of included studies – patient training methods and assessment of trainers

<table>
<thead>
<tr>
<th>Study author (year)</th>
<th>Study design</th>
<th>Intervention category</th>
<th>Intervention (experimental group)</th>
<th>Intervention (control group)</th>
<th>N</th>
<th>Duration of follow-up (months)</th>
<th>Effect of intervention on ESI</th>
<th>Effect of intervention on tunnel infection</th>
<th>Effect of intervention on erysipelotis</th>
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</thead>
<tbody>
<tr>
<td>Hall et al. (2004)</td>
<td>Observational</td>
<td>Method of patient training</td>
<td>Adult learning-based training</td>
<td>Conventional training</td>
<td>620</td>
<td>2160 patient-months (experimental group); 2863 patient-months (control group)</td>
<td>Decreased 18.5 versus 31.8 per 1000 patient-months, ( p = 0.004 )</td>
<td>Not stated</td>
<td>No effect 28.2 versus 36.7 per 1000 patient-months, ( p = 0.10 )</td>
</tr>
<tr>
<td>Gadola et al. 2013</td>
<td>Observational</td>
<td>Method of patient training</td>
<td>Multidisciplinary education programme</td>
<td>Conventional training</td>
<td>56</td>
<td>N/A</td>
<td>Not stated</td>
<td>Not stated</td>
<td>Reduced 0.28 episodes per patient-year versus 0.55 episodes per patient-year, ( p &lt; 0.05 )</td>
</tr>
<tr>
<td>Bernardini et al. (2006)</td>
<td>Cross sectional survey</td>
<td>Method of patient training</td>
<td>Longer total training time</td>
<td>Shorter total training time</td>
<td>N/A</td>
<td>N/A</td>
<td>Not stated</td>
<td>Not stated</td>
<td>No effect 0.43 versus 0.50 episodes per year, ( p = 0.38 )</td>
</tr>
<tr>
<td>Ellis et al. (2012)</td>
<td>Observational</td>
<td>Monitoring of patient technique</td>
<td>Home visit by trained dialysis nurse</td>
<td>No home visit</td>
<td>22</td>
<td>N/A</td>
<td>Not stated</td>
<td>Not stated</td>
<td>No effect 0.39 versus 0.75 episodes per patient-year, ( p = 0.25 ) (Advanced group = reference)</td>
</tr>
<tr>
<td>Yang et al. (2012)</td>
<td>Observational</td>
<td>Experience of nurses giving training</td>
<td>General medicine experience of nurse: (1) &lt;10 years (least); (2) 10 to &lt;15 years (moderate); (3) ( \geq 15 ) years (advanced)</td>
<td>N/A</td>
<td>305</td>
<td>13 582 patient-months</td>
<td>Not stated</td>
<td>Not stated</td>
<td>(Advanced group = reference) Moderate group, HR: 2.69 (1.03–6.98), ( p = 0.04 ) least group, HR: 3.16 (1.20–8.30), ( p = 0.02 )</td>
</tr>
</tbody>
</table>
### Table 2.4: Characteristics of included studies – prophylactic use of antifungal

<table>
<thead>
<tr>
<th>Study author (year)</th>
<th>Study design</th>
<th>Intervention category</th>
<th>Intervention (experimental group)</th>
<th>Intervention (control group)</th>
<th>N</th>
<th>Duration of follow-up (months)</th>
<th>Effect of intervention on ESI</th>
<th>Effect of intervention on tunnel infection</th>
<th>Effect of intervention on peritonitis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lo et al. (1996)</td>
<td>RCT</td>
<td>Prophylaxis to prevent fungal peritonitis</td>
<td>Oral nystatin with antibiotic course</td>
<td>No antifungal treatment with antibiotic course</td>
<td>397</td>
<td>18 (N), 16.6 (C)</td>
<td>N/A</td>
<td>N/A</td>
<td>Reduced Candida peritonitis episodes 4/199 versus 12/198 P &lt; 0.05</td>
</tr>
<tr>
<td>Restrepo et al. (2010)</td>
<td>RCT</td>
<td>Prophylaxis to prevent fungal peritonitis</td>
<td>Oral fluconazole with antibiotic course</td>
<td>No antifungal treatment with antibiotic course</td>
<td>420</td>
<td>1–5</td>
<td></td>
<td>Reduced (RR: 0.20 (0.06–0.68) P &lt; 0.05)</td>
<td></td>
</tr>
</tbody>
</table>
2.15 References


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2.10 Development of antibiotic resistance to mupirocin


2.10 Development of antibiotic resistance to mupirocin


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antibiotic exit site cream for prevention of exit site infection in peritoneal dialysis patients. J Am Soc Nephrol 2005; 16(2): 539-545


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2.10 Development of antibiotic resistance to mupirocin


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Chapter 3: Assessment of current practice and barriers to antimicrobial prophylaxis in peritoneal dialysis patients


3.1 Abstract

**Background:** Existing Australasian and international guidelines outline antibiotic and antifungal measures to prevent the development of treatment-related infection in peritoneal dialysis (PD) patients. Practice patterns and rates of PD-related infection vary widely across renal units in Australia and New Zealand and are known to vary significantly from guideline recommendations, resulting in PD technique survival rates that are lower than those achieved in many other countries. The aim of this study was to determine if there is an association between current practice and PD-related infection outcomes and to identify the barriers and enablers to good clinical practice.

**Methods:** Multicentre network study involving eight PD units in Australia and New Zealand, with a focus on adherence to guideline recommendations on antimicrobial prophylaxis in PD patients. Current practice was established by asking the PD unit heads to respond to a short survey about practice/protocols/policies and a ‘process map’ was constructed following a face to face interview with the primary PD nurse at each unit. The perceived barriers/enablers to adherence to the relevant guideline recommendations were
obtained from the completion of ‘cause and effect’ diagrams by the nephrologist and PD nurse at each unit. Data on PD-related infections were obtained for the period 1 January to 31 December 2011.

**Results:** Perceived barriers that may result in reduced adherence to guideline recommendations included lack of knowledge, procedural lapses, lack of a centralized patient database, patients with non-English speaking background, professional concern about antibiotic resistance, medication cost and the inability of nephrologists and infectious diseases staff to reach consensus on unit protocols. The definitions of PD-related infections used by some units varied from those recommended by the ISPD, particularly with exit site infection (ESI). Wide variations were observed in the rates of ESI (0.06 – 0.53 episodes per patient-year) and peritonitis (0.31 – 0.86 episodes per patient-year).

**Conclusions:** Despite the existence of strongly evidence-based guideline recommendations, there was wide variation in adherence to these recommendations between PD units which might contribute to PD-related infection rates, which varied widely between units. Although individual patient characteristics may account for some of this variability, inconsistencies in the processes of care to prevent infection in PD patients also play a role.

**KEY WORDS:** Antibiotic; antifungal agents; catheters, indwelling; drug resistance, microbial; peritoneal dialysis; peritonitis.

### 3.2 Background

Adherence to evidence-based clinical practice guidelines is thought to
improve patient outcomes, particularly when there are significant variations in practice, excessive morbidity and/or mortality is associated with a disease process, when treatment has the potential to reduce this, and when the services involved are costly (1). Even though most healthcare workers are aware of the existence of evidence-based guidelines, many are unfamiliar with the content of these guidelines and they are not routinely adopted into clinical practice (2). Active implementation programs are needed to engage with stakeholders. It is also essential to identify areas of non-adherence to these guidelines and implement changes in clinical practice in accordance with guideline recommendations (3).

Peritoneal dialysis is an accepted form of renal replacement therapy among Australians and New Zealanders with end-stage kidney disease (ESKD). More than 20% of all prevalent dialysis patients receive PD (4). However, PD technique survival in Australia and New Zealand is lower than in many other parts of the world, attributed to a higher incidence of peritonitis (5),(6). Clinical practice patterns are known to vary widely between centers in Australia and New Zealand and variations from clinical practice guidelines are known to contribute to poor infection outcomes (5). In 2008, over 30% of Australian and New Zealand PD units did not meet the ISPD minimum accepted peritonitis rate of 1 episode per 18 patient-months (0.67 episodes per patient-year) (5, 7-10). Peritoneal dialysis-related infections are also a key contributor to technique failure in PD patients in Australia and New Zealand with this being cited as the second and third most common cause of technique failure, respectively, in the 2012 ANZDATA registry report (9).

The Kidney Health Australia - Caring for Australasians with Renal Impairment
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(KHA-CARI) Guidelines are evidence-based clinical practice guidelines developed for use by healthcare workers primarily in Australia and New Zealand. The aim of these guidelines is to improve the health outcomes of patients with chronic kidney disease (CKD) by adhering to best clinical practice and improving the quality and cost-effectiveness of the care provided. The International Society for Peritoneal Dialysis (ISPD) is an international organization dedicated to the dissemination of education and research in the area of peritoneal dialysis (PD). Both organizations have developed guideline recommendations for the prevention of infections in patients maintained on PD (11-13).

The KHA-CARI Guidelines PD Implementation Project commenced in 2011 with the task of trying to improve PD outcomes through adherence to these established PD guidelines. The aims of this study were to accurately measure each participating PD unit’s performance with regard to infectious outcomes and to identify the barriers and enablers to adherence to best practice guidelines in an attempt to close the gap of continuous quality improvement between evidence and outcomes.

This paper describes the baseline data obtained during the baseline phase for the subsequent guideline implementation project.

3.3 Methods

Study design

The KHA-CARI Guidelines Peritoneal Dialysis Implementation Project is a prospective multicentre network study designed to assess the adherence to the KHA-CARI (published in 2004)(12) and ISPD guidelines (published in 2011)(13) targeting the prophylactic use of antibiotics at the time of Tenckhoff catheter insertion, the prophylactic use of antibiotics to prevent...
ESI, and the prophylactic use of antifungals during courses of antibiotic therapy [Appendix 1].

**Participants**

Eight PD units took part in the study. All Australian (78) and New Zealand (11) renal units were invited to participate by an ‘Expression of Interest’ letter that was sent out via the local professional nephrology society. Participating units were selected based on seven selection criteria defined by the steering committee [Appendix 2].

**Data collection**

A project coordinator (DC) was responsible for managing the project, for conducting interviews on site, and collecting information on PD-related infections in incident PD patients on a case report form developed for the study. The interviews were semi-structured and aimed to identify key features of the clinical pathway that an incident PD patient with ESKD follows once referred to a nephrologist. A ‘process map’ was then developed for each PD unit.

Data were collected using quantitative and qualitative approaches. Quantitative data included demographic and PD-related infection data for incident patients who experienced a PD-related infection during a baseline monitoring period. Qualitative data were collected by the project coordinator through face-to-face interviews with staff at each participating unit. The nephrologist and PD nurse from each unit attended two face-to-face meetings, as did the members of the project’s steering committee. At the initial meeting,
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each PD unit was asked to outline what they thought were the barriers and enablers to optimal infection prevention at their unit. The units were given a cause-and-effect diagram to help identify barriers and enablers to good clinical practice (14). Data on each PD unit’s protocols, policies and usual practices were also collected by asking each unit to complete a survey. Information for each unit on PD-related peritonitis was obtained from the ANZDATA registry for the 12 months from 1 January 2011 to 31 December 2011. The units were asked to provide data on ESIs for the same period. Currently, data on ESI are not submitted to ANZDATA.

Study outcomes
The following outcomes were assessed: 1) identification of key elements of current practice;

2) rates of ESI and PD-related peritonitis; and 3) identification of the barriers and enablers relating to the guideline recommendations for the prevention of catheter surgery-related infection, ESI/tunnel infection and PD-related peritonitis.

Statistical analysis
Results are expressed as frequencies and percentages for categorical variables, and medians and interquartile ranges for continuous variables. Peritonitis and ESI rates were calculated by totalling all the peritonitis or ESI episodes that occurred during the entire time on PD for all patients at each unit in the program during the period 1 January to 31 December 2011. The total was then divided by the time at risk in years. This follows the suggested method for reporting outlined by the ISPD (13).
3.4 Results

Unit and patient characteristics

Of the 10 PD units that responded, eight were selected by the steering committee. These units treated a total of 582 PD patients, which comprise 28.1% of the total PD population in Australia and New Zealand (9). The numbers of patients receiving care in the individual units during the period 1 January to 31 December 2011 were divided into quartiles and center size was categorized accordingly. Two of the units were categorized as large (>107 patients), two were categorized as medium-large (57-107 patients), two were classified as small-medium (32-56 patients) and two units were classified as small (<32 patients). There was one Australian PD unit with an inner regional location; the rest were located in major cities. The two PD units that were not selected were based at large metropolitan hospitals. All patients in all units had access to the full range of renal replacement therapy as all 8 units offered both haemodialysis and peritoneal dialysis. Four of the 8 units were also transplanting centers and the models of care in Australia and New Zealand are hub and spoke so that all patients at all centers had access to transplantation as well. Peritoneal dialysis is a home-based therapy in Australia and New Zealand. All patients trained would be expected to be self-sufficient in the technique either alone or with the assistance of their spouse/carer.

Table 1 shows the baseline demographic characteristics of patients in the individual units and the overall PD cohort. There were no significant differences between the PD units for sex, age, BMI or diabetes mellitus. There
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were significant differences between PD units for race, numbers of patients per unit, duration per patient of treatment with PD and the numbers receiving APD or CAPD. The number of patients on APD and CAPD ranged from 26% to 89% and 11% to 74%, respectively.

**Current practice and organizational features**

There was considerable variation in nurse to patient ratios (median, 1:19, range 1:12 - 1:58) and the proportion of experienced surgeons to junior surgeons working at a unit (median, 2:0.5, range 0:1 - 5:2). The NZ unit did not have an experienced surgeon available to it for Tenckhoff catheter insertions. A majority of the PD units completed patient PD training within 1 week (1-2 weeks) and 7 of 8 units offered home visits after commencement of PD.

**Prophylactic antibiotics**

All units had protocols in place for the administration of intravenous antibiotic to patients prior to catheter surgery. Seven of 8 units had protocols for the routine prescription of antibiotic prophylaxis against ESI and 5 of 8 units had protocols for the routine prescription of an antifungal agent during courses of antibiotics.

**PD-related infection definitions**

We found that the definitions of the PD-related infectious outcomes were not consistent across the units. Three units were using peritonitis definitions that differed from the ISPD definition (8). Definitions of ESI and tunnel infection used differed from ISPD definitions in five and six units, respectively (Table 2).
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Current ESI and peritonitis rates

Figure 1 shows that the reported peritonitis rates for the selected units for the period 1 January to 31 December 2011, ranged from 0.31-0.86 (95% CI: 0.23-1.39) episodes per patient-year. The reported ESI rates varied from 0.06-0.53 (95% CI: 0.03-0.83) episodes per patient-year (Figure 2). The two large and the two medium-large Australian units had the best peritonitis rates and three of these units also had the best ESI rates. One of the small-medium size units and one of the small units had the worst peritonitis rates; the same two units and the other small size unit had the worst ESI rates.

Of the six units that had a protocol prescribing ESI antibiotic prophylaxis, those that applied antibiotic to the exit site had better ESI rates than those that used nasal application. Of the two units that did not have such a protocol, one had a good ESI rate (Unit 4) while one had a poor ESI rate (Unit 3) [Table 3]. Of the five units that had a protocol directing that antifungal be given with any antibiotic course, two units had peritonitis rates close to the ISPD recommended standard of 0.36 episodes per patient-year. However, three units had peritonitis rates of 0.42 episodes per patient-year or greater. Interestingly, of the two units without this protocol, one unit had a good peritonitis rate while the other had a poor one [Table 3]. Thus, from the data there was not an obvious correlation between the presence of protocols and the perceived application of the protocols to the rates of infection.

Perceived barriers to prophylaxis against PD-related infections

Perceived organizational, medical staff and patient barriers to the use of antibiotic prophylaxis are summarised in Figure 3. At the time of Tenckhoff catheter insertion, the most common barrier reported by medical staff was the
nominated person forgetting to give antibiotic at surgery whereas the most common organization-based barrier was the lack of a centralized patient database so that staff could not check whether or not the antibiotic had been administered. Fifty per cent of the units did not have a centralized patient database.

The most common barriers to ESI prophylaxis reported by medical staff was concern by Infectious Diseases staff that routine use of mupirocin would result in the development of antibiotic resistance, difficulty in gaining agreement on the routine use of mupirocin at the exit site at units with more nephrologists on staff, and insufficient staff to test and treat patients if nasal carriage of *S. aureus* was to be routinely monitored. The most common organization-based barrier was when the unit had a blanket policy against the routine use of antibiotic at the exit site. Of the various patient-based barriers identified, the most common was distance from the PD unit and when the patient’s first language was other than English.

Perceived barriers to appropriate antifungal prophylaxis are outlined in Figure 4. The most common medical staff-based barriers included lack of awareness of junior doctors or of doctors outside the hospital system of the need to co-prescribe antifungal medication with an antibiotic course. The only organization-based barrier identified was the lack of a formal policy around the need for antifungal medication when an antibiotic course is prescribed to a PD patient. Of the patient-based barriers identified, the most common barriers were the taste of the antifungal medication, patient’s lack of understanding of the importance of taking the medication, and the cost of the medication. Only six fungal infections were reported over the study period,
with four of them occurring in units where antifungal prophylaxis was not routine.

3.5 Discussion

We found wide variation in the current practices in place at each PD unit. We found that clinical staff were generally aware of these clinical practice guideline recommendations but there was considerable variation in application of the recommendations in practice. All units had protocols in place for two of the three guideline recommendations of interest to this project but the variability in peritonitis and ESI rates experienced by the units raised questions as to how well these processes were being followed.

We also identified a wide variation in the PD-related infection rates at the units. The peritonitis rates for the Australian units ranged from 0.31-0.86 episodes per patient-year while the New Zealand unit had a rate of 0.52 episodes per patient-year. These compare with median rates for all PD units in Australia in 2011 of 0.55 episodes per patient-year and a median rate of 0.62 episodes per patient-year for all New Zealand PD units (4). Most of the units in this study did not meet the ISPD minimum recommended standard of 0.36 episodes per patient-year and the rate was vastly inferior to the reported rate for countries such as Korea, Japan, Hong Kong and China (5). The ESI rates for the study units varied hugely from 0.06-0.53 episodes per patient-year. It is not possible to compare these rates with other PD units in Australia and New Zealand because this information is not collected by the ANZDATA Registry. Other countries have reported ESI rates of 0.16 to 0.40 episodes per patient-year (15-18).
Several factors were identified that may explain the high rates of ESI and peritonitis seen at some units. Some of the selected PD units failed to adhere to the recommendations of the KHA-CARI and ISPD guidelines, particularly those on the routine use of antibiotics to prevent ESI and the need to co-prescribe antifungal medication when any course of antibiotics was given to a PD patient. Possible reasons for the non-adherence to guideline recommendations include the lack of policies/protocols (3 units), awareness of and attitudes towards the guideline recommendations (3 units), low (suboptimal) staff to patient ratios (2 units), lack of access to an experienced surgeon to do the catheter placement (1 unit), and resistance by Infectious Diseases staff to the routine use of mupirocin (3 units). No units identified the quality of the evidence underpinning the KHA-CARI guidelines or the ISPD guidelines as a reason for non-adherence.

The fact that some units had protocols in place consistent with clinical guideline recommendations and yet appeared to have had less favourable outcomes in terms of infection rates and some units appeared to have better outcomes but no formal protocols suggests that other factors/variables are likely to explain these results (e.g. patient selection, definition of infection). In addition, although protocols consistent with the published clinical trial data were in place, the application or implementation of the protocols might have been suboptimal. Furthermore, patients entered into clinical trials are selected on particular criteria and may not be totally representative of the broad population treated in a study such as this one.

The perceived barriers to putting into practice the guideline recommendations show the range of barriers that can occur across different
levels of health care. The perceived barriers were identified at three levels and included awareness of the relevant guideline recommendation and attitude to the guideline (healthcare providers); practical and cost impediments, knowledge and compliance issues (patients); and care processes, staffing and capacities (organization).

The clinical uptake or implementation of guideline recommendations does not automatically follow the production and dissemination of clinical practice guidelines. Recommendations are not always put into practice and many patients do not receive evidence-based care (2, 19, 20). Research into guideline implementation has found that strategies such as interactive small group meetings, educational outreach visits, reminders, computerised decision support, introduction of computers in practice, substitution of tasks, multiprofessional collaboration, mass media campaigns and financial interventions are effective at changing practice (21).

The use of educational materials, conferences/courses, opinion leaders, education, performance feedback and patient-mediated interventions were found to yield mixed effects in terms of practice change. Total quality management/continuous quality improvement strategies were found to have only limited effects. Most of the interventions studied had some effects on care improvement with an average change of about 10% for main targets (21).

This study has a number of strengths. Firstly, current practice data and individual patient data on ESI for the year prior to the start of the study were directly collected from the units. This gave an accurate assessment of the pathways from catheter insertion to the development of infection. Secondly, the combined patients at the 8 selected PD units treated 28.1% of the total
population of PD patients in Australia and New Zealand and therefore provided a good evaluation of PD practices in our region. The selected PD units were of varying sizes and locations and were identified as a good representation of the variability seen in the two countries. These features may make the results potentially generalizable to other PD patient populations. Barriers to the successful implementation of the antibiotic and antifungal prophylaxis guideline recommendations were identified by mapping the steps in the care process and by using the National Institute of Clinical Studies barrier tool (22).

This study also has some limitations. Due to resource constraints, more units were not able to be enrolled in the study. Secondly, the fact that the three process steps of interest were not directly audited was a limitation. For example, while the participating units were asked if they gave suitable antibiotics at catheter insertion, each unit was not specifically audited to establish if the antibiotics were reliably recorded when given and if they were given within an appropriate timeframe. In addition, patient-based barriers were reported by the healthcare professionals and not obtained directly from patient interviews. Furthermore, 6 of the 7 Australian PD units have a ‘major city’ classification according to the Australian Bureau of Statistics remote area index, which makes the patient population sample a mostly urban one (23). Lastly, participation in the study was voluntary with only 10 units offering to join the study.

**Implications for clinical practice**

The active implementation of nephrology guidelines based on appropriate evidence for reducing infections has the potential to improve a unit’s PD-
associated infection rates, catheter loss and technique failure rates, as a consequence. Although there are some caveats around the quality of evidence in some areas of PD practice, the consistent use of appropriate antibiotics at catheter insertion should be associated with reduced occurrence of post-surgery ESI and peritonitis. Our study does not conclusively show that mupirocin prevents exit site/tunnel infection and peritonitis. Although anti-fungal prophylaxis can be beneficial, its use by individual PD units should depend on the background rate of fungal peritonitis and local geographical and patient demographic factors, as demonstrated in our study, whereby one of the units that had such a protocol had a higher fungal peritonitis rate than the three units that did not have an anti-fungal protocol in place.

**Implications for clinical research**

Further research is needed to determine which prophylactic strategies involving the application of antibacterial creams or solutions are most effective in preventing catheter ESI. Our results suggest that the units that used nasal mupirocin prophylaxis generally had higher ESI and peritonitis rates than those that used exit-site mupirocin prophylaxis. It has previously been noted that there have been no direct head-to-head comparison studies of intranasal mupirocin against either exit-site mupirocin or exit-site gentamicin (6). In addition, the unit with the best infection rates did not use antibiotic at all but used daily application of povidone-iodine at the exit site.

As the barriers to adherence to clinical practice guidelines vary from individual to individual and from unit to unit, the results of a barrier analysis in one setting may not be generalizable to another. Research into the barriers to
guideline adherence at a unit will benefit from being conducted locally and any implementation plan to improve adherence will need to address the identified factors.

In conclusion, this study has identified several factors that may contribute to the high rates of ESI and peritonitis that occur in Australia and New Zealand compared with accepted international standards. Nearly all of these factors are potentially modifiable through improved education, creation of a centralized patient database, and routine checking of patient exit site care and exchange technique. The findings of this study will provide the first step in improving PD outcomes by having identified a number of perceived barriers and enablers to good antibiotic and antifungal practice in PD patients. Having an understanding of the barriers to good clinical practice that exist within each organisation can inform the development of a targeted implementation strategy aimed at improving PD-related infection outcomes (3).
### Table 3.1: Demographic characteristics and dialysis details of PD patients at the eight participating units

<table>
<thead>
<tr>
<th>Variables</th>
<th>Unit 1</th>
<th>Unit 2</th>
<th>Unit 3</th>
<th>Unit 4</th>
<th>Unit 5</th>
<th>Unit 6</th>
<th>Unit 7</th>
<th>Unit 8</th>
<th>P-value</th>
<th>All Unis</th>
<th>Australian PD population</th>
<th>P-value</th>
<th>New Zealand PD population</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Demographic characteristics</strong></td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>No. (%) patients</td>
<td>120 (21)</td>
<td>67 (12)</td>
<td>34 (6)</td>
<td>181 (32)</td>
<td>21 (4)</td>
<td>95 (17)</td>
<td>18 (3)</td>
<td>46 (8)</td>
<td>582 (100)</td>
<td>2074</td>
<td>792</td>
<td></td>
<td>0.54</td>
<td></td>
</tr>
<tr>
<td>No. (%) males</td>
<td>66 (55)</td>
<td>34 (51)</td>
<td>15 (44)</td>
<td>101 (56)</td>
<td>12 (57)</td>
<td>61 (64)</td>
<td>9 (50)</td>
<td>24 (52)</td>
<td>0.58</td>
<td>322 (35)</td>
<td>1164 (56)</td>
<td>0.83</td>
<td>450 (57)</td>
<td>0.46</td>
</tr>
<tr>
<td>Age in years (median, IQR)</td>
<td>62 (23)</td>
<td>62 (19)</td>
<td>62 (20)</td>
<td>62 (21)</td>
<td>72 (18)</td>
<td>63 (24)</td>
<td>68 (21)</td>
<td>65 (16)</td>
<td>0.08</td>
<td>65 (20)</td>
<td>63 (23)</td>
<td>0.17</td>
<td>61 (19)</td>
<td>0.46</td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. (%) Caucasian</td>
<td>93 (78)</td>
<td>47 (70)</td>
<td>34 (100)</td>
<td>98 (54)</td>
<td>12 (57)</td>
<td>59 (62)</td>
<td>16 (89)</td>
<td>12 (26)</td>
<td>&lt;0.001</td>
<td>371 (64)</td>
<td>1482 (72)</td>
<td>0.02</td>
<td>329 (42)</td>
<td>0.03</td>
</tr>
<tr>
<td>No. (%) Aboriginal/Torres Strait Islander</td>
<td>6 (5)</td>
<td>6 (9)</td>
<td>0 (0)</td>
<td>1 (1)</td>
<td>0 (0)</td>
<td>1 (1)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0.006</td>
<td>14 (2)</td>
<td>134 (7)</td>
<td>&lt;0.001</td>
<td>0 (0)</td>
<td></td>
</tr>
<tr>
<td>No. (%) Maori/Pacific Islander</td>
<td>6 (5)</td>
<td>5 (8)</td>
<td>0 (0)</td>
<td>17 (9)</td>
<td>0 (0)</td>
<td>3 (3)</td>
<td>0 (0)</td>
<td>19 (41)</td>
<td>&lt;0.001</td>
<td>50 (9)</td>
<td>72 (4)</td>
<td>0.003</td>
<td>365 (46)</td>
<td>0.53</td>
</tr>
<tr>
<td>No. (%) Asian</td>
<td>11 (9)</td>
<td>5 (8)</td>
<td>0 (0)</td>
<td>58 (32)</td>
<td>8 (38)</td>
<td>25 (26)</td>
<td>2 (11)</td>
<td>14 (30)</td>
<td>&lt;0.001</td>
<td>123 (21)</td>
<td>346 (17)</td>
<td>0.03</td>
<td>92 (12)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>No. (%) Other/unknown</td>
<td>4 (3)</td>
<td>4 (6)</td>
<td>0 (0)</td>
<td>7 (4)</td>
<td>1 (5)</td>
<td>7 (7)</td>
<td>0 (0)</td>
<td>1 (2)</td>
<td>0.52</td>
<td>23 (4)</td>
<td>40 (2)</td>
<td>&lt;0.001</td>
<td>6 (1)</td>
<td>0.27</td>
</tr>
<tr>
<td>No. (%) diabetes mellitus</td>
<td>46 (38)</td>
<td>25 (37)</td>
<td>9 (27)</td>
<td>83 (46)</td>
<td>11 (52)</td>
<td>28 (30)</td>
<td>9 (50)</td>
<td>22 (48)</td>
<td>0.07</td>
<td>233 (42)</td>
<td>840 (41)</td>
<td>&lt;0.001</td>
<td>395 (50)</td>
<td>0.004</td>
</tr>
<tr>
<td>BMI in kg/m² (median, IQR)</td>
<td>27 (9)</td>
<td>26 (8)</td>
<td>27 (7)</td>
<td>25 (7)</td>
<td>26 (7)</td>
<td>25 (6)</td>
<td>27 (7)</td>
<td>27 (8)</td>
<td>0.10</td>
<td>26 (7)</td>
<td>26 (7)</td>
<td>0.99</td>
<td>28 (7)</td>
<td>0.80</td>
</tr>
<tr>
<td>Dialysis</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. (%) patients on APD</td>
<td>41 (34)</td>
<td>44 (66)</td>
<td>26 (77)</td>
<td>85 (47)</td>
<td>11 (52)</td>
<td>64 (67)</td>
<td>16 (89)</td>
<td>12 (26)</td>
<td>&lt;0.001</td>
<td>299 (51)</td>
<td>1283 (62)</td>
<td>&lt;0.001</td>
<td>351 (44)</td>
<td>0.01</td>
</tr>
<tr>
<td>Duration of dialysis in years (FD), median (IQR)</td>
<td>1.8 (3.2)</td>
<td>1.9 (3.4)</td>
<td>1.3 (1.9)</td>
<td>1.7 (3.6)</td>
<td>1.9 (1.6)</td>
<td>2.4 (3.4)</td>
<td>3.4 (5.2)</td>
<td>2.8 (2.9)</td>
<td>&lt;0.001</td>
<td>2.2 (3.2)</td>
<td>2.1 (2.9)</td>
<td>0.57</td>
<td>2.1 (2.7)</td>
<td>0.59</td>
</tr>
</tbody>
</table>

QR, interquartile range; BMI, body mass index; CAPD, continuous ambulatory peritoneal dialysis; APD, automated peritoneal dialysis. The χ² test was used for univariate analysis among units. Units represented: Princess Alexandra Hospital, QLD; Australia; Royal Brisbane and Women’s Hospital, QLD; Australia; Gosford Hospital, NSW; Australia; Regional Renal Dialysis Centre, Blacktown, NSW; Australia; Home Therapists Unit, Western Hospital, VIC; Australia; Monash Health, Melbourne, VIC; Australia; Home Therapists Service, Royal Hobart Hospital, TAS; Australia; Auckland City Hospital, New Zealand. The χ² test was used for analysis between all Australian units and Australian peritoneal dialysis population data and for analysis between the New Zealand unit and the New Zealand peritoneal dialysis population data.
Table 3.2: The PD-related infection definitions in use at each PD unit

<table>
<thead>
<tr>
<th>Criteria used to define an ESI</th>
<th>Criteria used to define a tunnel infection</th>
<th>Criteria used to define peritonitis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Presence of purulent discharge, with or without erythema of the skin at the catheter-epidermal interface</td>
<td>Presence of pain/tenerness and/or swelling along the tunnel, with or without exit site infection; ultrasound of the tunnel identifying fluid collection</td>
<td>Presence of cloudy effluent with ≥ 100 white blood cells/µL, with ≥ 50% polymorphonuclear cells, or cloudy effluent; or fever, or abdominal pain, or patient is systemically unwell</td>
</tr>
<tr>
<td>Presence of purulent discharge and erythema around the catheter-epidermal interface</td>
<td>Presence of pain/tenerness and/or swelling along the tunnel, with or without exit site infection</td>
<td>Presence of cloudy effluent with ≥ 100 white blood cells/µL, with ≥ 50% polymorphonuclear cells, or cloudy effluent; or fever, or abdominal pain, or patient is systemically unwell</td>
</tr>
<tr>
<td>Presence of purulent discharge and/or pain and/or redness</td>
<td>Presence of subcutaneous tunnel and/or tunnel tract, and/or discharge at the exit site</td>
<td>Presence of cloudy effluent with ≥ 100 white blood cells/µL, with ≥ 50% polymorphonuclear cells, or cloudy effluent; or fever, or abdominal pain, or patient is systemically unwell</td>
</tr>
<tr>
<td>Presence of purulent discharge, with or without redness</td>
<td>Presence of redness over the subcutaneous tract, with or without erythema, ultrasound or CT evidence of infection</td>
<td>Presence of cloudy effluent with ≥ 100 white blood cells/µL, with ≥ 50% polymorphonuclear cells, or cloudy effluent; or fever, or abdominal pain, or patient is systemically unwell</td>
</tr>
<tr>
<td>Presence of purulent discharge and/or significant polymorphonuclear cells from wound swab</td>
<td>Presence of redness &gt; 3 mm with purulent discharge</td>
<td>Presence of cloudy effluent with ≥ 100 white blood cells/µL, with ≥ 50% polymorphonuclear cells, or cloudy effluent; or fever, or abdominal pain, or patient is systemically unwell</td>
</tr>
<tr>
<td>Presence of redness &gt; 3 mm with purulent discharge</td>
<td>Presence of redness, swelling at the tunnel with discharge at the exit site</td>
<td>Presence of cloudy effluent with ≥ 100 white blood cells/µL, with ≥ 50% polymorphonuclear cells, or cloudy effluent; or fever, or abdominal pain, or patient is systemically unwell</td>
</tr>
</tbody>
</table>
Table 3.3: Comparison of the exit site and peritonitis rates with unit protocols (January to December 2011)

<table>
<thead>
<tr>
<th>Unit number</th>
<th>Protocol to administer antibiotic prophylaxis at catheter surgery</th>
<th>Protocol to prescribe ESI antibiotic prophylaxis</th>
<th>Protocol to prescribe antifungal with antibiotic course</th>
<th>ESI rate (episodes/patient-year)</th>
<th>Peritonitis rate (episodes/patient-year)</th>
<th>Fungal peritonitis rate (episodes/patient-year)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unit 1</td>
<td>Yes (IV cephalosporin intra-operatively)</td>
<td>Yes—nasal</td>
<td>Yes</td>
<td>0.26</td>
<td>0.39</td>
<td>0.00</td>
</tr>
<tr>
<td>Unit 2</td>
<td>Yes (IV cephalosporin intra-operatively)</td>
<td>Yes—exit site</td>
<td>Yes</td>
<td>0.13</td>
<td>0.40</td>
<td>0.08</td>
</tr>
<tr>
<td>Unit 3</td>
<td>Yes (IV cephalosporin intra-operatively)</td>
<td>Yes—nasal</td>
<td>No</td>
<td>0.53</td>
<td>0.78</td>
<td>0.00</td>
</tr>
<tr>
<td>Unit 4</td>
<td>Yes (IV cephalosporin intra-operatively)</td>
<td>No (policy against routine use of mupirocin)</td>
<td>No</td>
<td>0.06</td>
<td>0.31</td>
<td>0.0005</td>
</tr>
<tr>
<td>Unit 5</td>
<td>Yes (IV cephalosporin intra-operatively)</td>
<td>Yes—exit site</td>
<td>Yes</td>
<td>0.21</td>
<td>0.46</td>
<td>0.00</td>
</tr>
<tr>
<td>Unit 6</td>
<td>Yes (IV cephalosporin pre- or intra-operatively)</td>
<td>Yes—exit site</td>
<td>Yes</td>
<td>0.11</td>
<td>0.42</td>
<td>0.01</td>
</tr>
<tr>
<td>Unit 7</td>
<td>Yes (IV cephalosporin intra-operatively)</td>
<td>Yes—nasal</td>
<td>Yes</td>
<td>0.27</td>
<td>0.86</td>
<td>0.00</td>
</tr>
<tr>
<td>Unit 8</td>
<td>Yes (IV cefuroxime on induction, 8 h post, 16 h post)</td>
<td>Yes—nasal</td>
<td>No</td>
<td>0.23</td>
<td>0.52</td>
<td>0.04</td>
</tr>
</tbody>
</table>

*Vancomycin given to MRSA positive patients and those allergic to cephalosporin or cefuroxime.

*Patients screened every 6 months for S. aureus nasal carriage and treated with mupirocin ointment if found positive.

*Only patients who screened positive for S. aureus nasal carriage at initial screening are screened every 6 months and treated with mupirocin ointment if found positive.

*Only patients who screened positive for S. aureus nasal carriage at initial screening are screened every 3 months and treated with mupirocin ointment if found positive. The treatment is repeated for the following 3 months. Those that are negative are re-swabbed annually.
Chapter 3: Assessment of current practice and barriers to antimicrobial prophylaxis in peritoneal dialysis patients

Figure 3.1: Peritonitis rates by unit (January to December 2011)

Figure 3.2: ESI rates by unit (January to December 2011)
Chapter 3: Assessment of current practice and barriers to antimicrobial prophylaxis in peritoneal dialysis patients

Figure 3.3: Perceived barriers to appropriate antibiotic prophylaxis in PD patients

Figure 3.4: Perceived barriers to appropriate antifungal prophylaxis in PD patients
3.6 References


Chapter 3: Assessment of current practice and barriers to antimicrobial prophylaxis in peritoneal dialysis patients

4.1 Abstract

Background

Peritoneal dialysis (PD) is an important therapy for patients with end-stage kidney disease (ESKD) and is used in more than 200,000 such patients globally (Jain 2012). However, its value is often limited by the development of infections such as peritonitis and exit-site and tunnel infections (Morton 2011). Multiple strategies have been developed to reduce the risk of peritonitis including antibiotics, topical disinfectants to the exit site and antifungal agents. However, the effectiveness of these strategies has been variable and are based on a small number of randomised controlled trials (RCTs). The optimal preventive strategies to reduce the occurrence of peritonitis remain unclear.

This is an update of a Cochrane review first published in 2004.

Objectives

To evaluate the effectiveness of antimicrobial agents designed to prevent peritonitis in PD patients.

Search methods

We searched the Cochrane Kidney and Transplant Specialised Register to 5 May 2015 through contact with the Trial Search Co-ordinator using search terms relevant to this review.
Selection criteria

Randomised controlled trials (RCTs) or quasi-RCTs in patients receiving chronic peritoneal dialysis, which evaluated any antimicrobial agents used systemically or locally to prevent peritonitis or exit-site/tunnel infection were included.

Data collection and analysis

Two reviewers independently assessed risk of bias and extracted data. Results were expressed as risk ratio (RR) with 95% confidence intervals (CI).

Main results

Thirty-nine trials, enrolling 4374, patients met our inclusion criteria. Twenty more trials (2183 patients) were included than in the original review of 2004. The risk of bias domains were often unclear or high with low risk of bias reported in 19 (49%) studies for sequence generation, in 22 (56%) studies for incomplete outcome reporting, in 18 (46%) studies for selective outcome reporting and in 12 (31%) studies for allocation concealment. Blinding of participants and personnel was considered low risk in 8 (21%) and blinding of outcome assessors was also low risk in 10 (26%) studies but it should be noted that blinding of participants and personnel was not possible in many of the studies because of the nature of the intervention or control treatment.

The use of oral or topical antibiotic compared with placebo/no treatment may reduce the risk of exit site/tunnel infection (3 trials, 191 patients, low quality evidence, RR 0.45, 95% CI 0.19 to 1.04) and may slightly reduce the risk of peritonitis (5 trials, 395 patients, low quality evidence, RR 0.82, 95% CI 0.57 to 1.19).

It is uncertain whether the use of nasal antibiotic compared with placebo
reduces the risk of exit-site/tunnel infection (3 trials, 338 patients, low quality evidence, RR 1.34, 95% CI 0.62 to 2.87) or the risk of peritonitis (3 trials, 338 patients, low quality evidence, RR 0.94, 95% CI 0.67 to 1.31).

Pre/perioperative intravenous vancomycin compared with no treatment appears to reduce the risk of early peritonitis (1 trial, 177 patients, low quality evidence, RR 0.08, 95% CI 0.01 to 0.61) but has uncertain effects on the risk of exit-site/tunnel infection (1 trial, 177 patients, low quality evidence, RR 0.36, 95% CI 0.10 to 1.32).

The use of topical disinfectant compared with standard care or other active treatment (antibiotic or other disinfectant) may lead to little or no difference in the risk of exit-site/tunnel infection (8 trials, 973 patients, low quality evidence, RR 1.00, 95% CI 0.75 to 1.33) but may slightly reduce the risk of peritonitis (6 trials, 853 patients, low quality evidence, RR 0.83, 95% CI 0.65 to 1.06).

Antifungal prophylaxis with oral nystatin/fluconazole compared with placebo/no treatment appears to reduce the risk of fungal peritonitis occurring after a patient has had an antibiotic course (2 trials, 817 patients, low quality evidence, RR 0.28, 95% CI 0.12 to 0.63).

No intervention reduced the risk of catheter removal or replacement.

**Authors' conclusions**

In this 2015 update, we identified limited data from RCTs and quasi-RCTs which evaluated strategies to prevent peritonitis and exit-site/tunnel infections. This review demonstrates that pre/peri-operative intravenous vancomycin appears to reduce the risk of early peritonitis and that antifungal
prophylaxis with oral nystatin or fluconazole appears to reduce the risk of fungal peritonitis following an antibiotic course. However, no other antimicrobial interventions have proven efficacy. Given the large number of patients on PD and the importance of peritonitis, the lack of adequately powered and high quality RCTs to inform decision making about strategies to prevent peritonitis is striking.

4.2 Plain language summary

People with kidney failure may be treated with peritoneal dialysis where a catheter is permanently inserted into the peritoneum (lining around abdominal contents) through the abdominal wall and sterile fluid is drained in and out a few times each day. The most common serious complication is infection of the peritoneum, which is called peritonitis. This may be caused by bacteria accidentally being transferred from the catheter. This review found that antibiotics given when a peritoneal dialysis catheter is implanted appear to reduce the risk of early peritonitis but not of exit-site/tunnel infection. Antifungal prophylaxis with oral nystatin or fluconazole appears to reduce the risk of fungal peritonitis following an antibiotic course. The available studies are of low quality evidence and consequently, it is uncertain if there is any benefit from using nasal mupirocin or topical disinfectants or other interventions to reduce exit-site/tunnel infection or peritonitis. More large scale trials are needed.

4.3 Background

Peritoneal dialysis (PD) is one of the renal replacement therapies available to people with end-stage kidney disease. There is considerable variation in its
use from country to country, with the proportion of total dialysis patients on PD in developed countries ranging from 3.3% (Japan), to 7.0% (United States), 8.3% (Greece), 17.0 % (United Kingdom), 36.3% (New Zealand), and up to 79.4% (Hong Kong) (Jain 2012). Because PD and haemodialysis have similar outcomes and patients feel that PD, compared with HD, allows them to live life more fully (Morton 2011), PD should be used more frequently than it is but the risk of peritonitis may prevent this from occurring (Heaf 2004; Piraino 1998).

Description of the condition

Peritonitis due to various organisms (e.g. *Staphylococcus aureus*, *Pseudomonas aeruginosa*, coagulase-negative staphylococci) is a leading complication of PD resulting in technique failure (Woodrow 1997), hospitalisation (Choi 2004; Churchill 1997), peritoneal membrane failure, switching to haemodialysis (Jaar 2009; Piraino 1989) and increased mortality (Annigeri 2001; Digenis 1990; Fried 1996; Piraino 2000). There has been a dramatic reduction in the rates of peritonitis from the start of continuous ambulatory PD (CAPD), but rates above the minimum acceptable peritonitis rate recommended by the International Society of Peritoneal Dialysis of 1 episode every 33 months (0.36 episodes/year at risk) are still common (Piraino 2011).

Risk factors for peritonitis include older age (Nessim 2009; Oxton 1994; Salusky 1997), depression (Troidle 2003), coexisting diseases such as diabetes (Chow 2005; Ghali 2011) and cardiovascular disease (McDonald 2004; Nolph 1987), obesity (McDonald 2004), connection methodology (Daly 2001),
Chapter 4: Antimicrobial agents for preventing peritonitis in peritoneal dialysis patients

presence of a peritoneal catheter exit-site infection (Lloyd 2013; van Diepen 2012), and the presence of nasal carriage of *S. aureus* (Golper 1996; Mupirocin SG 1996; Perez-Fontan 1993; Schaefer 2003). Race is also an independent risk factor, with African-American, native Canadian and indigenous Australian Aborigines on PD being shown to be at increased risk (Farias 1994; Fine 1994; Golper 1996; Holley 1993; Lim 2005).

**Description of the intervention**

Different antimicrobial interventions are used at PD catheter insertion and on an ongoing basis to prevent peritonitis. These include intravenous antibiotics, oral antibiotics, topical antibiotics (Thodis 2000), topical disinfectants, prophylactic treatment of *S. aureus* nasal carriage primarily with intranasal antibiotic ointment (Piraino 2002), different exit-site dressing systems and antifungal prophylaxis. All of these strategies, particularly the use of antibiotic at catheter insertion and the cleansing and disinfection of the exit-site, are widely accepted, but practice patterns are variable and it is not clear which practices have most benefit (Piraino 2011; Van Biesen 2014). Studies on preventing PD-related infections are limited in number and quality (Piraino 2011). International guidelines differ in their recommendations on preventing PD-related infections, with some countries not having relevant guidelines (Table 2).

None of these interventions are free of risks or without cost. Antibiotic prophylaxis carries the risk of gastrointestinal toxicity and may be a cause of antibiotic resistance (Annigeri 2001; Bernardini 1996); it may also be
ineffective when patients already have resistance to some antibiotics. Care should be taken that any disinfectant used is at a concentration that is non-cytotoxic (Piraino 2011).

**How the intervention might work**

For a patient to be able to successfully use PD as a dialysis therapy, PD-related infections (exit-site infections, tunnel infections and peritonitis) need to be avoided. The most important infection is peritonitis and a number of prophylactic strategies have been employed to limit its occurrence. Bacteria are known to be able to gain entry to the peritoneum in a variety of ways and hence, various strategies have been used to prevent this occurring (Campbell 2015).

Oral or topical or intraperitoneal antibiotics: Oral antibiotics such as rifampin have been given as prophylaxis to PD patients to reduce catheter infections and peritonitis due to *S. aureus* (Bernardini 1996; Zimmerman 1991). This organism is a major cause of PD catheter infections which can result in *S. aureus* peritonitis and catheter removal. *S. aureus* nasal carriage is known to be a significant risk factor for *S. aureus* PD-related infections (Bernardini 1996). Cyclic oral rifampin is superior to placebo in preventing *S. aureus* infections. Other oral antibiotics used include ofloxacin (Sesso 1994), cephalexin (Low 1980), and trimethoprim/sulphamethoxazole (Churchill 1988).

Topical antibiotics such as mupirocin have been applied to the exit site once daily because this antibiotic has good activity against gram-positive organisms such as staphylococci and streptococci, which are a common cause of exit-site infection and peritonitis in PD patients (Keane 2000;
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Troidle 1998; Ward 1986). However, mupirocin is less active against most gram-negative bacilli and anaerobes (Sutherland 1985). Sodium fusidate ointment (2%) has also been applied to the exit site at one-month intervals and is known to have activity against staphylococci (Sesso 1994). Gentamicin cream is active against both gram-positive and gram-negative organisms and has been used long term on a once-daily basis at the exit site as prophylaxis for exit-site infection (Bernardini 2005; Chu 2008). Gentamicin is active against both S. aureus and Pseudomonas aeruginosa, two important causes of exit-site infection (Bernardini 2005). Polysporin triple ointment (P3) consists of bacitracin/gramicidin/polymyxin and has bacteriostatic activity against a wide range of skin flora and other organisms including gram-negative bacteria (MP3 Study 2008).

Nasal antibiotic prophylaxis: Various antibiotic treatments have been trialled in attempts to eliminate S. aureus nasal carriage in PD patients. The nasal carriage of S. aureus is a well-recognised risk factor for the development of S. aureus infections in CAPD patients (Davies 1989; Luzar 1990; Piraino 1990). Neomycin sulphate ointment has been used prophylactically. Mupirocin has also been used to eliminate nasal S. aureus. While mupirocin is effective at reducing S. aureus nasal carriage rates, re-colonisation frequently occurs. Sodium fusidate ointment (2%) has also been used and is effective at reducing S. aureus nasal carriage rates (Sesso 1994).

Pre/peri-operative intravenous antibiotic prophylaxis: The administration of intravenous antibiotics at catheter insertion has been found to reduce the risk of peritonitis within the first month following PD catheter placement. Although the insertion of a PD catheter involves "clean surgery involving the
placement of a prosthesis or implant”, there is the potential for contamination of the peritoneum with microorganisms from the patient's own body during surgery. Hence, the giving of a single dose of antibiotic prophylaxis intravenously on starting anaesthesia is recommended (Collier 2008).

Topical disinfectants of the exit site: Topical disinfectants have been applied to the exit site for many years, in an attempt to reduce the bacterial load around the exit site. It has been shown that PD patients with a history of an exit-site infection have twice the risk of experiencing a peritonitis episode (Canadian CAPD Clinical Trials Group 1989) so it is important to keep the exit site infection-free. Povidone iodine ointment is a broad spectrum antiseptic ointment that has been used and has minimal adverse events associated with its use (Waite 1997). Povidone iodine solution (20g/L) has also been used and shown to successfully reduce the number of exit-site infections (Luzar 1990). Other antiseptic agents such as hydrogen peroxide, sodium hypochlorite and chlorhexidine have been used (Piraino 2011).

The daily use of antibacterial honey at the exit site was trialled in the HONEYPOT study. This agent was used because it does not induce antimicrobial resistance and has been shown to be active against a broad range of bacteria and fungi (Cho 2014).

Dressing systems for exit sites: A number of exit-site dressing systems have been devised, all with the aim of reducing exit-site/tunnel infection and any subsequent peritonitis. The agents used include topical disinfectants and different dressing types and require more or less frequent removal. More frequent removal is seen to risk damaging the skin around the exit site and less
frequent removal is felt to possibly encourage the growth of anaerobes. The concentration of topical disinfectants used need to be at non-cytotoxic levels.

Silver ring system on catheter: The addition of a silver ring device mounted onto the PD catheter was trialled by German researchers in the 1990s (SIPROCE 1997). The silver ring was used because of the antimicrobial properties of silver. The use of silver-coated catheters in animals had shown a reduction in infectious events (Dasgupta 1994; Fung 1996) and offered a non-pharmaceutical approach to reducing PD catheter-related infections.

Antistaphylococcal vaccine: An antistaphylococcal vaccine was trialled in the 1990s for the purpose of immunising patients with an anti-staphylococcal agent. The expectation was that the vaccine would promote a significant increase in the dialysate level of specific antibodies against S. aureus and that this would lead to reduced peritonitis and exit-site/tunnel infection rates (Poole-Warren 1991).

Antifungal agents: Antifungal prophylaxis to prevent fungal peritonitis when a PD patient receives an antibiotic course is based on the fact that most episodes of fungal peritonitis are preceded by courses of antibiotics (Piraino 2011). Patients receiving prolonged or repeated antibiotic courses are at increased risk of fungal peritonitis, mostly due to Candida spp. Trials that have given patients antifungal agents during antibiotic courses have shown fewer fungal peritonitis episodes arose (Lo 1996; Restrepo 2010).

Why it is important to do this review

The aim of this update was to include any new studies of antimicrobial interventions designed to prevent peritonitis in PD patients that have been
published since the original review was published in 2004. We also aim to provide a critical appraisal of the current available evidence. As peritonitis is a significant problem for patients using PD, frequently leading to morbidity and technique failure and sometimes to mortality, we have updated the review.

### 4.4 Objectives
To evaluate the benefits and harms of antimicrobial strategies used to prevent peritonitis in PD patients.

### 4.5 Methods

**Criteria for considering studies for this review**

**Types of studies**
We included randomised controlled trials (RCTs) and quasi-RCTs (studies in which allocation to treatment was obtained by alternation, use of alternate medical records, date of birth or other predictable methods) in which antimicrobial interventions designed to prevent peritonitis were compared in patients on PD.

**Types of participants**
We included adult and paediatric patients with ESKD who were undergoing PD treatment.

**Types of interventions**
We included studies involving the use of any antimicrobial agent, whether the interventions were tested between themselves (head-to-head) or against placebo/no treatment. The inclusion criteria have been expanded in this update, with the intervention "oral antibiotics" becoming "oral or topical or intraperitoneal antibiotics" and with the interventions "dressing systems for
exit sites" and "silver ring system on catheter" being added.

Specifically, the following antimicrobial interventions were analysed:

- Oral or topical or intraperitoneal antibiotics
- Nasal antibiotic prophylaxis (mupirocin, rifampicin, other)
- Pre/peri-operative intravenous antibiotic prophylaxis
- Topical disinfectants of the exit-site (povidone-iodine, chlorhexidine, triclosan, soap and water, other)
- Germicidal systems for connection devices
- Dressing systems for exit sites
- Silver ring system on catheter
- Antistaphylococcal vaccine
- Antifungal agents

Types of outcome measures

- Peritonitis-number of patients with peritonitis and peritonitis rate (peritonitis defined as dialysate count of > 100 cells/mm³ with > 50% being polymorphonuclear leukocytes; peritonitis rate defined as number of episodes of peritonitis over total patient months on PD)
- Peritonitis relapse (reoccurrence of peritonitis due to the same organism within 2-4 weeks)
- Death due to peritonitis
- All-cause mortality
- Exit-site and tunnel infection-number of patients with exit-site and tunnel infections and exit-site and tunnel infection rate
- Catheter removal/catheter replacement
• Technique failure (transfer from PD to haemodialysis/transplant due to peritonitis)

• Toxicity of antimicrobial treatments (nasal irritation, sneezing, generalised pruritus, headache, diarrhoea, nausea, vomiting, jaundice, local irritation, rash)

• Time to first peritonitis episode

**Primary outcomes**

• Peritonitis

• Exit-site infection/tunnel infection

• Catheter removal/catheter replacement

**Secondary outcomes**

• Peritonitis relapse

• Death due to peritonitis

• All-cause mortality

• Technique failure

• Toxicity of antimicrobial treatments

• Time to first peritonitis episode

**Search methods for identification of studies**

**Electronic searches**

We searched the Cochrane Kidney and Transplant Specialised Register to 5 May 2015 through contact with the Trials' Search Co-ordinator using search terms relevant to this review.

The Cochrane Kidney and Transplant Specialised Register contains studies identified from:
1. Monthly searches of the Cochrane Central Register of Controlled Trials CENTRAL;
2. Weekly searches of MEDLINE OVID SP;
3. Handsearching of renal-related journals & the proceedings of major renal conferences;
4. Searching of the current year of EMBASE OVID SP;
5. Weekly current awareness alerts for selected renal journals;
6. Searches of the International Clinical Trials Register (ICTRP) Search Portal & ClinicalTrials.gov

Studies contained in the Specialised Register are identified through search strategies for CENTRAL, MEDLINE, EMBASE based on the scope of Cochrane Kidney and Transplant. Details of these 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

- Reference lists of nephrology textbooks, review articles and relevant studies.
- Letters to investigators seeking information about unpublished or incomplete studies.

Data collection and analysis

Selection of studies

The search strategy described was used to obtain titles and abstracts of studies that were potentially relevant to the review. The titles and abstracts were screened independently by DC and GFMS, who discarded studies that were not applicable. However, studies and reviews that might include
relevant data or information on studies were retained initially. Two authors independently assessed retrieved abstracts and where necessary, the full text of these studies, to determine which satisfied the inclusion criteria.

**Data extraction and management**

Data extraction and assessment of the risk of bias were performed independently by the same authors using standardised data extraction forms. Studies reported in non-English language journals were translated before assessment. Where more than one publication of one study existed, only the publication with the most complete data was included. Where relevant outcomes were only published in earlier versions, these data were used. Any discrepancy between published versions was highlighted. Any further information required from the original author was requested by written correspondence and any relevant information obtained in this manner was included in the review.

**Assessment of risk of bias in included studies**

The following items were assessed using the risk of bias assessment tool (Higgins 2008) (see Appendix 2):

- Was there adequate sequence generation?
- Was allocation adequately concealed?
- Was knowledge of the allocated interventions adequately prevented during the study?
- Were incomplete outcome data adequately addressed?
- Are reports of the study free of suggestion of selective outcome reporting?
- Was the study apparently free of other problems that could put it at a risk of bias?
Measures of treatment effect

For dichotomous outcomes (peritonitis - number, peritonitis - rate, death due to peritonitis, all-cause mortality, exit-site/tunnel infection - number, exit-site/tunnel infection - rate, catheter removal/replacement, technique failure, toxicity of antimicrobial treatments) results were expressed as risk ratios (RR) with 95% confidence intervals (CI). No continuous outcomes were identified.

Unit of analysis issues

Where data on the number of subjects with events (e.g. number of subjects with one or more episodes of peritonitis) were available, the RR was calculated as the ratio of the incidence of the event (one or more episodes) in the experimental treatment group over the incidence in the control group.

Where data on the number of episodes were available the RR was calculated as the ratio of the rate of the outcome (e.g. the peritonitis rate) in the experimental treatment group (given by number of episodes of the outcome over total patient months on PD) over the rate in the control group.

Dealing with missing data

Where necessary, we contacted trialists to request missing patient data due to loss to follow-up and exclusion from study analyses in an effort to conduct intention-to-treat analyses. With the update, four authors responded to our requests. Where missing dichotomous data were few, and unlikely to affect the overall results, we analysed available data.
Assessment of heterogeneity

Heterogeneity was analysed using a Chi² test on N-1 degrees of freedom, with an alpha of 0.05 used for statistical significance and with the I² test (Higgins 2003). I² values of 25%, 50% and 75% correspond to low, medium and high levels of heterogeneity.

Assessment of reporting biases

The search strategy included searching major databases, conference proceedings and prospective trial registers without language restriction in an attempt to reduce publication bias related to failure of authors to publish negative results or inability to publish negative results in journals indexed in major databases. Insufficient studies were available to assess for publication bias using funnel plots. Where multiple publications of the same study were identified, data were included from the most recent publication, and preferably, the definitive publication. However, all publications were reviewed to identify outcomes not reported in the index publication in an attempt to reduce outcome reporting bias.

Data synthesis

Data were pooled using the random-effects model for dichotomous data.

Subgroup analysis and investigation of heterogeneity

Subgroup analysis was planned to explore potential sources of variability in observed treatment effect where possible (paediatric versus adult population, diabetic versus non-diabetic, time on PD before beginning of antimicrobial treatment). However, no subgroup analyses were performed.
due to lack of available data from the included studies.

**Sensitivity analysis**

Sensitivity analysis was planned to investigate the effect of year of study and study performance. However, there were insufficient studies to do this.

**Summarising and interpreting results**

We used the GRADE approach to assess the quality of evidence for each of the key outcomes (Schunemann 2009). We used the GRADE profiler to import data from Review Manager 5.3 and create 'Summary of Findings' tables.

For assessments of the overall quality of evidence for each outcome that included pooled data from RCTs, we downgraded the evidence from 'high quality' by one level for serious study limitations and by two levels for very serious study limitations. The evidence was appraised using the five GRADE considerations: risk of bias, imprecision of effect estimates, inconsistency, indirectness and potential publication bias. None were upgraded to moderate or high quality as most pooled estimates did not reveal a large magnitude of effect, there was potential for impact by confounders, and most did not show a strong dose-response gradient. The exception was the pooled estimate obtained for the comparison of the use of an antifungal agent versus placebo/no treatment for preventing fungal peritonitis, but the evidence was not upgraded from 'low' because only two studies contributed data for the outcome of fungal peritonitis and one of the studies had a high risk of bias. We used these assessments and the evidence for absolute benefit or harm of the interventions and the sum of available data on all important outcomes
from each study included for each comparison, to arrive at conclusions about the effectiveness of antimicrobial agents at preventing catheter-related infection or the need for catheter removal/replacement in PD patients.

'Summary of Findings' tables consisted of the following clinically important outcomes identified in the selected trials: Peritonitis (number of patients with one or more episodes); Exit-site/tunnel infection (number of patients with one or more episodes); Catheter removal or replacement (number of patients); Fungal peritonitis (number of patients with one or more episodes).

4.6 Results

Description of studies
See: Characteristics of included studies; Characteristics of excluded studies.

Results of the search

Search results are shown in Figure 1, Figure 2. Following full text review of the 57 potentially eligible reports, 22 studies (28 reports) were excluded and 20 studies (29 reports) were identified as eligible for inclusion. Therefore, 20 studies (29 reports) were added in this update; the original review had 19 studies (23 reports).

Included studies

We included 39 studies in the review, 19 of which had been included in the original review. Of the 20 additional studies, 11 had been published since the search was done for the previous review and ten (Axelrod 1973; Cheng 1999a; Cocksedge 1993; Fuchs 1990; Moore 1989; Ryckelynck 1987; Sharma 1971; SIPROCE 1997; Wadhwa 1995; Wadhwa 1997) had not been identified in previous searches. There was one four-arm trial (Swartz 1991), three three-arm trials (Fuchs 1990; Gadallah 2000; Sesso 1994), and the
remaining studies were two-arm trials. No cross over studies were identified.

Of the 39 studies included, all (4374 participants) were parallel group studies. All participants were chronic PD patients treated in centre or in satellite facilities. Two studies (Axelrod 1973; Sharma 1971) reported the number of dialyses but not the number of patients in each group and hence, the data from these studies could not be added to the meta-analyses. Most studies included only adult patients; two studies (Blowey 1994; Mendoza-Guevara 2007) included only children and young adults on PD. Twenty-six studies (Bernardini 2005; Bernardini 1996; Chu 2008; Cockseedge 1993; Fuchs 1990; Gadallah 2000; HONEYPOT Trial 2009; Lo 1996; Luzar 1990; Lye 1992; MP3 Study 2008; Mupirocin SG 1996; Nolph 1985; Nunez-Moral 2014; Perez-Fontan 1992; Poole-Warren 1991; Restrepo 2010; Sesso 1994; SIPROCE 1997; Swartz 1991; Wadhwa 1995; Wadhwa 1997; Waite 1997; Wikdahl 1997; Wong 2003; Zimmerman 1991) identified the proportion of patients who had diabetes mellitus.

Most studies reported only some of the primary outcomes of interest to this review. The primary outcomes reported in the studies were as follows: peritonitis - number of patients (22 studies), peritonitis rate (14 studies), exit-site/tunnel infection - number of patients (22 studies), exit-site/tunnel infection - rate (12 studies) and catheter removal/replacement (15 studies). Other outcomes reported included death due to peritonitis (2 studies), all-cause mortality (13 studies), technique failure (3 studies) and toxicity of antimicrobial treatments (5 studies). No studies had data on peritonitis relapse
and only two had time to first peritonitis episode (HONEYPOT Trial 2009; MP3 Study 2008).

Funnel plots to examine for publication bias were not done because there were insufficient studies.

**Oral or topical antibiotics versus placebo/no treatment**

In 7 trials (469 participants), patients were randomised to oral, or topical (exit site, nasal) or intraperitoneal prophylactic antibiotics versus placebo/no treatment (Blowey 1994; Churchill 1988; Low 1980; Sesso 1994; Swartz 1991; Wong 2003; Zimmerman 1991). The duration of follow-up ranged from 1 to 12 months.

**Oral or topical antibiotics versus other antibiotic**

Seven trials (640 participants) randomised patients to oral, or topical (exit site, nasal) or intraperitoneal antibiotics versus other antibiotics (Bernardini 1996; Bernardini 2005; Chu 2008; Danguilan 2003; MP3 Study 2008; Perez-Fontan 1992; Sesso 1994) with follow-up ranging from 7.8 to 18 months.

**Nasal antibiotic prophylaxis versus placebo/no treatment**

Three trials (338 participants) compared the use of nasal prophylactic antibiotics with placebo (Mupirocin SG 1996; Sesso 1994; Sit 2007). The duration of follow-up ranged from 7.8 to 18 months.

**Pre/peri-operative antibiotic prophylaxis versus placebo/no treatment or other antibiotic**

One trial (178 participants) assessed the use of vancomycin with cefazolin as perioperative intravenous prophylaxis head to head (Gadallah 2000) and four
trials (379 patients) compared the use of perioperative intravenous antibiotic prophylaxis against no antibiotic treatment (Bennet-Jones 1988; Gadallah 2000; Lye 1992; Wikdahl 1997). Follow-up periods ranged from 10 to 28 days.

**Topical disinfectants versus standard care or other active treatment (antibiotic or other disinfectant)**

Nine trials (1039 participants) evaluated the effect of topical disinfectants versus standard care or other intervention at the exit site on a range of outcomes (Cheng 1999a; HONEYPOT Trial 2009; Luzar 1990; Mendoza-Guevara 2007; Nunez-Moral 2014; Wadhwa 1995; Wadhwa 1997; Waite 1997; Wilson 1997). The duration of follow-up ranged from 6 to 24 months.

**Other interventions**

Other interventions included one trial (167 participants) which compared the use of an ultraviolet germicidal chamber to disinfect the spike and the solution bag outlet port versus no treatment (Nolph 1985) while another trial (50 participants) directed one group to soak their connectors in antiseptic before performing a bag exchange while the control group did not use antiseptic (Ryckelynck 1987). Three trials (140 participants) compared different dressing systems (Cocksedge 1993; Fuchs 1990; Moore 1989) and one trial (195 participants) compared the addition of a silver ring device on the catheter versus no ring (SIPROCE 1997).

One trial (124 participants) compared the antistaphylococcal vaccine Staphypan Berna against placebo (Poole-Warren 1991).

**Antifungal prophylaxis versus placebo/no treatment interventions**

Two trials (817 participants) compared the administration of an antifungal
agent with an antibiotic course against no treatment (Lo 1996; Restrepo 2010). Follow-up periods ranged from 1 to 18 months.

With the update, four trial authors responded to queries about study methods and/or requests for additional unpublished information (Ayliffe 1984; Chu 2008; Danguilan 2003; HONEYPOT Trial 2009).

**Excluded studies**

Twenty-two studies (28 reports) were excluded after full text review. The characteristics of the excluded studies are shown in "Characteristics of excluded studies". Reasons for excluding studies included having a non-randomised study design, focus of study was about treatment of PD-related infection not prevention, report was of a pharmacokinetics study, agent used in intervention was not an antimicrobial, and PD-related infection data was not readily available in the published report.

**Risk of bias in included studies**

The assessment of risk of bias is shown in Figure 3 and Figure 4. Figure 3 shows relative proportional rankings of studies for each risk of bias indicator. Figure 4 shows the risk of bias items for individual studies.

**Allocation (selection bias)**


Blinding (performance bias and detection bias)

Only eight studies (Axelrod 1973; Bennet-Jones 1988; Bernardini 2005; Churchill 1988; Low 1980; MP3 Study 2008; Poole-Warren 1991; Sharma 1971) reported methods of blinding for participants, investigators and outcome assessors. Blinding of participants was used in 9/38 (23.7%) trials, blinding of investigators in 9/38 (23.7%) trials, and outcome assessors were blinded in 9/38 (23.7%) trials.

Incomplete outcome data (attrition bias)

Outcomes data reporting was considered to be complete with a low risk of bias in 22 studies (Bennet-Jones 1988; Bernardini 1996; Bernardini 2005; Blowey 1994; Churchill 1988; Fuchs 1990; Gadallah 2000; Lo 1996; Low 1980; Luzar 1990; Lye 1992; MP3 Study 2008; Mupirocin SG 1996; Nunez-Moral 2014; Perez-Fontan 1992; Poole-Warren 1991; Sit 2007; Swartz 1991; Waite 1997; Wikdahl 1997; Wilson 1997; Wong 2003). Eight studies (Axelrod 1973; Chu 2008; Danguilan 2003; HONEYPOT Trial 2009; Nolph 1985; Sesso 1994; SIPROCE 1997; Zimmerman 1991) reported that from 9.2% to 77.7% of patients were excluded from analyses,
so were considered to be at high risk of bias. The risk of bias was unclear in 9 studies because there was insufficient information provided to determine if data from all patients who entered the study were included in the analysis.

**Selective reporting (reporting bias)**

We identified 19 studies (Bernardini 1996; Bernardini 2005; Chu 2008; HONEYPOT Trial 2009; Luzar 1990; Lye 1992; MP3 Study 2008; Mupirocin SG 1996; Nunez-Moral 2014; Poole-Warren 1991; Sesso 1994; SIPROCE 1997; Swartz 1991; Wadhwa 1995; Wadhwa 1997; Wikdahl 1997; Wilson 1997; Wong 2003; Zimmerman 1991) that were considered to have reported all outcomes based on the protocols described in the trial methods. Two studies (Axelrod 1973; Sharma 1971) reported outcomes incompletely so they could not be meta-analysed. It was unclear if outcomes were selectively reported in 11 studies because there was insufficient information provided to determine if data from all patients who entered the study were included in the analysis.

**Other potential sources of bias**

Nine studies (Axelrod 1973; Churchill 1988; HONEYPOT Trial 2009; Mupirocin SG 1996; Nolph 1985; Poole-Warren 1991; SIPROCE 1997; Waite 1997; Zimmerman 1991) reported receiving monetary support from pharmaceutical companies and 25 studies did not report study funding.

**Effects of interventions**

See: Summary of findings 1 Oral or topical or intraperitoneal antibiotics versus placebo/no treatment for preventing peritonitis in peritoneal dialysis
patients; Summary of findings 2 Nasal antibiotics versus no treatment for preventing peritonitis in peritoneal dialysis patients; Summary of findings 3 Topical disinfectants versus standard care or other active treatment (antibiotic or other disinfectant) for preventing peritonitis in peritoneal dialysis patients; Summary of findings 4 Antifungal versus placebo/no treatment for preventing fungal peritonitis in peritoneal dialysis patients.

In most studies, the primary outcomes were peritonitis (number of patients), peritonitis rate, exit site/tunnel infection (number of patients), exit site/tunnel infection rate, and catheter removal or replacement (number). Many studies only included one or two of these outcomes. Other outcomes included all-cause mortality, time to first catheter-related infection, hospitalisation, death due to catheter-related infection, technique failure, local pruritus/rash and toxicity.

**Effect on PD catheter-related infections, catheter removal/replacement and all-cause mortality of oral or topical antibiotics compared with placebo/no treatment**

The oral antibiotic used was either ofloxacin, cephalexin, rifampin or cotrimoxazole and the topical antibiotic used was mupirocin ointment (exit site, nasal). There was no significant difference between oral or topical antibiotic prophylaxis and placebo/no treatment for the risk of peritonitis (Analysis 1.1.1 (4 trials, 241 patients): RR 0.87, 95% CI 0.58 to 1.32; Analysis 1.1.2 (1 trial, 154 patients): RR 0.55, 95% CI 0.22 to 1.40). There was low to moderate heterogeneity across these trials ($I^2 = 33\%$). The risk of peritonitis outcome was assessed as low quality because of unclear or high risk of bias in 3 of 5 studies and because of wide confidence intervals.
in all 5 studies due to small patient numbers.

There was also no significant difference between the two interventions for the peritonitis rate (Analysis 1.2.1 (3 trials, 1440 patient-months): RR 0.68, 95% CI 0.40 to 1.14), the risk of exit-site and tunnel infection (Analysis 1.3.1 (3 trials, 191 patients): RR 0.45, 95% CI 0.19 to 1.04), the exit-site/tunnel infection rate (Analysis 1.4.1 (2 trials, 939 patient-months): RR 0.42, 95% CI 0.17 to 1.05), risk of catheter removal or replacement (Analysis 1.5.1 (5 trials, 395 patients): RR 0.82, 95% CI 0.46 to 1.46) and all-cause mortality (Analysis 1.6.1 (4 trials, 201 patients): RR 0.88, 95% CI 0.41 to 1.89), with no significant heterogeneity across trials for any of these analyses ($I^2 = 0\%$). The risk of exit-site/tunnel infection outcome was assessed as low quality because of unclear or high risk of bias in all 3 studies and because of wide confidence intervals in all 3 studies due to small patient numbers. The risk of catheter removal/replacement outcome was also assessed as low quality because of unclear or high risk of bias in 3 of 5 studies and because of wide confidence intervals in all 5 studies due to small patient numbers.

**Effect on PD catheter-related infections of oral or topical antibiotics compared with other antibiotic**

The use of antibiotic ointment prophylaxis (either sodium fusidate [exit site plus nasal] or mupirocin [exit site]) was compared with another antibiotic (either oral ofloxacin, oral rifampin or gentamicin cream [exit site]) in four trials. There was no significant difference between the interventions for the risk of peritonitis (Analysis 2.1 (4 trials, 314 patients): RR 1.28, 95% CI 0.89 to 1.84). There was low heterogeneity across these trials ($I^2 = 9\%$).
Similarly, there was no significant difference between topical antibiotic prophylaxis (either mupirocin ointment [exit site], sodium fusidate ointment [exit site plus nasal] or mupirocin cream [exit site]) compared with other antibiotic (either sodium fusidate ointment [exit site], oral ofloxacin or gentamicin cream [exit site]) for the risk of exit-site and tunnel infection (Analysis 2.3 (4 trials, 336 patients): RR 1.28, 95% CI 0.71 to 2.31). There was medium heterogeneity across these trials ($I^2 = 56\%$).

**Effect on PD catheter-related infections and catheter removal/replacement of nasal antibiotic prophylaxis compared with placebo/no treatment**

There were no significant differences between nasal antibiotic prophylaxis and placebo/no treatment for the risk of peritonitis (Analysis 3.1 (3 trials, 338 patients): RR 0.94, 95% CI 0.67 to 1.31), the peritonitis rate (Analysis 3.2 (2 trials, 2797 patient-months): RR 0.67, 95% CI 0.16 to 2.77), the risk of exit-site and tunnel infection (Analysis 3.3 (3 trials, 338 patients): RR 1.34, 95% CI 0.62 to 2.87), the exit-site and tunnel infection rate (Analysis 3.4 (2 trials, 2796 patient-months): RR 0.91, 95% CI 0.29 to 2.92), and the number of patients with catheter removal or replacement (Analysis 3.5 (2 trials, 289 patients): RR 0.92, 95% CI 0.48 to 1.78). There was no significant heterogeneity across the trials for any of these analyses.

Although in one trial, there was a significant reduction in the exit-site/tunnel infection rate when CAPD patients identified as *S. aureus* carriers (nasal) were treated with mupirocin ointment (nasal application, 2/day for 5 days, every 1 month), there were no significant differences with any of the other primary outcomes of interest (Mupirocin SG 1996).
The risk of peritonitis and the risk of exit-site/tunnel infection outcomes were assessed as low quality because of unclear or high risk of bias in all 3 studies and because of wide confidence intervals in all 3 studies due to small patient numbers. The risk of catheter removal/replacement outcome was assessed as low quality because of unclear to high risk of bias in the 2 studies and because of wide confidence intervals in the 2 studies due to small patient numbers.

**Effect on early peritonitis and early exit-site infection of pre/peri-operative antibiotic prophylaxis compared with placebo/no treatment or other antibiotic**

Pre/peri-operative intravenous antibiotic prophylaxis compared with no treatment significantly reduced the risk of early peritonitis (less than one month from catheter insertion) in one study (Gadallah 2000) but there was no significant difference between the interventions in three other studies using different antibiotics (Analysis 4.1 (4 trials, 379 patients). The single 3-arm study (Gadallah 2000) compared vancomycin with placebo, cefazolin with placebo and vancomycin with cefazolin and found the risk of peritonitis was significantly reduced by vancomycin compared with placebo (RR 0.08, 95% CI 0.01 to 0.61) and by vancomycin compared with cefazolin (RR 0.11, 95% CI 0.01 to 0.84); there was no significant difference between cefazolin compared with placebo. None of the antibiotic interventions made a significant difference to the risk of exit-site and tunnel infection (Analysis 4.2 (4 trials, 379 patients). When outcomes at more than one month after catheter insertion were considered, there was no significant difference between the interventions for the risk of peritonitis or exit-site/tunnel infection. Because each trial used a different antibiotic intervention, it
is not possible to comment on heterogeneity across the trials.

**Effect on PD catheter-related infections, catheter removal/replacement and all-cause mortality of topical disinfectants compared with standard care or other active treatment (antibiotic or other disinfectant)**

Eight studies reported on the use of disinfectant at the exit site versus standard care or other active treatment. There was no significant difference between topical disinfection of the exit-site with povidone iodine ointment or solution or dry power spray compared with no treatment or soap and water on the risk of peritonitis (Analysis 5.1.1 (3 trials, 393 patients): RR 0.81, 95% CI 0.52 to 1.26), exit-site/tunnel infection (Analysis 5.2.1 (4 trials, 453 patients): RR 0.74, 95% CI 0.45 to 1.20), catheter removal or replacement (Analysis 5.4.1 (2 trials, 266 patients): RR 0.73, 95% CI 0.34 to 1.55), or all-cause mortality (Analysis 5.5.1 (2 trials, 266 patients): RR 1.24, 95% CI 0.54 to 2.84), with no significant heterogeneity across trials for any of these analyses.

Topical disinfection of the exit-site with sodium hypochlorite solution 10% or sodium hypochlorite solution 5% or antibacterial honey was compared with standard care or standard care plus mupirocin ointment treatment nasally (only in *S. aureus* nasal carriers). There was no significant difference between the interventions for the risk of peritonitis (Analysis 5.1.2 (3 trials, 460 patients): RR 0.84, 95% CI 0.62 to 1.13), exit-site/tunnel infection (Analysis 5.2.2 (3 trials, 460 patients): RR 1.15, 95% CI 0.85 to 1.56), catheter removal or replacement (Analysis 5.4.2 (4 trials, 526 patients): RR 0.98, 95% CI 0.57 to 1.69), or all-cause mortality (Analysis 5.5.2 (1 trial, 371 patients): RR 0.77, 95% CI 0.40 to 1.51). There was low heterogeneity across trials for outcomes
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with data from more than one trial.

The risk of peritonitis outcome was assessed as low quality because of unclear allocation concealment and blinding in 4 of 6 studies and imprecision due to the small number of patients and events in 5 of 6 studies. The risk of exit-site/tunnel infection outcome was assessed as low quality because of unclear allocation concealment and blinding in 6 of 8 studies and imprecision due to the small number of patients and events in 7 of 8 studies. The risk of catheter removal/replacement outcome was assessed as low quality because of unclear allocation concealment and blinding in 5 of 7 studies and imprecision due to the small number of patients and events in 6 of 7 studies.

**Effect on PD-catheter-related infections and catheter removal/replacement of other interventions**

Seven studies reported on other interventions designed to reduce PD-related infections. There was no significant difference in the peritonitis rate with other interventions including:

- use of a germicidal chamber for connection devices or soaking of the connector in antiseptic prior to bag exchange versus none (Analysis 6.1 (2 trials, 1855 patient-months): RR 1.05, 95% CI 0.74 to 1.51)

- use of the Staphypan Berna antistaphylococcal vaccine (Analysis 9.1 (1 trial, 1099 patient-months): RR 1.11, 95% CI 0.77 to 1.59). Staphypan Berna compared with placebo was also shown to make no significant difference to the exit-site and tunnel infection rate (Analysis 9.2 (1 trial, 1107 patient-months): RR 0.98, 95% CI 0.65 to 1.48).

There was no significant difference between use of a silver ring on the PD
catheter versus none for the risk of peritonitis (Analysis 8.1 (1 trial, 195 patients): RR 0.90, 95% CI 0.49 to 1.66), risk of exit-site/tunnel infection (Analysis 8.2 (1 trial, 195 patients): RR 1.26, 95% CI 0.84 to 1.90) or risk of catheter removal/replacement (Analysis 8.3 (1 trial, 195 patients): RR 1.26, 95% CI 0.35 to 4.56).

Three studies reported on the use of different dressing systems. There was no significant difference between the comparisons for the number of patients with one or more episodes of exit-site/tunnel infection (Analysis 7.1 (3 trials, 140 patients) or the exit-site/tunnel infection rate (Analysis 7.2 (1 trial, 679 patient-months).

**Effect on fungal peritonitis of antifungal prophylaxis compared with placebo/no treatment interventions**

The use of antifungal agents (oral fluconazole or oral nystatin) compared with no antifungal agent being given when a patient receives a course of antibiotics for bacterial peritonitis were reported in 2 studies. The antifungal intervention showed a significant reduction in the risk of fungal peritonitis (Analysis 10.1 (2 trials, 817 patients): RR 0.28, 95% CI 0.12 to 0.63). There was low heterogeneity across the two trials for this analysis. The risk of fungal peritonitis outcome was assessed as low quality because of unclear risk of bias in 1 study and high risk of bias in 1 study and imprecision due to the small number of events and patient numbers.

One trial of oral nystatin in PD patients who were receiving treatment for bacterial peritonitis showed a significant reduction in the rate of fungal peritonitis due to *Candida* spp. with nystatin prophylaxis (Analysis 10.2 (1
trial, 6864 patient-months): RR 0.31, 95% CI 0.10 to 0.95).

**Adverse effects**

For the comparisons which included oral or topical antibiotics versus placebo/no treatment, two studies provided some information on adverse effects of therapy. They were reported in relation to the use of oral rifampin and sodium fusidate ointment (nasal and exit site). More patients reported adverse effects with oral rifampin therapy but the results did not achieve significance. Heterogeneity could not be determined (Analysis 1.8; 2 studies, 86 patients).

For the studies which included oral or topical antibiotics versus other antibiotic, three studies reported on adverse effects of therapy. The antibiotics used were applied daily/routinely to the exit site and included Polysporin triple ointment, gentamicin cream and cyclic oral rifampin against mupirocin ointment or cream. There were fewer patients who reported adverse effects with mupirocin but the result was not significantly different. There was low heterogeneity of results (Analysis 2.8; 3 studies, 419 patients: RR 0.54, 95% CI 0.21 to 1.39; I² = 40%).

Three studies compared nasal antibiotics against placebo/no treatment and two of them reported information on adverse effects of therapy. The antibiotics used included mupirocin ointment (nasal) and sodium fusidate ointment (nasal and exit site) versus placebo ointment (nasal) or placebo tablets. More patients reported adverse effects with the antibiotic treatments but the results did not achieve significance. Heterogeneity could not be determined (Analysis 3.7; 2 studies, 289 patients).

For the studies which included topical disinfectant versus standard care or
other active treatment at the exit site, four studies reported on adverse
effects of therapy. The interventions that these reports related to were
sodium hypochlorite solution, antibacterial honey and povidone iodine dry
powder spray against povidone iodine solution, mupirocin ointment
(nasal) or alcohol wipes. More patients reported adverse effects with use
of the former agents and a statistically significant increase in pruritus
occurred with topical disinfectants versus standard care. There was low
heterogeneity of results (Analysis 5.7; 4 studies, 609 patients: RR 2.80,
95% CI 1.21 to 6.48; $I^2 = 44\%$). Antibiotic resistance was not adequately
reported in the included studies (Table 3).

**Outcomes sought but not reported**

Very few studies reported on peritonitis relapse, development of antibiotic
resistance (topical use), hospitalisation due to PD-related infections or
peritonitis, time to first peritonitis episode, technique failure (transfer from
PD to haemodialysis/transplant due to peritonitis), or death due to peritonitis.

**4.7 Discussion**

**Summary of main results**

We identified 39 studies that compared antimicrobial agents with placebo/no
treatment or other antimicrobial agent or standard care in CKD patients on
PD. A range of antimicrobial agents were found and studies using antibiotic
prophylaxis showed wide variability regarding the dose and duration of the
interventions trialled. The duration of studies ranged from 1 month to 8 years.
The quality of the evidence for all of the findings listed below was low.
Key findings are as follows:

- The use of oral or topical antibiotic may reduce the risk of exit-site/tunnel infection and may slightly reduce the risk of peritonitis.

- It is uncertain whether the topical administration of antibiotic ointment to the anterior nares of PD patients (sodium fusidate or mupirocin ointment) reduces the risk of exit-site/tunnel infection or the risk of peritonitis.

- Pre/peri-operative intravenous vancomycin appears to reduce the risk of early peritonitis in the first few weeks (< 1 month) following Tenckhoff catheter insertion but has an uncertain effect on the risk of exit-site/tunnel infection. The comparisons using other antibiotics (i.e. IV gentamicin; IV cefazolin plus gentamicin; IV cefuroxime plus cefuroxime intraperitoneal) did not reduce the risk of peritonitis or exit site/tunnel infection.

- The use of topical disinfectant may lead to little or no difference in the risk of exit-site/tunnel infection but may slightly reduce the risk of peritonitis.

- Oral antifungal prophylaxis (fluconazole or nystatin) with each antibiotic course given to a PD patient appears to reduce the risk of fungal peritonitis.

- No intervention reduced the risk of catheter removal or replacement.

None of the following interventions (oral or topical antibiotics versus placebo/no treatment; oral or topical antibiotics versus other antibiotic; nasal antibiotics versus placebo/no treatment; pre-peri-operative prophylaxis...
versus placebo/no treatment or other antibiotic; topical disinfectants versus standard care or other active treatment; germicidal chamber versus none; silver ring system on catheter versus none) made a significant difference to mortality (all-cause). Neither of the following interventions (oral or topical antibiotics versus other antibiotic; topical disinfectants versus standard care or other active treatment) made a significant difference to the risk of technique failure.

Heterogeneity among the studies was low except for the interventions 'oral or topical antibiotics versus placebo/no treatment' and 'oral or topical antibiotics versus other antibiotic'.

Heterogeneity in the former comparison for the risk of peritonitis was 33% and was likely related to the variety of antibiotics used, the frequency of administration (daily, monthly, every 3 months), the route of administration (oral, topical) and the population studied (adults in Brazil, Canada, USA, Hong Kong). Heterogeneity in the latter comparison for the risk of exit-site/tunnel infection was 56% and was probably related to the range of antibiotics used, the frequency of administration (twice daily, daily, every 2 days, weekly), the route of administration (oral, topical) and the population studied (adults in the Philippines, Brazil, Hong Kong, USA).

**Overall completeness and applicability of evidence**

Ten studies reported on all three primary outcomes of interest (peritonitis, exit-site/tunnel infection, catheter removal/replacement); 16 studies reported on two primary outcomes of interest; 11 studies reported on one primary outcome of interest and two studies reported on primary outcomes in a way that was not usable (Axelrod 1973; Sharma 1971). Our meta-
analyses identified that use of oral or topical antibiotics may reduce the risk of exit-site/tunnel infection and the risk of peritonitis but did not appear to affect the exit-site/tunnel infection rate, the peritonitis rate or the risk of catheter removal/replacement. It is unclear if the use of nasal mupirocin in identified nasal carriers of *S. aureus* reduces the risk of exit-site/tunnel infection or peritonitis. The use of pre/peri-operative intravenous antibiotic at PD catheter insertion reduces the occurrence of early peritonitis (within 1 month of insertion) with vancomycin being the most effective antibiotic to use. The use of topical disinfectant appears to lead to little or no difference in the risk of exit-site/tunnel infection but may slightly reduce the risk of peritonitis. The co-administration of antifungal agents with an antibiotic course appears to reduce the risk of fungal peritonitis developing in a PD patient.

No RCT was found which had the comparison of routine courses of intranasal mupirocin versus daily exit-site mupirocin. Likewise, no RCT was found which compared *S. aureus* nasal carriage eradication at the time of PD catheter insertion versus no eradication of *S. aureus* nasal carriage. In addition, some outcomes were either not addressed (development of antibiotic resistance with topical use) or not often addressed (peritonitis relapse, hospitalisation rates due to PD-related infections or peritonitis, technique failure due to peritonitis). It should also be mentioned that for most comparisons there are only a few studies and small numbers of patients.

**Quality of the evidence**

Our review included 39 studies that involved 4374 participants, of whom all were either on peritoneal dialysis (CAPD, CCPD or APD) or were having
surgery to insert the Tenckhoff catheter prior to commencing peritoneal dialysis. Two studies had paediatric populations, two studies had a mix of adults and children, with the remainder having only adult participants.

We found the quality of evidence for all outcomes to be of low quality mainly due to unclear or high risk of bias in a majority of studies and imprecise results because of small patient numbers and events. This means that further research is likely to have an important impact on our confidence in the estimates of effect and is likely to change those estimates.

Of the 39 included studies, four were available only as abstracts; 18 reported adequate sequence generation, and 12 had adequate allocation concealment. Hence, allocation concealment was either unclear or inadequate in two-thirds of the studies. Studies that do not have adequate allocation concealment are felt to be at increased risk of bias (Moher 1998; Schulz 1995). Eight studies reported adequate blinding of participants and personnel, and 10 studies reported adequate blinding of outcome assessment. Therefore, blinding methodology was either unclear or inadequate in three-quarters of the studies. We found that 21 studies provided complete data reporting, and 10 reported all primary outcomes. Nine of the included studies reported receiving some form of sponsorship from pharmaceutical companies, 6 studies reported funding from an institute or government organisation and 25 studies did not report any funding source. In this review, we did not observe a difference between studies that were sponsored by pharmaceutical companies and those that were not. Of the nine pharma-sponsored studies, six had adequate allocation concealment; of the six studies with partial or full funding from an institute/government organisation, five reported
adequate allocation concealment; and of the 25 studies that did not report a
funding source, only three demonstrated adequate allocation concealment.
Likewise, in terms of selective outcome reporting, five of the nine pharma-
sponsored studies reported expected outcomes; four of the six institute/
government-sponsored studies reported expected outcomes; and 10 of the 25
studies without a declared funding source included all expected primary
outcomes.

For the comparison of oral or topical antibiotics versus placebo/no
treatment, the variable quality of relevant studies and the small patient
numbers, meant the quality of evidence was rated as low for the outcomes
of peritonitis, exit-site/tunnel infection and catheter removal/replacement
(Summary of findings table 1). For the comparison of nasal antibiotics
versus placebo/no treatment, the variable quality of relevant studies and the
small patient numbers, reduced the quality of evidence to low for the
outcomes of peritonitis, exit-site/tunnel infection and catheter
removal/replacement (Summary of findings table 2). With the comparison
of topical disinfectants versus standard care or other active treatment, the
unclear allocation in several studies and imprecision due to small patient
numbers and events in several studies, meant the quality of evidence was
rated as low for the outcomes of peritonitis, exit-site/tunnel infection and
catheter removal/replacement (Summary of findings table 3). With the
comparison of antifungal prophylaxis versus placebo/no treatment, the
quality of evidence for the outcome of fungal peritonitis was considered to
be low because of high risk of bias in one study and modest patient numbers
and the limited number of studies reporting this outcome (Summary of
findings table 4).

**Potential biases in the review process**

Four of the included studies were available only as abstracts (4/38) but this was not considered a major source of bias. Since the original version of this review was published, the literature search has been run several times (up to April 2015), to increase the chance that all eligible studies published before that time have been included. Although the Cochrane Kidney and Transplant Specialised Register includes references of reports of studies identified by handsearching resources including conference proceedings, it is a possibility that relevant studies may have been added since our last search of the register. Some outcomes were reported in only a few studies, which increased the risk of the non-randomised selection of patients for the intervention or control group in a study. For example, the outcome of fungal peritonitis was reported in two studies (817 patients), with one study finding a significant difference between the fungal prophylaxis and control groups, while the second study did not have this finding. In addition, adverse effects were reported in only five studies.

**Agreements and disagreements with other studies or reviews**

A systematic review was performed as part of the HONEYPOT trial published in 2014. The authors systematically reviewed trials of topical antimicrobial prophylaxis for prevention of infections in peritoneal dialysis. Nine trials were identified using a search strategy that included electronic searches of Medline (through Ovid) and the Cochrane Central Register of Controlled Trials (Johnson 2014). Our
review included all of the studies included by Johnson 2014, as well as two studies not reported in that review (Chu 2008; Danguilan 2003). The 2014 review concluded that the evidence from the nine trials was inconclusive for nasal mupirocin, exit-site mupirocin and exit-site gentamicin prophylaxis. In the present review, we reached a similar conclusion, with some individual studies making a significant difference to the risk of exit-site/tunnel infection or the exit-site/tunnel infection rate but not having an effect on the other outcomes of peritonitis, catheter removal/replacement and technique failure.

The Renal Association (UK) guidelines currently recommend that "topical antibiotic administration be used to reduce the frequency of S. aureus and Gram-negative exit-site infection and peritonitis" (Woodrow 2010). The suggested antibiotics are mupirocin ointment or gentamicin cream (the latter for patients with a known history of Pseudomonas infections). The International Society for Peritoneal Dialysis (ISPD) position statement on exit-site care to prevent peritonitis (Piraino 2011) states that "antibiotic protocols against S. aureus are effective in reducing the risk of S. aureus catheter infections" and that "all PD patients should use topical antibiotic either at the catheter exit-site or intranasally or both". The Kidney Health Australia-Caring for Australasians with Renal Impairment guidelines (Walker 2014) recommend that "prophylactic therapy using mupirocin ointment be used, especially for S. aureus carriage (intranasally or at the exit site) to decrease the risk of S. aureus catheter exit site/tunnel infections and peritonitis" and suggest that the "PD catheter exit site be cleaned daily and a topical antimicrobial agent (either mupirocin or gentamicin) be applied". This
review found that the use of oral antibiotic or mupirocin ointment (at the exit site) may reduce the risk of exit-site/tunnel infection and the risk of peritonitis but was not seen to reduce the exit-site/tunnel infection rate, the peritonitis rate or the number of patients with catheter removal/replacement. The head to head comparison of application of mupirocin ointment or cream against gentamicin cream is based on two trials and shows that there is no significant difference between the effectiveness of mupirocin and gentamicin in terms of preventing exit-site/tunnel infection and peritonitis. It is unclear if the nasal application of mupirocin reduces the risk of exit-site/tunnel infection or the risk of peritonitis.

The Renal Association (UK) guidelines state it is "recommended that initial catheter insertion be accompanied by antibiotic prophylaxis" and refer to the RCT evidence supporting the use of vancomycin (Wilkie 2010; Woodrow 2010). The ISPD position statement says that "prophylactic antibiotics administered at the time of insertion decrease the infection risk. A first-generation cephalosporin or vancomycin can be used, but suggested each program should weigh the potential benefit against the risk of vancomycin use (development of resistant organisms)" (Piraino 2011). The KHA-CARI guidelines say it is "recommended that intravenous antibiotic prophylaxis be used prior to peritoneal dialysis catheter insertion to reduce the risk of early peritonitis" and "vancomycin, cephalosporins and gentamicin have demonstrated effectiveness in reducing the risk of peritonitis" (Walker 2014). The inclusion of first generation cephalosporins is based on extrapolations from the results of pre-operative antibiotic trials in patients without chronic kidney disease. However, our study indicates
that the evidence supporting the use of first generation cephalosporins in PD patients undergoing Tenckhoff catheter insertion is scant. In the present review, we identified four RCTs of different pre-operative antibiotic prophylaxis regimens, including parenteral gentamicin, vancomycin, cephazolin and cefuroxime, with only two evaluating a first generation cephalosporin. One small trial involving 50 PD patients found that cephazolin and gentamicin were no better than no treatment (Lye 1992). The largest of the trials (265 patients) showed that cephazolin was inferior to vancomycin in preventing post-operative catheter-associated infections (7% versus 1%, respectively; P<0.05) (Gadallah 2000). However, the recommendation to use a first generation cephalosporin or vancomycin is understandable because of the risk of selecting for resistant organisms such as vancomycin-resistant enterococci and *S. aureus* (Hospital 1995) and the development of *Clostridium difficile* colitis (Wilkie 2010). Postoperative incidence of peritonitis in the control arms of three of the evaluated trials were high, ranging from 14% to 46% (Bennet-Jones 1988; Gadallah 2000; Wikdahl 1997) and the applicability of these data to PD units with lower infection rates following PD catheter insertion is unclear.

The ISPD position statement suggests "most episodes of fungal peritonitis are preceded by courses of antibiotics" and "fungal prophylaxis during antibiotic therapy may prevent some cases of *Candida* peritonitis in programs that have high rates of fungal peritonitis" (Piraino 2011). The KHA-CARI guidelines recommend "oral antifungal prophylaxis should be considered when antibiotics are administered to patients undergoing peritoneal dialysis to reduce the risk of developing fungal peritonitis"
This review indicates that fluconazole reduced the risk of fungal peritonitis following antibiotic treatment and that nystatin reduced the rate of *Candida* peritonitis in PD patients. The authors of the fluconazole trial (Restrepo 2010) noted that a growing number of *Candida* strains were resistant to fluconazole during their trial, and this will limit its use.

The ISPD no longer recommends that the exit-site be regularly disinfected with antibacterial soap or a medical antiseptic to keep the exit-site clean and reduce the numbers of resident bacteria. The current position statement states that "water and antibacterial soap are recommended by many centres. Use of an antiseptic to clean the exit site is preferred in some programs, but the agent must be non-cytotoxic" (Piraino 2011). The four trials in this review which compared the use of disinfectant against standard care did not show any benefit with the use of disinfectant (povidone-iodine 10% ointment; povidone-iodine 2.5% dry powder spray; povidone-iodine 20g/L solution; or sodium hypochlorite 10% solution) compared with standard care (povidone-iodine 10% solution; alcohol chlohexidine hand wash and use of alcohol wipes; non-disinfectant soap and water; or pH neutral soap and water). Three of the studies did not report on adverse effects of the interventions and one study observed that skin rashes/pruritis occurred in 6% of patients following use of the povidone-iodine dry powder spray (Wilson 1997). The three trials in this review which looked at the use of disinfectant versus antibiotic or other disinfectant also did not show any benefit with the use of disinfectant (sodium hypochlorite 10% solution; sodium hypochlorite 5% solution; antibacterial honey 10 mg) compared with antibiotic (2% mupirocin...
ointment) or other disinfectant (povidone iodine 10% solution). Adverse effects were reported in each of these studies. Sodium hypochlorite solution was associated with more irritation around the exit site than povidone iodine solution (Wadhwa 1995; Wadhwa 1997) and 5.9% of patients using antibacterial honey at the exit site in the HONEYPOT trial reported local reaction as the reason for withdrawing from the study whereas no patients in the control group reported this adverse effect (HONEYPOT Trial 2009).

4.8 Authors' conclusions

Implications for practice

This update of a systematic review identified low quality evidence for the outcomes under consideration. Our findings are as follows:

- The use of oral or topical antibiotic may reduce the risk of exit-site/tunnel infection and may slightly reduce the risk of peritonitis.
- It is uncertain whether the use of nasal antibiotic reduces the risk of exit-site/tunnel infection or the risk of peritonitis.
- The use of pre/perioperative intravenous vancomycin appears to reduce the risk of early peritonitis but does not appear to reduce the risk of exit-site/tunnel infection.
- The use of topical disinfectant may lead to little or no difference in the risk of exit-site/tunnel infection but may slightly reduce the risk of peritonitis.
- Antifungal prophylaxis with oral nystatin/fluconazole appears to reduce the risk of fungal peritonitis occurring after a PD patient has had an antibiotic course.
Implications for research

Many of the studies included in this review have significant methodological limitations, including lack of statistical power, and potential for bias. Further large randomised studies with sufficiently long follow-up periods are required. These need to assess patient-important outcomes such as adverse effects of the interventions given as well as quality of life. Studies need to be designed so they yield useful data on the key outcomes of exit-site/tunnel infection, peritonitis, catheter loss/replacement and technique failure due to infection.

These studies should be large enough to enable subgroup analyses to determine which patients would benefit most from a prophylactic intervention and to clearly identify any harms associated with an intervention. There is a pressing need for more well-designed RCTs in this area, which adequately assess safety, as well as efficacy.
### Table 4.1: Characteristics of included studies

**Axelrod 1973**

| Methods | Study design: parallel RCT  
Study duration/time frame: 2 months at Bronx VA Hospital; 12 months at Mt Sinai Hospital |
|---------|---------------------------------------------------------------------|
| Participants | Inclusion criteria  
Setting: 2 tertiary centres  
Country: USA  
Health status: Peritoneal dialysis patients  
Number: 36 patients (no numbers given for intervention and control group)  
Mean age: NS  
Sex (M/F): Bronx VA Hospital 24/0; Mt Sinai Hospital 3/9  
Proportion of diabetic patients (%): Bronx VA Hospital 8.3%; Mt Sinai Hospital 8.3% |
| Exclusion criteria: NS |
| Interventions | Cephalothin added to 2 L bottle of dialysate (100 micrograms/mL) versus placebo solution added to 2 L bottle of dialysate |
| Outcomes | Peritonitis - number of dialyses |
| Notes | Funding source: Public Health Service grant and Eli Lilly & Company, Indianapolis.  
Follow-up period: NS  
Loss to follow-up: NS  
Excluded from analysis: 10 dialyses were excluded (no numbers given for intervention and control group breakdown)  
Exclusions post-randomisation but pre-intervention: NS  
Stop or end point/s: NS |

<table>
<thead>
<tr>
<th>Bias</th>
<th>Authors' judgement</th>
<th>Support for judgement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Random sequence generation (selection bias)</td>
<td>Low risk</td>
<td>Random number table. &quot;Patients were selected to receive placebo or antibiotic according to a random number list kept by the pharmacy...&quot;</td>
</tr>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>Low risk</td>
<td>Central allocation (pharmacy)</td>
</tr>
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<td>Blinding of participants and personnel (performance bias)</td>
<td>Low risk</td>
<td>Blinding, and unlikely that the blinding could have been broken.</td>
</tr>
<tr>
<td>Blinding of outcome assessment (detection bias)</td>
<td>Low risk</td>
<td>Blinding, and unlikely that the blinding could have been broken. &quot;We conducted a random double-blind trial of cephalothin sodium as the prophylactic agent.&quot;</td>
</tr>
</tbody>
</table>
### Bennet-Jones 1988

#### Methods
- Study design: parallel RCT
- Study duration/time frame: 28 days

#### Participants
- Inclusion criteria
  - Setting: Single centre
  - Country: UK
  - Health status: All patients who were to undergo the insertion of a Tenckhoff catheter prior to starting CAPD
  - Number: 27 patients randomised; IV gentamicin 13; no antibiotic 14
  - Mean age ± SD: IV gentamicin 52.7 ± 18.6 years; no antibiotic 53.1 ± 13.0 years
  - Sex (M/F): IV gentamicin 8/5; no antibiotic 9/4
  - Proportion of diabetic patients (%): 0% in either group
- Exclusion criteria
  - Receiving any antibiotic in the previous 7 days; receiving vancomycin in the previous 3 weeks; history of gentamicin toxicity; any pre-existing hearing deficit

#### Interventions
- Gentamicin (i.v.) 1.5 mg/kg at time of catheter placement versus none

#### Outcomes
- Peritonitis - number of patients; exit-site/tunnel infection - number of patients

#### Notes
- Funding source: None reported
- Follow-up period: 28 days
- Loss to follow-up: 0
- 1 (7%) excluded from analysis in control group due to catheter removal
- Exclusions post-randomisation but pre-intervention: 0
- Stop or end point/s: review after 25 patients had completed 28 day follow-up period
Chapter 4: Antimicrobial agents for preventing peritonitis in peritoneal dialysis patients

Risk of bias table

<table>
<thead>
<tr>
<th>Bias</th>
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<th>Support for judgement</th>
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<td>Random sequence generation (selection bias)</td>
<td>Low risk</td>
<td>Consecutively numbered sealed envelopes</td>
</tr>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>Low risk</td>
<td>&quot;Patients were randomised by being assigned consecutively numbered sealed envelopes, which contained either a prescription for gentamicin to be administered with the anaesthetic, or an instruction to the anaesthetist to give no antibiotic.&quot;</td>
</tr>
<tr>
<td>Blinding of participants and personnel (performance bias)</td>
<td>Low risk</td>
<td>&quot;Neither the surgeon nor physician knew whether or not the patient had received the antibiotic.&quot;</td>
</tr>
<tr>
<td>Blinding of outcome assessment (detection bias)</td>
<td>Low risk</td>
<td>&quot;Neither the surgeon nor physician knew whether or not the patient had received the antibiotic.&quot; Physician assessing outcomes did not know whether patient had received antibiotic or not.</td>
</tr>
<tr>
<td>Incomplete outcome data (attrition bias)</td>
<td>Low risk</td>
<td>Only 1/27 (3.7%) patients not included in the analysis.</td>
</tr>
<tr>
<td>Selective reporting (reporting bias)</td>
<td>High risk</td>
<td>2 of 3 primary outcomes of interest reported (exit site infection, peritonitis). No report of adverse effects of intervention.</td>
</tr>
<tr>
<td>Other bias</td>
<td>Unclear risk</td>
<td>No information provided about funding source.</td>
</tr>
</tbody>
</table>

Bernardini 1996

Methods

| Study design: parallel RCT                                                                                         |
| Study duration/time frame: August 1992 - end September 1994                                                        |

Participants

| Inclusion criteria                                                                                     |
| Setting: 2 tertiary centres                                                                              |
| Country: USA                                                                                             |
| Health status: Adult CAPD and CCPD patients - prevalent and incident; no catheter infection or peritonitis; no antibiotics for at least 2 weeks prior to the study. |
| Number: 82 patients randomised; oral rifampin 41; mupirocin ointment 41                                    |
| Mean age: NS                                                                                             |
| Sex (M/F): oral rifampin 24/17; mupirocin ointment 20/21                                                    |
| Proportion of diabetic patients (%): oral rifampin 27%; mupirocin ointment 41%                           |

Exclusion criteria

| Refusal to participate; contraindication to rifampin; patient on daily erythromycin therapy                |

Interventions

| Mupirocin ointment (2%) daily application to exit site versus rifampin (oral) 300 mg x 2/day x 5 days, every 3 months |
Chapter 4: Antimicrobial agents for preventing peritonitis in peritoneal dialysis patients

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Peritonitis - rate; peritonitis - number of patients; catheter removal/replacement; adverse effects</th>
</tr>
</thead>
</table>
| Notes | Funding source: None reported  
Follow-up period: 1 year (mean)  
Loss to follow-up: NS  
Analysis was "intention to treat"  
Exclusions post-randomisation but pre-intervention: NS  
Stop or end point/s: When patient ceased peritoneal dialysis or study ended. Additional data requested from authors: Further information on methods and more detailed results were obtained from the corresponding author. |

Risk of bias table

<table>
<thead>
<tr>
<th>Bias</th>
<th>Authors' judgement</th>
<th>Support for judgement</th>
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<td>Random sequence generation (selection bias)</td>
<td>Unclear risk</td>
<td>Study said to be randomised but no further information provided.</td>
</tr>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>Unclear risk</td>
<td>Study said to be randomised but no further information provided.</td>
</tr>
<tr>
<td>Blinding of participants and personnel (performance bias)</td>
<td>High risk</td>
<td>Blinding not possible - topical antibiotic ointment vs oral antibiotic therapy. The outcome could be influenced by lack of blinding and knowledge of the interventions.</td>
</tr>
<tr>
<td>Blinding of outcome assessment (detection bias)</td>
<td>High risk</td>
<td>&quot;Catheter infections were defined as ... and were diagnosed by the peritoneal dialysis nurse and physician, who were not blinded to the patient's treatment arm.&quot;</td>
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<tr>
<td>Incomplete outcome data (attrition bias)</td>
<td>Low risk</td>
<td>All patients included in analysis including patients who ceased therapy.</td>
</tr>
<tr>
<td>Selective reporting (reporting bias)</td>
<td>Low risk</td>
<td>All pre-specified outcomes for this review were reported</td>
</tr>
<tr>
<td>Other bias</td>
<td>Unclear risk</td>
<td>No information on funding provided</td>
</tr>
</tbody>
</table>

Bernardini 2005

| Methods | Study design: parallel RCT  
Study duration/time frame: NS |
<table>
<thead>
<tr>
<th></th>
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</thead>
<tbody>
<tr>
<td>Participants</td>
<td>Inclusion criteria</td>
</tr>
</tbody>
</table>
| Setting: 3 tertiary centres  
Country: USA  
Health status: >=18 yrs age, on PD, able to give informed consent, already enrolled in a registry permitting data collection  
Number: 133 patients; gentamicin cream 67; mupirocin cream 66  
Mean age ± SD: gentamicin 54 ± 15; mupirocin 51 ± 15 years  
Sex (M/F): gentamicin 34/33; mupirocin 38/28  
Proportion of diabetic patients (%): gentamicin 40%; mupirocin 41% |
| Exclusion criteria | Allergy to either study cream; those in another interventional study; those with catheter infections or peritonitis in the past 30 days |
Chapter 4: Antimicrobial agents for preventing peritonitis in peritoneal dialysis patients

<table>
<thead>
<tr>
<th>Interventions</th>
<th>Daily application of gentamicin cream (gentamicin sulfate 0.1%) versus mupirocin cream (mupirocin 2%) at exit site</th>
</tr>
</thead>
<tbody>
<tr>
<td>Outcomes</td>
<td>Primary = P. aeruginosa and S. aureus catheter infection rate. Secondary = Gram-negative and Gram-positive peritonitis, overall catheter infection rate, overall peritonitis rate, causative organisms, catheter removal (due to infection), time to first catheter infection.</td>
</tr>
<tr>
<td>Notes</td>
<td>Funding source: National Kidney Foundation of Western Pennsylvania, National Kidney Foundation of Upstate New York, Paul Teschan Fund of Dialysis Clinic, Inc. Follow-up period: 8 months (median)</td>
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<tr>
<td>Bias</td>
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<td>Blinding of outcome assessment (detection bias)</td>
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<tr>
<td>Incomplete outcome data (attrition bias)</td>
</tr>
<tr>
<td>Selective reporting (reporting bias)</td>
</tr>
<tr>
<td>Other bias</td>
</tr>
</tbody>
</table>

Loss to follow-up: nil
Analysis was "intention to treat"
Exclusions post-randomisation but pre-intervention: 3 in mupirocin group (did not start PD)
Stop or end point/s: stopped at 118 patient-years when a difference in peritonitis rates between the groups was found
## Chapter 4: Antimicrobial agents for preventing peritonitis in peritoneal dialysis patients

### Blowey 1994

| **Methods** | **Study design:** parallel RCT  
**Study duration/time frame:** 1991 - 1993 |
|-------------|------------------------------------------|
| **Participants** | **Inclusion criteria**  
Setting: Single centre  
Country: USA  
Health status: no evidence of a dialysis-related infection in the preceding month; no antibiotic therapy in the preceding month; duration of dialysis of at least 3 months  
Number: 34 patients; positive for nasal S. aureus - Rifampin + bacitracin 7; no treatment 8; negative for nasal S. aureus - no treatment 19  
Mean age (range): 11.5 years (8 mths-21 years)  
Sex (M/F): no details for intervention groups  
Proportion of diabetic patients: NS  
Exclusion criteria: NS |
| **Interventions** | Oral rifampin 20 mg/kg/day in 2 doses for 5 days + bacitracin (mupirocin) [nasal] 2 times/day x 7 days versus none |
| **Outcomes** | Peritonitis - number of patients; exit-site/tunnel infection - number of patients |
| **Notes** | Funding source: None reported  
Follow-up period: 1 month  
Loss to follow-up: NS  
Excluded from analysis: NS  
Exclusions post-randomisation but pre-intervention: NS  
Stop or end point/s: NS |

### Risk of bias table

<table>
<thead>
<tr>
<th><strong>Bias</strong></th>
<th><strong>Authors' judgement</strong></th>
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<td>Patients said to be randomised but no further information provided.</td>
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<tr>
<td>Blinding of participants and personnel (performance bias)</td>
<td>High risk</td>
<td>Blinding not done - oral antibiotic + topical antibiotic ointment vs no therapy. The outcome could be influenced by lack of blinding and knowledge of the interventions.</td>
</tr>
<tr>
<td>Blinding of outcome assessment (detection bias)</td>
<td>High risk</td>
<td>Clinical assessment of outcome could be influenced by knowledge of treatment group.</td>
</tr>
<tr>
<td>Incomplete outcome data (attrition bias)</td>
<td>Low risk</td>
<td>All patients completed the study</td>
</tr>
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<td>Selective reporting (reporting bias)</td>
<td>Unclear risk</td>
<td>Only 2 of 3 primary outcomes of interest for this review were reported (exit site/tunnel infection, peritonitis)</td>
</tr>
<tr>
<td>Other bias</td>
<td>Unclear risk</td>
<td>No information on funding provided</td>
</tr>
</tbody>
</table>
Chapter 4: Antimicrobial agents for preventing peritonitis in peritoneal dialysis patients

### Cheng 1999a

| Methods | Study design: parallel RCT  
Study duration/time frame: NS |
|---------|-----------------------------|
| Participants | Inclusion criteria  
Setting: Single centre  
Country: Hong Kong  
Health status: CAPD patients with infection-free exit sites  
Number: 66 patients; chlorhexidine soap 33; povidone iodine 33  
Mean age: NS  
Sex (M/F): NS  
Proportion of diabetic patients (%): NS |
| Exclusion criteria: NS |
| Interventions | Use of chlorhexidine soap vs povidone iodine at exit site (daily) |
| Outcomes | Exit site infection - rate; catheter removal - number |
| Notes | Funding source: NS  
Follow-up period: chlorhexidine soap 17.2 ± 5 months; povidone iodine 16.6 ± 6 months  
Loss to follow-up: NS |

**Risk of bias table**

<table>
<thead>
<tr>
<th>Bias</th>
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<th>Support for judgement</th>
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<td>Study said to be randomised but no information on method provided.</td>
</tr>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>Unclear risk</td>
<td>Study said to be randomised but no information on method provided.</td>
</tr>
<tr>
<td>Blinding of participants and personnel (performance bias)</td>
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<td>Blinding of outcome assessment (detection bias)</td>
<td>High risk</td>
<td>Knowledge of interventions could influence outcome assessment</td>
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<tr>
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<td>Unclear risk</td>
<td>Insufficient information to permit judgement. Abstract only available</td>
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<td>Selective reporting (reporting bias)</td>
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<td>Only 2 of 3 expected primary outcomes were reported (exit site infection, catheter removal)</td>
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<tr>
<td>Other bias</td>
<td>Unclear risk</td>
<td>No information on funding provided</td>
</tr>
</tbody>
</table>
Chapter 4: Antimicrobial agents for preventing peritonitis in peritoneal dialysis patients

Chu 2008

| Methods | Study design: quasi RCT  
Study duration/time frame: NS |
|---------|-------------------------|
| Participants | Inclusion criteria  
Setting: Single centre  
Country: Hong Kong  
Health status: Adult PD patient without any exclusion criteria  
Number: 95 patients; no details of initial randomised numbers; completed the study - gentamicin 43; mupirocin 38  
Mean age: gentamicin 57.6 years; mupirocin 61.2 years  
Sex (M/F): gentamicin 27/16; mupirocin 31/7  
Proportion of diabetic patients (%): gentamicin 41.9%; mupirocin 28.9% |
| Exclusion criteria | Active infection; ESI or peritonitis within the previous 4 weeks; allergy to either gentamicin or mupirocin; inability to apply the drug; inability to give consent. |
| Interventions | Daily application of gentamicin cream vs mupirocin ointment at the exit site |
| Outcomes | Peritonitis - number of patients; peritonitis rate; exit site/tunnel infection - number of patients; exit site/tunnel infection rate; all-cause mortality |
| Notes | Funding source: NS  
Follow-up period: NS  
Loss to follow-up: nil |

Excluded from analysis: 14 (14.7%) excluded from analysis for various reasons - do not know how many per intervention group. Exclusions post-randomisation but pre-intervention: NS  
Stop or end point/s: NS  
Additional data requested from authors: Further information on methods were obtained from the corresponding author (KH Chu).

Risk of bias table

<table>
<thead>
<tr>
<th>Bias</th>
<th>Authors' judgement</th>
<th>Support for judgement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Random sequence generation (selection bias)</td>
<td>High risk</td>
<td>Alternate allocation. &quot;The patients were assigned to either drug on a one-to-one alternate basis.&quot;</td>
</tr>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>High risk</td>
<td>Alternate allocation. &quot;The patients were assigned to either drug on a one-to-one alternate basis.&quot;</td>
</tr>
<tr>
<td>Blinding of participants and personnel (performance bias)</td>
<td>High risk</td>
<td>&quot;Patients were not informed of which cream/ointment they were using. However the cream/ointment were not covered or blinded.&quot; (email from author)</td>
</tr>
<tr>
<td>Blinding of outcome assessment (detection bias)</td>
<td>High risk</td>
<td>No blinding and knowledge of interventions could influence outcome assessment</td>
</tr>
<tr>
<td>Incomplete outcome data (attrition bias)</td>
<td>High risk</td>
<td>14/95 (15%) withdrew from the study and were excluded from analysis.</td>
</tr>
</tbody>
</table>
## Chapter 4: Antimicrobial agents for preventing peritonitis in peritoneal dialysis patients

### Selective reporting

**Selective reporting (reporting bias)**
- **Unclear risk**
  - Only 2 of 3 expected primary outcomes were reported (peritonitis, exit site/tunnel infection).

### Other bias

**Other bias**
- **Unclear risk**
  - No information on funding provided

### Churchill 1988

#### Methods

- **Study design:** parallel RCT
- **Study duration/time frame:** 12 months

#### Participants

##### Inclusion criteria
- Setting: 4 tertiary centres
- Country: Canada
- Health status: CAPD patients aged 18 to 80 years
- Number: 105 patients; trimethoprim 160 mg/sulfamethoxazole 800 mg/day 56; placebo 49
- Mean age: NS
- Sex (M/F): NS
- Proportion of diabetic patients (%): NS

##### Exclusion criteria
- Allergy to either trimethoprim or sulfamethoxazole; elective transplantation; move from study area; unlikely to survive the study period; noncompliance; active tunnel infection; no previous peritonitis in patients who had been on CAPD for 18 months or more

#### Interventions

- Trimethoprim 160 mg/sulfamethoxazole 800 mg/day x 12 months versus none

#### Outcomes

- All-cause mortality, mortality due to peritonitis, peritonitis - number of patients, transfers to hemodialysis or transplantation, withdrawals, adverse reactions, response to peritonitis treatment, peritoneal catheter loss.

#### Notes

- Funding source: Hoffman La Roche supplied the antibiotic (cotrimoxazole) and placebo tablets
- Follow-up period: 12 months
- Loss to follow-up: 20 in cotrimoxazole group (35.7%); 9 in placebo group (18.4%)
- Excluded from analysis: "Intention to treat" analysis was used.
- Exclusions post-randomisation but pre-intervention: 49 eligible patients refused to participate
- Stop or end point/s: 12 months from start of treatment
- Additional data requested from authors: Further information on methods and more detailed results were obtained from the corresponding author.

### Risk of bias table

<table>
<thead>
<tr>
<th>Bias</th>
<th>Authors' judgement</th>
<th>Support for judgement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Random sequence generation (selection bias)</td>
<td>Low risk</td>
<td>Stratified or block randomisation</td>
</tr>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>Low risk</td>
<td>Central allocation by pharmacy</td>
</tr>
</tbody>
</table>
Chapter 4: Antimicrobial agents for preventing peritonitis in peritoneal dialysis patients

Blinding of participants and personnel (performance bias) | Low risk | Blinding, and unlikely that the blinding could have been broken
Blinding of outcome assessment (detection bias) | Low risk | Blinding, and unlikely that the blinding could have been broken
Incomplete outcome data (attrition bias) | Low risk | Intention to treat analysis for primary outcome
Selective reporting (reporting bias) | High risk | 2 of 3 primary outcomes not reported (exit site/tunnel infection, catheter removal/replacement)
Other bias | High risk | Hoffman La Roche supplied the antibiotic (cotrimoxazole) and placebo tablets

Cocksedge 1993

| Methods | Study design: parallel RCT  
Study duration/time frame: 1 January 1988 to 31 December 1989 |
| Participants | Inclusion criteria |
| Setting: Single tertiary centre  
Country: Australia  
Health status: Current and new adult CAPD patients  
Number: 60 patients; shower and gauze 30; dressing pack and Fixomull 30  
Mean age: NS (most patients were >60 years)  
Sex (M/F): NS  
Proportion of diabetic patients (%): 11.7% (7/60) - do not know how many per intervention group |
| Exclusion criteria: NS |
| Interventions | Shower and gauze versus dressing pack and Fixomull dressing at exit site |
| Outcomes | Exit site infection - rate, exit site infection - number of patients |
| Notes | Funding source: NS  
Follow-up period: NS  
Loss to follow-up: NS  
Excluded from analysis: NS  
Exclusions post-randomisation but pre-intervention: NS  
Stop or end point/s: NS |

Risk of bias table

<table>
<thead>
<tr>
<th>Bias</th>
<th>Authors' judgement</th>
<th>Support for judgement</th>
</tr>
</thead>
</table>
| Random sequence generation (selection bias) | Unclear risk | Sealed envelopes. "New patients to the program were asked to select a sealed envelope from a pack. Each envelope contained a card allocating the patient to either Method One or Method Two."
| Allocation concealment (selection bias) | Unclear risk | Do not know if the envelope was opaque or not. |
| Blinding of participants and personnel (performance bias) | High risk | No blinding and the outcome is likely to be influenced by lack of blinding. |
### Danguilan 2003

#### Methods
- **Study design:** parallel RCT
- **Study duration/time frame:** NS

#### Participants
- **Inclusion criteria**
  - **Setting:** Single centre
  - **Country:** Philippines
  - **Health status:** New exit site infection-free CAPD patients
  - **Number:** 100 patients; sodium fusidate 50; mupirocin 50
  - **Mean age:** NS
  - **Sex (M/F):** NS
  - **Proportion of diabetic patients (%):** NS

- **Exclusion criteria:** NS

#### Interventions
- Sodium fusidate ointment at exit site after dressing change versus mupirocin ointment at exit site after dressing change (weekly)

#### Outcomes
- **Exit site infection - number of patients; exit site infection - rate**

#### Notes
- **Funding source:** NS
- **Follow-up period:** 1.5 years
- **Loss to follow-up:** NS
- **Excluded from analysis:** nil. Intention-to-treat analysis used.
- **Exclusions post-randomisation but pre-intervention:** NS
- **Stop or end point/s:** NS
- **Additional data requested from authors:** Further information on methods and results were obtained from the corresponding author (R Danguilan)

#### Risk of bias table

<table>
<thead>
<tr>
<th>Bias</th>
<th>Authors' judgement</th>
<th>Support for judgement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Random sequence generation (selection bias)</td>
<td>Unclear risk</td>
<td>Randomization method not stated. &quot;One hundred patients were enrolled in the study... 50 patients were randomly assigned to each treatment group.&quot;</td>
</tr>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>Unclear risk</td>
<td>No details given re concealment of patient allocation.</td>
</tr>
<tr>
<td>Blinding of participants and personnel (performance bias)</td>
<td>High risk</td>
<td>No blinding and the outcome is likely to be influenced by lack of blinding and knowledge of the interventions.</td>
</tr>
</tbody>
</table>
### Fuchs 1990

**Methods**
- Study design: parallel RCT
- Study duration/time frame: 1 October 1987 to 31 December 1988

**Participants**
- Setting: Single centre
- Country: USA
- Health status: CAPD and APD patients over 18 years of age with well-healed non-inflamed exit sites; no previous exit site infection associated with the current catheter.
- Number: 51 patients; chlorhexidine gluconate 18; sodium hypochlorite 13; povidone iodine 20
- Mean age: chlorhexidine gluconate 46 years; sodium hypochlorite 47 years; povidone iodine 55 years
- Sex (M/F): chlorhexidine gluconate 7/11; sodium hypochlorite 7/6; povidone iodine 13/7.
- Proportion of diabetic patients (%): chlorhexidine gluconate 55.6%; sodium hypochlorite 53.8%; povidone iodine 25%

**Interventions**
- Exit site cleaning with chlorhexidine gluconate and water versus sodium hypochlorite solution versus povidone-iodine solution

**Outcomes**
- Exit site infection - number of patients

**Notes**
- Funding source: NS
- Follow-up period: 15 months
- Loss to follow-up: NS
- Excluded from analysis: nil
- Exclusions post-randomisation but pre-intervention: nil
- Stop or end point/s: NS

### Risk of bias table

<table>
<thead>
<tr>
<th>Bias</th>
<th>Authors' judgement</th>
<th>Support for judgement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blinding of outcome assessment (detection bias)</td>
<td>High risk</td>
<td>No blinding and knowledge of interventions could influence outcome assessment. &quot;Exit sites were monitored weekly during regular follow up.&quot;</td>
</tr>
<tr>
<td>Incomplete outcome data (attrition bias)</td>
<td>High risk</td>
<td>Total of 22/100 dropouts from the study (22%). Proportion missing enough to have a clinically relevant effect.</td>
</tr>
<tr>
<td>Selective reporting (reporting bias)</td>
<td>Unclear risk</td>
<td>Only 2 of 3 expected primary outcomes are reported (exit site infection, peritonitis)</td>
</tr>
<tr>
<td>Other bias</td>
<td>Unclear risk</td>
<td>No report of funding source.</td>
</tr>
</tbody>
</table>
Chapter 4: Antimicrobial agents for preventing peritonitis in peritoneal dialysis patients

### Gadallah 2000

#### Methods
- Study design: parallel RCT
- Study duration/time frame: 8 years

#### Participants
- Inclusion criteria
  - Setting: Single tertiary centre
  - Country: USA
  - Health status: Patients undergoing permanent peritoneal dialysis catheter placement
  - Number: 265 patients; IV vancomycin 90; IV cefazolin 88; no antibiotic 87
  - Mean age (range): IV vancomycin 46 (15-72) years; IV cefazolin 47 (20-81) years; no antibiotic 45 (19-76) years
  - Sex (M/F): IV vancomycin 38/52; IV cefazolin 43/45; no antibiotic 38/49
  - Proportion of diabetic patients (%): IV vancomycin 35.6%; IV cefazolin 34.1%; no antibiotic 32.2%
- Exclusion criteria: NS

#### Interventions
- Vancomycin (i.v.) 1000 mg 12 h before catheter placement versus cefazolin (i.v.) 1000 mg 3 h before catheter placement versus no antibiotic treatment

#### Outcomes
- Peritonitis - number of patients; exit site/tunnel infection - number of patients (within 14 days of date of catheter insertion)

#### Notes
- Funding source: NS
- Follow-up period: 14 days
- Loss to follow-up: NS
- Excluded from analysis: Data for exit site/tunnel infection excluded from analysis (IV vancomycin 3; IV cefazolin 6; no antibiotic 8)
- Exclusions post-randomisation but pre-intervention: NS
- Stop or end point/s: NS

#### Risk of bias table

<table>
<thead>
<tr>
<th>Bias</th>
<th>Authors' judgement</th>
<th>Support for judgement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Random sequence generation (selection bias)</td>
<td>High risk</td>
<td>Consecutive allocation of intervention - &quot;first patient received vancomycin; second, cefazolin; third, neither; fourth, vancomycin; and so on.&quot;</td>
</tr>
</tbody>
</table>
### Allocation concealment (selection bias)
- **Risk:** High
- **Description:** Non-random, predictable sequence

### Blinding of participants and personnel (performance bias)
- **Risk:** High
- **Description:** No blinding and the outcome is likely to be influenced by lack of blinding and knowledge of the interventions.

### Blinding of outcome assessment (detection bias)
- **Risk:** High
- **Description:** No blinding and knowledge of interventions could influence outcome assessment.

### Incomplete outcome data (attrition bias)
- **Risk:** Low
- **Description:** No missing data re peritonitis outcome.

### Selective reporting (reporting bias)
- **Risk:** Unclear
- **Description:** 2 of 3 expected outcomes of interest are reported.

### Other bias
- **Risk:** Unclear
- **Description:** No report of funding source.

## HONEYPOT Trial 2009

### Methods
- **Study design:** parallel RCT
- **Study duration/time frame:** 17 September 2008 to 16 June 2012

### Participants
- **Setting:** 26 tertiary centres
- **Country:** Australia; New Zealand
- **Health status:** Adults and children of all ages with end-stage kidney disease who were undergoing peritoneal dialysis.
- **Number:** 371 patients; antibacterial honey 186; intranasal mupirocin 185
- **Mean age ± SD:** antibacterial honey (adult) 61.2 ± 14.5 years; intranasal mupirocin (adult) 62.1 ± 14.6 years.
- **Sex (M/F):** antibacterial honey 108/78; intranasal mupirocin 116/69.
- **Proportion of diabetic patients (%):** antibacterial honey 34%; intranasal mupirocin 28%

**Exclusion criteria:**
- Exit site infection, tunnel infection or peritonitis in the preceding month; current or recent (within the preceding 4 weeks) treatment with an antibiotic administered by any route; nasal carriage of mupirocin-resistant S. aureus; known hypersensitivity to or intolerance of honey or mupirocin; inability to provide informed consent; history of psychological illness or disorder that interfered with the ability to understand or comply with the requirements of the study.

### Interventions
- **Daily topical exit-site application of antibacterial honey (10 mg) plus standard exit site care vs intranasal application of mupirocin ointment (2% mupirocin) (only in carriers of nasal S. aureus) plus standard exit site care. Mupirocin to be applied 2 x daily for 5 days, each month.

### Outcomes
- **Primary:** time to first episode of exit-site infection, tunnel infection or peritonitis, whichever came first.
- **Secondary:** time to first exit-site infection, time to first tunnel infection, time to first peritonitis, time to infection-associated catheter removal, death, and serious adverse events.
Chapter 4: Antimicrobial agents for preventing peritonitis in peritoneal dialysis patients

Notes

Funding source: Baxter Healthcare; Queensland government; Comvita; Gambro
Follow-up period: minimum of 12 months; maximum of 24 months.
Loss to follow-up: 1 in honey group (0.5%); 3 in mupirocin group (1.6%)
Excluded from analysis: nil
Exclusions post-randomisation but pre-intervention: nil
Stop or end point/s: Once 185 individuals per group had been followed up for at least 12 months.
Additional data requested from authors: Further information about results were obtained from the biostatistician (E Pascoe).

Risk of bias table

<table>
<thead>
<tr>
<th>Bias</th>
<th>Authors' judgement</th>
<th>Support for judgement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Random sequence generation (selection bias)</td>
<td>Low risk</td>
<td>Minimization method. &quot;Participants were randomly assigned in a 1:1 ratio by use of an adaptive allocation algorithm designed to minimise imbalance in treatment groups for the three variables.&quot;</td>
</tr>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>Low risk</td>
<td>Central allocation (web). &quot;To ensure adequate concealment of allocation, the randomisation was done with a password-protected internet-based system.&quot;</td>
</tr>
<tr>
<td>Blinding of participants and personnel (performance bias)</td>
<td>High risk</td>
<td>No blinding and the outcome is likely to be influenced by lack of blinding and knowledge of the interventions. &quot;Blinding of investigators and patients is not possible because of the completely different characteristics of Medihoney and mupirocin ointment.&quot;</td>
</tr>
<tr>
<td>Blinding of outcome assessment (detection bias)</td>
<td>High risk</td>
<td>No blinding and knowledge of the interventions could influence outcome assessment. &quot;The trial was open label, but microbiology staff at the local laboratories were not informed of the treatment allocation.&quot;</td>
</tr>
<tr>
<td>Incomplete outcome data (attrition bias)</td>
<td>High risk</td>
<td>Missing data not balanced between groups. 17/185 (9.2%) withdrew from control group; 54/186 (29%) withdrew from honey group.</td>
</tr>
<tr>
<td>Selective reporting (reporting bias)</td>
<td>Low risk</td>
<td>3 of 3 expected primary outcomes are reported.</td>
</tr>
<tr>
<td>Other bias</td>
<td>Unclear risk</td>
<td>The study appears to be free of other sources of risk. Although 3 of 4 funders are pharmaceutical companies, there is an explicit statement about their role on page 26 of the paper.</td>
</tr>
</tbody>
</table>

Lo 1996

Methods

Study design: parallel RCT
Study duration/time frame: 1 May 1991 to 30 April 1993
Chapter 4: Antimicrobial agents for preventing peritonitis in peritoneal dialysis patients

### Participants

<table>
<thead>
<tr>
<th>Inclusion criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Setting: 2 tertiary centres</td>
</tr>
<tr>
<td>Country: Hong Kong</td>
</tr>
<tr>
<td>Health status: All patients receiving CAPD</td>
</tr>
<tr>
<td>Number: 397 patients; oral nystatin 199; control 198</td>
</tr>
<tr>
<td>Mean age ± SD: 48.4 ± 14.5 years; control 48.5 ± 14.2 years</td>
</tr>
<tr>
<td>Sex (M/F): Oral nystatin 86/113; control 98/100</td>
</tr>
<tr>
<td>Proportion of diabetic patients (%): Oral nystatin 18.6%; control 15.2%</td>
</tr>
</tbody>
</table>

Exclusion criteria: NS

### Interventions

Nystatin 500,000 units x 4/day (whenever antibiotics were prescribed to patient) versus none

### Outcomes

Peritonitis - number of patients, peritonitis - rate (due to Candida spp.)

### Notes

Trial focusing on prophylaxis to prevent Candida peritonitis in CAPD patients receiving antibiotics for any indication

Funding source: NS

Follow-up period (mean ± SD): Oral nystatin 18.0 ± 7.6 months; control 16.6 ± 8.5 months

Loss to follow-up: NS

Excluded from analysis: NS

Exclusions post-randomisation but pre-intervention: NS

Stop or end point/s: NS

### Risk of bias table

<table>
<thead>
<tr>
<th>Bias</th>
<th>Authors' judgement</th>
<th>Support for judgement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Random sequence generation (selection bias)</td>
<td>High risk</td>
<td>Patients were randomised according to odd or even identity numbers.</td>
</tr>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>High risk</td>
<td>A non-random, predictable sequence was used.</td>
</tr>
<tr>
<td>Blinding of participants and personnel (performance bias)</td>
<td>High risk</td>
<td>No blinding and the outcome is likely to be influenced by lack of blinding and knowledge of the interventions.</td>
</tr>
<tr>
<td>Blinding of outcome assessment (detection bias)</td>
<td>High risk</td>
<td>No blinding and knowledge of the interventions could influence outcome assessment.</td>
</tr>
<tr>
<td>Incomplete outcome data (attrition bias)</td>
<td>Low risk</td>
<td>Intention to treat analysis for primary outcome.</td>
</tr>
<tr>
<td>Selective reporting (reporting bias)</td>
<td>Low risk</td>
<td>The expected primary outcome is reported.</td>
</tr>
<tr>
<td>Other bias</td>
<td>Unclear risk</td>
<td>No report of funding source.</td>
</tr>
</tbody>
</table>
**Low 1980**

| **Methods** | Study design: parallel RCT  
Study duration/time frame: April to September 1979 |
|-------------|--------------------------------------------------|
| **Participants** | Inclusion criteria  
Setting: 2 tertiary centres  
Country: Canada  
Health status: Patients receiving CAPD  
Number: 50 patients; oral cefalexin 25; placebo 25  
Mean age: NS  
Sex (M/F): NS  
Proportion of diabetic patients: NS  
Exclusion criteria: NS |
| **Interventions** | Cefalexin 500 mg x 2/day versus none |
| **Outcomes** | Peritonitis - number of patients; peritonitis - rate; catheter removal/replacement - number of patients |
| **Notes** | Funding source: National Institutes of Health  
Follow-up period: NS  
Loss to follow-up: NS  
Excluded from analysis: NS  
Exclusions post-randomisation but pre-intervention: NS  
Stop or end point/s: NS |

### Risk of bias table

<table>
<thead>
<tr>
<th>Bias</th>
<th>Authors' judgement</th>
<th>Support for judgement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Random sequence generation (selection bias)</td>
<td>Low risk</td>
<td>Minimisation method used.</td>
</tr>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>Low risk</td>
<td>Allocation done by a third party</td>
</tr>
<tr>
<td>Blinding of participants and personnel (performance bias)</td>
<td>Low risk</td>
<td>Blinding, and unlikely that the blinding could have been broken.</td>
</tr>
<tr>
<td>Blinding of outcome assessment (detection bias)</td>
<td>Low risk</td>
<td>Blinding, and unlikely that the blinding could have been broken.</td>
</tr>
<tr>
<td>Incomplete outcome data (attrition bias)</td>
<td>Low risk</td>
<td>No missing data.</td>
</tr>
<tr>
<td>Selective reporting (reporting bias)</td>
<td>Unclear risk</td>
<td>1 of 3 primary outcomes not reported (exit site/tunnel infection).</td>
</tr>
<tr>
<td>Other bias</td>
<td>Low risk</td>
<td>Study appears to be free of other sources of risk.</td>
</tr>
</tbody>
</table>

Funding was from a National Institutes of Health contract.
## Chapter 4: Antimicrobial agents for preventing peritonitis in peritoneal dialysis patients

### Luzar 1990

| Methods | Study design: parallel RCT  
Study duration/time frame: May 1987 to September 1988 |
|---------|------------------------------------------------------|
| Participants | Inclusion criteria  
Setting: 8 tertiary centres  
Country: UK, France, Belgium  
Health status: New and current CAPD patients  
Number: 127 patients; povidone iodine 74; control 53  
Mean age: NS  
Sex (M/F): Povidone iodine 47/27; control 31/22  
Proportion of diabetic patients (%): Povidone iodine 17%; control 11% |
| Exclusion criteria: Patients with any current infection. |
| Interventions | Povidone iodine (20 g/L) and nonocclusive dressing 2-3 times/week versus none (nondisinfectant soap and water) |
| Outcomes | All-cause mortality, peritonitis - rate, exit-site/tunnel infection - rate |
| Notes | Funding source: NS but lead author employed by Baxter R & D Europe, Belgium  
Follow-up period: 9.03 months per patient  
Loss to follow-up: 8 of 127 (6.3%)  
Excluded from analysis: NS  
Exclusions post-randomisation but pre-intervention: 9 patients randomised to control group refused to do that type of exit site care  
Stop or end point/s: 1 year of follow-up per patient or until a significant difference in rate of exit-site infection.  
Four patients in Group 2 (soap and water) changed to Group 1 (povidone iodine and dressing). |

### Risk of bias table

<table>
<thead>
<tr>
<th>Bias</th>
<th>Authors' judgement</th>
<th>Support for judgement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Random sequence generation (selection bias)</td>
<td>Low risk</td>
<td>Random number table</td>
</tr>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>Low risk</td>
<td>Central allocation</td>
</tr>
<tr>
<td>Blinding of participants and personnel (performance bias)</td>
<td>High risk</td>
<td>No blinding and the outcome is likely to be influenced by lack of blinding and knowledge of the interventions.</td>
</tr>
<tr>
<td>Blinding of outcome assessment (detection bias)</td>
<td>High risk</td>
<td>No blinding and knowledge of interventions could influence outcome assessment.</td>
</tr>
<tr>
<td>Incomplete outcome data (attrition bias)</td>
<td>Low risk</td>
<td>Proportion missing not enough to have a clinically relevant effect</td>
</tr>
<tr>
<td>Selective reporting (reporting bias)</td>
<td>Low risk</td>
<td>3 of 3 primary outcomes of interest are reported</td>
</tr>
<tr>
<td>Other bias</td>
<td>High risk</td>
<td>Funding source not specified but seems to be Baxter Healthcare Corporation</td>
</tr>
</tbody>
</table>
Lye 1992

| Methods | Study design: parallel RCT  
Study duration/time frame: 1 May 1989 to 31 May 1990 |
|---------|--------------------------------------------------|
| Participants | Inclusion criteria  
Setting: Single tertiary centre  
Country: Singapore  
Health status: Patients having CAPD catheters inserted  
Number: 66 patients; cefazolin + gentamicin 33; control 33  
Mean age ± SD: Cefazolin + gentamicin 56.2 ± 12.3 years; control 55.6 ± 13.4 years  
Sex (M/F): Cefazolin + gentamicin 12/21; control 18/15  
Proportion of diabetic patients (%): Cefazolin + gentamicin 68%; control 52%  
Exclusion criteria:  
Recognised infection at the time of surgery; antibiotic therapy in the week prior to surgery; vancomycin therapy in the 2 weeks before surgery; history of allergy to beta-lactam antibiotics and aminoglycosides |
| Interventions | Cefazolin (i.v.) 500 mg and gentamicin (i.v.) 80 mg 0.5-1.0 hour before catheter placement versus none |
| Outcomes | All-cause mortality, peritonitis - number of patients, exit-site/tunnel infection - number of patients (within 4 weeks of catheter insertion) |
| Notes | Funding source: NS  
Follow-up period: NS  
Loss to follow-up: NS  
4 (16%) excluded from analysis in cefazolin + gentamicin group due to lack of effect of study antibiotics on MRSA bacteria; 3 (12%) excluded from analysis in control group for the same reason  
Exclusions post-randomisation but pre-intervention: NS  
Stop or end point/s: NS |

Risk of bias table

<table>
<thead>
<tr>
<th>Bias</th>
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<th>Support for judgement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Random sequence generation (selection bias)</td>
<td>High risk</td>
<td>Alternate allocation</td>
</tr>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>High risk</td>
<td>Non-random, predictable sequence</td>
</tr>
<tr>
<td>Blinding of participants and personnel (performance bias)</td>
<td>High risk</td>
<td>No blinding and the outcome is likely to be influenced by lack of blinding and knowledge of the interventions.</td>
</tr>
<tr>
<td>Blinding of outcome assessment (detection bias)</td>
<td>High risk</td>
<td>No blinding and knowledge of interventions could influence outcome assessment.</td>
</tr>
<tr>
<td>Incomplete outcome data (attrition bias)</td>
<td>Low risk</td>
<td>Missing data balanced across groups, and reasons similar</td>
</tr>
</tbody>
</table>
Chapter 4: Antimicrobial agents for preventing peritonitis in peritoneal dialysis patients

| Selective reporting (reporting bias) | Low risk | 3 of 3 primary outcomes of interest are reported |
| Other bias | Unclear risk | No report of funding source |

### Mendoza-Guevara 2007

#### Methods
- Study design: parallel RCT
- Study duration/time frame: 22 January 2004 to 15 March 2005

#### Participants
- **Inclusion criteria**
  - Setting: Single centre
  - Country: Mexico
  - Health status: Cyclic continuous PD patients that had been at least 3 months on the PD program and free of peritonitis or exit-site infection for at least 1 month since the last episode.
  - Number: 60 patients (paediatric); Amuchina 10% 30; pH neutral soap 30
  - Median age (Q25-75): Amuchina 10% 12 (10-14) years; pH neutral soap 12 (8.75-14.25) years
  - Sex (M/F): Amuchina 10% 19/11; pH neutral soap 11/19
  - Proportion of diabetic patients (%): NA

- **Exclusion criteria:**
  - Patients on steroids; patients with cancer; HIV positive patients

#### Interventions
- Use of Amuchina 10% (sodium hypochlorite) solution versus pH neutral soap for cleaning of exit site

#### Outcomes
- Exit site infection - number of patients

#### Notes
- Funding source: NS
- Follow-up period: NS
- Loss to follow-up: NS
- Excluded from analysis: NS
- Exclusions post-randomisation but pre-intervention: NS
- Stop or end point/s: NS

### Risk of bias table

<table>
<thead>
<tr>
<th>Bias</th>
<th>Authors' judgement</th>
<th>Support for judgement</th>
</tr>
</thead>
</table>
| Random sequence generation (selection bias) | Low risk           | Random number tables. "Patients were assigned 1:1 in two groups, with only one treatment; the Rand Corporation tables were used for randomization."
| Allocation concealment (selection bias)   | Unclear risk       | No details of allocation method given                                                 |
| Blinding of participants and personnel (performance bias) | Unclear risk | Patient cleans own exit site - impossible to conceal intervention allocation. "The study was blind for the investigators and laboratory personnel." |
| Blinding of outcome assessment (detection bias) | Low risk           | Blinding, and unlikely that the blinding could have been broken. "The study was blind for the investigators and laboratory personnel." |
Chapter 4: Antimicrobial agents for preventing peritonitis in peritoneal dialysis patients

Moore 1989

Methods
- Study design: parallel quasi RCT
- Study duration/time frame: 1 October 1987 to 1 February 1988

Participants
- Inclusion criteria:
  - Setting: Single centre
  - Country: USA
  - Health status: Current CAPD patient (adult)
  - Number: 29 patients; Blisterfilm 15; gauze 14
  - Mean age (range): Blisterfilm 54 (30-75) years; gauze 59 (28-72) years
  - Sex (M/F): NS
  - Proportion of diabetic patients (%): NS

- Exclusion criteria:
  - Patients with a history of exit-site infection 2 months prior to possible study admission

Interventions
- Blisterfilm adhesive dressing versus gauze dressing at exit site

Outcomes
- Exit site infection - number of patients

Notes
- Funding source: NS
- Follow-up period: 4 months.
- Loss to follow-up: NS
- Excluded from analysis: NS
- Exclusions post-randomisation but pre-intervention: NS
- Stop or end point/s: NS

Risk of bias table

<table>
<thead>
<tr>
<th>Bias</th>
<th>Authors' judgement</th>
<th>Support for judgement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Random sequence generation (selection bias)</td>
<td>High risk</td>
<td>Alternate allocation. &quot;The numbering was consecutive so all participants were given an equal chance of being admitted to either group.&quot; &quot;Odd numbers were admitted to the Blisterfilm group and even numbers admitted to the gauze group.&quot;</td>
</tr>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>High risk</td>
<td>Non-random, predictable sequence. However, allocation concealment not possible - the two dressings are of different sizes and types.</td>
</tr>
<tr>
<td>Blinding of participants and personnel (performance bias)</td>
<td>High risk</td>
<td>No blinding and the outcome is likely to be influenced by lack of blinding and knowledge of interventions.</td>
</tr>
</tbody>
</table>
Blinding of outcome assessment (detection bias) | High risk | No blinding and knowledge of the interventions could influence outcome assessment.
---|---|---
Incomplete outcome data (attrition bias) | Unclear risk | The published report states percentage of patients in each group that experienced exit-site infection but does not state actual patient numbers. No report of loss to follow-up, withdrawals etc.
Selective reporting (reporting bias) | High risk | Only 1 of 3 expected primary outcomes of interest reported (exit-site infection)
Other bias | Unclear risk | No report of funding source

**MP3 Study 2008**

**Methods**
Study design: parallel RCT
Study duration/time frame: NS

**Participants**
Inclusion criteria

- Setting: 3 tertiary centres
- Country: Canada
- Health status: Current or new PD patients; aged 18 years or more; have a PD catheter in situ; are medically stable.
- Number: 204 patients (adults); P3 ointment 103; mupirocin ointment 101
- Mean age ± SD: P3 ointment 59.36 ± 15.04 years; mupirocin ointment 61.02 ± 13.66 years
- Sex (M/F): P3 ointment 63/37; mupirocin ointment 66/34
- Proportion of diabetic patients (%): P3 ointment 45.5%; mupirocin ointment 42%

Exclusion criteria:

- Patients with acute renal failure; catheter-related infection at the time of recruitment or within the previous 3 months; use of an oral, intravenous or intraperitoneal antibiotic at the time of randomisation or within the previous 1 week; a known allergy to any component of P3 or mupirocin; or a scheduled date for living donor transplant surgery within 6 months of the study completion date.

**Interventions**
Application of Polysporin Triple (P3) antibiotic ointment (bacitracin 500 U/g, gramicidin 0.25 mg/g, polymyxin B 10 000 U/g) at exit site when dressing is changed versus mupirocin ointment

**Outcomes**
Primary = Time to first catheter-related infection (ESI, tunnel infection, PD peritonitis). Secondary = catheter removal (catheter-related infection); hospitalization (catheter-related infection); death due to catheter-related infection; all-cause mortality; technique failure (i.e. transfer to HD)

**Notes**
Funding source: Kidney Foundation of Canada
Follow-up period: Median (range): 18 (0.1-18) months
Loss to follow-up: 2 from each group
Excluded from analysis: Data for 3 patients from 1 site were excluded
Exclusions post-randomisation but pre-intervention: nil
Stop or end point/s: NS
Chapter 4: Antimicrobial agents for preventing peritonitis in peritoneal dialysis patients

Risk of bias table

<table>
<thead>
<tr>
<th>Bias</th>
<th>Authors' judgement</th>
<th>Support for judgement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Random sequence generation (selection bias)</td>
<td>Low risk</td>
<td>Computer random number generator. &quot;All randomization is determined by a computer-generated random number list...&quot; &quot;...201 patients from two centers were randomly assigned to either mupirocin or P3 using stratified block randomization as per protocol.&quot;</td>
</tr>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>Low risk</td>
<td>Central allocation (pharmacy). &quot;Randomization occurs centrally in coordination with the central clinical trials pharmacy... The ointments are placed in containers that are labeled only with the site investigator, study number, and expiry date.&quot;</td>
</tr>
<tr>
<td>Blinding of participants and personnel (performance bias)</td>
<td>Low risk</td>
<td>Blinding, and unlikely that the blinding could have been broken. &quot;The treatments resemble each other in odor, color, and consistency to allow for a double blinded controlled trial.&quot; &quot;Neither the healthcare workers not the participants know which intervention the participant will receive.&quot;</td>
</tr>
<tr>
<td>Blinding of outcome assessment (detection bias)</td>
<td>Low risk</td>
<td>Blinding, and unlikely that the blinding could have been broken.</td>
</tr>
<tr>
<td>Incomplete outcome data (attrition bias)</td>
<td>Low risk</td>
<td>Missing data balanced across groups, and reasons similar.</td>
</tr>
<tr>
<td>Selective reporting (reporting bias)</td>
<td>Low risk</td>
<td>Protocol is available and all pre-specified outcomes of interest to the review are reported in the pre-specified way.</td>
</tr>
<tr>
<td>Other bias</td>
<td>Low risk</td>
<td>Funded by the Kidney Foundation of Canada. Study appears to be free of other sources of risk.</td>
</tr>
</tbody>
</table>

Mupirocin SG
1996

Methods
- Study design: parallel RCT
- Study duration/time frame: up to 18 months

Participants
- Inclusion criteria:
  - Setting: 9 centres
  - Country: Europe
  - Health status: Patients undergoing CAPD who were identified as S. aureus nasal carriers
  - Number: 267 patients; mupirocin ointment 134; placebo ointment 133
  - Mean age: Mupirocin ointment 60.3 years; placebo ointment 60.3 years
  - Sex (M/F): Mupirocin ointment 81/53; placebo ointment 80/53
  - Proportion of diabetic patients (%): Mupirocin ointment 17.2%; placebo ointment 22.6%
- Exclusion criteria:
  - Patient negative for S. aureus nasal carriage; patient who had received antibiotics for a PD-related infection within the preceding month; patient with active exit site infection.

Interventions
- Mupirocin (2%) nasal ointment 2/day x 5 days, every 1 month versus
### Risk of bias table

<table>
<thead>
<tr>
<th>Bias</th>
<th>Authors' judgement</th>
<th>Support for judgement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Random sequence generation (selection bias)</td>
<td>Unclear risk</td>
<td>No details given re randomisation method used.</td>
</tr>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>Unclear risk</td>
<td>Not stated.</td>
</tr>
<tr>
<td>Blinding of participants and personnel (performance bias)</td>
<td>Unclear risk</td>
<td>Blinding, and unlikely that patients were aware of treatment group. Unclear if personnel were aware of patient treatment groups.</td>
</tr>
<tr>
<td>Blinding of outcome assessment (detection bias)</td>
<td>Unclear risk</td>
<td>No details given re who did the outcome assessment and if they were blind to patient treatment group.</td>
</tr>
<tr>
<td>Incomplete outcome data (attrition bias)</td>
<td>Low risk</td>
<td>Missing data balanced across groups, and reasons similar</td>
</tr>
<tr>
<td>Selective reporting (reporting bias)</td>
<td>Low risk</td>
<td>3 of 3 expected primary outcomes of interest are reported</td>
</tr>
<tr>
<td>Other bias</td>
<td>High risk</td>
<td>Funding source: SmithKline Beecham, UK, and Baxter Healthcare, USA</td>
</tr>
</tbody>
</table>

### Nolph 1985

#### Methods
- Study design: parallel RCT
- Study duration/time frame: 9 months

#### Participants
- Inclusion criteria
  - Setting: 10 tertiary centres
  - Country: USA
  - Health status: Patients with end stage renal disease being treated with CAPD.
  - Number: 167 patients; test group 74; control 93
  - Mean age ± SD: Test group 49 ± 14 years; control 49 ± 14 years
  - Sex (M/F): Test group 50/24; control 49/44.
  - Proportion of diabetic patients (%): Test group 16.2%; control 23.7%

- Exclusion criteria: NS

#### Interventions
- Ultraviolet germicidal chamber for spike and bag outlet port versus none

#### Outcomes
- All-cause mortality, peritonitis - number of patients, peritonitis - rate

#### Notes
- Funding source: Travenol Laboratories Inc., USA
### Risk of bias table

<table>
<thead>
<tr>
<th>Bias</th>
<th>Authors' judgement</th>
<th>Support for judgement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Random sequence generation (selection bias)</td>
<td>Low risk</td>
<td>Random number table.</td>
</tr>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>Low risk</td>
<td>Central allocation (Travenol Laboratories).</td>
</tr>
<tr>
<td>Blinding of participants and personnel (performance bias)</td>
<td>High risk</td>
<td>No blinding and the outcome is likely to be influenced by lack of blinding and knowledge of the interventions.</td>
</tr>
<tr>
<td>Blinding of outcome assessment (detection bias)</td>
<td>High risk</td>
<td>No blinding and knowledge of the interventions could influence outcome assessment.</td>
</tr>
<tr>
<td>Incomplete outcome data (attrition bias)</td>
<td>High risk</td>
<td>12.9% withdrew from control group; 24.3% withdrew from intervention group. Proportion missing enough to have a clinically relevant effect.</td>
</tr>
<tr>
<td>Selective reporting (reporting bias)</td>
<td>High risk</td>
<td>Only 1 of 3 primary expected outcomes of interest is reported (peritonitis).</td>
</tr>
<tr>
<td>Other bias</td>
<td>High risk</td>
<td>Funding source: Travenol Laboratories Inc., USA.</td>
</tr>
</tbody>
</table>

### Nunez-Moral 2014

**Methods**
- Study design: parallel RCT
- Study duration/time frame: 12 months

**Participants**
- Inclusion criteria
  - Setting: Single tertiary centre
  - Country: Spain
  - Health status: patients older than 18 years in PD program in which a peritoneal catheter had been implanted at least 6 weeks before; absence of infectious complications which had required either hospital admission or antibiotic treatment at least three months before entering the study; absence of known reaction or contingent polyhexanide intolerance; the patient or representatives had signed the informed consent form.
  - Number: 60 patients; polyhexanide solution 30; control 30
  - Mean age ± SD: Polyhexanide group 61 ± 15 years; control 60 ± 19 years
  - Sex (M/F): Polyhexanide group 17/13; control 16/14
  - Proportion of diabetic patients (%): Polyhexanide group 41%; control 40%
- Exclusion criteria: Presence of exit-site infection at randomization time; history of bad adherence to treatment and/or medical advice; withdrawal of the informed consent.

**Interventions**
- Use of polyhexanide solution at exit site versus standard care (0.9% saline)
### Chapter 4: Antimicrobial agents for preventing peritonitis in peritoneal dialysis patients

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>All-cause mortality; exit site/tunnel infection - number of patients; exit site/tunnel infection - rate; catheter removal or replacement (due to infection)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Notes</td>
<td>Funding source: Nephrological Nursing Investigation Baxter award 2010 Follow up period: 12 months Loss to follow up: nil Excluded from analysis: nil Exclusions post-randomisation but pre-intervention: nil Stop or end point/s: NS Additional data requested from authors: Further information on peritonitis data were requested from the corresponding author.</td>
</tr>
</tbody>
</table>

#### Risk of bias table

<table>
<thead>
<tr>
<th>Bias</th>
<th>Authors' judgement</th>
<th>Support for judgement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Random sequence generation</td>
<td>Low risk</td>
<td>Random number table. &quot;Randomization was performed by means of a randomization code via random number table...&quot;</td>
</tr>
<tr>
<td>Allocation concealment</td>
<td>Unclear risk</td>
<td>Randomisation stated but no information on method used is available.</td>
</tr>
<tr>
<td>Blinding of participants and personnel</td>
<td>Unclear risk</td>
<td>Insufficient information to permit judgement</td>
</tr>
<tr>
<td>Blinding of outcome assessment</td>
<td>Unclear risk</td>
<td>Insufficient information to permit judgement</td>
</tr>
<tr>
<td>Incomplete outcome data</td>
<td>Low risk</td>
<td>No missing outcome data</td>
</tr>
<tr>
<td>Selective reporting</td>
<td>Unclear risk</td>
<td>Only 2 of 3 expected primary outcomes of interest reported fully.</td>
</tr>
<tr>
<td>Other bias</td>
<td>Unclear risk</td>
<td>Disclosure states that &quot;Part of these data belong to Baxter S. L. funds as we received the Nephrological Nursing Investigation Baxter award 2010&quot;.</td>
</tr>
</tbody>
</table>

#### Perez-Fontan 1992

<table>
<thead>
<tr>
<th>Methods</th>
<th>Study design: parallel RCT Study duration/time frame: 3 - 15 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Participants</td>
<td>Inclusion criteria</td>
</tr>
<tr>
<td>Setting: Single centre Country: Spain Health status: Patients undergoing CAPD and their assisting partners Number: 22 patients, 3 partners; mupirocin 12 patients, 1 partner; neomycin 10 patients, 2 partners Mean age ± SD: Mupirocin 51 ± 15 years; neomycin 48 ± 21 years Sex (M/F): Mupirocin 5/7; neomycin 5/5 Proportion of diabetic patients (%): Mupirocin 25%; neomycin 20%</td>
<td></td>
</tr>
</tbody>
</table>
### Exclusion criteria
NS

### Interventions
- **Mupirocin (2%) nasal ointment t.i.d. x 7 days versus neomycin sulphate (0.1%) nasal ointment t.i.d. x 7 days**

### Outcomes
- Peritonitis - number of patients, peritonitis - rate, exit-site/tunnel infection - number of patients, exit site/tunnel infection - rate

### Notes
- Funding source: None reported
- Follow up period: 9.5 ± 3.3 months
- Loss to follow up: NS
- Excluded from analysis: NS
- Exclusions post-randomisation but pre-intervention: NS
- Stop or end point/s: NS

#### Risk of bias table

<table>
<thead>
<tr>
<th>Bias</th>
<th>Authors' judgement</th>
<th>Support for judgement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Random sequence generation (selection bias)</td>
<td>Low risk</td>
<td>Stratified randomization method used. &quot;Staph. aureus nasal carriers were assigned to one of two groups, randomized for age, time on CAPD and prevalence of diabetes.&quot;</td>
</tr>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>Unclear risk</td>
<td>No details given.</td>
</tr>
<tr>
<td>Blinding of participants and personnel (performance bias)</td>
<td>Unclear risk</td>
<td>Insufficient information to permit judgement.</td>
</tr>
<tr>
<td>Blinding of outcome assessment (detection bias)</td>
<td>Unclear risk</td>
<td>Insufficient information to permit judgement.</td>
</tr>
<tr>
<td>Incomplete outcome data (attrition bias)</td>
<td>Low risk</td>
<td>Reasons for missing data not related to outcome. &quot;Patients of Group 2 in whom eradication was not obtained after two neomycin cycles were treated with mupirocin.&quot;</td>
</tr>
<tr>
<td>Selective reporting (reporting bias)</td>
<td>Unclear risk</td>
<td>2 of 3 expected primary outcomes of interest are reported.</td>
</tr>
<tr>
<td>Other bias</td>
<td>Unclear risk</td>
<td>No report of funding source.</td>
</tr>
</tbody>
</table>

### Poole-Warren 1991

#### Methods
- Study design: parallel RCT
- Study duration/time frame: 12 months

#### Participants
- **Inclusion criteria**
  - Setting: 8 tertiary centres
  - Country: Australia and New Zealand
  - Health status: Current CAPD patients stabilised on the therapy
  - Number: 124 patients; Staphypan Berna 65; saline placebo 59
  - Mean age ± SD: Staphypan Berna 54 ± 11 years; saline placebo 52 ± 14 years
  - Sex (M/F): Staphypan Berna 1/5; saline placebo 0/7
  - Proportion of diabetic patients (%): Staphypan Berna 18.5%; saline placebo 15.3%
<table>
<thead>
<tr>
<th>Exclusion criteria:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Current peritoneal infection; receipt of an antibiotic course within the 2 week period prior to study enrolment; use of assist devices; use of disconnect systems.</td>
</tr>
</tbody>
</table>

### Interventions

Staphypan Berna vaccine versus saline placebo

### Outcomes

Peritonitis - number of patients, peritonitis - rate, exit-site/tunnel infection - number of patients, exit-site/tunnel infection - rate

### Notes

- Funding source: Baxter Healthcare Corporation, USA
- Follow-up period: 12 months
- Loss to follow-up: NS
- Excluded from analysis: NS
- Exclusions post-randomisation but pre-intervention: NS
- Stop or end point/s: 43 patient years per treatment group

### Risk of bias table

<table>
<thead>
<tr>
<th>Bias</th>
<th>Authors' judgement</th>
<th>Support for judgement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Random sequence generation (selection bias)</td>
<td>Unclear risk</td>
<td>Randomization method not stated. &quot;Patients were randomly assigned by an independent third party to either the vaccinated group or the saline solution (SS) placebo administered group.&quot;</td>
</tr>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>Low risk</td>
<td>Central allocation (independent third party). &quot;The assigned injection group was not known to either patient or staff immediately connected with the patient's care at any time during the study.&quot;</td>
</tr>
<tr>
<td>Blinding of participants and personnel (performance bias)</td>
<td>Low risk</td>
<td>Blinding, and unlikely that the blinding could have been broken.</td>
</tr>
<tr>
<td>Blinding of outcome assessment (detection bias)</td>
<td>Low risk</td>
<td>Blinding, and unlikely that the blinding could have been broken.</td>
</tr>
<tr>
<td>Incomplete outcome data (attrition bias)</td>
<td>Low risk</td>
<td>Missing data balanced across groups, and reasons similar.</td>
</tr>
<tr>
<td>Selective reporting (reporting bias)</td>
<td>Low risk</td>
<td>3 of 3 expected primary outcomes of interest are reported.</td>
</tr>
<tr>
<td>Other bias</td>
<td>High risk</td>
<td>Funding source: Baxter Healthcare Corporation, USA</td>
</tr>
</tbody>
</table>

### Restrepo 2010

#### Methods

- Study design: parallel RCT
- Study duration/time frame: 1 June 2004 to 30 October 2007

#### Participants

- Inclusion criteria
  - Setting: Single centre
  - Country: Colombia
  - Health status: Chronic kidney disease patients stage 5 on PD (CAPD or APD) were included if they experienced peritonitis, exit-site infection or
Chapter 4: Antimicrobial agents for preventing peritonitis in peritoneal dialysis patients

tunnel infection.
Number: 340 patients; 226 patients with peritonitis; 114 patients with ESI or TI
Mean age: 50.9 years (men); 47.9 years (women); unable to calculate mean age per intervention group
Sex (M/F): Oral fluconazole 93/117; no oral fluconazole 116/94
Proportion of diabetic patients (%): Oral fluconazole 33.3%; no oral fluconazole 37.1%

Exclusion criteria:
Allergy to fluconazole, imidazoles, or triazoles; hepatic disease; pregnancy; less than 18 years of age; more than 70 years of age; patients that did not wish to participate

<table>
<thead>
<tr>
<th>Interventions</th>
<th>Oral fluconazole (200 mg every 48 hours) vs no oral fluconazole with an antibiotic course for a PD-related infection</th>
</tr>
</thead>
<tbody>
<tr>
<td>Outcomes</td>
<td>Fungal peritonitis in the time period 30-150 days following the end of antibacterial treatment</td>
</tr>
<tr>
<td>Notes</td>
<td>Funding source: None reported Follow-up period: 30-150 days after the end of treatment Loss to follow-up: NS Excluded from analysis: NS Exclusions post-randomisation but pre-intervention: NS Stop or end point/s: When 434 episodes of peritonitis had occurred</td>
</tr>
</tbody>
</table>

**Risk of bias table**

<table>
<thead>
<tr>
<th>Bias</th>
<th>Authors' judgement</th>
<th>Support for judgement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Random sequence generation (selection bias)</td>
<td>Low risk</td>
<td>Drawing of lots. &quot;The randomization procedure was performed by drawing from a bag cards indicating whether the patient would or would not receive this treatment.&quot;</td>
</tr>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>Unclear risk</td>
<td>No details of allocation method stated.</td>
</tr>
<tr>
<td>Blinding of participants and personnel (performance bias)</td>
<td>Unclear risk</td>
<td>Insufficient information to permit judgement.</td>
</tr>
<tr>
<td>Blinding of outcome assessment (detection bias)</td>
<td>Unclear risk</td>
<td>Insufficient information to permit judgement.</td>
</tr>
<tr>
<td>Incomplete outcome data (attrition bias)</td>
<td>Unclear risk</td>
<td>No details of missing data given.</td>
</tr>
<tr>
<td>Selective reporting (reporting bias)</td>
<td>Unclear risk</td>
<td>The expected primary outcome is reported. However, adverse effects of antifungal use are not reported.</td>
</tr>
<tr>
<td>Other bias</td>
<td>Unclear risk</td>
<td>No report of funding source.</td>
</tr>
</tbody>
</table>

**Ryckelynck 1987**

| Methods | Study design: parallel quasi RCT |
Chapter 4: Antimicrobial agents for preventing peritonitis in peritoneal dialysis patients

<table>
<thead>
<tr>
<th>Study duration/time frame: NS</th>
</tr>
</thead>
</table>

**Participants**
Inclusion criteria

- Setting: 5 tertiary centres
- Country: France
- Health status: Current CAPD patients using Y-line systems
- Number: 50 patients; Antiseptic soak 24; no antiseptic 26
- Mean age: NS
- Sex (M/F): NS
- Proportion of diabetic patients (%): NS

Exclusion criteria: NS

**Interventions**
Connector soaked in antiseptic prior to bag exchange versus no use of antiseptic

**Outcomes**
Peritonitis - rate

**Notes**
Funding source: NS
Follow-up period: NS
Loss to follow-up: NS
Excluded from analysis: NS
Exclusions post-randomisation but pre-intervention: NS
Stop or end point/s: NS

### Risk of bias table

<table>
<thead>
<tr>
<th>Bias</th>
<th>Authors' judgement</th>
<th>Support for judgement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Random sequence generation (selection bias)</td>
<td>Unclear risk</td>
<td>Randomisation method not stated. &quot;24 patients using a single use Y-set and 26 using a reusable Y-set (O-set) were separately randomized into two groups.&quot;</td>
</tr>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>Unclear risk</td>
<td>Not stated</td>
</tr>
<tr>
<td>Blinding of participants and personnel (performance bias)</td>
<td>Unclear risk</td>
<td>Insufficient information to permit judgement.</td>
</tr>
<tr>
<td>Blinding of outcome assessment (detection bias)</td>
<td>Unclear risk</td>
<td>Insufficient information to permit judgement.</td>
</tr>
<tr>
<td>Incomplete outcome data (attrition bias)</td>
<td>Unclear risk</td>
<td>No details of missing data given.</td>
</tr>
<tr>
<td>Selective reporting (reporting bias)</td>
<td>High risk</td>
<td>Only 1 of 3 expected primary outcomes is reported.</td>
</tr>
<tr>
<td>Other bias</td>
<td>Unclear risk</td>
<td>No report of funding source.</td>
</tr>
</tbody>
</table>

### Sesso 1994

**Methods**
Study design: parallel RCT
Study duration/time frame: January 1991 through June 1992

**Participants**
Inclusion criteria

- Setting: Single centre
- Country: Brazil
Chapter 4: Antimicrobial agents for preventing peritonitis in peritoneal dialysis patients

Health status: Continuing and new patients undergoing CAPD identified as S. aureus carriers  
Number: 31 patients; S. aureus nasal carriers - oral ofloxacin 9; sodium fusidate ointment 9; control 13  
Mean age ± SE: Oral ofloxacin 36.6 ± 4.6 years; sodium fusidate 46.1 ± 3.8 years; control 42.1 ± 4.6 years  
Sex (M/F): Oral ofloxacin 6/3; sodium fusidate 6/3; control 9/4  
Proportion of diabetic patients (%): Oral ofloxacin 33.3%; sodium fusidate 11.1%; control 7.7%

Exclusion criteria:

Patients who had peritonitis or exit site infection within 1 month of the beginning of the study were excluded until being asymptomatic for at least 1 month; patients who had received antimicrobial therapy within 78 hours before the start of the study; patients younger than 15 years.

Interventions

<table>
<thead>
<tr>
<th>Ofloxacin 200 mg every 2 days over 5 days versus sodium fusidate (2%) ointment applied twice daily (nasal and exit site) x 5 days versus placebo tablets [all treatments repeated monthly]</th>
</tr>
</thead>
</table>

Outcomes

All-cause mortality, peritonitis - number of patients, peritonitis - rate, exit-site/tunnel infection - number of patients, exit-site/tunnel infection - rate, catheter removal or replacement, nasal irritation

Notes

Funding source: Instituto Paulista de Estudos e Pesquisas em Nefrologia e Hipertensao  
Follow up period: 7.8 months (mean)  
Loss to follow up: 7 in oral ofloxacin group (77.8%); 4 in sodium fusidate group (44.4%); 7 in control group (53.9%)  
Excluded from analysis: NS  
Exclusions post-randomisation but pre-intervention: NS  
Stop or end point/s: June 1992 or date patient ceased CAPD, if earlier.

Risk of bias table

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<thead>
<tr>
<th>Bias</th>
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</thead>
<tbody>
<tr>
<td>Random sequence generation (selection bias)</td>
<td>Unclear risk</td>
<td>Randomisation method not stated. &quot;Each carrier was then randomly assigned to one of the three groups&quot;.</td>
</tr>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>Unclear risk</td>
<td>Not stated.</td>
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<tr>
<td>Blinding of participants and personnel (performance bias)</td>
<td>Unclear risk</td>
<td>Insufficient information to permit judgement.</td>
</tr>
<tr>
<td>Blinding of outcome assessment (detection bias)</td>
<td>Unclear risk</td>
<td>Insufficient information to permit judgement.</td>
</tr>
</tbody>
</table>
| Incomplete outcome data (attrition bias) | High risk | 44.4% withdrew from sodium fusidate group; 77.7% withdrew from ofloxacin group; 53.8% withdrew from control group. Proportion missing enough to have a
Selective reporting (reporting bias) | Low risk | 3 of 3 expected primary outcomes of interest are reported.
---|---|---
Other bias | Low risk | Supported by a grant from Instituto Paulista de Estudos e Pesquisas em Nefrologia e Hipertensao. Study appears to be free of other sources of risk.

**Sharma 1971**

| Methods | Study design: parallel RCT  
Study duration/time frame: NS |
|---|---|
| Participants | Inclusion criteria  
Setting: Single tertiary centre  
Country: USA  
Health status: Peritoneal dialysis patients with acute or chronic renal failure.  
Number: 41 patients  
Age range: 11 to 75 years  
Sex (M/F): 22/19 (no details for each treatment group)  
Proportion of diabetic patients (%): NS  
Exclusion criteria: NS |
| Interventions | Oral neomycin 0.5 g in suspension every 12 hours vs placebo |
| Outcomes | Peritonitis - number of dialyses |
| Notes | Funding source: None reported  
Follow-up period: NS  
Loss to follow-up: Six dialyses excluded from analysis  
Excluded from analysis: 6 dialyses excluded (6.3%)  
Exclusions post-randomisation but pre-intervention: NS  
Stop or end point/s: NS |

**Risk of bias table**

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<thead>
<tr>
<th>Bias</th>
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<tr>
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<td>Unclear risk</td>
<td>Randomisation method not stated.</td>
</tr>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>Low risk</td>
<td>Central allocation (pharmacy).</td>
</tr>
<tr>
<td>Blinding of participants and personnel (performance bias)</td>
<td>Low risk</td>
<td>Blinding, and unlikely that the blinding could have been broken.</td>
</tr>
<tr>
<td>Blinding of outcome assessment (detection bias)</td>
<td>Low risk</td>
<td>Blinding, and unlikely that the blinding could have been broken.</td>
</tr>
<tr>
<td>Incomplete outcome</td>
<td>Unclear risk</td>
<td>No details of missing data given on a patient basis.</td>
</tr>
</tbody>
</table>
Chapter 4: Antimicrobial agents for preventing peritonitis in peritoneal dialysis patients

**Risk of bias table**

<table>
<thead>
<tr>
<th>Bias</th>
<th>Authors' judgement</th>
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</thead>
<tbody>
<tr>
<td>Random sequence generation (selection bias)</td>
<td>Low risk</td>
<td>Stratified randomisation. &quot;After informed consent had been obtained, the patients were stratified by diabetes mellitus status (types I and II) and randomly assigned by the coordinating study center (Berlin) to either the silver ring or</td>
</tr>
<tr>
<td>Bias</td>
<td>Risk</td>
<td>Description</td>
</tr>
<tr>
<td>------</td>
<td>------</td>
<td>-------------</td>
</tr>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>Low risk</td>
<td>Central allocation (coordinating study centre).</td>
</tr>
<tr>
<td>Blinding of participants and personnel (performance bias)</td>
<td>High risk</td>
<td>No blinding and the outcome is likely to be influenced by lack of blinding and knowledge of the interventions.</td>
</tr>
<tr>
<td>Blinding of outcome assessment (detection bias)</td>
<td>High risk</td>
<td>No blinding and knowledge of the interventions could influence outcome assessment.</td>
</tr>
<tr>
<td>Incomplete outcome data (attrition bias)</td>
<td>High risk</td>
<td>Proportion missing enough to have a clinically relevant effect. Dropouts: 29/97 (29.9%) in silver ring group; 30/98 (30.6%) in control group. Withdrawals: 6/97 (6.2%) in silver ring group; 0/98 (0%) in control group.</td>
</tr>
<tr>
<td>Selective reporting (reporting bias)</td>
<td>Low risk</td>
<td>3 of 3 expected primary outcomes are reported.</td>
</tr>
<tr>
<td>Other bias</td>
<td>Unclear risk</td>
<td>Supported in part by Baxter Deutschland GmbH, Ettlingen, Germany.</td>
</tr>
</tbody>
</table>

### Sit 2007

#### Methods
- Study design: parallel RCT
- Study duration/time frame: NS

#### Participants
- Inclusion criteria:
  - Setting: Single tertiary centre
  - Country: Turkey
  - Health status: Current CAPD patients (on CAPD for at least 6 months)
  - Number: 49 patients; Mupirocin 25; control 24
  - Mean age ± SD: Mupirocin 42.0 ± 12.1 years; control 37.5 ± 12.9 years
  - Sex (M/F): Mupirocin 10/13; control 11/13
  - Proportion of diabetic patients (%): NS
- Exclusion criteria:
  - Patients who had been treated with intranasal mupirocin before randomisation; those with a known allergy to intranasal mupirocin; those with infection related to CAPD who were transferred to hemodialysis or transplantation.

#### Interventions
- Intranasal mupirocin ointment applied to nares 2 x day for 5 days every 4 weeks versus no ointment

#### Outcomes
- Peritonitis - number of patients
Chapter 4: Antimicrobial agents for preventing peritonitis in peritoneal dialysis patients

**Notes**

Funding source: None reported.
Follow-up period: 12 months
Loss to follow-up: NS
Excluded from analysis: 2 (8%) excluded from analysis in mupirocin group due to renal transplantation (1) and death (1).
Exclusions post-randomisation but pre-intervention: nil
Stop or end point/s: When patient had been followed for 12 months.

---

**Risk of bias table**

<table>
<thead>
<tr>
<th>Bias</th>
<th>Authors' judgement</th>
<th>Support for judgement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Random sequence generation (selection bias)</td>
<td>Low risk</td>
<td>Coin toss. &quot;Randomization was guided by the flip of a coin...&quot;</td>
</tr>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>Unclear risk</td>
<td>Not stated</td>
</tr>
<tr>
<td>Blinding of participants and personnel (performance bias)</td>
<td>Unclear risk</td>
<td>Insufficient information to permit judgement.</td>
</tr>
<tr>
<td>Blinding of outcome assessment (detection bias)</td>
<td>Unclear risk</td>
<td>Insufficient information to permit judgement.</td>
</tr>
<tr>
<td>Incomplete outcome data (attrition bias)</td>
<td>Low risk</td>
<td>Proportion missing not enough to have a clinically relevant effect.</td>
</tr>
<tr>
<td>Selective reporting (reporting bias)</td>
<td>Unclear risk</td>
<td>2 of 3 expected primary outcomes are reported (exit site/tunnel infection, peritonitis).</td>
</tr>
<tr>
<td>Other bias</td>
<td>Unclear risk</td>
<td>No report of funding source.</td>
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</tbody>
</table>

---

**Swartz 1991**

**Methods**

Study design: parallel RCT
Study duration/time frame: Early 1987-1991

**Participants**

Inclusion criteria:

Setting: Single tertiary centre
Country: USA
Health status: Patients beginning chronic PD with a new catheter
Number: 59 patients; antibiotic prophylaxis 29; control 30
Mean age ± SE: antibiotic prophylaxis 49 ± 3.4 years; control 51 ± 3.1 years
Sex (M/F): antibiotic prophylaxis 16/13; control 16/14
Proportion of diabetic patients: antibiotic prophylaxis 34.5 (%); control 33.3%

Exclusion criteria:

Patients beginning chronic PD with a new catheter but also: pediatric age group; extensive prior surgery; given general anesthesia; catheter placement incidental to another surgical procedure

**Interventions**

Trimethoprim/sulfamethoxazole (low dose) or cepahlexin (250 mg) or clindamycin (300 mg) [3 days/week] versus none
## Outcomes

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>All-cause mortality, peritonitis - rate, exit-site/tunnel infection - rate</th>
</tr>
</thead>
</table>

## Notes

<table>
<thead>
<tr>
<th>Notes</th>
<th>Funding source: NS Follow-up period (mean ± SE): antibiotic prophylaxis 11.4 ± 1.3 months; control 12.3 ± 1.4 months Loss to follow-up: 2 of 29 in antibiotic prophylaxis group (6.9%) Excluded from analysis: NS Exclusions post-randomisation but pre-intervention: NS Stop or end point/s: NS</th>
</tr>
</thead>
</table>

### Risk of bias table

<table>
<thead>
<tr>
<th>Bias</th>
<th>Authors' judgement</th>
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</tr>
</thead>
<tbody>
<tr>
<td>Random sequence generation (selection bias)</td>
<td>Low risk</td>
<td>Random number table</td>
</tr>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>Unclear risk</td>
<td>Not stated.</td>
</tr>
<tr>
<td>Blinding of participants and personnel (performance bias)</td>
<td>Unclear risk</td>
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</tr>
<tr>
<td>Blinding of outcome assessment (detection bias)</td>
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<td>Insufficient information to permit judgement.</td>
</tr>
<tr>
<td>Incomplete outcome data (attrition bias)</td>
<td>Low risk</td>
<td>Missing data balanced across groups, and reasons similar</td>
</tr>
<tr>
<td>Selective reporting (reporting bias)</td>
<td>Low risk</td>
<td>3 of 3 expected primary outcomes of interest are reported</td>
</tr>
<tr>
<td>Other bias</td>
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<td>No report of funding source.</td>
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</table>

### Wadhwa 1995

<table>
<thead>
<tr>
<th>Methods</th>
<th>Study design: parallel quasi RCT Study duration/time frame: NS</th>
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</thead>
<tbody>
<tr>
<td>Participants</td>
<td>Inclusion criteria</td>
</tr>
<tr>
<td></td>
<td>Setting: Single centre</td>
</tr>
<tr>
<td></td>
<td>Country: USA</td>
</tr>
<tr>
<td></td>
<td>Health status: PD patients (presume they were current)</td>
</tr>
<tr>
<td></td>
<td>Number: 50 patients; Amuchina 10% 25; povidone iodine 10% 25</td>
</tr>
<tr>
<td></td>
<td>Mean age: Amuchina 10% 59 years; povidone iodine 10% 53 years</td>
</tr>
<tr>
<td></td>
<td>Sex (M/F): NS</td>
</tr>
<tr>
<td></td>
<td>Proportion of diabetic patients (%): Amuchina 10% 48%; povidone iodine 10% 32%</td>
</tr>
<tr>
<td></td>
<td>Exclusion criteria: NS</td>
</tr>
<tr>
<td>Interventions</td>
<td>Application of Amuchina 10% (sodium hypochlorite) vs povidone iodine 10% solution at exit site</td>
</tr>
<tr>
<td>Outcomes</td>
<td>Exit site infection - number of patients; peritonitis - number of patients; catheter removal - number of patients</td>
</tr>
<tr>
<td>Notes</td>
<td>Funding source: NS Follow-up period: NS Loss to follow-up: NS</td>
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</table>
Chapter 4: Antimicrobial agents for preventing peritonitis in peritoneal dialysis patients

<table>
<thead>
<tr>
<th>Bias</th>
<th>Authors’ judgement</th>
<th>Support for judgement</th>
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</thead>
<tbody>
<tr>
<td>Random sequence generation (selection bias)</td>
<td>Unclear risk</td>
<td>Randomisation method not stated. &quot;Fifty PD patients were prospectively randomized to perform daily exit site care with soap and water followed by Amuchina 10% or Povidone Iodine 10% solution.&quot;</td>
</tr>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>Unclear risk</td>
<td>Not stated.</td>
</tr>
<tr>
<td>Blinding of participants and personnel (performance bias)</td>
<td>Unclear risk</td>
<td>Not stated.</td>
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<td>Unclear risk</td>
<td>Not stated.</td>
</tr>
<tr>
<td>Incomplete outcome data (attrition bias)</td>
<td>Unclear risk</td>
<td>Insufficient information to permit judgement. No details re missing data provided.</td>
</tr>
<tr>
<td>Selective reporting (reporting bias)</td>
<td>Low risk</td>
<td>3 of 3 expected primary outcomes are reported (exit site infection, peritonitis, catheter loss).</td>
</tr>
<tr>
<td>Other bias</td>
<td>Unclear risk</td>
<td>No report of funding source.</td>
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</tbody>
</table>

Wadhwa 1997

<table>
<thead>
<tr>
<th>Methods</th>
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</tr>
</thead>
<tbody>
<tr>
<td>Study duration/time frame</td>
<td>NS</td>
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<tr>
<th>Participants</th>
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<tbody>
<tr>
<td>Setting: Single centre</td>
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</tr>
<tr>
<td>Country: USA</td>
<td></td>
</tr>
<tr>
<td>Health status: PD patients (presume they were current)</td>
<td></td>
</tr>
<tr>
<td>Number: 39 patients; Amuchina 5% 18; povidone iodine 10% 21</td>
<td></td>
</tr>
<tr>
<td>Mean age: Amuchina 5% 55 years; povidone iodine 10% 60 years</td>
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</tr>
<tr>
<td>Sex (M/F): NS</td>
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</tr>
<tr>
<td>Proportion of diabetic patients (%): Amuchina 5% 27.8%; povidone iodine 10% 28.6%</td>
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<td>Exclusion criteria: NS</td>
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<table>
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<th>Interventions</th>
<th>Application of Amuchina 5% (sodium hypochlorite) vs povidone iodine 10% solution at exit site</th>
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<table>
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<td>Follow-up period: NS</td>
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<td>Loss to follow-up: NS</td>
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<tr>
<td>Excluded from analysis: NS</td>
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<td>Randomisation method not stated. &quot;Thirty nine PD patients were prospectively randomized to perform daily exit site care with soap and water followed by Amuchina 5% or povidone iodine 10% solution.&quot;</td>
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<td>Allocation concealment (selection bias)</td>
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<td>3 of 3 expected primary outcomes are reported (exit site infection, peritonitis, catheter loss).</td>
</tr>
<tr>
<td>Other bias</td>
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#### Waite 1997

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<thead>
<tr>
<th>Methods</th>
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<tr>
<td></td>
<td>Study duration/time frame: NS</td>
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</table>

<table>
<thead>
<tr>
<th>Participants</th>
<th>Inclusion criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Setting: Single tertiary centre</td>
<td>Country: Canada</td>
</tr>
<tr>
<td>Health status: Patients with ESKD requiring PD catheter insertion</td>
<td></td>
</tr>
<tr>
<td>Number: 117 patients; povidone iodine ointment 61; standard care 56</td>
<td></td>
</tr>
<tr>
<td>Mean age ± SD: povidone iodine ointment 54.4 ± 15.1 years; standard care 53.2 ± 14.5 years</td>
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</tr>
<tr>
<td>Sex (M/F): povidone iodine ointment 33/28; standard care 30/26</td>
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</tr>
<tr>
<td>Proportion of diabetic patients (%): povidone iodine ointment 31.2%; standard care 35.7%</td>
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<td>Exclusion criteria: NS</td>
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<table>
<thead>
<tr>
<th>Interventions</th>
<th>Povidone iodine (10%) ointment 3.5 g at every dressing change versus none</th>
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</table>

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>All-cause mortality, peritonitis - number of patients, exit-site/tunnel infection - number of patients, catheter removal or replacement</th>
</tr>
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<table>
<thead>
<tr>
<th>Notes</th>
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<td>Follow-up period: 6 months.</td>
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<td></td>
<td>3 (2.5%) excluded from analysis due to withdrawal (2) and failure to have PD catheter inserted (1) - group allocation NS</td>
</tr>
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### Risk of bias table

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<td>Random number table</td>
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<td>Allocation concealment (selection bias)</td>
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</tr>
<tr>
<td>Blinding of participants and personnel (performance bias)</td>
<td>Unclear risk</td>
<td>Insufficient information to permit judgement.</td>
</tr>
<tr>
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<td>&quot;Investigators assessing response (presence or absence of infection) were blinded to the treatment received by the individual patients&quot;.</td>
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<td>Low risk</td>
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<tr>
<td>Selective reporting (reporting bias)</td>
<td>Unclear risk</td>
<td>2 of 3 expected primary outcomes of interest are reported.</td>
</tr>
<tr>
<td>Other bias</td>
<td>High risk</td>
<td>Funding source: Purdue-Frederick</td>
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</tbody>
</table>

### Wikdahl 1997

#### Methods

- Study design: parallel RCT
- Study duration/time frame: 27 months

#### Participants

- Setting: Single tertiary centre
- Country: Sweden
- Health status: New peritoneal dialysis patients
- Number: 38 patients; cefuroxime 18; control 20
- Mean age: Cefuroxime 56 (33-84) years; control 61 (34-84) years
- Sex (M/F): Cefuroxime 12/6; control 15/5
- Proportion of diabetic patients (%): Cefuroxime 33.3%; control 35%
- Exclusion criteria: NS

#### Interventions

- Cefuroxime (i.v.) 1.5 g 0.5-2.0 hr before surgery + 250 mg i.p. in first dialysis bag versus none

#### Outcomes

- Peritonitis - number of patients, exit-site/tunnel infection - number of patients (within 10 days of catheter insertion)

#### Notes

- Funding source: NS
- Follow-up period: 10 days post surgery
- Loss to follow-up: NS
- Excluded from analysis: NS
- Exclusions post-randomisation but pre-intervention: NS
- Stop or end point/s:
Chapter 4: Antimicrobial agents for preventing peritonitis in peritoneal dialysis patients

Risk of bias table

<table>
<thead>
<tr>
<th>Bias</th>
<th>Authors' judgement</th>
<th>Support for judgement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Random sequence generation (selection bias)</td>
<td>Unclear risk</td>
<td>Closed envelopes used but insufficient details given</td>
</tr>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>High risk</td>
<td>Envelopes without all safeguards</td>
</tr>
<tr>
<td>Blinding of participants and personnel (performance bias)</td>
<td>Unclear risk</td>
<td>Not stated.</td>
</tr>
<tr>
<td>Blinding of outcome assessment (detection bias)</td>
<td>Unclear risk</td>
<td>Not stated.</td>
</tr>
<tr>
<td>Incomplete outcome data (attrition bias)</td>
<td>Low risk</td>
<td>No missing data.</td>
</tr>
<tr>
<td>Selective reporting (reporting bias)</td>
<td>Low risk</td>
<td>3 of 3 expected primary outcomes of interest are reported.</td>
</tr>
<tr>
<td>Other bias</td>
<td>Unclear risk</td>
<td>No report of funding source.</td>
</tr>
</tbody>
</table>

Wilson 1997

Methods

Study design: parallel RCT
Study duration/time frame: NS

Participants

Inclusion criteria

- Setting: Single tertiary centre
- Country: UK
- Health status: All patients in the peritoneal dialysis program
- Number: 149 patients; povidone iodine spray 77; no spray 72
- Mean age (range): Povidone iodine spray 53 (18-82) years; no spray 51 (21-76) years
- Sex (M/F): Povidone iodine spray 55/22; no spray 43/29
- Proportion of diabetic patients (%): NS

Exclusion criteria: NS

Interventions

Povidone iodine (2.5%) dry powder spray at exit site at every dressing change versus none

Outcomes

All-cause mortality, peritonitis - number of patients, exit-site/tunnel infection - number of patients, catheter removal or replacement, technique failure due to infection, local pruritus/rash

Notes

Funding source: NS.
Follow-up period: 12 months
Loss to follow-up: 1 in spray group (1.3%), 3 in control group (4.2%)
Withdrawals: 5 in spray group (6.5%) (adverse events)
1 (1.3%) excluded from analysis in povidone iodine spray group due to missing results
Exclusions post-randomisation but pre-intervention: NS
Stop or end point/s: 12 months or until a significant difference was found between groups
Additional data requested from authors: Further information on methods and more detailed results were obtained from the corresponding author.
Chapter 4: Antimicrobial agents for preventing peritonitis in peritoneal dialysis patients

Risk of bias table

<table>
<thead>
<tr>
<th>Bias</th>
<th>Authors' judgement</th>
<th>Support for judgement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Random sequence generation</td>
<td>Low risk</td>
<td>Random number table</td>
</tr>
<tr>
<td>Allocation concealment</td>
<td>Unclear risk</td>
<td>Not stated.</td>
</tr>
<tr>
<td>Blinding of participants and</td>
<td>Unclear risk</td>
<td>Not stated.</td>
</tr>
<tr>
<td>personnel</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Blinding of outcome assessment</td>
<td>Unclear risk</td>
<td>Not stated.</td>
</tr>
<tr>
<td>Incomplete outcome data</td>
<td>Low risk</td>
<td>Proportion missing not enough to have a</td>
</tr>
<tr>
<td>(attrition bias)</td>
<td></td>
<td>clinically relevant effect</td>
</tr>
<tr>
<td>Selective reporting</td>
<td>Low risk</td>
<td>3 of 3 expected primary outcomes of</td>
</tr>
<tr>
<td>(reporting bias)</td>
<td></td>
<td>interest are reported</td>
</tr>
<tr>
<td>Other bias</td>
<td>Unclear risk</td>
<td>No report of funding source.</td>
</tr>
</tbody>
</table>

Wong 2003

Methods

Study design: parallel RCT
Study duration/time frame: 5 months

Participants

Inclusion criteria

Setting: Single tertiary centre
Country: Hong Kong SAR, China
Health status: current CAPD patients
Number: 154 patients; mupirocin 73; control 81
Mean age ± SD: mupirocin 60 ± 12 years; control 59 ± 13 years
Sex (M/F): mupirocin 32/41; control 47/34
Proportion of diabetic patients (%): mupirocin 26%; control 33.3%

Presence of significant mental disorder; presence of a significant skin problem; antibiotic treatment within 1 month of the start of the study; regular daily mupirocin ointment prophylaxis at the catheter exit site already prescribed before the start of the study; active exit site infection or peritonitis; ill health; use of any exit site dressing method other than 10% povidone iodine.

Interventions

Application of mupirocin ointment to exit site 1 x day after routine exit-site dressing versus usual daily exit-site care

Outcomes

Exit site infection - number of patients, exit site infection - rate, peritonitis - number of patients, peritonitis - rate

Notes

Funding source: NS
Follow-up period: NS
Loss to follow-up: 1 withdrawal (not stated which intervention group)
Excluded from analysis: 5 (6.4%) from mupirocin group; 7 (8.0%) from control group
Exclusions post-randomisation but pre-intervention: NS
### Risk of bias table

<table>
<thead>
<tr>
<th>Bias</th>
<th>Authors' judgement</th>
<th>Support for judgement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Random sequence generation (selection bias)</td>
<td>Unclear risk</td>
<td>Randomisation method not stated. &quot;Patients not excluded were randomized into two groups.&quot; No description of sequence generation.</td>
</tr>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>Unclear risk</td>
<td>No description of sequence generation.</td>
</tr>
<tr>
<td>Blinding of participants and personnel (performance bias)</td>
<td>Unclear risk</td>
<td>Not stated.</td>
</tr>
<tr>
<td>Blinding of outcome assessment (detection bias)</td>
<td>Unclear risk</td>
<td>Not stated.</td>
</tr>
<tr>
<td>Incomplete outcome data (attrition bias)</td>
<td>Low risk</td>
<td>Missing data balanced across groups, and reasons similar. Outcome data for tunnel infection not reported - this is ok as this infection is the least frequent one in PD patients.</td>
</tr>
<tr>
<td>Selective reporting (reporting bias)</td>
<td>Low risk</td>
<td>3 of 3 expected primary outcomes are reported (exit site infection, peritonitis, catheter loss).</td>
</tr>
<tr>
<td>Other bias</td>
<td>Unclear risk</td>
<td>No report of funding source.</td>
</tr>
</tbody>
</table>

### Zimmerman 1991

**Methods**
- Study design: parallel RCT
- Study duration/time frame: 1 September 1987 - 31 May 1989

**Participants**
- Inclusion criteria
  - Setting: Single tertiary centre
  - Country: USA
  - Health status: Adults who had completed at least 6 months of peritoneal dialysis
  - Number: 64 patients; rifampin 32; control 32
  - Mean age ± SEM: Rifampin 53 ± 3 years; control 55 ± 4 years
  - Sex (M/F): Rifampin 17/15; control 24/8
  - Proportion of diabetic patients (%): Rifampin 43.8%; control 37.5%

- Exclusion criteria: NS

**Interventions**
- Rifampin 300 mg x 2/day x 5 days, every 3 months versus none

**Outcomes**
- Peritonitis - number of patients, peritonitis - rate, catheter removal or replacement, toxicity

**Notes**
- Funding source: Baxter Healthcare
- Follow-up period (mean ± SEM): Rifampin 10.2 ± 1.2 months; control 12.0 ± 1.3 months
- Loss to follow-up: NS
- Withdrawals: Rifampin 4/32 (12.5%); nil in control group
- Excluded from analysis: NS
- Exclusions post-randomisation but pre-intervention: NS
Chapter 4: Antimicrobial agents for preventing peritonitis in peritoneal dialysis patients

Risk of bias table

<table>
<thead>
<tr>
<th>Bias</th>
<th>Authors' judgement</th>
<th>Support for judgement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Random sequence generation (selection bias)</td>
<td>Low risk</td>
<td>Random number table</td>
</tr>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>Unclear risk</td>
<td>No details of allocation method given.</td>
</tr>
<tr>
<td>Blinding of participants and personnel (performance bias)</td>
<td>High risk</td>
<td>No blinding and the outcomes are likely to be influenced by lack of blinding and knowledge of the interventions.</td>
</tr>
<tr>
<td>Blinding of outcome assessment (detection bias)</td>
<td>High risk</td>
<td>No blinding and knowledge of the interventions could influence outcome assessment.</td>
</tr>
<tr>
<td>Incomplete outcome data (attrition bias)</td>
<td>High risk</td>
<td>12.5% in rifampin group withdrew; 0% in control group withdrew. Proportion missing enough to have a clinically relevant effect.</td>
</tr>
<tr>
<td>Selective reporting (reporting bias)</td>
<td>Low risk</td>
<td>Protocol not available but all expected outcomes of interest are reported.</td>
</tr>
<tr>
<td>Other bias</td>
<td>High risk</td>
<td>Funding source: Baxter Healthcare</td>
</tr>
</tbody>
</table>

Table 4.2: Characteristics of excluded studies

<table>
<thead>
<tr>
<th>Reason for exclusion</th>
<th>Al Hwiesh 2008</th>
<th>Not an RCT. A cohort study</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reason for exclusion</td>
<td>Ayliffe 1984</td>
<td>Not an RCT</td>
</tr>
<tr>
<td>Reason for exclusion</td>
<td>Casey 2000</td>
<td>Not an RCT. A cohort study</td>
</tr>
<tr>
<td>Reason for exclusion</td>
<td>Cavdar 2004</td>
<td>Not an intervention of interest</td>
</tr>
<tr>
<td>Reason for exclusion</td>
<td>Churchill 1989</td>
<td>Not an intervention of interest</td>
</tr>
<tr>
<td>Reason for exclusion</td>
<td>Crabtree 2003</td>
<td>Not an intervention of interest</td>
</tr>
<tr>
<td>Reason for exclusion</td>
<td>de Fijter 1989</td>
<td>Treatment study not prevention. Not an RCT</td>
</tr>
</tbody>
</table>
### Chapter 4: Antimicrobial agents for preventing peritonitis in peritoneal dialysis patients

<table>
<thead>
<tr>
<th>Study</th>
<th>Reason for exclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>de Fijter 1992a</td>
<td>Pharmacokinetics study not prevention</td>
</tr>
<tr>
<td>Fong 1993</td>
<td>Preliminary results of an ongoing study. Not an RCT. No reply from authors to query email</td>
</tr>
<tr>
<td>Gadallah 2000c</td>
<td>Urokinase is not an antimicrobial agent. Treatment study not prevention</td>
</tr>
<tr>
<td>Klaus 2002</td>
<td>It is an RCT but peritonitis data is not readily available. No reply from authors to query email</td>
</tr>
<tr>
<td>Maiorca 1983</td>
<td>Not an intervention of interest</td>
</tr>
<tr>
<td>Munoz 1989</td>
<td>Not an RCT. No control group</td>
</tr>
<tr>
<td>Naylor 1997</td>
<td>Small pilot study</td>
</tr>
<tr>
<td>Plum 1997a</td>
<td>Treatment study not prevention</td>
</tr>
<tr>
<td>Read 1985</td>
<td>Not an RCT. No control group</td>
</tr>
<tr>
<td>Rodriguez-Perez 1989</td>
<td>Not an intervention of interest</td>
</tr>
<tr>
<td>Ryckelynck 1988</td>
<td>Not an RCT. No control group</td>
</tr>
<tr>
<td>Stegmayr 1991</td>
<td>Not an RCT. A cohort study with consecutive interventions</td>
</tr>
<tr>
<td>Thomae 1982</td>
<td>Study only went for 84 hours. Of the 7 patients, 3 had previously had peritonitis</td>
</tr>
<tr>
<td>Trooskin 1990</td>
<td>Not an intervention of interest</td>
</tr>
<tr>
<td>Verger 1987</td>
<td>Not an intervention of interest</td>
</tr>
</tbody>
</table>
Table 4.3: Summary of findings tables

1 Oral or topical or intraperitoneal antibiotics versus placebo/no treatment for preventing peritonitis in peritoneal dialysis patients

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Illustrative comparative risks* (95% CI)</th>
<th>Relative effect (95% CI)</th>
<th>No of Participants (studies)</th>
<th>Quality of the evidence (GRADE)</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Peritonitis</strong> (number of patients with one or more episodes)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>Oral or topical or intraperitoneal antibiotics versus placebo/no treatment</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Study population</td>
<td>360 per 1000</td>
<td>295 per 1000 (205 to 428)</td>
<td>RR 0.82 (0.57 to 1.19)</td>
<td>395 (5 studies)</td>
<td>⊕⊕⊕⊕ low&lt;sup&gt;12&lt;/sup&gt;</td>
</tr>
<tr>
<td>Moderate</td>
<td>385 per 1000</td>
<td>316 per 1000 (219 to 458)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Exit-site/tunnel infection</strong> (number of patients with one or more episodes)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Study population</td>
<td>176 per 1000</td>
<td>79 per 1000 (34 to 184)</td>
<td>RR 0.45 (0.19 to 1.04)</td>
<td>191 (3 studies)</td>
<td>⊕⊕⊕⊕ low&lt;sup&gt;2&lt;/sup&gt;</td>
</tr>
<tr>
<td>Moderate</td>
<td>231 per 1000</td>
<td>104 per 1000 (44 to 240)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Catheter removal or replacement</strong> (number of patients)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Study population</td>
<td>115 per 1000</td>
<td>94 per 1000 (53 to 168)</td>
<td>RR 0.82 (0.46 to 1.46)</td>
<td>395 (5 studies)</td>
<td>⊕⊕⊕⊕ Low&lt;sup&gt;12&lt;/sup&gt;</td>
</tr>
<tr>
<td>Moderate</td>
<td>156 per 1000</td>
<td>128 per 1000 (72 to 228)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: Confidence interval; RR: Risk ratio;

GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
### Nasal Antibiotics versus Placebo/No Treatment for Preventing Peritonitis in Peritoneal Dialysis Patients

**Patient or population:** Patients with CKD on peritoneal dialysis  
**Settings:** Tertiary settings  
**Intervention:** Nasal antibiotics versus placebo/no treatment

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Illustrative comparative risks* (95% CI)</th>
<th>Relative effect (95% CI)</th>
<th>No of participants (studies)</th>
<th>Quality of the evidence (GRADE)</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Peritonitis</strong></td>
<td></td>
<td>RR 0.94 (0.67 to 1.31)</td>
<td>338 (3 studies)</td>
<td>⊕⊕⊝⊕   low¹²</td>
<td></td>
</tr>
<tr>
<td>(number of patients with one or more episodes)</td>
<td>Study population 294 per 1000</td>
<td>RR 1.34 (0.62 to 2.87)</td>
<td>338 (3 studies)</td>
<td>⊕⊕⊝⊕   low¹²</td>
<td></td>
</tr>
<tr>
<td></td>
<td>276 per 1000 (197 to 385)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>331 per 1000</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>311 per 1000 (222 to 434)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Exit site/ tunnel infection</strong></td>
<td></td>
<td>RR 0.92 (0.48 to 1.78)</td>
<td>289 (2 studies)</td>
<td>⊕⊕⊝⊕   low¹²</td>
<td></td>
</tr>
<tr>
<td>(number of patients with one or more episodes)</td>
<td>Study population 103 per 1000</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>95 per 1000 (49 to 183)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>265 per 1000</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>244 per 1000 (127 to 472)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

**Footnotes**

1. Unclear or high risk of bias in 3 of 5 studies  
2. Wide confidence intervals due to small patient numbers

**Very low quality:** We are very uncertain about the estimate.
### Topical disinfectants versus standard care or other active treatment (antibiotic or other disinfectant) for preventing peritonitis in peritoneal dialysis patients

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Illustrative comparative risks* (95% CI)</th>
<th>Relative effect (95% CI)</th>
<th>No of Participants (studies)</th>
<th>Quality of the evidence (GRADE)</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Peritonitis</strong> (number of patients with one or more episodes)</td>
<td>Study population</td>
<td>RR 0.83 (0.65 to 1.06)</td>
<td>853 (6 studies)</td>
<td>⊕⊕⊝⊝ low¹,²</td>
<td>235 per 1000&lt;br&gt;195 per 1000 (153 to 250)</td>
</tr>
<tr>
<td></td>
<td>Moderate</td>
<td></td>
<td></td>
<td></td>
<td>152 per 1000&lt;br&gt;126 per 1000 (99 to 161)</td>
</tr>
<tr>
<td><strong>Exit site/tunnel infection</strong> (number of patients with one or more episodes)</td>
<td>Study population</td>
<td>RR 0.97 (0.74 to 1.27)</td>
<td>913 (7 studies)</td>
<td>⊕⊕⊝⊝ low¹,²</td>
<td>238 per 1000&lt;br&gt;230 per 1000 (176 to 302)</td>
</tr>
<tr>
<td></td>
<td>Moderate</td>
<td></td>
<td></td>
<td></td>
<td>222 per 1000&lt;br&gt;215 per 1000 (164 to 282)</td>
</tr>
<tr>
<td><strong>Catheter removal or replacement</strong> (number of patients)</td>
<td>Study population</td>
<td>RR 0.89 (0.57 to 1.38)</td>
<td>792 (6 studies)</td>
<td>⊕⊕⊝⊝ low¹,²</td>
<td>97 per 1000&lt;br&gt;86 per 1000 (55 to 134)</td>
</tr>
</tbody>
</table>

---

1. Unclear risk of bias for allocation concealment in largest study (Mupirocin SG 1996)
2. Wide confidence intervals due to small patient numbers

Abbreviations: CI - confidence interval; RR - risk ratio; GRADE - Grading of Recommendations Assessment, Development and Evaluation
Chapter 4: Antimicrobial agents for preventing peritonitis in peritoneal dialysis patients

<table>
<thead>
<tr>
<th>patients)</th>
<th>93 per 1000</th>
<th>83 per 1000 (53 to 128)</th>
</tr>
</thead>
</table>

*The basis for the assumed risk (e.g. the median control group risk across studies) is provided in footnotes. The corresponding risk (and its 95% confidence interval) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).

CI: Confidence interval; RR: Risk ratio;

GRADE Working Group grades of evidence

High quality: Further research is very unlikely to change our confidence in the estimate of effect.

Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.

Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.

Very low quality: We are very uncertain about the estimate.

Footnotes

1 Unclear allocation in several studies
2 Imprecision due to small number of patients and events in several studies

4 Antifungal versus placebo/no treatment for preventing peritonitis in peritoneal dialysis patients

Antifungal versus placebo/no treatment for preventing fungal peritonitis in peritoneal dialysis patients

| Patient or population: | Patients with CKD on peritoneal dialysis
| Settings: | Tertiary settings
| Intervention: | Antifungal versus placebo/no treatment during antibiotic course

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Illustrative comparative risks* (95% CI)</th>
<th>Relative effect (95% CI)</th>
<th>No of Participants (studies)</th>
<th>Quality of the evidence (GRADE)</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Assumed risk</td>
<td>Corresponding risk</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>Antifungal versus placebo/no treatment</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fungal peritonitis (number of patients with one or more episodes)</td>
<td>Study population</td>
<td>64 per 1000</td>
<td>18 per 1000 (8 to 40)</td>
<td>RR 0.28 (0.12 to 0.63)</td>
<td>817 (2 studies)</td>
</tr>
<tr>
<td>Moderate</td>
<td>64 per 1000</td>
<td>18 per 1000 (8 to 40)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*The basis for the assumed risk (e.g. the median control group risk across studies) is provided in footnotes. The corresponding risk (and its 95% confidence interval) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).

CI: Confidence interval; RR: Risk ratio;

GRADE Working Group grades of evidence

High quality: Further research is very unlikely to change our confidence in the estimate of effect.

Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.

Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.

Very low quality: We are very uncertain about the estimate.
### Footnotes

1 High risk of bias in one study (Lo 1996)

2 Imprecision due to small number of events and studies

### Table 4.4: Additional tables

1 **Comparisons in original review and updated review**

<table>
<thead>
<tr>
<th>Comparisons in original review</th>
<th>Comparisons in updated review</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral antibiotics versus none</td>
<td>Oral or topical antibiotics versus placebo/no treatment</td>
</tr>
<tr>
<td>Nasal antibiotics versus none</td>
<td>Oral or topical antibiotics versus other antibiotic</td>
</tr>
<tr>
<td>Peri-operative IV prophylaxis versus none</td>
<td>Nasal antibiotics versus no treatment</td>
</tr>
<tr>
<td>Peri-operative IV prophylaxis head-to-head</td>
<td>Pre/peri-operative IV prophylaxis versus none or head-to-head</td>
</tr>
<tr>
<td>Topical disinfectants versus none</td>
<td>Topical disinfectants versus standard care or other active treatment (antibiotic or other disinfectant)</td>
</tr>
<tr>
<td>Germicidal chamber versus none</td>
<td>Germicidal chamber versus none</td>
</tr>
<tr>
<td>Antistaphylococcal vaccine (Staphypan) versus placebo</td>
<td>Dressing systems (any)</td>
</tr>
<tr>
<td>Antibiotic prophylaxis head-to-head agents</td>
<td>Silver ring system on catheter versus none</td>
</tr>
<tr>
<td></td>
<td>Antistaphylococcal vaccine (Staphypan) versus placebo</td>
</tr>
<tr>
<td></td>
<td>Antifungal versus placebo/no treatment</td>
</tr>
</tbody>
</table>
## Guidelines on antimicrobial interventions to prevent peritonitis in PD

<table>
<thead>
<tr>
<th>Guideline</th>
<th>Country</th>
<th>Year</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kidney-Disease Outcomes Quality Initiative</td>
<td>United States of America</td>
<td>NA</td>
<td>No guideline</td>
</tr>
<tr>
<td>The Renal Association</td>
<td>United Kingdom</td>
<td>April 2008</td>
<td>Guideline 3.1 - PD Access: Implantation Protocol. Recommended that renal units have clear protocols for peri-operative catheter care including the use of antibiotic prophylaxis (1A).</td>
</tr>
<tr>
<td></td>
<td></td>
<td>July 2010</td>
<td>Guideline 5.1.4 - PD Infectious Complications: Prevention Strategies Recommended that initial catheter insertion be accompanied by antibiotic prophylaxis (1B).</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Guideline 5.1.5 - PD Infectious Complications: Prevention Strategies Recommended that invasive procedures be accompanied by antibiotic prophylaxis and emptying the abdomen of dialysis fluid for a period commensurate with the procedure (1C).</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Guideline 5.1.6 - PD Infectious Complications: Prevention Strategies Recommended that topical antibiotic administration be used to reduce the frequency of S. aureus and Gram-negative exit-site infection and peritonitis (1A).</td>
</tr>
<tr>
<td>Canadian Society of Nephrology</td>
<td>Canada</td>
<td>NA</td>
<td>No guideline</td>
</tr>
<tr>
<td>European Renal Best Practice</td>
<td>Europe</td>
<td>NA</td>
<td>No guideline</td>
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<tr>
<td>International Society for Peritoneal Dialysis</td>
<td>NA</td>
<td>July 2010 to November 2011</td>
<td></td>
</tr>
<tr>
<td>---------------------------------------------</td>
<td>----</td>
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</tr>
</tbody>
</table>

**Guideline 3.1: Implantation Protocol (1A)**

Recommended that renal units have clear protocols for perioperative catheter care, including the use of antibiotic prophylaxis. Recommended that perioperative catheter care protocol include screening for methicillin-resistant S. aureus (MRSA) and nasal carriage of S. aureus. Recommended that prophylactic antibiotics be administered to reduce the risk of catheter-site infection, peritonitis and wound sepsis and there is randomised controlled trial (RCT) evidence for the use of vancomycin.

**Position Statement: Catheter Placement to Prevent Catheter Infections and the Related Peritonitis Episodes**

Prophylactic antibiotics administered at the time of insertion decrease the infection risk. A first-generation cephalosporin or vancomycin can be used, but suggested each program should weigh the potential benefit against the risk of vancomycin use (development of resistant organisms). There is no data on the effectiveness of obtaining nose cultures before catheter insertion, and treating patients positive for S. aureus nasal carriage.

**Position Statement: Exti-Site Care to Prevent Peritonitis**

Antibiotic protocols against S. aureus are effective in reducing the risk of S. aureus catheter infections. All PD patients should use topical antibiotic either at the catheter exit-site or intranasally or both. Topical antibiotic ointments (as opposed to antibiotic creams) should not be used at the exit site of polyurethane catheters.

**Position Statement: Prevention of Fungal Peritonitis**

Most episodes of fungal peritonitis are preceded by courses of antibiotics. Fungal prophylaxis during antibiotic therapy may prevent some cases of Candida peritonitis in programs that have high rates of fungal peritonitis.
<table>
<thead>
<tr>
<th>Kidney Health Australia-Caring for Australasians with Renal Impairment</th>
<th>Australia/New Zealand</th>
<th>February 2014</th>
</tr>
</thead>
</table>

**Guideline 6. Prophylactic Antibiotics for Insertion of PD Catheters**

Recommended that intravenous antibiotic prophylaxis be used prior to peritoneal dialysis catheter insertion to reduce the risk of early peritonitis. Vancomycin, cephalosporins and gentamicin have demonstrated effectiveness in reducing the risk of peritonitis.

**Guideline 8. Treatment of Peritoneal Dialysis-Associated Fungal Peritonitis**

Oral antifungal prophylaxis should be considered when antibiotics are administered to patients undergoing peritoneal dialysis to reduce the risk of developing fungal peritonitis. Prophylactic antifungals should be administered before gynaecological procedures.

**Guideline 10. Prophylaxis for Exit Site/Tunnel Infections Using Mupirocin**

Recommended that prophylactic therapy using mupirocin ointment be used, especially for S. aureus carriage (intranasally or at the exit site) to decrease the risk of S. aureus catheter exit site/tunnel infections and peritonitis. Suggested that clean the PD catheter exit site daily and apply a topical antimicrobial agent (either mupirocin or gentamicin).
Chapter 4: Antimicrobial agents for preventing peritonitis in peritoneal dialysis patients

3 Other outcomes analysed

<table>
<thead>
<tr>
<th>Outcome analysed</th>
<th>Number of studies</th>
<th>Number of patients</th>
<th>RR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral antibiotic prophylaxis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pruritus</td>
<td>1</td>
<td>64</td>
<td>3.00 (0.13 to 71.00)</td>
</tr>
<tr>
<td>Diarrhoea</td>
<td>1</td>
<td>64</td>
<td>0.09 (0.01 to 1.58)</td>
</tr>
<tr>
<td>Nausea</td>
<td>1</td>
<td>64</td>
<td>9.00 (0.50 to 160.59)</td>
</tr>
<tr>
<td>Allergy</td>
<td>1</td>
<td>64</td>
<td>5.00 (0.25 to 100.20)</td>
</tr>
<tr>
<td>Nasal antibiotic prophylaxis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nasal irritation</td>
<td>1</td>
<td>15</td>
<td>2.10 (0.10 to 44.40)</td>
</tr>
<tr>
<td>Rhinitis</td>
<td>1</td>
<td>267</td>
<td>0.74 (0.27 to 2.09)</td>
</tr>
<tr>
<td>Headache</td>
<td>1</td>
<td>267</td>
<td>0.99 (0.14 to 6.94)</td>
</tr>
<tr>
<td>Diarrhoea</td>
<td>1</td>
<td>267</td>
<td>1.65 (0.40 to 6.78)</td>
</tr>
<tr>
<td>Nausea</td>
<td>1</td>
<td>267</td>
<td>0.99 (0.14 to 6.94)</td>
</tr>
<tr>
<td>Vomiting</td>
<td>1</td>
<td>267</td>
<td>2.98 (0.61 to 14.94)</td>
</tr>
<tr>
<td>Pruritus</td>
<td>1</td>
<td>267</td>
<td>1.49 (0.25 to 8.77)</td>
</tr>
<tr>
<td>Topical disinfectants</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Technique failure</td>
<td>1</td>
<td>149</td>
<td>0.19 (0.01 to 3.83)</td>
</tr>
<tr>
<td>Pruritus</td>
<td>1</td>
<td>149</td>
<td>10.29 (0.58 to 182.92)</td>
</tr>
</tbody>
</table>

Table 4.5: Data and analyses tables

1 Oral or topical antibiotics versus placebo/no treatment

<table>
<thead>
<tr>
<th>Outcome or Subgroup</th>
<th>Studies</th>
<th>Participants</th>
<th>Statistical Method</th>
<th>Effect Estimate</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.1 Peritonitis (number of patients with one or more episodes)</td>
<td>5</td>
<td>395</td>
<td>Risk Ratio (M-H, Random, 95% CI)</td>
<td>0.82 [0.57, 1.19]</td>
</tr>
<tr>
<td>1.1.1 Oral antibiotic versus placebo</td>
<td>4</td>
<td>241</td>
<td>Risk Ratio (M-H, Random, 95% CI)</td>
<td>0.87 [0.58, 1.32]</td>
</tr>
<tr>
<td>1.1.2 Mupirocin ointment versus standard care</td>
<td>1</td>
<td>154</td>
<td>Risk Ratio (M-H, Random, 95% CI)</td>
<td>0.55 [0.22, 1.40]</td>
</tr>
<tr>
<td>1.2 Peritonitis rate (episodes/total patient-months on PD)</td>
<td>3</td>
<td>1440</td>
<td>Risk Ratio (M-H, Random, 95% CI)</td>
<td>0.68 [0.40, 1.14]</td>
</tr>
<tr>
<td>1.2.1 Any systemic antibiotic versus placebo/no treatment (excluding nystatin)</td>
<td>3</td>
<td>1440</td>
<td>Risk Ratio (M-H, Random, 95% CI)</td>
<td>0.68 [0.40, 1.14]</td>
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</tbody>
</table>
### Chapter 4: Antimicrobial agents for preventing peritonitis in peritoneal dialysis patients

<table>
<thead>
<tr>
<th>Section</th>
<th>Number</th>
<th>Total</th>
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<th>Risk Ratio (M-H, Random, 95% CI)</th>
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<tr>
<td>1.3 Exit-site/tunnel infection (number of patients with one or more episodes)</td>
<td>3</td>
<td>191</td>
<td>0.45 [0.19, 1.04]</td>
<td>0.45 [0.19, 1.04]</td>
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<tr>
<td>1.3.1 Any systemic antibiotic versus placebo/no treatment</td>
<td>3</td>
<td>191</td>
<td>0.45 [0.19, 1.04]</td>
<td>0.45 [0.19, 1.04]</td>
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<tr>
<td>1.4 Exit-site/tunnel infection rate (episodes/total patient-months on PD)</td>
<td>2</td>
<td>939</td>
<td>0.42 [0.17, 1.05]</td>
<td>0.42 [0.17, 1.05]</td>
</tr>
<tr>
<td>1.4.1 Any systemic antibiotic versus placebo/no treatment</td>
<td>2</td>
<td>939</td>
<td>0.42 [0.17, 1.05]</td>
<td>0.42 [0.17, 1.05]</td>
</tr>
<tr>
<td>1.5 Catheter removal or replacement (number of patients)</td>
<td>5</td>
<td>395</td>
<td>0.82 [0.46, 1.46]</td>
<td>0.82 [0.46, 1.46]</td>
</tr>
<tr>
<td>1.5.1 Any systemic antibiotic versus placebo/no treatment</td>
<td>5</td>
<td>395</td>
<td>0.82 [0.46, 1.46]</td>
<td>0.82 [0.46, 1.46]</td>
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<tr>
<td>1.6 Mortality (all-cause)</td>
<td>4</td>
<td>201</td>
<td>0.88 [0.41, 1.89]</td>
<td>0.88 [0.41, 1.89]</td>
</tr>
<tr>
<td>1.6.1 Any systemic antibiotic versus placebo/no treatment</td>
<td>4</td>
<td>201</td>
<td>0.88 [0.41, 1.89]</td>
<td>0.88 [0.41, 1.89]</td>
</tr>
<tr>
<td>1.7 Mortality due to peritonitis</td>
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<td>No totals</td>
<td>No totals</td>
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<tr>
<td>1.7.1 Oral antibiotic versus placebo</td>
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<td></td>
<td>No totals</td>
<td>No totals</td>
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<tr>
<td>1.8 Adverse effects</td>
<td>2</td>
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<td>No totals</td>
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<tr>
<td>1.8.1 Diarrhoea</td>
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<td>No totals</td>
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<tr>
<td>1.8.2 Nausea</td>
<td>1</td>
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<td>No totals</td>
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<tr>
<td>1.8.3 Pruritis (generalised)</td>
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<td>No totals</td>
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<td>1.8.4 Nasal irritation</td>
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<td>No totals</td>
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<tr>
<td>1.8.5 Allergy</td>
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<td>No totals</td>
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</table>
## 2 Oral or topical antibiotics versus other antibiotic

<table>
<thead>
<tr>
<th>Outcome or Subgroup</th>
<th>Studies</th>
<th>Participants</th>
<th>Statistical Method</th>
<th>Effect Estimate</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.1 Peritonitis (number of patients with one or more episodes)</td>
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<td>314</td>
<td>Risk Ratio (M-H, Random, 95% CI)</td>
<td>1.28 [0.89, 1.84]</td>
</tr>
<tr>
<td>2.1.1 Sodium fusidate ointment versus ofloxacin (oral)</td>
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<td>Risk Ratio (M-H, Random, 95% CI)</td>
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<td>2.1.2 Mupirocin ointment versus rifampin (oral)</td>
<td>1</td>
<td>82</td>
<td>Risk Ratio (M-H, Random, 95% CI)</td>
<td>1.25 [0.67, 2.33]</td>
</tr>
<tr>
<td>2.1.3 Mupirocin ointment/cream versus gentamicin cream (topical)</td>
<td>2</td>
<td>214</td>
<td>Risk Ratio (M-H, Random, 95% CI)</td>
<td>1.39 [0.93, 2.07]</td>
</tr>
<tr>
<td>2.2 Peritonitis rate (episodes/total patient-months on PD)</td>
<td>5</td>
<td></td>
<td>Risk Ratio (M-H, Random, 95% CI)</td>
<td>No totals</td>
</tr>
<tr>
<td>2.2.1 Mupirocin ointment versus polysporin triple ointment (exit site)</td>
<td>1</td>
<td></td>
<td>Risk Ratio (M-H, Random, 95% CI)</td>
<td>No totals</td>
</tr>
<tr>
<td>2.2.2 Sodium fusidate ointment versus ofloxacin (oral)</td>
<td>1</td>
<td></td>
<td>Risk Ratio (M-H, Random, 95% CI)</td>
<td>No totals</td>
</tr>
<tr>
<td>2.2.3 Mupirocin ointment versus neomycin sulphate ointment (nasal)</td>
<td>1</td>
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<td>Risk Ratio (M-H, Random, 95% CI)</td>
<td>No totals</td>
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<tr>
<td>2.2.4 Mupirocin ointment versus rifampin (oral)</td>
<td>1</td>
<td></td>
<td>Risk Ratio (M-H, Random, 95% CI)</td>
<td>No totals</td>
</tr>
<tr>
<td>2.2.5 Mupirocin ointment versus gentamicin cream (exit site)</td>
<td>1</td>
<td></td>
<td>Risk Ratio (M-H, Random, 95% CI)</td>
<td>No totals</td>
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<td>2.3 Exit-site/tunnel infection (number of patients with one or more episodes)</td>
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<td>336</td>
<td>Risk Ratio (M-H, Random, 95% CI)</td>
<td>1.28 [0.71, 2.31]</td>
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<tr>
<td>2.3.1 Mupirocin ointment versus sodium fusidate ointment (topical)</td>
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<td>100</td>
<td>Risk Ratio (M-H, Random, 95% CI)</td>
<td>0.91 [0.42, 1.95]</td>
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<tr>
<td>2.3.2 Sodium fusidate ointment versus ofloxacin (oral)</td>
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<tr>
<td>2.3.3 Mupirocin ointment/cream versus gentamicin cream (topical)</td>
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<td>Risk Ratio (M-H, Random, 95% CI)</td>
<td>1.19 [0.41, 3.46]</td>
</tr>
<tr>
<td>2.4 Exit-site/tunnel infection rate (episodes/total patient-months on PD)</td>
<td>3</td>
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<td>Risk Ratio (M-H, Random, 95% CI)</td>
<td>No totals</td>
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<tr>
<td>2.4.1 Mupirocin ointment versus polysporin triple ointment (exit site)</td>
<td>1</td>
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<td>Risk Ratio (M-H, Random, 95% CI)</td>
<td>No totals</td>
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<tr>
<td>2.4.2 Mupirocin ointment versus gentamicin cream (exit site)</td>
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<td>Risk Ratio (M-H, Random, 95% CI)</td>
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<tr>
<td>2.4.3 Sodium fusidate ointment versus ofloxacin (oral)</td>
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<td>Risk Ratio (M-H, Random, 95% CI)</td>
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<tr>
<td>2.5 Catheter removal or replacement (number of patients)</td>
<td>4</td>
<td>Risk Ratio (M-H, Random, 95% CI)</td>
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<tr>
<td>2.5.1 Mupirocin ointment versus polysporin triple ointment (exit site)</td>
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<td>Risk Ratio (M-H, Random, 95% CI)</td>
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<tr>
<td>2.5.2 Sodium fusidate ointment versus ofloxacin (oral)</td>
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<td>Risk Ratio (M-H, Random, 95% CI)</td>
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<tr>
<td>2.5.3 Mupirocin ointment (exit site) versus rifampin (oral)</td>
<td>1</td>
<td>Risk Ratio (M-H, Random, 95% CI)</td>
<td>No totals</td>
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<tr>
<td>2.5.4 Mupirocin cream versus gentamicin cream (exit site)</td>
<td>1</td>
<td>Risk Ratio (M-H, Random, 95% CI)</td>
<td>No totals</td>
<td></td>
</tr>
<tr>
<td>2.6 Mortality (all-cause)</td>
<td>4</td>
<td>Risk Ratio (M-H, Random, 95% CI)</td>
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<td></td>
</tr>
<tr>
<td>2.6.1 Mupirocin ointment vs polysporin triple ointment (exit site)</td>
<td>1</td>
<td>Risk Ratio (M-H, Random, 95% CI)</td>
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<tr>
<td>2.6.2 Sodium fusidate ointment versus ofloxacin (oral)</td>
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<td>Risk Ratio (M-H, Random, 95% CI)</td>
<td>No totals</td>
<td></td>
</tr>
<tr>
<td>2.6.3 Mupirocin ointment versus rifampin (oral)</td>
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<td>Risk Ratio (M-H, Random, 95% CI)</td>
<td>No totals</td>
<td></td>
</tr>
<tr>
<td>2.6.4 Mupirocin ointment versus gentamicin cream (exit site)</td>
<td>1</td>
<td>Risk Ratio (M-H, Random, 95% CI)</td>
<td>No totals</td>
<td></td>
</tr>
<tr>
<td>2.7 Technique failure</td>
<td>1</td>
<td>Risk Ratio (M-H, Random, 95% CI)</td>
<td>No totals</td>
<td></td>
</tr>
<tr>
<td>2.7.1 Mupirocin ointment versus polysporin triple ointment (exit site)</td>
<td>1</td>
<td>Risk Ratio (M-H, Random, 95% CI)</td>
<td>No totals</td>
<td></td>
</tr>
<tr>
<td>2.8 Adverse effects</td>
<td>3</td>
<td>419</td>
<td>Risk Ratio (M-H, Random, 95% CI)</td>
<td>0.54 [0.21, 1.39]</td>
</tr>
<tr>
<td>2.8.1 Nausea</td>
<td>1</td>
<td>82</td>
<td>Risk Ratio (M-H, Random, 95% CI)</td>
<td>0.09 [0.01, 1.59]</td>
</tr>
<tr>
<td>2.8.2 Pruritus (local)</td>
<td>2</td>
<td>337</td>
<td>Risk Ratio (M-H, Random, 95% CI)</td>
<td>0.65 [0.29, 1.49]</td>
</tr>
</tbody>
</table>
3 Nasal antibiotics versus placebo/no treatment

<table>
<thead>
<tr>
<th>Outcome or Subgroup</th>
<th>Studies</th>
<th>Participants</th>
<th>Statistical Method</th>
<th>Effect Estimate</th>
</tr>
</thead>
<tbody>
<tr>
<td>3.1 Peritonitis (number of patients with one or more episodes)</td>
<td>3</td>
<td>338</td>
<td>Risk Ratio (M-H, Random, 95% CI)</td>
<td>0.94 [0.67, 1.31]</td>
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<tr>
<td>3.2 Peritonitis rate (episodes/total patient-months on PD)</td>
<td>2</td>
<td>2797</td>
<td>Risk Ratio (M-H, Random, 95% CI)</td>
<td>0.67 [0.16, 2.77]</td>
</tr>
<tr>
<td>3.3 Exit site and tunnel infection (number of patients with one or more episodes)</td>
<td>3</td>
<td>338</td>
<td>Risk Ratio (M-H, Random, 95% CI)</td>
<td>1.34 [0.62, 2.87]</td>
</tr>
<tr>
<td>3.4 Exit site and tunnel infection rate (episodes/total patient-months on PD)</td>
<td>2</td>
<td>2796</td>
<td>Risk Ratio (M-H, Random, 95% CI)</td>
<td>0.91 [0.29, 2.92]</td>
</tr>
<tr>
<td>3.5 Catheter removal or replacement (number of patients)</td>
<td>2</td>
<td>289</td>
<td>Risk Ratio (M-H, Random, 95% CI)</td>
<td>0.92 [0.48, 1.78]</td>
</tr>
<tr>
<td>3.6 Mortality (all-cause)</td>
<td>3</td>
<td>338</td>
<td>Risk Ratio (M-H, Random, 95% CI)</td>
<td>0.89 [0.53, 1.47]</td>
</tr>
<tr>
<td>3.7 Adverse effects</td>
<td>2</td>
<td>1624</td>
<td>Risk Ratio (M-H, Random, 95% CI)</td>
<td>1.28 [0.70, 2.32]</td>
</tr>
<tr>
<td>3.7.1 Headache</td>
<td>1</td>
<td>267</td>
<td>Risk Ratio (M-H, Random, 95% CI)</td>
<td>0.99 [0.14, 6.94]</td>
</tr>
<tr>
<td>3.7.2 Diarrhoea</td>
<td>1</td>
<td>267</td>
<td>Risk Ratio (M-H, Random, 95% CI)</td>
<td>1.65 [0.40, 6.78]</td>
</tr>
<tr>
<td>3.7.3 Nausea</td>
<td>1</td>
<td>267</td>
<td>Risk Ratio (M-H, Random, 95% CI)</td>
<td>0.99 [0.14, 6.94]</td>
</tr>
<tr>
<td>3.7.4 Vomiting</td>
<td>1</td>
<td>267</td>
<td>Risk Ratio (M-H, Random, 95% CI)</td>
<td>2.98 [0.61, 14.49]</td>
</tr>
<tr>
<td>3.7.5 Pruritis</td>
<td>1</td>
<td>267</td>
<td>Risk Ratio (M-H, Random, 95% CI)</td>
<td>1.49 [0.25, 8.77]</td>
</tr>
<tr>
<td>3.7.6 Nasal irritation/rhinitis</td>
<td>2</td>
<td>289</td>
<td>Risk Ratio (M-H, Random, 95% CI)</td>
<td>0.93 [0.30, 2.94]</td>
</tr>
</tbody>
</table>

4 Pre/peri-operative prophylaxis versus placebo/no treatment or other antibiotic

<table>
<thead>
<tr>
<th>Outcome or Subgroup</th>
<th>Studies</th>
<th>Participants</th>
<th>Statistical Method</th>
<th>Effect Estimate</th>
</tr>
</thead>
<tbody>
<tr>
<td>4.1 Peritonitis (number of patients with one or more episodes)</td>
<td>4</td>
<td></td>
<td>Risk Ratio (M-H, Random, 95% CI)</td>
<td>No totals</td>
</tr>
<tr>
<td>4.1.1 Vancomycin versus placebo</td>
<td>1</td>
<td></td>
<td>Risk Ratio (M-H, Random, 95% CI)</td>
<td>No totals</td>
</tr>
<tr>
<td>4.1.2 Cefazolin versus placebo</td>
<td>1</td>
<td></td>
<td>Risk Ratio (M-H, Random, 95% CI)</td>
<td>No totals</td>
</tr>
</tbody>
</table>
4.1.3 IV gentamicin versus no antibiotics

| 4.1.3 IV gentamicin versus no antibiotics | 1 | Risk Ratio (M-H, Random, 95% CI) | No totals |

4.1.4 IV cefazolin + gentamicin versus no antibiotics

| 4.1.4 IV cefazolin + gentamicin versus no antibiotics | 1 | Risk Ratio (M-H, Random, 95% CI) | No totals |

4.1.5 IV cefuroxime + cefuroxime (intraperitoneal) versus no antibiotics

| 4.1.5 IV cefuroxime + cefuroxime (intraperitoneal) versus no antibiotics | 1 | Risk Ratio (M-H, Random, 95% CI) | No totals |

4.1.6 Vancomycin versus cefazolin

| 4.1.6 Vancomycin versus cefazolin | 1 | Risk Ratio (M-H, Random, 95% CI) | No totals |

4.2 Exit site/tunnel infection (number of patients with one or more episodes)

| 4.2 Exit site/tunnel infection (number of patients with one or more episodes) | 4 | Risk Ratio (M-H, Random, 95% CI) | No totals |

4.2.1 Vancomycin versus placebo

| 4.2.1 Vancomycin versus placebo | 1 | Risk Ratio (M-H, Random, 95% CI) | No totals |

4.2.2 Cefazolin versus placebo

| 4.2.2 Cefazolin versus placebo | 1 | Risk Ratio (M-H, Random, 95% CI) | No totals |

4.2.3 IV gentamicin versus no antibiotics

| 4.2.3 IV gentamicin versus no antibiotics | 1 | Risk Ratio (M-H, Random, 95% CI) | No totals |

4.2.4 IV cefazolin + gentamicin versus no antibiotics

| 4.2.4 IV cefazolin + gentamicin versus no antibiotics | 1 | Risk Ratio (M-H, Random, 95% CI) | No totals |

4.2.5 IV cefuroxime + cefuroxime (intraperitoneal) versus no antibiotics

| 4.2.5 IV cefuroxime + cefuroxime (intraperitoneal) versus no antibiotics | 1 | Risk Ratio (M-H, Random, 95% CI) | No totals |

4.2.6 Vancomycin versus cefazolin

| 4.2.6 Vancomycin versus cefazolin | 1 | Risk Ratio (M-H, Random, 95% CI) | No totals |

4.3 Catheter removal or replacement (number of patients)

| 4.3 Catheter removal or replacement (number of patients) | 1 | Risk Ratio (M-H, Random, 95% CI) | No totals |

4.4 Mortality (all-cause)

| 4.4 Mortality (all-cause) | 1 | Risk Ratio (M-H, Random, 95% CI) | No totals |

5 Topical disinfectants versus standard care or other active treatment (antibiotic or other disinfectant)

<table>
<thead>
<tr>
<th>Outcome or Subgroup</th>
<th>Studies</th>
<th>Participants</th>
<th>Statistical Method</th>
<th>Effect Estimate</th>
</tr>
</thead>
<tbody>
<tr>
<td>5.1 Peritonitis (number of patients with one or more episodes)</td>
<td>6</td>
<td>853</td>
<td>Risk Ratio (M-H, Random, 95% CI)</td>
<td>0.83 [0.65, 1.06]</td>
</tr>
<tr>
<td>5.1.1 Disinfectant versus standard care</td>
<td>3</td>
<td>393</td>
<td>Risk Ratio (M-H, Random, 95% CI)</td>
<td>0.81 [0.52, 1.26]</td>
</tr>
<tr>
<td>5.1.2 Disinfectant versus other active treatment (antibiotics, other disinfectant)</td>
<td>3</td>
<td>460</td>
<td>Risk Ratio (M-H, Random, 95% CI)</td>
<td>0.84 [0.62, 1.13]</td>
</tr>
<tr>
<td>5.2 Exit site/tunnel infection (number of patients with one or more episodes)</td>
<td>8</td>
<td>973</td>
<td>Risk Ratio (M-H, Random, 95% CI)</td>
<td>1.00 [0.75, 1.33]</td>
</tr>
</tbody>
</table>
### Chapter 4: Antimicrobial agents for preventing peritonitis in peritoneal dialysis patients

#### 5.2.1 Disinfectant versus standard care

<table>
<thead>
<tr>
<th>Outcome or Subgroup</th>
<th>Studies</th>
<th>Participants</th>
<th>Statistical Method</th>
<th>Effect Estimate</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>4</td>
<td>453</td>
<td>Risk Ratio (M-H, Random, 95% CI)</td>
<td>0.74 [0.45, 1.20]</td>
</tr>
</tbody>
</table>

#### 5.2.2 Disinfectant versus other active treatment (antibiotics, other disinfectant)

<table>
<thead>
<tr>
<th>Outcome or Subgroup</th>
<th>Studies</th>
<th>Participants</th>
<th>Statistical Method</th>
<th>Effect Estimate</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>4</td>
<td>520</td>
<td>Risk Ratio (M-H, Random, 95% CI)</td>
<td>1.19 [0.89, 1.60]</td>
</tr>
</tbody>
</table>

#### 5.3 Exit site/tunnel infection rate (episodes/total patient-months on PD)

<table>
<thead>
<tr>
<th>Outcome or Subgroup</th>
<th>Studies</th>
<th>Participants</th>
<th>Statistical Method</th>
<th>Effect Estimate</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2</td>
<td>1752</td>
<td>Risk Ratio (M-H, Random, 95% CI)</td>
<td>1.25 [0.31, 4.93]</td>
</tr>
</tbody>
</table>

#### 5.3.1 Disinfectant versus other active treatment (antibiotics, other disinfectant)

<table>
<thead>
<tr>
<th>Outcome or Subgroup</th>
<th>Studies</th>
<th>Participants</th>
<th>Statistical Method</th>
<th>Effect Estimate</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2</td>
<td>1752</td>
<td>Risk Ratio (M-H, Random, 95% CI)</td>
<td>1.25 [0.31, 4.93]</td>
</tr>
</tbody>
</table>

#### 5.4 Catheter removal or replacement (number of patients)

<table>
<thead>
<tr>
<th>Outcome or Subgroup</th>
<th>Studies</th>
<th>Participants</th>
<th>Statistical Method</th>
<th>Effect Estimate</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>7</td>
<td>852</td>
<td>Risk Ratio (M-H, Random, 95% CI)</td>
<td>0.89 [0.57, 1.38]</td>
</tr>
</tbody>
</table>

#### 5.4.1 Disinfectant versus standard care

<table>
<thead>
<tr>
<th>Outcome or Subgroup</th>
<th>Studies</th>
<th>Participants</th>
<th>Statistical Method</th>
<th>Effect Estimate</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2</td>
<td>266</td>
<td>Risk Ratio (M-H, Random, 95% CI)</td>
<td>0.73 [0.34, 1.55]</td>
</tr>
</tbody>
</table>

#### 5.4.2 Disinfectant versus other active treatment (antibiotics, other disinfectant)

<table>
<thead>
<tr>
<th>Outcome or Subgroup</th>
<th>Studies</th>
<th>Participants</th>
<th>Statistical Method</th>
<th>Effect Estimate</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>5</td>
<td>586</td>
<td>Risk Ratio (M-H, Random, 95% CI)</td>
<td>0.98 [0.57, 1.69]</td>
</tr>
</tbody>
</table>

#### 5.5 Mortality (all-cause)

<table>
<thead>
<tr>
<th>Outcome or Subgroup</th>
<th>Studies</th>
<th>Participants</th>
<th>Statistical Method</th>
<th>Effect Estimate</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>4</td>
<td>697</td>
<td>Risk Ratio (M-H, Random, 95% CI)</td>
<td>0.88 [0.53, 1.44]</td>
</tr>
</tbody>
</table>

#### 5.5.1 Disinfectant versus standard care

<table>
<thead>
<tr>
<th>Outcome or Subgroup</th>
<th>Studies</th>
<th>Participants</th>
<th>Statistical Method</th>
<th>Effect Estimate</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2</td>
<td>266</td>
<td>Risk Ratio (M-H, Random, 95% CI)</td>
<td>1.24 [0.54, 2.84]</td>
</tr>
</tbody>
</table>

#### 5.5.2 Disinfectant versus other active treatment (antibiotics, other disinfectant)

<table>
<thead>
<tr>
<th>Outcome or Subgroup</th>
<th>Studies</th>
<th>Participants</th>
<th>Statistical Method</th>
<th>Effect Estimate</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2</td>
<td>431</td>
<td>Risk Ratio (M-H, Random, 95% CI)</td>
<td>0.73 [0.39, 1.35]</td>
</tr>
</tbody>
</table>

#### 5.6 Technique failure

<table>
<thead>
<tr>
<th>Outcome or Subgroup</th>
<th>Studies</th>
<th>Participants</th>
<th>Statistical Method</th>
<th>Effect Estimate</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1</td>
<td></td>
<td>Risk Ratio (M-H, Random, 95% CI)</td>
<td>No totals</td>
</tr>
</tbody>
</table>

#### 5.7 Pruritus (local)

<table>
<thead>
<tr>
<th>Outcome or Subgroup</th>
<th>Studies</th>
<th>Participants</th>
<th>Statistical Method</th>
<th>Effect Estimate</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>4</td>
<td>609</td>
<td>Risk Ratio (M-H, Random, 95% CI)</td>
<td>2.80 [1.21, 6.48]</td>
</tr>
</tbody>
</table>

### 6 Germicidal chamber versus none

<table>
<thead>
<tr>
<th>Outcome or Subgroup</th>
<th>Studies</th>
<th>Participants</th>
<th>Statistical Method</th>
<th>Effect Estimate</th>
</tr>
</thead>
<tbody>
<tr>
<td>6.1 Peritonitis rate (episodes/total patient-months on PD)</td>
<td>2</td>
<td>1855</td>
<td>Risk Ratio (M-H, Random, 95% CI)</td>
<td>1.05 [0.74, 1.51]</td>
</tr>
<tr>
<td>6.2 Mortality (all-cause)</td>
<td>1</td>
<td></td>
<td>Risk Ratio (M-H, Random, 95% CI)</td>
<td>No totals</td>
</tr>
</tbody>
</table>
### 7 Dressing systems (any)

<table>
<thead>
<tr>
<th>Outcome or Subgroup</th>
<th>Studies</th>
<th>Participants</th>
<th>Statistical Method</th>
<th>Effect Estimate</th>
</tr>
</thead>
<tbody>
<tr>
<td>7.1 Exit site/tunnel infection (number of patients with one or more episodes)</td>
<td>3</td>
<td></td>
<td>Risk Ratio (M-H, Random, 95% CI)</td>
<td>No totals</td>
</tr>
<tr>
<td>7.1.1 Chlorhexidine gluconate plus water versus povidone-iodine solution</td>
<td>1</td>
<td></td>
<td>Risk Ratio (M-H, Random, 95% CI)</td>
<td>No totals</td>
</tr>
<tr>
<td>7.1.2 Sodium hypochlorite solution versus povidone-iodine solution</td>
<td>1</td>
<td></td>
<td>Risk Ratio (M-H, Random, 95% CI)</td>
<td>No totals</td>
</tr>
<tr>
<td>7.1.3 Shower plus gauze versus dressing pack plus fixomull</td>
<td>1</td>
<td></td>
<td>Risk Ratio (M-H, Random, 95% CI)</td>
<td>No totals</td>
</tr>
<tr>
<td>7.1.4 Blisterfilm versus gauze</td>
<td>1</td>
<td></td>
<td>Risk Ratio (M-H, Random, 95% CI)</td>
<td>No totals</td>
</tr>
<tr>
<td>7.2 Exit site/tunnel infection rate (episodes/total patient-months on PD)</td>
<td>1</td>
<td></td>
<td>Risk Ratio (M-H, Random, 95% CI)</td>
<td>No totals</td>
</tr>
<tr>
<td>7.2.1 Shower plus gauze versus dressing pack plus fixomull</td>
<td>1</td>
<td></td>
<td>Risk Ratio (M-H, Random, 95% CI)</td>
<td>No totals</td>
</tr>
</tbody>
</table>

### 8 Silver ring system on catheter versus none

<table>
<thead>
<tr>
<th>Outcome or Subgroup</th>
<th>Studies</th>
<th>Participants</th>
<th>Statistical Method</th>
<th>Effect Estimate</th>
</tr>
</thead>
<tbody>
<tr>
<td>8.1 Peritonitis (number of patients with one or more episodes)</td>
<td>1</td>
<td></td>
<td>Risk Ratio (M-H, Random, 95% CI)</td>
<td>No totals</td>
</tr>
<tr>
<td>8.2 Exit site/tunnel infection (number of patients with one or more episodes)</td>
<td>1</td>
<td></td>
<td>Risk Ratio (M-H, Random, 95% CI)</td>
<td>No totals</td>
</tr>
<tr>
<td>8.3 Catheter removal or replacement (number of patients)</td>
<td>1</td>
<td></td>
<td>Risk Ratio (M-H, Random, 95% CI)</td>
<td>No totals</td>
</tr>
<tr>
<td>8.4 Mortality (all-cause)</td>
<td>1</td>
<td></td>
<td>Risk Ratio (M-H, Random, 95% CI)</td>
<td>No totals</td>
</tr>
</tbody>
</table>

### 9 Antistaphylococcal vaccine (Staphypan) versus placebo

<table>
<thead>
<tr>
<th>Outcome or Subgroup</th>
<th>Studies</th>
<th>Participants</th>
<th>Statistical Method</th>
<th>Effect Estimate</th>
</tr>
</thead>
<tbody>
<tr>
<td>9.1 Peritonitis rate (episodes/total patient-months on PD)</td>
<td>1</td>
<td></td>
<td>Risk Ratio (M-H, Random, 95% CI)</td>
<td>No totals</td>
</tr>
<tr>
<td>9.2 Exit site/tunnel infection rate (episodes/total patient-months on PD)</td>
<td>1</td>
<td></td>
<td>Risk Ratio (M-H, Random, 95% CI)</td>
<td>No totals</td>
</tr>
</tbody>
</table>
10 **Antifungal versus placebo/no treatment**

<table>
<thead>
<tr>
<th>Outcome or Subgroup</th>
<th>Studies</th>
<th>Participants</th>
<th>Statistical Method</th>
<th>Effect Estimate</th>
</tr>
</thead>
<tbody>
<tr>
<td>10.1 Fungal peritonitis (number of patients with one or more episodes)</td>
<td>2</td>
<td>817</td>
<td>Risk Ratio (M-H, Random, 95% CI)</td>
<td>0.28 [0.12, 0.63]</td>
</tr>
<tr>
<td>10.2 Fungal peritonitis rate (episodes/total patient-months on PD)</td>
<td>1</td>
<td></td>
<td>Risk Ratio (M-H, Random, 95% CI)</td>
<td>No totals</td>
</tr>
</tbody>
</table>
### Table 4.6: Electronic search strategies

<table>
<thead>
<tr>
<th>Database searched</th>
<th>Search terms</th>
</tr>
</thead>
</table>
| CENTRAL           | peritoneal next dialysis  
  PERITONEAL DIALYSIS (MeSH explode))  
  pd or capd or ccpd  
  #1 or #2 or #3  
  PERITONITIS (MeSH)  
  periton*  
  #5 or #6  
  #4 and #7 |
| MEDLINE           | exp Peritoneal Dialysis/  
  peritoneal dialysis.tw.  
  (PD or CAPD or CCPD).tw.  
  or/1-3  
  Peritonitis/  
  peritonitis.tw.  
  (periton$ and infect$).tw.  
  or/8-10  
  and/4,7,11 |
| EMBASE            | peritoneal dialysis/  
  continuous ambulatory peritoneal dialysis/  
  (PD or CAPD or CCPD).tw.  
  peritoneal dialysis.tw.  
  or/1-4  
  exp Peritonitis/  
  Catheter Infection/  
  peritonitis.tw.  
  infect$.tw.  
  or/6-9  
  and/5,10 |
### Table 4.7: Risk of bias assessment tool

<table>
<thead>
<tr>
<th>Potential source of bias</th>
<th>Assessment criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Random sequence generation</strong></td>
<td><strong>Low risk of bias:</strong> 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).</td>
</tr>
<tr>
<td>Selection bias (biased allocation to interventions) due to inadequate generation of a randomised sequence</td>
<td><strong>High risk of bias:</strong> 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.</td>
</tr>
<tr>
<td><strong>Allocation concealment</strong></td>
<td><strong>Low risk of bias:</strong> 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).</td>
</tr>
<tr>
<td>Selection bias (biased allocation to interventions) due to inadequate concealment of allocations prior to assignment</td>
<td><strong>High risk of bias:</strong> 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.</td>
</tr>
<tr>
<td><strong>Blinding of participants and personnel</strong></td>
<td><strong>Low risk of bias:</strong> 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.</td>
</tr>
<tr>
<td>Performance bias due to knowledge of the allocated interventions by participants and personnel during the study</td>
<td><strong>High risk of bias:</strong> 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.</td>
</tr>
<tr>
<td><strong>Blinding of outcome assessment</strong></td>
<td><strong>Low risk of bias:</strong> 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.</td>
</tr>
<tr>
<td>Detection bias due to knowledge of the allocated interventions by outcome assessors.</td>
<td><strong>High risk of bias:</strong> 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.</td>
</tr>
<tr>
<td><strong>Incomplete outcome data</strong></td>
<td><strong>Low risk of bias:</strong> No missing outcome data; reasons for missing data available.</td>
</tr>
<tr>
<td><strong>Unclear:</strong> Insufficient information to permit judgement</td>
<td></td>
</tr>
<tr>
<td><strong>Unclear:</strong> Insufficient information to permit judgement</td>
<td></td>
</tr>
<tr>
<td><strong>Unclear:</strong> Insufficient information to permit judgement</td>
<td></td>
</tr>
</tbody>
</table>
## Attrition bias due to amount, nature or handling of incomplete outcome data.

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 standardized 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.

**High risk of bias:** 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.

**Unclear:** Insufficient information to permit judgement

## Selective reporting

**Reporting bias due to selective outcome reporting**

**Low risk of bias:** 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).

**High risk of bias:** 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.

**Unclear:** Insufficient information to permit judgement

## Other bias

**Bias due to problems not covered elsewhere in the table**

**Low risk of bias:** The study appears to be free of other sources of bias.

**High risk of bias:** 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.

**Unclear:** Insufficient information to assess whether an important risk of bias exists; insufficient rationale or evidence that an identified problem will introduce bias.
Figure 4.1: Study flow diagram (updated)

MEDLINE, EMBASE, CENTRAL, Renal Register
2004 review: 382 reports screened

Included studies: 19 (23 reports)
Excluded studies: 2 (4 reports)
Ongoing studies: 0

2015 review update
Renal Register: 57 reports identified

New included studies: 20 (29 reports)
New ongoing studies: 0
Excluded studies: 22 (28 reports) (not RCT, not intervention of interest)

2015 review update
Total included studies: 39 (52 reports)
Total excluded studies: 22 (28 reports)
Ongoing studies: 0

Comparisons
oral or topical or intraperitoneal antibiotics versus placebo/no treatment: 7 studies (469 participants)
oral or topical or intraperitoneal antibiotics versus other antibiotic: 7 studies (640 participants)
nasal antibiotics versus no treatment: 3 studies (338 participants)
pre/peri-operative IV prophylaxis versus none or head-to-head: 4 studies (379 participants)
topical disinfectants versus standard care or other active treatment: 9 studies (1039 participants)
germicidal chamber versus none: 2 studies (217 participants)
dressing systems (any): 3 studies (140 participants)
silver ring system on catheter versus none: 1 study (195 participants)
antistaphylococcal vaccine (Staphypan) versus placebo: 1 study (124 participants)
antifungal versus placebo/no treatment: 2 studies (817 participants)
Figure 4.2: Study flow diagram (original)
Figure 4.3: Risk of bias graph: review authors’ judgements about each risk of bias item presented as percentages across all included studies.

Risk of bias graph: review authors’ judgements about each risk of bias item presented as percentages across all included studies.
Figure 4.4: Risk of bias summary: review authors’ judgements about each risk of bias item for each included study
Figure 4.4: Risk of bias summary: review authors’ judgements about each risk of bias item for each included study (continued)

<table>
<thead>
<tr>
<th>Study</th>
<th>Random Sequence Generation</th>
<th>Allocation Concealment</th>
<th>Blinding of Participants</th>
<th>Blinding of Outcome Assessment</th>
<th>Selective Reporting</th>
<th>Other Bias</th>
</tr>
</thead>
<tbody>
<tr>
<td>MP3 Study 2008</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Mupirocin Study 1996</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Nolp 1985</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Nunez-Moral 2014</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Perez-Fonot 1992</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Poole-Warren 1991</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Restrepo 2010</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Ryckelynck 1987</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Sesso 1994</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Sharma 1971</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>SIPROCE Study 1997</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>St 2007</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Swartz 1991</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Wadhwa 1995</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
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<td>No</td>
</tr>
<tr>
<td>Wadhwa 1997</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Wyate 1997</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Wriedahl 1997</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Wilson 1997</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Wong 2003</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Zimmerman 1991</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
</tr>
</tbody>
</table>

Risk of bias summary: review authors’ judgements about each risk of bias item for each included study.
Figure 4.5: Analysis 1.1 Comparison 1 – Oral or topical antibiotics versus placebo/no treatment, Outcome 1 Peritonitis (number of patients with one or more episodes)

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Treatment Events</th>
<th>Control Events</th>
<th>Total Events</th>
<th>Control Total</th>
<th>Risk Ratio M-H, Random, 95% CI</th>
<th>Risk Ratio M-H, Random, 95% CI</th>
<th>Risk of Bias</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.1.1 Oral antibiotic versus placebo</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sesso 1994</td>
<td>4</td>
<td>9</td>
<td>13</td>
<td>11.0%</td>
<td>1.16 [0.42, 3.15]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low 1980</td>
<td>9</td>
<td>25</td>
<td>34</td>
<td>13.7%</td>
<td>1.50 [0.63, 3.59]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Zimmerman 1991</td>
<td>8</td>
<td>32</td>
<td>40</td>
<td>19.6%</td>
<td>0.47 [0.24, 0.93]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Churchill 1988</td>
<td>33</td>
<td>56</td>
<td>89</td>
<td>43.2%</td>
<td>0.90 [0.67, 1.22]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>122</td>
<td>119</td>
<td>241</td>
<td>87.5%</td>
<td>0.87 [0.58, 1.32]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total events</td>
<td>54</td>
<td>60</td>
<td>114</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
| Heterogeneity: Tau^2 = 0.07; Chi^2 = 5.00, df = 3 (P = 0.17); I^2 = 40%
Test for overall effect: Z = 0.64 (P = 0.52)

1.1.2 Mupirocin ointment versus standard care

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Treatment Events</th>
<th>Control Events</th>
<th>Total Events</th>
<th>Control Total</th>
<th>Risk Ratio M-H, Random, 95% CI</th>
<th>Risk of Bias</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wong 2003</td>
<td>6</td>
<td>73</td>
<td>79</td>
<td>12.5%</td>
<td>0.55 [0.22, 1.40]</td>
<td></td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>73</td>
<td>81</td>
<td>154</td>
<td>12.5%</td>
<td>0.55 [0.22, 1.40]</td>
<td></td>
</tr>
<tr>
<td>Total events</td>
<td>6</td>
<td>12</td>
<td>18</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
| Heterogeneity: Not applicable
Test for overall effect: Z = 1.24 (P = 0.21)

Total (95% CI) | 195             | 200            | 100.0%       | 0.82 [0.57, 1.19] |                                |
| Total events      | 60              | 72             | 132          |             |                                |              |
| Heterogeneity: Tau^2 = 0.06; Chi^2 = 5.97, df = 4 (P = 0.20); I^2 = 33%
Test for overall effect: Z = 1.03 (P = 0.30)
Test for subgroup differences: Chi^2 = 0.76, df = 1 (P = 0.38), I^2 = 0%
Risk of bias legend:
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias
Figure 4.6: Analysis 1.2 Comparison 1 – Oral or topical antibiotics versus placebo/no treatment, Outcome 2 Peritonitis rate (episodes/total patient-months on PD)
Figure 4.7: Analysis 1.3 Comparison 1 - Oral or topical antibiotics versus placebo/no treatment, Outcome 3 Exit-site/tunnel infection (number of patients with one or more episodes)

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Treatment</th>
<th>Control</th>
<th>Risk Ratio</th>
<th>Risk Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Events</td>
<td>Events</td>
<td>Total</td>
<td>M-H, Random, 95% CI</td>
</tr>
<tr>
<td>Blowey 1994</td>
<td>0</td>
<td>7</td>
<td>2</td>
<td>8, 8.7%</td>
</tr>
<tr>
<td>Sesso 1994</td>
<td>2</td>
<td>9</td>
<td>3</td>
<td>13, 29.0%</td>
</tr>
<tr>
<td>Wong 2003</td>
<td>4</td>
<td>73</td>
<td>13</td>
<td>81, 62.3%</td>
</tr>
<tr>
<td><strong>Subtotal (95% CI)</strong></td>
<td><strong>89</strong></td>
<td><strong>102</strong></td>
<td><strong>100.0%</strong></td>
<td><strong>0.45 [0.19, 1.04]</strong></td>
</tr>
</tbody>
</table>

Total events: 6
Heterogeneity: $\hat{Tau}^2 = 0.00$; $\chi^2 = 1.40$, df = 2 ($P = 0.50$); $I^2 = 0$
Test for overall effect: $Z = 1.87$ ($P = 0.06$)

Total (95% CI): 89
Heterogeneity: $\hat{Tau}^2 = 0.00$; $\chi^2 = 1.40$, df = 2 ($P = 0.50$); $I^2 = 0$
Test for overall effect: $Z = 1.87$ ($P = 0.06$)
Test for subgroup differences: Not applicable

Risk of bias legend:
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias
Figure 4.8: Analysis 1.4 Comparison 1 - Oral or topical antibiotics versus placebo/no treatment, Outcome 4 Exit-site/tunnel infection rate (episodes/total patient-months on PD)

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Treatment Events</th>
<th>Control Events</th>
<th>Total Events</th>
<th>Total Weight</th>
<th>Risk Ratio M-H, Random, 95% CI</th>
<th>Risk of Bias</th>
<th>Risk Ratio M-H, Random, 95% CI</th>
<th>Risk of Bias</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1.4.1 Any systemic antibiotic versus placebo/no treatment</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sesso 1984</td>
<td>2</td>
<td>73</td>
<td>4</td>
<td>96</td>
<td>30.7%</td>
<td></td>
<td>0.66 [0.12, 3.49]</td>
<td><img src="image" alt="Risk of Bias" /></td>
</tr>
<tr>
<td>Wong 2003</td>
<td>4</td>
<td>365</td>
<td>13</td>
<td>405</td>
<td>58.3%</td>
<td></td>
<td>0.34 [0.11, 1.04]</td>
<td><img src="image" alt="Risk of Bias" /></td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>6</td>
<td>438</td>
<td>501</td>
<td>100.0%</td>
<td>0.42 [0.17, 1.05]</td>
<td><img src="image" alt="Risk of Bias" /></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Total events 17
Heterogeneity: Tau² = 0.00; Chi² = 0.41, df = 1 (P = 0.52); I² = 0%
Test for overall effect: Z = 1.85 (P = 0.06)

Risk of bias legend
- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias
Chapter 4: Antimicrobial agents for preventing peritonitis in peritoneal dialysis patients

Figure 4.9: Analysis 1.5 Comparison 1 - Oral or topical antibiotics versus placebo/no treatment, Outcome 5 Catheter removal or replacement (number of patients)

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Treatment Events</th>
<th>Treatment Total</th>
<th>Control Events</th>
<th>Control Total</th>
<th>Risk Ratio M–H, Random, 95% CI</th>
<th>Risk Ratio M–H, Random, 95% CI</th>
<th>Risk of Bias</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low 1990</td>
<td>3</td>
<td>25</td>
<td>1</td>
<td>25</td>
<td>6.9%</td>
<td>3.00 [0.33, 26.92]</td>
<td>![Risk of Bias Icon]</td>
</tr>
<tr>
<td>Wong 2003</td>
<td>4</td>
<td>73</td>
<td>2</td>
<td>81</td>
<td>11.9%</td>
<td>2.22 [0.42, 11.76]</td>
<td>![Risk of Bias Icon]</td>
</tr>
<tr>
<td>Zimmerman 1991</td>
<td>2</td>
<td>32</td>
<td>5</td>
<td>37</td>
<td>13.5%</td>
<td>0.40 [0.08, 1.91]</td>
<td>![Risk of Bias Icon]</td>
</tr>
<tr>
<td>Sesso 1994</td>
<td>3</td>
<td>9</td>
<td>6</td>
<td>13</td>
<td>27.7%</td>
<td>0.72 [0.24, 2.16]</td>
<td>![Risk of Bias Icon]</td>
</tr>
<tr>
<td>Churchill 1988</td>
<td>7</td>
<td>56</td>
<td>9</td>
<td>49</td>
<td>40.0%</td>
<td>0.68 [0.27, 1.69]</td>
<td>![Risk of Bias Icon]</td>
</tr>
<tr>
<td><strong>Subtotal (95% CI)</strong></td>
<td><strong>195</strong></td>
<td><strong>200</strong></td>
<td><strong>9</strong></td>
<td><strong>49</strong></td>
<td><strong>100.0%</strong></td>
<td><strong>0.82 [0.46, 1.46]</strong></td>
<td>![Risk of Bias Icon]</td>
</tr>
<tr>
<td><strong>Total events</strong></td>
<td><strong>19</strong></td>
<td><strong>23</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>![Risk of Bias Icon]</td>
</tr>
</tbody>
</table>

Heterogeneity: Tau² = 0.00; Chi² = 3.76, df = 4 (P = 0.44); I² = 0%

Test for overall effect: Z = 0.67 (P = 0.50)

Risk of bias legend:
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias
### Figure 4.10: Analysis 1.6 Comparison 1 - Oral or topical antibiotics versus placebo/no treatment, Outcome 6 Mortality (all-cause)

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Treatment</th>
<th>Control</th>
<th>Risk Ratio</th>
<th>Risk of Bias</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Events</td>
<td>Events</td>
<td>M-H, Random, 95% CI</td>
<td>M-H, Random, 95% CI</td>
</tr>
<tr>
<td>Blowey 1994</td>
<td>0</td>
<td>7</td>
<td>0.23 [0.04, 4.02]</td>
<td>-</td>
</tr>
<tr>
<td><strong>Subtotal (95% CI)</strong></td>
<td><strong>101</strong></td>
<td><strong>100</strong></td>
<td><strong>0.88 [0.41, 1.89]</strong></td>
<td>-</td>
</tr>
</tbody>
</table>

**Total events** 11 13

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 1.62$, df = 3 ($P = 0.65$); $I^2 = 0$

Test for overall effect: $Z = 0.32$ ($P = 0.75$)

**Total (95% CI)** 101 100 100.0% 0.88 [0.41, 1.89]

Total events 11 13

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 1.62$, df = 3 ($P = 0.65$); $I^2 = 0$

Test for overall effect: $Z = 0.32$ ($P = 0.75$)

Test for subgroup differences: Not applicable

**Risk of bias legend**
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias
Figure 4.11: Analysis 1.7 Comparison 1 - Oral or topical antibiotics versus placebo/no treatment, Outcome 7 Mortality due to peritonitis

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Treatment</th>
<th>Control</th>
<th>Risk Ratio M-H, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Churchill 1988</td>
<td>2/55</td>
<td>0/49</td>
<td>4.39 [0.22, 89.20]</td>
</tr>
</tbody>
</table>

Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias
Figure 4.12: Analysis 1.8 Comparison 1 - Oral or topical antibiotics versus placebo/no treatment, Outcome 8 Adverse effects

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Treatment Events</th>
<th>Control Events</th>
<th>Risk Ratio M-H, Random, 95% CI</th>
<th>Risk of Bias</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>1.8.1 Diarrhoea</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Zimmerman 1991</td>
<td>0</td>
<td>5</td>
<td>0.09 [0.01, 1.58]</td>
<td></td>
</tr>
<tr>
<td><strong>1.8.2 Nausea</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Zimmerman 1991</td>
<td>4</td>
<td>0</td>
<td>9.00 [0.50, 160.59]</td>
<td></td>
</tr>
<tr>
<td><strong>1.8.3 Pruritis (generalised)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Zimmerman 1991</td>
<td>1</td>
<td>0</td>
<td>3.00 [0.13, 71.00]</td>
<td></td>
</tr>
<tr>
<td><strong>1.8.4 Nasal irritation</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sesso 1994</td>
<td>1</td>
<td>0</td>
<td>4.20 [0.19, 92.86]</td>
<td></td>
</tr>
<tr>
<td><strong>1.8.5 Allergy</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Zimmerman 1991</td>
<td>2</td>
<td>0</td>
<td>5.00 [0.25, 100.20]</td>
<td></td>
</tr>
</tbody>
</table>

**Risk of bias legend**
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias
Chapter 4: Antimicrobial agents for preventing peritonitis in peritoneal dialysis patients

Figure 4.13: Analysis 2.1 Comparison 2 - Oral or topical antibiotics versus other antibiotic, Outcome 1 Peritonitis (number of patients with one or more episodes)

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Treatment Events</th>
<th>Control Events</th>
<th>Total Events</th>
<th>Weight</th>
<th>Risk Ratio M-H, Random, 95% CI</th>
<th>Risk Ratio M-H, Random, 95% CI</th>
<th>Risk of Bias A B C D E F G</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.1.1 Sodium fusidate ointment versus ofloxacin (oral)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Secco 1994</td>
<td>9</td>
<td>9</td>
<td>9</td>
<td>3.2%</td>
<td>0.25 [0.03, 1.82]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>9</td>
<td>9</td>
<td>9</td>
<td>3.2%</td>
<td>0.25 [0.03, 1.82]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total events</td>
<td>1</td>
<td>4</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td>Heterogeneity: Not applicable</td>
<td></td>
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</tr>
<tr>
<td>Test for overall effect: $I^2 = 13.7$ ($p = 0.17$)</td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2.1.2 Mupirocin ointment versus rifampin (oral)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bernardini 1996</td>
<td>15</td>
<td>41</td>
<td>12</td>
<td>41</td>
<td>29.7%</td>
<td>1.25 [0.67, 2.33]</td>
<td></td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>41</td>
<td>41</td>
<td>29.7%</td>
<td>1.25 [0.67, 2.33]</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total events</td>
<td>15</td>
<td>12</td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Heterogeneity: Not applicable</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Test for overall effect: $I^2 = 0.70$ ($p = 0.48$)</td>
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<td></td>
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<td></td>
</tr>
<tr>
<td>2.1.3 Mupirocin ointment/cream versus gentamicin cream (topical)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chw 2008</td>
<td>15</td>
<td>28</td>
<td>6</td>
<td>43</td>
<td>14.8%</td>
<td>1.89 [0.76, 4.70]</td>
<td></td>
</tr>
<tr>
<td>Bernardini 2005</td>
<td>28</td>
<td>66</td>
<td>22</td>
<td>67</td>
<td>52.3%</td>
<td>1.29 [0.83, 2.01]</td>
<td></td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>104</td>
<td>110</td>
<td>67.0%</td>
<td>1.39 [0.93, 2.07]</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Total events</td>
<td>38</td>
<td>28</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heterogeneity: Tau² = 0.00, Chi² = 0.54, df = 1 ($p = 0.46$), I² = 0%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Test for overall effect: $I^2 = 1.61$ ($p = 0.11$)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>154</td>
<td>160</td>
<td>100.0%</td>
<td>1.28 [0.89, 1.84]</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total events</td>
<td>54</td>
<td>44</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heterogeneity: Tau² = 0.00, Chi² = 3.31, df = 2 ($p = 0.28$), I² = 0%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for subgroup differences: Chi² = 2.76, df = 2 ($p = 0.25$), I² = 27.5%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

0.05 0.2 1 5 20
Favours treatment Favours control
Figure 4.14: Analysis 2.2 Comparison 2 - Oral or topical antibiotics versus other antibiotic, Outcome 2 Peritonitis rate (episodes/total patient-months on PD)

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Treatment Events</th>
<th>Control Events</th>
<th>Risk Ratio M–H, Random, 95% CI</th>
<th>Risk Ratio M–H, Random, 95% CI</th>
<th>Risk of Bias A B C D E F G</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>2.2.1 Mupirocin ointment versus polysporin triple ointment (exit site)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MP3 Study 2008</td>
<td>48 / 1442</td>
<td>40 / 1298</td>
<td>1.08 [0.71, 1.63]</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>2.2.2 Sodium fusidate ointment versus ofloxacin (oral)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sesso 1994</td>
<td>1 / 75</td>
<td>5 / 72</td>
<td>0.19 [0.02, 1.60]</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>2.2.3 Mupirocin ointment versus neomycin sulphate ointment (nasal)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Perez-Fontan 1992</td>
<td>5 / 133</td>
<td>4 / 76</td>
<td>0.71 [0.20, 2.58]</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>2.2.4 Mupirocin ointment versus rifampin (oral)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bernardini 1996</td>
<td>22 / 538</td>
<td>22 / 488</td>
<td>0.91 [0.51, 1.62]</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>2.2.5 Mupirocin ointment versus gentamicin cream (exit site)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chu 2008</td>
<td>12 / 538</td>
<td>13 / 476</td>
<td>0.82 [0.38, 1.77]</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias
Chapter 4: Antimicrobial agents for preventing peritonitis in peritoneal dialysis patients

Figure 4.15: Analysis 2.3 Comparison 2 - Oral or topical antibiotics versus other antibiotic, Outcome 3 Exit-site/tunnel infection (number of patients with one or more episodes)

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Treatment</th>
<th>Control</th>
<th>Total</th>
<th>Weight</th>
<th>Risk Ratio</th>
<th>Risk Ratio</th>
<th>Risk of Bias</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Events</td>
<td>Events</td>
<td>Total</td>
<td></td>
<td></td>
<td>M-H, Random, 95% CI</td>
<td>M-H, Random, 95% CI</td>
</tr>
<tr>
<td><strong>2.3.1 Mupirocin ointment versus sodium fusidate ointment (topical)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dongui 2003</td>
<td>10</td>
<td>50</td>
<td>11</td>
<td>56</td>
<td>0.81 [0.2, 1.95]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>50</td>
<td>50</td>
<td>10</td>
<td>50</td>
<td>0.91 [0.42, 1.95]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total events</td>
<td>10</td>
<td>11</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Heterogeneity: Not applicable</td>
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</tr>
<tr>
<td>Test for overall effect: Z = 0.25 (P = 0.81)</td>
<td></td>
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<td></td>
</tr>
<tr>
<td><strong>2.3.2 Sodium fusidate ointment versus ofloxacin (oral)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sesso 1994</td>
<td>5</td>
<td>9</td>
<td>3</td>
<td>13</td>
<td>2.41 [0.76, 7.62]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>9</td>
<td>13</td>
<td>5</td>
<td>22</td>
<td>2.41 [0.76, 7.62]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total events</td>
<td>5</td>
<td>3</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heterogeneity: Not applicable</td>
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</tr>
<tr>
<td>Test for overall effect: Z = 1.50 (P = 0.13)</td>
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</tr>
<tr>
<td><strong>2.3.3 Mupirocin ointment/cream versus gentamicin cream (topical)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chu 2008</td>
<td>7</td>
<td>38</td>
<td>12</td>
<td>43</td>
<td>0.68 [0.23, 1.50]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gentamicin 2005</td>
<td>29</td>
<td>66</td>
<td>15</td>
<td>87</td>
<td>1.98 [1.16, 3.34]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>104</td>
<td>116</td>
<td>57</td>
<td>163</td>
<td>1.19 [0.41, 3.46]</td>
<td></td>
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</tr>
<tr>
<td>Total events</td>
<td>36</td>
<td>27</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Heterogeneity: Tau² = 0.47; Chi² = 4.81; df = 1 (P = 0.03); I² = 79%</td>
<td></td>
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</tr>
<tr>
<td>Test for overall effect: Z = 0.33 (P = 0.74)</td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td>163</td>
<td>173</td>
<td>100</td>
<td>1.28 [0.71, 2.34]</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total events</td>
<td>51</td>
<td>41</td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Heterogeneity: Tau² = 0.20; Chi² = 0.83; df = 3 (P = 0.06); I² = 60%</td>
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</tr>
<tr>
<td>Test for overall effect: Z = 0.02 (P = 0.41)</td>
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<td></td>
</tr>
<tr>
<td>Test for subgroup differences: Chi² = 1.91; df = 2 (P = 0.38); I² = 0%</td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias
Figure 4.16: Analysis 2.4 Comparison 2 - Oral or topical antibiotics versus other antibiotic, Outcome 4 Exit-site/tunnel infection rate (episodes/total patient-months on PD)

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Treatment Events</th>
<th>Treatment Total</th>
<th>Control Events</th>
<th>Control Total</th>
<th>Risk Ratio M−H, Random, 95% CI</th>
<th>Risk Ratio M−H, Random, 95% CI</th>
<th>Risk of Bias A B C D E F G</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>2.4.1 Mupirocin ointment versus polymyxin triple ointment (exit site)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MP3 Study 2008</td>
<td>14</td>
<td>1442</td>
<td>30</td>
<td>1298</td>
<td>0.42 [0.22, 0.79]</td>
<td></td>
<td>⬤⬤⬤⬤⬤⬤⬤⬤</td>
</tr>
<tr>
<td><strong>2.4.2 Mupirocin ointment versus gentamicin cream (exit site)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chu 2008</td>
<td>9</td>
<td>538</td>
<td>15</td>
<td>476</td>
<td>0.53 [0.23, 1.20]</td>
<td></td>
<td>⬤⬤⬤⬤⬤⬤⬤⬤</td>
</tr>
<tr>
<td><strong>2.4.3 Sodium fusidate ointment versus ofloxacin (oral)</strong></td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
</tbody>
</table>

**Risk of bias legend**
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Risk of bias assessments: ⬤=Low, ⬤⬤=Moderate, ⬤⬤⬤=High
Figure 4.17: Analysis 2.5 Comparison 2 - Oral or topical antibiotics versus other antibiotic, Outcome 5 Catheter removal or replacement (number of patients)

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Treatment</th>
<th>Control</th>
<th>Risk Ratio</th>
<th>Risk Ratio</th>
<th>Risk of Bias</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Events Total</td>
<td>Events Total</td>
<td>M-H, Random, 95% CI</td>
<td>M-H, Random, 95% CI</td>
<td>A B C D E F G</td>
</tr>
<tr>
<td>2.5.1 Mupirocin ointment versus polysporin triple ointment (exit site)</td>
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<td></td>
</tr>
<tr>
<td>MP3 Study 2008</td>
<td>4  101</td>
<td>9  103</td>
<td>0.45 [0.14, 1.42]</td>
<td></td>
<td><img src="image" alt="Bias Legend" /></td>
</tr>
<tr>
<td>2.5.2 Sodium fusidate ointment versus ofloxacin (oral)</td>
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<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sesso 1994</td>
<td>4  9</td>
<td>3  9</td>
<td>1.33 [0.41, 4.33]</td>
<td></td>
<td><img src="image" alt="Bias Legend" /></td>
</tr>
<tr>
<td>2.5.3 Mupirocin ointment (exit site) versus rifampin (oral)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bernardini 1996</td>
<td>4  41</td>
<td>5  41</td>
<td>0.80 [0.23, 2.77]</td>
<td></td>
<td><img src="image" alt="Bias Legend" /></td>
</tr>
<tr>
<td>2.5.4 Mupirocin cream versus gentamicin cream (exit site)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bernardini 2005</td>
<td>7  66</td>
<td>6  67</td>
<td>1.18 [0.42, 3.34]</td>
<td></td>
<td><img src="image" alt="Bias Legend" /></td>
</tr>
</tbody>
</table>

Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias
Figure 4.18: Analysis 2.6 Comparison 2 - Oral or topical antibiotics versus other antibiotic, Outcome 6 Mortality (all-cause)

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Treatment Events</th>
<th>Control Events</th>
<th>Risk Ratio M–H, Random, 95% CI</th>
<th>Risk Ratio M–H, Random, 95% CI</th>
<th>Risk of Bias</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>2.6.1 Mupirocin ointment vs polyclinic triple ointment (exit site)</strong></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MP3 Study 2008</td>
<td>8 101</td>
<td>12 103</td>
<td>0.68 [0.29, 1.59]</td>
<td></td>
<td>☀️ ☀️ ☀️ ☀️ ☀️ ☀️ ☀️</td>
</tr>
<tr>
<td><strong>2.6.2 Sodium fusidate ointment versus ofloxacin (oral)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>☐ ☐ ☐ ☐ ☐ ☐ ☑</td>
</tr>
<tr>
<td>Sesso 1994</td>
<td>0 9</td>
<td>1 9</td>
<td>0.33 [0.02, 7.24]</td>
<td></td>
<td>☐ ☐ ☐ ☐ ☐ ☐ ☑</td>
</tr>
<tr>
<td><strong>2.6.3 Mupirocin ointment versus rifampin (oral)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>☐ ☐ ☐ ☐ ☐ ☐ ☑</td>
</tr>
<tr>
<td>Bernardini 1996</td>
<td>4 41</td>
<td>1 41</td>
<td>4.00 [0.47, 34.28]</td>
<td></td>
<td>☐ ☐ ☐ ☐ ☐ ☐ ☑</td>
</tr>
<tr>
<td><strong>2.6.4 Mupirocin ointment versus gentamicin cream (exit site)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>☐ ☐ ☐ ☐ ☐ ☐ ☑</td>
</tr>
<tr>
<td>Chu 2008</td>
<td>5 38</td>
<td>3 43</td>
<td>1.89 [0.48, 7.37]</td>
<td></td>
<td>☐ ☐ ☐ ☐ ☐ ☐ ☑</td>
</tr>
</tbody>
</table>

Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

0.01 0.1 1 10 100
Favours treatment Favours control
Figure 4.19: Analysis 2.7 Comparison 2 - Oral or topical antibiotics versus other antibiotic, Outcome 7 Technique failure

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Treatment Events</th>
<th>Treatment Total</th>
<th>Control Events</th>
<th>Control Total</th>
<th>Risk Ratio M-H, Random, 95% CI</th>
<th>Risk Ratio M-H, Random, 95% CI</th>
<th>Risk of Bias</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.7.1 Mupirocin ointment versus polysporin triple ointment (exit site)</td>
<td>0</td>
<td>101</td>
<td>13</td>
<td>103</td>
<td>0.71 [0.32, 1.58]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MP3 Study 2008</td>
<td>0</td>
<td>101</td>
<td>13</td>
<td>103</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias
Figure 4.20: Analysis 2.8 Comparison 2 - Oral or topical antibiotics versus other antibiotic, Outcome 8 Adverse effects

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Treatment Events</th>
<th>Control Events</th>
<th>Total Events</th>
<th>Weight</th>
<th>M-H, Random, 95% CI</th>
<th>Risk Ratio M-H, Random, 95% CI</th>
<th>Risk of Bias</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>2.8.1 Nausea</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bernardini 1996</td>
<td>0</td>
<td>41</td>
<td>41</td>
<td>9.5%</td>
<td>0.09 [0.01, 1.59]</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Subtotal (95% Cl)</strong></td>
<td>41</td>
<td>41</td>
<td>82</td>
<td>9.5%</td>
<td>0.09 [0.01, 1.59]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total events</td>
<td>0</td>
<td>5</td>
<td>5</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heterogeneity: Not applicable</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for overall effect: ( Z = 1.64 ) (( P = 0.10 ))</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>2.8.2 Pruritus (local)</strong></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Bernardini 2005</td>
<td>7</td>
<td>66</td>
<td>71</td>
<td>43.6%</td>
<td>1.02 [0.38, 2.73]</td>
<td></td>
</tr>
<tr>
<td>MP3 Study 2008</td>
<td>6</td>
<td>101</td>
<td>107</td>
<td>46.9%</td>
<td>0.44 [0.17, 1.09]</td>
<td></td>
</tr>
<tr>
<td><strong>Subtotal (95% Cl)</strong></td>
<td>167</td>
<td>170</td>
<td>337</td>
<td>90.5%</td>
<td>0.65 [0.29, 1.49]</td>
<td></td>
</tr>
<tr>
<td>Total events</td>
<td>13</td>
<td>21</td>
<td>34</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heterogeneity: ( \tau^2 = 0.12 ); ( \chi^2 = 1.50 ); ( df = 1 ) (( P = 0.22 )); ( I^2 = 33% )</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for overall effect: ( Z = 1.02 ) (( P = 0.31 ))</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

| **Total (95% Cl)**           | 208               | 211         | 419    | 100.0%  | 0.54 [0.21, 1.39]   |                               |              |
| Total events                 | 13                | 26          | 39      |        |                     |                               |              |
| Heterogeneity: \( \tau^2 = 0.27 \); \( \chi^2 = 3.32 \); \( df = 2 \) (\( P = 0.19 \)); \( I^2 = 40\% \) |
| Test for overall effect: \( Z = 1.27 \) (\( P = 0.20 \)) |
| Test for subgroup differences: \( \chi^2 = 1.68 \); \( df = 1 \) (\( P = 0.20 \)); \( I^2 = 40.4\% \) |

**Risk of bias legend**

(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias
Figure 4.21: Analysis 3.1 Comparison 3 - Nasal antibiotics versus placebo/no treatment, Outcome 1 Peritonitis (number of patients with one or more episodes)

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Treatment Events</th>
<th>Treatment Total</th>
<th>Control Events</th>
<th>Control Total</th>
<th>Weight</th>
<th>Risk Ratio M-H, Random, 95% CI</th>
<th>Risk Ratio M-H, Random, 95% CI</th>
<th>Risk of Bias</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sit 2007</td>
<td>1</td>
<td>25</td>
<td>1</td>
<td>24</td>
<td>1.5%</td>
<td>0.96 [0.66, 1.45]</td>
<td></td>
<td>✔️ ? ? ? ? ? ? ? ?</td>
</tr>
<tr>
<td>Sesso 1994</td>
<td>1</td>
<td>9</td>
<td>5</td>
<td>13</td>
<td>2.9%</td>
<td>0.29 [0.04, 2.07]</td>
<td></td>
<td>✔️ ✔️ ✔️ ✔️ ? ? ? ?</td>
</tr>
<tr>
<td>Mupirocin Study 1996</td>
<td>43</td>
<td>134</td>
<td>44</td>
<td>133</td>
<td>95.5%</td>
<td>0.97 [0.69, 1.37]</td>
<td></td>
<td>✔️ ✔️ ✔️ ✔️ ✔️ ✔️ ✔️</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>168</td>
<td>170</td>
<td>100.0%</td>
<td></td>
<td>0.94</td>
<td>[0.67, 1.31]</td>
<td></td>
<td>✔️ ✔️ ✔️ ✔️ ✔️ ✔️ ✔️</td>
</tr>
</tbody>
</table>

Total events: 45, 50
Heterogeneity: Tau² = 0.00; Chi² = 1.43, df = 2 (P = 0.49); I² = 0%
Test for overall effect: Z = 0.38 (P = 0.70)

Risk of bias legend:
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias
Figure 4.22: Analysis 3.2 Comparison 3 - Nasal antibiotics versus placebo/no treatment, Outcome 2 Peritonitis rate (episodes/total patient-months on PD)

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Treatment Events</th>
<th>Treatment Total</th>
<th>Control Events</th>
<th>Control Total</th>
<th>Weight</th>
<th>Risk Ratio M-H, Random, 95% CI</th>
<th>Risk Ratio M-H, Random, 95% CI</th>
<th>Risk of Bias</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sessó 1994</td>
<td>1</td>
<td>75</td>
<td>6</td>
<td>96</td>
<td>28.4%</td>
<td>0.21 [0.03, 1.73]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mupirocin Study 1996</td>
<td>76</td>
<td>1390</td>
<td>64</td>
<td>1236</td>
<td>71.6%</td>
<td>1.06 [0.76, 1.46]</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td><strong>1465</strong></td>
<td><strong>1332</strong></td>
<td>100.0%</td>
<td></td>
<td></td>
<td><strong>0.67 [0.16, 2.77]</strong></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Total events 77
Heterogeneity: Tau² = 0.70; Chi² = 2.20, df = 1 (P = 0.14); I² = 55%
Test for overall effect: Z = 0.55 (P = 0.58)

Risk of bias legend:
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias
Figure 4.23: Analysis 3.3 Comparison 3 - Nasal antibiotics versus placebo/no treatment, Outcome 3 Exit site and tunnel infection (number of patients with one or more episodes)

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Treatment Events</th>
<th>Control Events</th>
<th>Total</th>
<th>Weight</th>
<th>Risk Ratio M-H, Random, 95% CI</th>
<th>Risk Ratio M-H, Random, 95% CI</th>
<th>Risk of Bias</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>M-H, Random, 95% CI</td>
<td>M-H, Random, 95% CI</td>
<td></td>
</tr>
<tr>
<td>Sit 2007</td>
<td>0</td>
<td>25</td>
<td>0</td>
<td>24</td>
<td>Not estimable</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sesso 1994</td>
<td>5</td>
<td>9</td>
<td>3</td>
<td>13</td>
<td>2.41 [0.76, 7.62]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mupirocin Study 1996</td>
<td>26</td>
<td>134</td>
<td>25</td>
<td>133</td>
<td>1.03 [0.63, 1.69]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>168</td>
<td>170</td>
<td>100.0%</td>
<td>1.34</td>
<td>[0.62, 2.87]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total events</td>
<td>31</td>
<td>28</td>
<td></td>
<td>0.16</td>
<td>1.76, df = 1 (P = 0.18); I² = 43%</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Risk of bias legend:
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias
Figure 4.24: Analysis 3.4 Comparison 3 - Nasal antibiotics versus placebo/no treatment, Outcome 4 Exit site and tunnel infection rate (episodes/total patient-months on PD)

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Treatment Events</th>
<th>Treatment Total</th>
<th>Control Events</th>
<th>Control Total</th>
<th>Weight</th>
<th>M-H, Random, 95% CI</th>
<th>Risk Ratio</th>
<th>Risk Ratio</th>
<th>Risk of Bias</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sessio 1994</td>
<td>6</td>
<td>74</td>
<td>4</td>
<td>96</td>
<td>38.1%</td>
<td>1.95 [0.57, 6.65]</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mupirocin Study 1996</td>
<td>42</td>
<td>1390</td>
<td>65</td>
<td>1236</td>
<td>61.9%</td>
<td>0.57 [0.39, 0.84]</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>1464</td>
<td>1332</td>
<td>100.0%</td>
<td></td>
<td></td>
<td>0.91 [0.29, 2.92]</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Total events 48 69
Heterogeneity $\tau^2 = 0.53$; $\chi^2 = 3.46, df = 1 (P = 0.06); I^2 = 71$
Test for overall effect: $Z = 0.15 (P = 0.88)$

Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias
Figure 4.25: Analysis 3.5 Comparison 3 - Nasal antibiotics versus placebo/no treatment, Outcome 5 Catheter removal or replacement (number of patients)

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Treatment</th>
<th>Control</th>
<th>Risk Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Events</td>
<td>Total</td>
<td>M-H, Random, 95% CI</td>
</tr>
<tr>
<td>Sesso 1994</td>
<td>4</td>
<td>9</td>
<td>0.96 [0.38, 2.46]</td>
</tr>
<tr>
<td>Mupirocin Study 1996</td>
<td>8</td>
<td>134</td>
<td>0.88 [0.35, 2.22]</td>
</tr>
</tbody>
</table>

Total (95% CI) 143 146 100.0% 0.92 [0.48, 1.78]

Heterogeneity: $\tau^2 = 0.00$, $\chi^2 = 0.02$, df = 1 ($P = 0.89$); $I^2 = 0$

Test for overall effect: $Z = 0.25$ ($P = 0.81$)

Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias
Chapter 4: Antimicrobial agents for preventing peritonitis in peritoneal dialysis patients

Figure 4.26: Analysis 3.6 Comparison 3 - Nasal antibiotics versus placebo/no treatment, Outcome 6 Mortality (all-cause)

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Treatment Events</th>
<th>Total Events</th>
<th>Control Events</th>
<th>Total Events</th>
<th>Weight</th>
<th>Risk Ratio M-H, Random, 95% CI</th>
<th>Risk Ratio M-H, Random, 95% CI</th>
<th>Risk of Bias</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sitt 2007</td>
<td>1</td>
<td>25</td>
<td>0</td>
<td>24</td>
<td>2.6%</td>
<td>2.88 [0.12, 67.53]</td>
<td></td>
<td>(? ? ? ? ? ? ?)</td>
</tr>
<tr>
<td>Sesso 1994</td>
<td>0</td>
<td>9</td>
<td>1</td>
<td>13</td>
<td>2.7%</td>
<td>0.47 [0.02, 10.32]</td>
<td></td>
<td>(? ? ? ? ? ? ?)</td>
</tr>
<tr>
<td>Mupirocin Study 1996</td>
<td>22</td>
<td>134</td>
<td>25</td>
<td>133</td>
<td>94.7%</td>
<td>0.87 [0.52, 1.47]</td>
<td></td>
<td>(? ? ? ? ? ? ?)</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>168</td>
<td>170</td>
<td>100.0%</td>
<td></td>
<td></td>
<td>0.89 [0.53, 1.47]</td>
<td></td>
<td>(? ? ? ? ? ? ?)</td>
</tr>
</tbody>
</table>

Heterogeneity: $\tau^2 = 0.00; \chi^2 = 0.71, df = 2 (P = 0.70); I^2 = 0$

Test for overall effect: $Z = 0.47 (P = 0.64)$

Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias
Chapter 4: Antimicrobial agents for preventing peritonitis in peritoneal dialysis patients

Figure 4.27: Analysis 3.7 Comparison 3 - Nasal antibiotics versus placebo/no treatment, Outcome 7 Adverse effects

| Study of Subgroup | Treatment Events Total Weight Risk Ratio M-H Random, 95% Cl Risk Ratio M-H Random, 95% Cl Risk of Bias | A | B | C | D | E | F | G |
|------------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| 3.7.1 Headache   |                 |                 |                 |                 |                 |                 |                 |                 |                 |
| Mupirocin Study 1998 | 2 134 | 2 133 | 9.5% | 0.90 (0.14, 6.94) |                 |                 |                 |                 |
| Subtotal (95% Cl) | 134 | 133 | 9.5% | 0.90 (0.14, 6.94) |                 |                 |                 |                 |
| Total events | 2 | 2 |                 |                 |                 |                 |                 |                 |
| Heterogeneity: Not applicable |                 |                 |                 |                 |                 |                 |                 |                 |
| Test for overall effect Z = 0.01 (P = 0.99) |                 |                 |                 |                 |                 |                 |                 |                 |
| 3.7.2 Diarrhoea   |                 |                 |                 |                 |                 |                 |                 |                 |                 |
| Mupirocin Study 1998 | 5 134 | 3 133 | 10.0% | 1.96 (0.40, 6.76) |                 |                 |                 |                 |
| Subtotal (95% Cl) | 134 | 133 | 18.0% | 1.65 (0.40, 6.76) |                 |                 |                 |                 |
| Total events | 5 | 3 |                 |                 |                 |                 |                 |                 |
| Heterogeneity: Not applicable |                 |                 |                 |                 |                 |                 |                 |                 |
| Test for overall effect Z = 0.70 (P = 0.48) |                 |                 |                 |                 |                 |                 |                 |                 |
| 3.7.3 Nasal soreness |                 |                 |                 |                 |                 |                 |                 |                 |                 |
| Mupirocin Study 1998 | 2 134 | 2 133 | 9.5% | 0.90 (0.14, 6.94) |                 |                 |                 |                 |
| Subtotal (95% Cl) | 134 | 133 | 9.5% | 0.90 (0.14, 6.94) |                 |                 |                 |                 |
| Total events | 2 | 2 |                 |                 |                 |                 |                 |                 |
| Heterogeneity: Not applicable |                 |                 |                 |                 |                 |                 |                 |                 |
| Test for overall effect Z = 0.01 (P = 0.99) |                 |                 |                 |                 |                 |                 |                 |                 |
| 3.7.4 Vomiting    |                 |                 |                 |                 |                 |                 |                 |                 |                 |
| Mupirocin Study 1998 | 6 134 | 2 133 | 14.3% | 2.68 [0.61, 14.48] |                 |                 |                 |                 |
| Subtotal (95% Cl) | 134 | 133 | 14.3% | 2.68 [0.61, 14.48] |                 |                 |                 |                 |
| Total events | 6 | 2 |                 |                 |                 |                 |                 |                 |
| Heterogeneity: Not applicable |                 |                 |                 |                 |                 |                 |                 |                 |
| Test for overall effect Z = 1.35 (P = 0.18) |                 |                 |                 |                 |                 |                 |                 |                 |
| 3.7.5 Pruritus     |                 |                 |                 |                 |                 |                 |                 |                 |                 |
| Mupirocin Study 1998 | 3 134 | 2 133 | 11.4% | 1.49 [0.45, 6.77] |                 |                 |                 |                 |
| Subtotal (95% Cl) | 134 | 133 | 11.4% | 1.49 [0.45, 6.77] |                 |                 |                 |                 |
| Total events | 3 | 2 |                 |                 |                 |                 |                 |                 |
| Heterogeneity: Not applicable |                 |                 |                 |                 |                 |                 |                 |                 |
| Test for overall effect Z = 0.44 (P = 0.66) |                 |                 |                 |                 |                 |                 |                 |                 |
| 3.7.6 Nasal irritation/anosmia |                 |                 |                 |                 |                 |                 |                 |                 |                 |
| Sesoo 1994 | 1 9 | 0 13 | 3.7% | 4.20 [0.19, 92.36] |                 |                 |                 |                 |
| Mupirocin Study 1998 | 0 134 | 0 133 | 33.7% | 0.74 [0.27, 2.09] |                 |                 |                 |                 |
| Subtotal (95% Cl) | 134 | 133 | 33.7% | 0.74 [0.27, 2.09] |                 |                 |                 |                 |
| Total events | 7 | 8 |                 |                 |                 |                 |                 |                 |
| Heterogeneity: Tau² = 0.12, Chi² = 0.82, df = 7 (P = 0.90), P = 0.8% |                 |                 |                 |                 |                 |                 |                 |                 |
| Test for overall effect Z = 0.76 (P = 0.45) |                 |                 |                 |                 |                 |                 |                 |                 |
| Total (95% Cl) | 913 | 911 | 100.0% | 1.29 [0.70, 2.33] |                 |                 |                 |                 |
| Total events | 25 | 19 |                 |                 |                 |                 |                 |                 |
| Heterogeneity: Tau² = 0.00, Chi² = 3.02, df = 8 (P = 0.81), P = 0.8% |                 |                 |                 |                 |                 |                 |                 |                 |
| Test for overall effect Z = 0.30 (P = 0.94) |                 |                 |                 |                 |                 |                 |                 |                 |
| Risk of bias legend |                 |                 |                 |                 |                 |                 |                 |                 |
| (A) Random sequence generation (selection bias) |                 |                 |                 |                 |                 |                 |                 |                 |
| (B) Allocation concealment (selection bias) |                 |                 |                 |                 |                 |                 |                 |                 |
| (C) Blinding of participants and personnel/performance bias |                 |                 |                 |                 |                 |                 |                 |                 |
| (D) Blinding of outcome assessment (detection bias) |                 |                 |                 |                 |                 |                 |                 |                 |
| (E) Incomplete outcome data (attrition bias) |                 |                 |                 |                 |                 |                 |                 |                 |
| (F) Selective reporting (reporting bias) |                 |                 |                 |                 |                 |                 |                 |                 |
| (G) Other bias |                 |                 |                 |                 |                 |                 |                 |                 |
Figure 4.28: Analysis 4.1 Comparison 4 – Pre/peri-operative prophylaxis versus placebo/no treatment or other antibiotic, Outcome 1 Peritonitis (number of patients with one or more episodes)

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Treatment</th>
<th>Control</th>
<th>Risk Ratio</th>
<th>Risk of Bias</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Events</td>
<td>Total</td>
<td>M-H, Random, 95% CI</td>
<td>A</td>
</tr>
<tr>
<td><strong>4.1.1 Vancomycin versus placebo</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gadallah 2000c</td>
<td>1</td>
<td>90</td>
<td>12 87</td>
<td>0.08 [0.01, 0.61]</td>
</tr>
<tr>
<td><strong>4.1.2 Cefazolin versus placebo</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gadallah 2000c</td>
<td>9</td>
<td>88</td>
<td>12 87</td>
<td>0.74 [0.33, 1.67]</td>
</tr>
<tr>
<td><strong>4.1.3 IV gentamicin versus no antibiotics</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bennet-Jones 1988</td>
<td>1</td>
<td>13</td>
<td>6 13</td>
<td>0.17 [0.02, 1.20]</td>
</tr>
<tr>
<td><strong>4.1.4 IV cefazolin + gentamicin versus no antibiotics</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lye 1992</td>
<td>2</td>
<td>25</td>
<td>1 25</td>
<td>2.00 [0.19, 20.67]</td>
</tr>
<tr>
<td><strong>4.1.5 IV cefuroxime + cefuroxime (intraperitoneal) versus no antibiotics</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wikdahl 1997</td>
<td>0</td>
<td>18</td>
<td>4 20</td>
<td>0.12 [0.01, 2.13]</td>
</tr>
<tr>
<td><strong>4.1.6 Vancomycin versus cefazolin</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gadallah 2000c</td>
<td>1</td>
<td>90</td>
<td>9 88</td>
<td>0.11 [0.01, 0.84]</td>
</tr>
</tbody>
</table>

Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias
Chapter 4: Antimicrobial agents for preventing peritonitis in peritoneal dialysis patients

Figure 4.29: Analysis 4.2 Comparison 4 - Pre/peri-operative prophylaxis versus placebo/no treatment or other antibiotic, Outcome 2 Exit site/tunnel infection (number of patients with one or more episodes)

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Treatment Events</th>
<th>Control Events</th>
<th>Risk Ratio M-H, Random, 95% CI</th>
<th>Risk of Bias</th>
</tr>
</thead>
<tbody>
<tr>
<td>4.2.1 Vancomycin versus placebo</td>
<td>90</td>
<td>87</td>
<td>0.36 [0.10, 1.32]</td>
<td></td>
</tr>
<tr>
<td>Gadallah 2000c</td>
<td>3</td>
<td>8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4.2.2 Cefazolin versus placebo</td>
<td>88</td>
<td>87</td>
<td>0.74 [0.27, 2.05]</td>
<td></td>
</tr>
<tr>
<td>Gadallah 2000c</td>
<td>6</td>
<td>8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4.2.3 IV gentamicin versus no antibiotics</td>
<td>13</td>
<td>13</td>
<td>0.07 [0.00, 1.06]</td>
<td></td>
</tr>
<tr>
<td>Bennet–Jones 1988</td>
<td>0</td>
<td>7</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4.2.4 IV cefazolin + gentamicin versus no antibiotics</td>
<td>25</td>
<td>25</td>
<td>0.86 [0.34, 2.19]</td>
<td></td>
</tr>
<tr>
<td>Lye 1992</td>
<td>6</td>
<td>7</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4.2.5 IV cefuroxime + cefuroxime (intraperitoneal) versus no antibiotics</td>
<td>20</td>
<td>Not estimable</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wikdañl 1997</td>
<td>0</td>
<td>18</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4.2.6 Vancomycin versus cefazolin</td>
<td>88</td>
<td>6</td>
<td>0.49 [0.13, 1.89]</td>
<td></td>
</tr>
<tr>
<td>Gadallah 2000c</td>
<td>3</td>
<td>90</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias
Figure 4.30: Analysis 4.3 Comparison 4 - Pre/peri-operative prophylaxis versus placebo/no treatment or other antibiotic, Outcome 3 Catheter removal or replacement (number of patients)

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Treatment Events</th>
<th>Control Events</th>
<th>M–H, Random, 95% CI</th>
<th>Risk Ratio M–H, Random, 95% CI</th>
<th>Risk of Bias</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bennet–Jones 1988</td>
<td>0</td>
<td>13</td>
<td>1</td>
<td>0.36 [0.02, 8.06]</td>
<td>💥</td>
</tr>
</tbody>
</table>

Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias
Chapter 4: Antimicrobial agents for preventing peritonitis in peritoneal dialysis patients

Figure 4.31: Analysis 4.4 Comparison 4 - Pre/peri-operative prophylaxis versus placebo/no treatment or other antibiotic, Outcome 4 Mortality (all-cause)

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Treatment</th>
<th>Control</th>
<th>Risk Ratio M-H, Random, 95% CI</th>
<th>Risk Ratio M-H, Random, 95% CI</th>
<th>Risk of Bias</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lye 1992</td>
<td>1 25</td>
<td>1 25</td>
<td>1.00 [0.07, 15.12]</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias
Figure 4.32: Analysis 5.1 Comparison 5 – Topical disinfectants versus standard care or other active treatment (antibiotic or other disinfectant), Outcome 1 Peritonitis (number of patients with one or more episodes)
Figure 4.33: Analysis 5.2 Comparison 5 - Topical disinfectants versus standard care or other active treatment (antibiotic or other disinfectant), Outcome 2 Exit site/tunnel infection (number of patients with one or more episodes)

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Treatment</th>
<th>Control</th>
<th>Risk Ratio</th>
<th>Risk of Bias</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Events</td>
<td>Total</td>
<td>M-H, Random, 95% CI</td>
<td>A  B  C  D  E  F  G</td>
</tr>
<tr>
<td><strong>5.2.1 Disinfectant versus standard care</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mendoza-Guevara 2007</td>
<td>0 30</td>
<td>9 30</td>
<td>1.0% 0.05 [0.00, 0.87]</td>
<td></td>
</tr>
<tr>
<td>Wolfe 1997</td>
<td>9 61</td>
<td>11 56</td>
<td>10.7% 0.75 [0.34, 1.68]</td>
<td></td>
</tr>
<tr>
<td>Wilson 1997</td>
<td>14 77</td>
<td>15 72</td>
<td>14.8% 0.87 [0.45, 1.68]</td>
<td></td>
</tr>
<tr>
<td>Luzar 1990</td>
<td>15 74</td>
<td>14 53</td>
<td>15.4% 0.77 [0.41, 1.45]</td>
<td></td>
</tr>
<tr>
<td><strong>Subtotal (95% CI)</strong></td>
<td>242</td>
<td>211</td>
<td>42.0% 0.74 [0.45, 1.20]</td>
<td></td>
</tr>
<tr>
<td>Total events</td>
<td>28</td>
<td>49</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heterogeneity: Tau² = 0.07; Chi² = 4.09, df = 3 (P = 0.25); I² = 27%</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for overall effect: Z = 1.23 (P = 0.22)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

| **5.2.2 Disinfectant versus other active treatment (antibiotics, other disinfectant)** |           |         |                |              |
| Nunez-Moral 2014        | 6 30      | 2 30    | 3.4% 3.00 [0.66, 13.69] |               |
| Wadhwa 1995             | 7 25      | 5 25    | 7.3% 1.40 [0.51, 3.82]  |               |
| Wadhwa 1997             | 10 18     | 10 21   | 16.5% 1.17 [0.63, 2.25]  |               |
| HONEYPOT Thai 2009      | 46 186    | 41 185  | 30.8% 1.12 [0.77, 1.61]  |               |
| **Subtotal (95% CI)**   | 259       | 261     | 58.0% 1.19 [0.89, 1.60]  |               |
| Total events            | 69        | 58      |            |               |
| Heterogeneity: Tau² = 0.00; Chi² = 1.65, df = 3 (P = 0.65); I² = 0% |
| Test for overall effect: Z = 2.18 (P = 0.04) |

| **Total (95% CI)**      | 501       | 472     | 100.0% 1.00 [0.75, 1.33] |               |
| Total events            | 107       | 107     |            |               |
| Heterogeneity: Tau² = 0.04; Chi² = 8.86, df = 7 (P = 0.26); I² = 21% |
| Test for overall effect: Z = 0.61 (P = 0.99) |
| Test for subgroup differences: Chi² = 2.75, df = 1 (P = 0.10), I² = 63.8% |
| Risk of bias legend:    | (A) Random sequence generation (selection bias) |
|                         | (B) Allocation concealment (selection bias) |
|                         | (C) Blinding of participants and personnel (performance bias) |
|                         | (D) Blinding of outcome assessment (detection bias) |
|                         | (E) Incomplete outcome data (attrition bias) |
|                         | (F) Selective reporting (reporting bias) |
|                         | (G) Other bias |

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Figure 4.34: Analysis 5.3 Comparison 5 - Topical disinfectants versus standard care or other active treatment (antibiotic or other disinfectant), Outcome 3 Exit site/tunnel infection rate (episodes/total patient-months on PD)

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Treatment</th>
<th>Control</th>
<th>Risk Ratio M–H, Random, 95% CI</th>
<th>Risk Ratio N–H, Random, 95% CI</th>
<th>Risk of Bias</th>
</tr>
</thead>
<tbody>
<tr>
<td>5.3.1 Disinfectant versus other active treatment (antibiotics, other disinfectant)</td>
<td>Nunez-Moral 2014</td>
<td>9 329 3 308 42.6% 2.81 [0.77, 10.28]</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cheng 1999a</td>
<td>12 567 17 548 57.4% 0.68 [0.33, 1.42]</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>896 856 100.0% 1.25 [0.31, 4.93]</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total events</td>
<td>21 20</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heterogeneity: Tau² = 0.72; Chi² = 3.49, df = 1 (P = 0.06); I² = 71%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for overall effect: Z = 0.31 (P = 0.75)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>896 856 100.0% 1.25 [0.31, 4.93]</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total events</td>
<td>21 20</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heterogeneity: Tau² = 0.72; Chi² = 3.49, df = 1 (P = 0.06); I² = 71%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for overall effect: Z = 0.31 (P = 0.75)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for subgroup differences: Not applicable</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias
### Figure 4.35: Analysis 5.4 Comparison 5 - Topical disinfectants versus standard care or other active treatment (antibiotic or other disinfectant), Outcome 4 Catheter removal or replacement (number of patients)

#### 5.4.1 Disinfectant versus standard care

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Treatment Events</th>
<th>Control Events</th>
<th>Total Events</th>
<th>Weight</th>
<th>Risk Ratio M-H, Random, 95% CI</th>
<th>Risk Ratio M-H, Random, 95% CI</th>
<th>Risk of Bias</th>
</tr>
</thead>
<tbody>
<tr>
<td>Waite 1997</td>
<td>5</td>
<td>5</td>
<td>10</td>
<td>13.9%</td>
<td>0.92 [0.28, 3.00]</td>
<td></td>
<td>?</td>
</tr>
<tr>
<td>Wilson 1997</td>
<td>6</td>
<td>77</td>
<td>83</td>
<td>20.2%</td>
<td>0.62 [0.23, 1.66]</td>
<td></td>
<td>?</td>
</tr>
<tr>
<td><strong>Subtotal (95% CI)</strong></td>
<td><strong>156</strong></td>
<td><strong>128</strong></td>
<td><strong>284</strong></td>
<td><strong>54.1%</strong></td>
<td><strong>0.73 [0.54, 1.53]</strong></td>
<td></td>
<td>? ? ? ? ? ?</td>
</tr>
<tr>
<td><strong>Total events</strong></td>
<td><strong>11</strong></td>
<td><strong>14</strong></td>
<td><strong>25</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: Tau² = 0.00; Ch² = 0.24, df = 1 (P = 0.62); I² = 0%
Test for overall effect: Z = 0.82 (P = 0.41)

#### 5.4.2 Disinfectant versus other active treatment (antibiotics, other disinfectant)

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Treatment Events</th>
<th>Control Events</th>
<th>Total Events</th>
<th>Weight</th>
<th>Risk Ratio M-H, Random, 95% CI</th>
<th>Risk Ratio M-H, Random, 95% CI</th>
<th>Risk of Bias</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nunez-Moral 2014</td>
<td>0</td>
<td>30</td>
<td>30</td>
<td></td>
<td>Not estimable</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cheng 1999a</td>
<td>3</td>
<td>33</td>
<td>36</td>
<td>10.7%</td>
<td>0.60 [0.16, 2.31]</td>
<td></td>
<td>? ? ? ? ? ?</td>
</tr>
<tr>
<td>HONEYFOT Trial 2009</td>
<td>17</td>
<td>186</td>
<td>193</td>
<td>49.0%</td>
<td>0.94 [0.50, 1.77]</td>
<td></td>
<td>? ? ? ? ? ?</td>
</tr>
<tr>
<td><strong>Subtotal (95% CI)</strong></td>
<td><strong>292</strong></td>
<td><strong>294</strong></td>
<td><strong>586</strong></td>
<td><strong>65.9%</strong></td>
<td><strong>0.98 [0.57, 1.69]</strong></td>
<td></td>
<td>? ? ? ? ? ?</td>
</tr>
<tr>
<td><strong>Total events</strong></td>
<td><strong>24</strong></td>
<td><strong>24</strong></td>
<td><strong>48</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: Tau² = 0.00; Ch² = 2.34, df = 3 (P = 0.51); I² = 0%
Test for overall effect: Z = 0.07 (P = 0.95)

**Total (95% CI)**: 430 / 422 = 100.0% 0.89 [0.57, 1.38]

**Total events**: 35 / 38 = 92.1% 0.28 [0.12, 0.68]

Heterogeneity: Tau² = 0.00; Ch² = 2.97, df = 5 (P = 0.71); I² = 0%
Test for overall effect: Z = 0.53 (P = 0.59)
Test for subgroup differences: Ch² = 0.35, df = 1 (P = 0.55); I² = 0%

**Risk of bias legend**
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias
Chapter 4: Antimicrobial agents for preventing peritonitis in peritoneal dialysis patients

Figure 4.36: Analysis 5.5 Comparison 5 - Topical disinfectants versus standard care or other active treatment (antibiotic or other disinfectant), Outcome 5 Mortality (all-cause)

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Treatment</th>
<th>Control</th>
<th>Risk Ratio M-H, Random, 95% CI</th>
<th>Risk Ratio M-H, Random, 95% CI</th>
<th>Risk of Bias</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Events</td>
<td>Total</td>
<td>Events</td>
<td>Total</td>
<td>Weight</td>
</tr>
<tr>
<td>Disinfectant versus standard care</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Waite 1997</td>
<td>5</td>
<td>61</td>
<td>4</td>
<td>56</td>
<td>15.4%</td>
</tr>
<tr>
<td>Wilson 1997</td>
<td>7</td>
<td>77</td>
<td>5</td>
<td>72</td>
<td>20.2%</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>138</td>
<td>128</td>
<td>35.6%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total events</td>
<td>12</td>
<td>9</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heterogeneity Tau²</td>
<td>0.00</td>
<td>Chi² = 0.02, df = 1 (P = 0.88);</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for overall effect: Z = 0.50 (P = 0.62)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Disinfectant versus other active treatment (antibiotics, other disinfectant)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nunez-Moral 2014</td>
<td>2</td>
<td>30</td>
<td>4</td>
<td>30</td>
<td>9.4%</td>
</tr>
<tr>
<td>HONEYFOT Trial 2009</td>
<td>14</td>
<td>186</td>
<td>18</td>
<td>185</td>
<td>55.0%</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>216</td>
<td>215</td>
<td>64.4%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total events</td>
<td>16</td>
<td>22</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heterogeneity Tau²</td>
<td>0.00</td>
<td>Chi² = 0.24, df = 1 (P = 0.63);</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for overall effect: Z = 1.02 (P = 0.31)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>354</td>
<td>343</td>
<td>100.0%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total events</td>
<td>23</td>
<td>31</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heterogeneity Tau²</td>
<td>0.00</td>
<td>Chi² = 1.28, df = 3 (P = 0.73);</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for overall effect: Z = 0.52 (P = 0.61)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for subgroup differences: Chi² = 1.02, df = 1 (P = 0.31),</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Risk of bias legend</td>
<td>(A) Random sequence generation (selection bias)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(B) Allocation concealment (selection bias)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(C) Blinding of participants and personnel (performance bias)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(D) Blinding of outcome assessment (detection bias)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(E) Incomplete outcome data (attrition bias)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(F) Selective reporting (reporting bias)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(G) Other bias</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Figure 4.37: Analysis 5.6 Comparison 5 - Topical disinfectants versus standard care or other active treatment (antibiotic or other disinfectant), Outcome 6 Technique failure

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Treatment Events</th>
<th>Control Events</th>
<th>Risk Ratio M–H, Random, 95% CI</th>
<th>Risk Ratio M–H, Random, 95% CI</th>
<th>Risk of Bias</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wilson 1997</td>
<td>0</td>
<td>2</td>
<td>0.19 [0.01, 3.33]</td>
<td></td>
<td>+ ? ? ? ? ? ?</td>
</tr>
</tbody>
</table>

Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias
Figure 4.38: Analysis 5.7 Comparison 5 - Topical disinfectants versus standard care or other active treatment (antibiotic or other disinfectant), Outcome 7 Pruritus (local)

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Treatment</th>
<th>Control</th>
<th>Risk Ratio M-H, Random, 95% CI</th>
<th>Risk of Bias</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wilson 1997</td>
<td>5/77</td>
<td>0/72</td>
<td>10.29 [0.58, 182.92]</td>
<td>☟</td>
</tr>
<tr>
<td>HONEYPOT Trial 2009</td>
<td>11/186</td>
<td>0/185</td>
<td>22.88 [1.36, 385.40]</td>
<td>☟</td>
</tr>
<tr>
<td>Wachwa 1997</td>
<td>14/25</td>
<td>6/25</td>
<td>2.33 [1.07, 5.09]</td>
<td>☟ ☟ ☟ ☟ ☟ ☟ ☟</td>
</tr>
<tr>
<td>Wachwa 1997</td>
<td>11/18</td>
<td>7/21</td>
<td>1.83 [0.90, 3.72]</td>
<td>☟ ☟ ☟ ☟ ☟ ☟ ☟</td>
</tr>
</tbody>
</table>

Total (95% CI) 306/303 100.0% 2.80 [1.21, 6.48]

Heterogeneity: Tau² = 0.29; Chi² = 5.39, df = 3 (P = 0.15); I² = 44%
Test for overall effect: Z = 2.41 (P = 0.02)

Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F)Selective reporting (reporting bias)
(G) Other bias
### Figure 4.39: Analysis 6.1 Comparison 6 – Germicidal chamber versus none, Outcome 1 Peritonitis rate (episodes/total patient-months on PD)

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Treatment Events</th>
<th>Control Events</th>
<th>Total Weight</th>
<th>Risk Ratio M-H, Random, 95% CI</th>
<th>Risk of Bias</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ryckewick 1987</td>
<td>9</td>
<td>7</td>
<td>235</td>
<td>1.14 [0.43, 3.00]</td>
<td></td>
</tr>
<tr>
<td>Nolph 1985</td>
<td>44</td>
<td>53</td>
<td>753</td>
<td>1.04 [0.71, 1.53]</td>
<td></td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>867</td>
<td>988</td>
<td>100%</td>
<td>1.05 [0.74, 1.51]</td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: Tau² = 0.00; Chi² = 0.03, df = 1 (P = 0.87); I² = 0%

Test for overall effect: Z = 0.28 (P = 0.78)

Risk of bias legend:
- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Blinding of outcome assessment (detection bias)
- (E) Incomplete outcome data (attrition bias)
- (F) Selective reporting (reporting bias)
- (G) Other bias

Favours chamber Favours control
**Figure 4.40: Analysis 6.2 Comparison 6 - Germicidal chamber versus none, Outcome 2 Mortality (all-cause)**

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Treatment Events</th>
<th>Treatment Total</th>
<th>Control Events</th>
<th>Control Total</th>
<th>Risk Ratio M-H, Random, 95% CI</th>
<th>Risk Ratio M-H, Random, 95% CI</th>
<th>Risk of Bias</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nolph 1985</td>
<td>4</td>
<td>74</td>
<td>11</td>
<td>93</td>
<td>0.46 [0.15, 1.38]</td>
<td></td>
<td>⬤ ⬤ ⬤ ⬤ ⬤ ⬤ ⬤</td>
</tr>
</tbody>
</table>

**Risk of bias legend**

(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias
Figure 4.41: Analysis 7.1 Comparison 7 – Dressing systems (any), Outcome 1 Exit site/tunnel infection (number of patients with one or more episodes)

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Treatment Events</th>
<th>Treatment Total</th>
<th>Control Events</th>
<th>Control Total</th>
<th>Risk Ratio M–H, Random, 95% CI</th>
<th>Risk Ratio M–H, Random, 95% CI</th>
<th>Risk of Bias</th>
</tr>
</thead>
<tbody>
<tr>
<td>7.1.1 Chlorhexidine gluconate plus water versus povidone-iodine solution</td>
<td>1 18</td>
<td>0 20</td>
<td>3.32 [0.14, 76.60]</td>
<td></td>
<td><img src="image" alt="Risk of Bias" /></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7.1.2 Sodium hypochlorite solution versus povidone-iodine solution</td>
<td>2 13</td>
<td>0 20</td>
<td>7.50 [0.39, 144.75]</td>
<td></td>
<td><img src="image" alt="Risk of Bias" /></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7.1.3 Shower plus gauze versus dressing pack plus fixomull</td>
<td>11 30</td>
<td>16 30</td>
<td>0.69 [0.39, 1.22]</td>
<td></td>
<td><img src="image" alt="Risk of Bias" /></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7.1.4 Blisterfilm versus gauze</td>
<td>3 15</td>
<td>6 14</td>
<td>0.47 [0.14, 1.52]</td>
<td></td>
<td><img src="image" alt="Risk of Bias" /></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias
Figure 4.42: Analysis 7.2 Comparison 7 – Dressing systems (any), Outcome 2 Exit site/tunnel infection rate (episodes/total patient-months on PD)

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Treatment Events</th>
<th>Control Events</th>
<th>Risk Ratio M–H, Random, 95% CI</th>
<th>Risk Ratio M–H, Random, 95% CI</th>
<th>Risk of Bias A B C D E F G</th>
</tr>
</thead>
<tbody>
<tr>
<td>7.2.1 Shower plus gauze versus dressing pack plus fixomull</td>
<td>16 337 25 342</td>
<td>0.65 [0.35, 1.19]</td>
<td></td>
<td></td>
<td>? ? ● ● ● ? ● ?</td>
</tr>
</tbody>
</table>

Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias
Figure 4.43: Analysis 8.1 Comparison 8 – Silver ring system on catheter versus none, Outcome 1 Peritonitis (number of patients with one or more episodes)

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Experimental Events</th>
<th>Control Events</th>
<th>Risk Ratio M–H, Random, 95% CI</th>
<th>Risk Ratio M–H, Random, 95% CI</th>
<th>Risk of Bias A</th>
<th>B</th>
<th>C</th>
<th>D</th>
<th>E</th>
<th>F</th>
<th>G</th>
</tr>
</thead>
<tbody>
<tr>
<td>SIPROCE Study 1997</td>
<td>16</td>
<td>18</td>
<td>0.90 [0.49, 1.66]</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Risk bar: 0.01 0.1 1 10 100
Favours silver ring Favours control
Figure 4.44: Analysis 8.2 Comparison 8 – Silver ring system on catheter versus none, Outcome 2 Exit site/tunnel infection (number of patients with one or more episodes)

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Experimental Events</th>
<th>Control Events</th>
<th>Risk Ratio M–H, Random, 95% CI</th>
<th>Risk Ratio M–H, Random, 95% CI</th>
<th>Risk of Bias</th>
</tr>
</thead>
<tbody>
<tr>
<td>SIPROCE Study 1997</td>
<td>35</td>
<td>28</td>
<td>1.26 [0.84, 1.90]</td>
<td></td>
<td>✳</td>
</tr>
</tbody>
</table>

**Risk of bias legend**
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias
Chapter 4: Antimicrobial agents for preventing peritonitis in peritoneal dialysis patients

Figure 4.45: Analysis 8.3 Comparison 8 - Silver ring system on catheter versus none, Outcome 3 Catheter removal or replacement (number of patients)

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Experimental Events</th>
<th>Total</th>
<th>Control Events</th>
<th>Total</th>
<th>Risk Ratio M-H, Random, 95% CI</th>
<th>Risk Ratio M-H, Random, 95% CI</th>
<th>Risk of Bias</th>
</tr>
</thead>
<tbody>
<tr>
<td>SIFROCE Study 1997</td>
<td>5</td>
<td>97</td>
<td>4</td>
<td>98</td>
<td>1.26 [0.35, 4.56]</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias
## Figure 4.46: Analysis 8.4 Comparison 8 - Silver ring system on catheter versus none, Outcome 4 Mortality (all-cause)

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Experimental Events</th>
<th>Total</th>
<th>Control Events</th>
<th>Total</th>
<th>Risk Ratio M-H, Random, 95% CI</th>
<th>Risk Ratio M-H, Random, 95% CI</th>
<th>Risk of Bias</th>
</tr>
</thead>
<tbody>
<tr>
<td>SIPROCE Study 1997</td>
<td>5</td>
<td>97</td>
<td>8</td>
<td>98</td>
<td>0.63 [0.21, 1.86]</td>
<td></td>
<td>F</td>
</tr>
</tbody>
</table>

**Risk of bias legend**

(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias
Figure 4.47: Analysis 9.1 Comparison 9 – Antistaphylococcal vaccine (Staphypan) versus placebo, Outcome 1 Peritonitis rate (episodes/total patient-months on PD)

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Treatment Events</th>
<th>Treatment Total</th>
<th>Control Events</th>
<th>Control Total</th>
<th>Risk Ratio M–H, Random, 95% CI</th>
<th>Risk Ratio M–H, Random, 95% CI</th>
<th>Risk of Bias A</th>
<th>Risk of Bias B</th>
<th>Risk of Bias C</th>
<th>Risk of Bias D</th>
<th>Risk of Bias E</th>
<th>Risk of Bias F</th>
<th>Risk of Bias G</th>
</tr>
</thead>
<tbody>
<tr>
<td>Poole-Warren 1991</td>
<td>57</td>
<td>552</td>
<td>51</td>
<td>547</td>
<td>1.11 [0.77, 1.59]</td>
<td></td>
<td>?</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>

Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias
Figure 4.48: Analysis 9.2 Comparison 9 - Antistaphylococcal vaccine (Staphypan) versus placebo, Outcome 2 Exit site/tunnel infection rate (episodes/total patient-months on PD)

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Treatment</th>
<th>Control</th>
<th>Risk Ratio M−H, Random, 95% CI</th>
<th>Risk Ratio M−H, Random, 95% CI</th>
<th>Risk of Bias</th>
</tr>
</thead>
<tbody>
<tr>
<td>Poole–Warren 1991</td>
<td>43 565</td>
<td>42 542</td>
<td>0.98 [0.65, 1.48]</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Risk of bias legend**
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias
Figure 4.49: Analysis 10.1 Comparison 10 – Antifungal versus placebo/no treatment, Outcome 1 Fungal peritonitis (number of patients with one or more episodes)

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Experimental Events</th>
<th>Control Events</th>
<th>Weight</th>
<th>Risk Ratio M-H, Random, 95% CI</th>
<th>Risk Ratio M-H, Random, 95% CI</th>
<th>Risk of Bias</th>
</tr>
</thead>
<tbody>
<tr>
<td>Restrepo 2010</td>
<td>3</td>
<td>15</td>
<td>45.9%</td>
<td>0.20 [0.06, 0.68]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lo 1996</td>
<td>4</td>
<td>11</td>
<td>54.1%</td>
<td>0.36 [0.12, 1.12]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>409</td>
<td>408</td>
<td>100.0%</td>
<td>0.28 [0.12, 0.63]</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Total events: 7

Heterogeneity: $\tau^2 = 0.00$, $\chi^2 = 0.49$, df = 1 ($P = 0.48$); $I^2 = 0$

Test for overall effect: $Z = 3.04$ ($P = 0.002$)

Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Favours prophylaxis Favours control
Figure 4.50: Analysis 10.2 Comparison 10 - Antifungal versus placebo/no treatment, Outcome 2 Fungal peritonitis rate (episodes/total patient-months on PD)

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Experimental Events</th>
<th>Experimental Total</th>
<th>Control Events</th>
<th>Control Total</th>
<th>Risk Ratio M-H, Random, 95% CI</th>
<th>Risk Ratio M-H, Random, 95% CI</th>
<th>Risk of Bias</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lo 1996</td>
<td>4</td>
<td>3576</td>
<td>12</td>
<td>3288</td>
<td>0.31 [0.10, 0.95]</td>
<td></td>
<td>☣ ☣ ☣ ☣ ☣ ☣ ☣ ?</td>
</tr>
</tbody>
</table>

Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias
4.9 References

References to studies: Included studies

**Axelrod 1973**

**Bennet-Jones 1988**

**Bernardini 1996**

**Bernardini 2005**
Blowey 1994

Cheng 1999a

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5.1 Abstract

Background: Clinical practice guidelines exist to reduce the rates of peritoneal dialysis (PD) - related infections, a common complication of PD in end-stage kidney disease patients. We describe the clinical practices used by Australian and New Zealand nephrologists to prevent PD-related infections in PD patients.

Methods: A survey of PD practices in relation to the use of antibiotic and antifungal prophylaxis in PD patients was conducted of practising nephrologists identified via the Australia and New Zealand Society of Nephrology (ANZSN) membership in 2013.

Results: Of 333 nephrologists approached, 133 (39.9%) participated. Overall, 127 (95.5%) nephrologists prescribed antibiotics at the time of Tenckhoff catheter insertion, 85 (63.9%) routinely screened for nasal S. aureus carriage, with 76 (88.4%) reporting they treated S. aureus carriers with mupirocin ointment. Following Tenckhoff catheter insertion, 79 (59.4%) prescribed mupirocin ointment at the exit site or intranasally, and 93 (69.9%) nephrologists routinely prescribed a course of oral antifungal agent whenever their PD patients were given a course of antibiotics.

Conclusions: Although the majority of nephrologists prescribe antibiotics at the time of Tenckhoff catheter insertion, less than 70%
routinely prescribe mupirocin ointment and/or prophylactic antifungal therapy. This variation in practice in Australia and New Zealand may contribute to the disparity in PD-related infection rates that is seen between units.

Key words: Antibiotic prophylaxis; antifungal agents; kidney failure, chronic; peritoneal dialysis; practice guideline.

### 5.2 Introduction

Peritoneal dialysis (PD) is an effective home-based dialysis modality suitable for many patients with end-stage kidney disease (ESKD).

Recurrent or severe exit-site infections (ESIs) and peritonitis are frequent complications which often result in Tenckhoff catheter removal and PD technique failure (1, 2). Up to one-third of all PD peritonitis episodes result in hospitalization and 5 - 10% of cases lead to death (3, 4). Hence, reducing PD-related infections may be both cost-saving and lead to reduced morbidity and mortality in PD patients.

Peritoneal dialysis technique survival in Australia and New Zealand (ANZ) is lower than in most other developed countries (5). From 2002 - 2005, the median technique survival in Australia was 1.8 years while in New Zealand it was 2.4 years (5). In comparison, Thailand had a reported median technique survival of 3.4 years (1995 - 2005) and Mexico a median technique survival of 4.0 years (1985 - 1997) (5). Peritonitis rates in ANZ are significantly greater than those reported in many other countries. According to the International Society for Peritoneal Dialysis (ISPD) guidelines, the PD peritonitis rate should not exceed 0.36 episodes per
patient-year (6). As reported in the 2013 ANZDATA Registry Report, the overall peritonitis rate in Australia was 0.50 episodes per patient-year while in New Zealand it was 0.57 episodes per patient-year for the period 1 January to 31 December 2012 (7). These rates are worse than the revised ISPD minimum peritonitis rate of 0.36 episodes per patient-year (6). The majority of ANZ PD units do not meet the revised minimum peritonitis rate (7).

With regard to infection prophylaxis, the appropriate use of antibiotics at the time of and after Tenckhoff catheter insertion, care of exit sites and the judicious use of prophylactic antifungal agent are essential to reduce the risk of PD-related infections and associated technique failure. Post-operative infection after catheter placement has been shown to be reduced by the use of intravenous antibiotic administration prior to or at the time of Tenckhoff catheter insertion (8). Exit-site colonisation and infection is one of the recognized ways for peritonitis to start (9). The development of ESI places patients at increased risk of developing peritonitis, with this association being present up to 60 days after initial diagnosis (10). Episodes of fungal peritonitis are known to be frequently preceded by a course of antibiotics and patients taking prolonged or frequent courses are most at risk. It has been shown that fungal prophylaxis during antibiotic therapy may prevent cases of *Candida* and other fungal peritonitis (6). Fungal peritonitis is associated with significant morbidity and mortality, a high likelihood of Tenckhoff catheter removal and high rates of permanent transfer to hemodialysis due to peritoneal membrane injury (11).

Although both ISPD and the local KHA-CARI guidelines explicitly recommend appropriate prophylactic antibiotic and antifungal use to reduce
PD-related infections, a survey of Australian and New Zealand nephrologists conducted in 2009 showed that many failed to adhere to these guidelines, with 14 of 30 PD units (47%) reporting the absence of a local protocol that included prophylaxis against exit-site infections (12). A study which looked at Australian registry data found that antifungal prophylaxis during treatment for bacterial peritonitis was only given in 7% of peritonitis episodes (11). There is substantial variation in the peritonitis rates between PD units in Australia and New Zealand (7,13,14), with the lack of consistency in PD program management or guideline implementation being blamed (5,15). With continuing high rates of PD-related peritonitis being reported, it is therefore imperative to determine if nephrologists are adhering to best practice guidelines.

Guideline implementation in PD units is dependent on the actions of the treating physician, PD nursing staff, and/or those in charge of the PD program. There is little data on the current antimicrobial prophylactic practices in place at PD units in Australia and New Zealand. We therefore designed a self-administered survey to elicit information about current practice in ANZ PD units around the topic of PD-related infection prevention.

5.3 Methods

Survey Instrument

Draft survey questions were developed by a project officer and piloted among several nephrologists in Australia and New Zealand. Revisions were made in response to the comments received.
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The survey was composed of 4 parts. The first assessed current practice in relation to the use of prophylactic antibiotics at Tenckhoff catheter insertion; the second, the use of prophylactic antibiotics to prevent exit-site/tunnel infection; the third asked about the concurrent use of antifungal agents when a PD patient is given a course of antibiotics; the fourth asked for details regarding the type of Tenckhoff catheter inserted, the specialty of the operator and the surgical technique used. Demographic details of the respondents were also collected (gender, age, years of practice in nephrology, place of residence, location of current practice/s). These aspects of infection prevention in PD patients were chosen because of their importance in reducing peritonitis incidence and there are evidence-based guideline recommendations on which to base practice. The questions about access surgery were included as it was felt that practice was changing, and the survey provided an opportunity to gather this data.

Participants

The link for the web-based survey was emailed to all members of the Australian and New Zealand Society of Nephrology (ANZSN) through the ANZSN office in June 2013. A cover letter invited consultant nephrologists caring for PD patients to participate, explained the aims of the survey and gave instructions on how to access the survey. Reminder emails were sent 1, 3 and 4 weeks after the initial email. A further email was sent to nephrologists listed in the KHA-CARI database in August 2013 to obtain more responses. The survey ended in September 2013.

Statistical analyses

The proportions of respondents who gave antibiotic prophylaxis at
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Tenckhoff catheter insertion, who screened and treated nasal *S. aureus* carriers, who used antibiotic prophylaxis at the exit site, and who gave antifungal prophylaxis whenever a PD patient received an antibiotic course were calculated. The type of antibiotic, duration of treatment and use of other cleaning agents was also calculated. Data relating to Tenckhoff catheter insertion practices were also categorized and calculated.

### 5.4 Results

We report data obtained in relation to the first 3 parts of the survey. One hundred and thirty-three (39.9%) of the 333 actively practising nephrologists responded to all questions in the survey. For Australia, data from 44/68 (64.7%) centres covering 2894/3358 (86.2%) patients were received. Of these, 15 were large-size units with >60 PD patients, 15 were medium-size units with >30 but <60 PD patients, and 14 were small-size units with <30 PD patients. For the key questions about prophylactic practice, nephrologists working at large centres contributed an average of 51.3% of the responses.

For New Zealand, responses were received from 11/12 centres with prevalent PD patients, covering 819/849 patients (96.5%). Three of the centres could be classified as large-size units with >100 PD patients, 4 were medium-size units with >40 but <100 PD patients and 4 were small-size units with ≤40 PD patients. For the key prophylaxis questions, nephrologists at large centres contributed 43.8% of the responses. Chi-squared analysis of the responses to the 3 key questions according to unit size found no significant difference between the practices at units according to size, with the exception of the data for New Zealand regarding the use of mupirocin. For this practice, there was greater use of mupirocin at medium- and small-size units than at large-size
The baseline characteristics of nephrologists participating in the survey are shown in Table 1. Over 70% were men with 65% aged less than 50 years. Almost 30% have over 20 years of clinical experience.

Respondences to the questions about the use of antibiotic prophylaxis and the screening and treatment of nasal *S. aureus* carriers are detailed in Table 2. Overall, 95.5% of all respondents give antibiotics at catheter insertion, 63.9% screen for nasal *S. aureus*, 88.4% treat identified *S. aureus* carriers, and 59.4% apply mupirocin ointment intranasally or at the exit site on a regular basis. Responses to the questions regarding the use of antifungal prophylaxis are shown in Table 3. A total of 69.9% of respondents give antifungal prophylaxis to PD patients when they are prescribed an antibiotic course.

**Respondents’ prophylaxis practices at catheter insertion**

The prophylactic antibiotic most commonly given at the time of Tenckhoff catheter insertion was a cephalosporin (88.7%) followed by vancomycin (22.6%), with some stating that vancomycin is used when a patient has previously screened positive for methicillin-resistant *S. aureus* (MRSA) or is allergic to penicillin.

**Respondents’ prophylaxis practices to prevent exit-site/tunnel infections**

Eighty-five respondents (63.9%) reported that they swab to detect nasal carriage of *S. aureus* and 76 (88.4%) said they treated anyone identified as a nasal *S. aureus* carrier. The length of antibiotic treatment given varied widely, with the most common treatment length being for 3-7 days (23 respondents [31.9%]) followed by 2 weeks (13 respondents [18.1%]).
Seventy-nine respondents (59.4%) stated that exit-site care to prevent *S. aureus* colonization at the exit site included the use of mupirocin ointment. Other practices included antibacterial wash (43 respondents [32.3%]), use of betadine wipes (31 respondents [23.3%]), and soap and water (36 respondents [27.1%]). Others (27 respondents [20.3%]) used nothing, saline wash or medicated honey.

**Respondents’ prophylaxis practices to prevent fungal peritonitis**

Ninety-three individuals (69.9%) reported that they routinely give antifungal prophylaxis with an antibiotic course in PD patients. The duration of treatment varied, with 55 (59.1%) saying they give the antifungal for the same length of time as the antibiotics and 37 (39.8%) saying that they give it for 3 days longer than the antibiotic course.

**5.5 Discussion**

Adherence to international and national guidelines to prevent PD-related infections has been shown to reduce the rates of technique failure and infection-related morbidity (16, 17). In Australia and New Zealand in 2012, PD peritonitis rates varied between 1.0 and 0.1 episodes per patient-year, with 21 of 62 (33.9%) centers with peritonitis rates above the recommended minimum rate of 0.36 episodes per patient-year. Our survey of 133 practising nephrologists in Australia and New Zealand showed a wide variation in clinical practice, with approx. 30 - 40% not adhering to published guidelines, particularly regarding the screening of patients for *S. aureus* nasal carriage, the use of mupirocin ointment either nasally or at the exit site, and the use of antifungal prophylaxis with an antibiotic
course, which are likely to contribute to the higher rates of PD-related infections observed in the 2 countries. The guideline recommendations chosen as the focus of this survey are either based on the findings of randomized controlled trials (RCTs) or a systematic review of all relevant RCTs.

The KHA-CARI guidelines published in 2004 recommended that antibiotic prophylaxis using a first generation cephalosporin should be administered at the time of PD catheter insertion to reduce the risk of PD-related infections, including catheter-site infection, peritonitis, and wound sepsis (18). The guidelines also recommended that vancomycin not be prescribed routinely because of the potential for developing resistant microorganisms (18). There was a slight amendment to the 2004 KHA-CARI guidelines in August 2013, which suggested that a single intravenous dose of vancomycin, cephalosporin, or gentamicin can be prescribed prior to PD catheter insertion, although vancomycin should be used cautiously to avoid the emergence of vancomycin-resistant enterococci and S. aureus (19). The ISPD guidelines, published in 2011, provided similar recommendations to those of the 2013 KHA-CARI guidelines (6). Ninety-five per cent of survey respondents stated that antibiotic was given with PD catheter insertion with 24.4% being given prior to surgery and 72.4% being given intra-operatively. Cephalosporin was the antibiotic most frequently used (88.7%) followed by vancomycin (22.6%). Nearly 46% of respondents reported using vancomycin in PD patients who were screened positive for methicillin-resistant S. aureus (MRSA) and nearly 32% of respondents prescribed this in patients with penicillin allergy. These behaviours broadly reflect the
guideline recommendations but only one quarter of respondents stated that the prophylactic antibiotic is given before PD catheter surgery. There is evidence supporting the administration of antibiotic in the 2 hours before surgery commences rather than at the same time as surgery is performed, which ensures the attainment of high concentrations of antibiotics in the wound during the operation (20-23).

Nasal carriage of *S. aureus* is considered to be a strong risk factor for the development of ESI and peritonitis (24). The 2004 KHA-CARI guidelines stated that the prophylactic use of mupirocin ointment, particularly in *S. aureus* nasal carriers, is recommended to decrease the risk of *S. aureus* catheter exit-site/tunnel infections and peritonitis (18). The updated KHA-CARI guidelines recommend that mupirocin ointment be used intranasally or topically at the exit site to reduce the risk of *S. aureus* catheter exit-site/tunnel infections and peritonitis (19). The ISPD guidelines recommend that all PD patients use topical antibiotic at the catheter exit site and/or intranasally (6). The survey responses show that 63.9% perform nasal swabs to identify patients/carers/staff who are *S. aureus* carriers and almost 90.0% treated those patients who were identified as *S. aureus* nasal carriers. It is unclear from our survey what the rationale is for why 10% of clinicians do not treat *S. aureus* nasal carriers after a positive result. However, this preventive approach to reduce *S. aureus* ESI and peritonitis has often been criticised for the lack of proven cost-effectiveness, being difficult to implement in clinical practice and for its potential to promote *S. aureus* resistance (25,26). Duration of treatment for those who screen positive varied widely, ranging from 3 - 7 days (31.9%), which is in line with published recommendations, to 3 months (20.8%) (27).
The survey responses reveal that 59.4% instruct patients to routinely apply mupirocin ointment either intranasally or to the exit site in addition to using various cleansing/antiseptic agents while 20.3% of respondents said they use ‘other’ means of caring for the exit site. The majority of respondents prescribed antiseptics and/or antibiotics but 7 (5.3%) do not routinely use any agents. There is RCT evidence supporting the use of mupirocin at the exit site and its ability to reduce the incidence or rates of ESI and peritonitis attributed to *S. aureus* or Gram-positive organisms (17,28). A recent systematic review confirmed the ability of mupirocin applied intranasally to significantly reduce the risk of ESI and peritonitis due to *S. aureus*, based on three RCTs (29).

Intranasal mupirocin was also found to reduce the risk of ESI by 46% but did not reduce the risk of peritonitis due to all organisms (29). When this survey was conducted, some units were participating in the HONEYPOT trial and had been randomized to have their patients apply medicated honey at the exit site or to use nasal mupirocin prophylaxis in identified *S. aureus* carriers (30,31). Participation in this trial would explain some of the 40.6% of respondents who report they do not instruct patients to use mupirocin ointment at the exit site. The use of topical antiseptics for chronic exit-site care and the application of mupirocin only in PD patients identified as *S. aureus* carriers is common in some countries (32). It has been suggested that this approach is likely to reflect the concerns of clinicians and nurses of the emergence of bacterial resistance to mupirocin or aminoglycosides in general and the positive selection of other pathogenic organisms such as *Pseudomonas* spp., when topical antibiotic is used routinely in long-term patients.
Both the ISPD and KHA-CARI guidelines recommend the routine prophylactic use of antifungal agent such as nystatin to prevent fungal peritonitis occurring when a PD patient is prescribed a course of antibiotics. The KHA-CARI guideline recommendations on antifungal prophylaxis published in 2004 state that the use of oral nystatin should be considered at the time of antibiotic administration to PD patients (18). The updated guideline continues these recommendations (19). They also suggest that oral nystatin is preferred to fluconazole as prophylaxis because of the risk of development of resistance to fluconazole with increased exposure. The ISPD guidelines outline that most episodes of fungal peritonitis are preceded by courses of antibiotics and that fungal prophylaxis during antibiotic therapy may prevent some cases of peritonitis due to Candida spp. in programs that have high rates of fungal peritonitis (6). Our survey results show that almost 1 in 3 nephrologists do not routinely give an antifungal agent when a PD patient receives an antibiotic course. The evidence supporting these recommendations comes from a number of observational studies and 2 RCTs (33,34) which have shown benefit in terms of reducing episodes of fungal peritonitis. The trial by Lo et al. (33) investigated whether Candida peritonitis (CP) was prevented when continuous ambulatory PD (CAPD) patients in Hong Kong were given oral nystatin concomitant with antibiotic therapy. The treatment group (199 patients) received nystatin tablets 500,000 units 4 times a day whenever antibiotics were prescribed while the control group (198 patients) received only their antibiotic therapy. At 2 years, the probability of being free of CP was higher in the antifungal treatment vs control group (0.974 vs 0.915; p < 0.05). The authors concluded that giving oral nystatin
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prophylaxis with each antibiotic prescription reduced the CP rate in patients.

The trial conducted by Restrepo et al. (34) in Colombia assessed whether giving oral fluconazole whenever a PD patient was treated for bacterial peritonitis, exit-site infection, or tunnel infection could prevent the development of fungal peritonitis. Patients in the treatment group received oral fluconazole (200 mg every 48 hours) for the entire time that they received therapeutic antibiotics by any route. In those patients who received oral fluconazole, 3 occurrences of fungal peritonitis were found within 30 – 150 days following the end of antibiotic therapy. In contrast, the group that received no antifungal therapy had 15 occurrences of fungal peritonitis over the same timeframe. For patients treated for bacterial peritonitis, the difference between the 2 groups regarding the development of secondary fungal peritonitis was significant (p = 0.0051). The authors concluded that in patients treated for bacterial peritonitis, the administration of fluconazole during the period they received antibiotics significantly reduced the appearance of secondary fungal peritonitis.

The ISPD guideline recommendations are less defined than are the KHA-CARI recommendations and emphasize that the use of antifungal therapy should be modified by local microbiology. The fact that we found nearly 1 in 3 nephrologists do not use antifungal prophylaxis may reflect a lack of awareness of the guideline recommendations or a belief that the local rates of fungal peritonitis are low and prophylaxis is not warranted. However, this response represents an improvement in antifungal prescribing having previously been reported that 92% of peritonitis episodes in Australian patients did not receive antifungal prophylaxis (5).
Our study has several limitations. Firstly, our response rate of 39.9% was low but similar to the response rates reported by other similar surveys (12, 35-37). The response rate might have been improved by the inclusion of PD nurses in the survey. Secondly, the responses given may only represent how nephrologists would ideally practice. Only an audit of practice could reliably ascertain actual practice. Thirdly, those who completed the survey may be more interested in the care of PD patients than non-respondents and hence, be a self-selected group whose practice might be significantly different to the rest of the ANZ nephrology community. Fourthly, 73% of respondents were in the 41 to 60 age group and it may be that the responses of younger nephrologists are under-represented. Lastly, we did not include a question asking why nephrologists choose not to follow a guideline recommendation. It is known that there are many reasons for physician non-adherence to guideline recommendations, including lack of awareness, lack of familiarity, disagreement with a recommendation, perceived lack of self-efficacy, lack of faith in achievement of the desired outcome, the inertia of previous practice, and external barriers, which can be guideline-related, patient-related or environmental in nature (38).

A strength of the study is that the sample of nephrologists was mostly obtained via the Australia and New Zealand Society of Nephrology database, so is representative of the practising nephrologists in Australia and New Zealand.

In Australia and New Zealand, there is a wide variation in clinical practice to prevent PD-related infections, with most variation occurring around the use of mupirocin to prevent exit-site infection and the co-administration of an
antifungal agent with an antibiotic course. Despite wide dissemination, guidelines on their own have a limited effect on changing clinical practice (39,40). It has been shown that multifaceted interventions that target a number of barriers to change are more likely to be effective than a single intervention in changing clinical behavior (41). One approach to improve PD practice involves the setting up of quality improvement collaboratives where groups of preofessionals from several centers learn fom and motivate each other to achieve a common objective (42–44). These often involve the delivery of a care bundle based on the guidance. Other means of improving practice include the publishing of comparative PD outcomes (e.g. by nephrology registries), the use of multidisciplinary team-based meetings with a focus on quality improvement (45), the performance of a root-cause analysis to each peritonitis episode to identify aspects that need improvement (46), and the sharing of clinical practice routines by those units that have excellent peritonitis rates so that others may benefit from their experience (6). The findings of this study show that practice varies widely between centers and the 2 countries involved in the survey and we outline some of the means by which the gap between health services research and health care delivery might be reduced.
**Table 5.1: Baseline characteristics of survey respondents (n=133)**

<table>
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<td>Rural</td>
<td>14</td>
<td>9.2</td>
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</tbody>
</table>

*Numbers are not additive as some individuals work in more than one location*
Table 5.2: Practice patterns for antibiotic prophylaxis and nasal screening and treatment in PD patients

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Response</th>
<th>n</th>
<th>%</th>
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<tbody>
<tr>
<td><strong>Give antibiotic at catheter insertion</strong></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Give antibiotic at catheter insertion</td>
<td>Yes</td>
<td>127</td>
<td>95.5</td>
</tr>
<tr>
<td><strong>Timing of antibiotic administration</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prior to surgery</td>
<td></td>
<td>31</td>
<td>24.4</td>
</tr>
<tr>
<td>At time of surgery</td>
<td></td>
<td>92</td>
<td>72.4</td>
</tr>
<tr>
<td>Other*</td>
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<td>3.2</td>
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<tr>
<td><strong>Antibiotic given</strong></td>
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</tr>
<tr>
<td>Vancomycin</td>
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<td>30</td>
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</tr>
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<td>None</td>
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<td>3.0</td>
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<tr>
<td>Other</td>
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<td>6</td>
<td>4.5</td>
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Table 5.2: Practice patterns for antibiotic prophylaxis and nasal screening and treatment in PD patients (continued)

| Practice patterns for the screening (n = 133) and treatment (n = 86) of nasal *S. aureus* carriers |
|---------------------------------------------|---------------------------------|-----------------|
| Characteristic                             | Response                        | n   | %     |
| Swab for nasal *S. aureus*                 | Yes                             | 85  | 63.9  |
| Treat identified carriers                  | Yes                             | 76  | 88.4  |
| Length of antibiotic treatment (n = 72)     | Single dose                     | 1   | 1.3   |
| 3-7 days                                    |                                 | 23  | 31.9  |
| 2 weeks                                     |                                 | 13  | 18.1  |
| 3-6 weeks                                   |                                 | 10  | 13.9  |
| 3 months                                    |                                 | 15  | 20.8  |
| Other                                       |                                 | 10  | 13.9  |

| Practice patterns for care of the exit site (n = 133) |
|-----------------------------------------------|-----------------|-----------------|
| Characteristic                               | Response        | n   | %     |
| Exit site care practice                      | Mupirocin ointment† | 79  | 59.4  |
|                                              | Antibacterial wash | 43  | 32.3  |
|                                              | Betadine wipes    | 31  | 23.3  |
|                                              | Soap and water   | 36  | 27.1  |
|                                              | Other            | 27  | 20.3  |

*Both times are used, depending on who is inserting the catheter; †includes nasal or exit site application
### Table 5.3: Practice patterns for antifungal prophylaxis in PD patients

<table>
<thead>
<tr>
<th>Characteristic</th>
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<tbody>
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<td>Give antifungal agent</td>
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<td>69.9</td>
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<td>Duration of treatment</td>
<td>Same duration as the antibiotics</td>
<td>55</td>
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<tr>
<td></td>
<td>For 3 days longer than the antibiotics</td>
<td>37</td>
<td>39.8</td>
</tr>
</tbody>
</table>
Chapter 5: Infection prophylaxis in peritoneal dialysis patients: results from an Australia/New Zealand survey

5.6 References


34. Restrepo C, Chacon J, Manjarres G. Fungal peritonitis in peritoneal dialysis patients: successful prophylaxis with fluconazole, as demonstrated by prospective randomized control trial. [Erratum


43. Toussaint ND, McMahon LP, Dowling G, Soding J, Safe M, Knight


Chapter 6: Patients’ perspectives on the prevention and treatment of peritonitis in peritoneal dialysis: a semi-structured interview study

6.1 Abstract

Background: Peritoneal dialysis (PD) is recommended for adults with residual kidney function and without significant comorbidities. However, peritonitis is a serious and common complication that is associated with hospitalization, pain, catheter loss and death. This study aims to describe the beliefs, needs, and experiences of PD patients about peritonitis, to inform the training, support, and care of these patients.

Methods: Qualitative semi-structured interviews were conducted with 29 patients from 3 renal units in Australia who had previous or current experience of PD. The interviews were conducted between November 2014 and November 2015. Transcripts were analyzed thematically.

Results: We identified 4 themes: constant vigilance for prevention (conscious of vulnerability, sharing responsibility with family, demanding attention to detail, ambiguity of detecting infection, ineradicable inhabitation, jeopardizing PD success); invading harm (life-threatening, wreaking internal damage, debilitating pain, losing control and dignity); incapacitating lifestyle interference (financial strain, isolation and separation, exacerbating burden on family); and exasperation with hospitalization (dread of hospital admission, exposure to infection, gruelling follow-up schedule, exposure to harm).

Conclusions: Patients perceived that peritonitis could threaten their health,
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treatment modality, and lifestyle, which motivated vigilance and attention to hygiene. They felt a loss of control due to debilitating symptoms including pain, having to be hospitalized, and were uncertain about how to monitor for signs of peritonitis. Providing patients with education about the causes and signs of peritonitis and addressing their concerns about lifestyle impact, financial impact, hospitalization, and peritonitis-related anxieties may improve treatment satisfaction and outcomes for patients requiring PD.

6.2 Introduction

Although incidence rates of peritonitis have decreased substantially with technological advances in peritoneal dialysis (PD), peritonitis rates in many countries still exceed 0.4 episodes per patient year (1, 2). Worldwide, peritonitis is the direct cause of 4% of deaths in patients on PD and is a “contributing factor” in at least 16% of deaths on PD. Furthermore, peritonitis is a leading cause of hospitalization and technique failure in PD whereby patients must transfer to hemodialysis (3-10).

To minimize the risk of peritonitis, patients are required to perform an exchange following the procedure they have been taught, paying attention to aseptic technique and ensuring excellent hand hygiene. They also need to clean and care for their exit site as taught and assess the exit site regularly for any signs of infection. They need to be aware that severe constipation or diarrhea can lead to peritonitis and take steps to prevent the occurrence of constipation, and they should also be aware that certain medical procedures can lead to peritonitis and that they need to be given antibiotics with these procedures (11). All of these demands on the patient can interfere with lifestyle and cause anxiety.
A systematic review of qualitative studies of the perspectives of adults on PD found that PD can offer a sense of control, independence, self-efficacy, and freedom but patients also reported impaired self-esteem, physical incapacitation, and reduced social functioning (12). However, there were limited data specifically about peritonitis and comparisons between automated PD (APD) and continuous ambulatory PD (CAPD) were sparse.

This study aims to describe patients’ beliefs, needs, and experiences about peritonitis in PD. An understanding of their beliefs and attitudes can inform strategies to help and empower patients in preventing peritonitis. Awareness of their concerns and needs when receiving treatment for peritonitis can inform support structures and lead to better treatment and health outcomes.

### 6.3 Methods

We used the Consolidated Criteria for Reporting Qualitative Health Research (COREQ) to report this study (13).

**Participants and setting**

Participants were eligible for interview if they were English-speaking, over 18 years of age, able to give informed voluntary consent, and had previous or current experience with PD. Purposive sampling was used to include participants with a range of ages, gender, experiences of APD and CAPD, and peritonitis episodes. Participants were recruited from Princess Alexandra Hospital, Brisbane; Westmead Hospital, Sydney; and Monash Medical Centre, Melbourne. Ethics approval was obtained from all 3 sites.
Data collection

We developed the interview guide after a review of the literature based on a systematic review of patients’ experiences of PD and discussion among the research team (Table S1). Face-to-face interviews were performed by the primary investigator (DC) between November 2014 and November 2015. DC is a researcher with training in public health and interest in PD. Recruitment ceased once theoretical saturation was observed in the concurrent analysis, when little or no new data was obtained after 3 consecutive interviews. All interviews were recorded digitally and transcribed verbatim.

Data analysis

The transcripts were imported into HyperRESEARCH (Version 2.8.3; Research Ware Inc., MA, US) to facilitate thematic analysis. The principles of grounded theory were followed (i.e. the development of a theory or explanation grounded in the data collected) (14). Each transcript was reviewed line by line by DC and meaningful segments of text were highlighted and given an appropriate code according to the concepts that had been identified inductively in the data. Similar concepts were grouped into themes. The coding was reviewed by AT who also read the interview transcripts. A schema was developed to show conceptual relationships between the themes. The preliminary concepts were discussed among the study authors (investigator triangulation). DC revised the coding structure until it included all concepts about patient beliefs and experiences regarding peritonitis.
6.4 Results

Twenty-nine patients from 3 Australian states participated (88% response rate). Non-participation (n = 4) was due to refusal or inability to set a suitable interview time after 3 attempts. The average duration of the interview was 40 minutes, which was conducted in person (n = 27) or via Skype (n = 2). The participant demographic characteristics are shown in Table 1.

We identified 4 major themes: constant vigilance for prevention, invading harm, incapacitating lifestyle interference, and exasperation with hospitalization. The themes and related subthemes are described in the following section with illustrative quotations provided in Table 2. A thematic schema showing the patterns and relationships among themes is provided in Figure 1.

Constant vigilance for prevention

Conscious of vulnerability: Peritonitis was “always in the back of your mind” and represented a threat to participants’ health and lives. Participants who had experienced peritonitis were fearful of recurrence and felt particularly susceptible during a bag exchange or when they made a mistake as “germs could get in.” Those who had not had peritonitis were “mindful” of the possibility of peritonitis because they had seen other patients with peritonitis. For some, they felt “panic” during the first few times they did an exchange.

Sharing responsibility with family: Some participants stressed family members had to be “educated as much as we are” so that their family would not be overwhelmed. Participants wanted to be able to depend on them for help. Others felt that their family members demonstrated a lack
Chapter 6: Patients’ perspectives on the prevention and treatment of peritonitis in peritoneal dialysis: a semi-structured interview study

of care and consideration “because they just don’t understand how
important it is.”

Demanding attention to detail: The cleaning demands of doing an exchange
were rigorous, such that patients felt it “just drives you insane.” They were
careful to “follow all of the instructions.” Some deliberately did an exchange
in a slow methodical manner, some timed how long they washed their hands
for, turned off anything that would move air around the room (e.g. fan, heater,
air conditioner) and closed the windows and doors before they commenced an
exchange. Others checked the dates of their dialysate bags, gauze and any
other items they used. Participants were careful to not “have shortcuts” and to
avoid becoming “careless or [overly] confident with their cleaning” as this
could result in peritonitis. One man felt under siege and that the attention to
detail required was overwhelming – “It could be anything … can’t wear a
fleecey shirt. A bit of fleece gets in there, you’re finished.”

Ambiguity of detecting infection: Participants had trouble identifying the first
signs of peritonitis and thought instead that they had the flu or that they had
gastrointestinal problems. Some experienced only localized pain which they
realized later was due to peritonitis. One participant recounted that their
general practitioner diagnosed a lower bowel infection but did not suspect
peritonitis. Women noticed that their bags became cloudy during ovulation
and menstruation, and panicked and went to hospital.

Ineradicable inhabitation: After experiencing peritonitis, some believed that
they “never fully clear the germs” and would always be prone to peritonitis.
Even after antibiotics, they believed the cause of the infection remained in
their system. Others said it had taken “a long time” to get rid of the infection.
Some participants who had a spontaneous infection, believed the peritonitis was caused by “a bug that just kind of happens” and that “the peritoneum … reacts to it [the fluid] and it gives you peritonitis.”

_Jeopardizing PD success:_ Participants wanted to remain on PD because it suited their lifestyle and offered more freedom and did not require cannulation. Aware that peritonitis could cause PD failure, patients were “worried” about being forced to go onto hemodialysis. Some hoped that they could “still do dialysis this way once [the peritonitis] cleared up.” Some had been warned that if they had 3 episodes of peritonitis, the decision could be made “to take you off peritoneal dialysis … and they will have to put a fistula in.”

**Invading harm**

_Life-threatening:_ Some were worried that they could die from peritonitis. Others were fatalistic, saying “If you die, you die because of my problem” while some said they felt so sick at the time that they thought “I just need to die.”

_Wreaking internal damage:_ Some participants anticipated that peritonitis would cause their “internal lining” to be “scarred” and “damaged.” They spoke of being “hit” with peritonitis and said that following peritonitis “everything changes” and that physically, they were “tender.”

_Debilitating pain:_ Although they had been told that peritonitis could be painful, participants were unprepared for the pain which they described as “enormous”, “massive”, “crumpling” and like “labour pain.” They became
unable to function as they were “hunched over” and “couldn’t do anything” and could “hardly move” or talk. They described the pain as quickly coming on and escalating rapidly to an “unbelievable” level.

Losing control and dignity: When going through a peritonitis episode, unpredictable occurrences such as falling unconscious in public, being unable to get off the toilet in the ward without assistance, and vomiting in public caused participants to feel embarrassed. Participants spoke of having “no control over your body” and the humiliation of other patients in the ward “knowing what’s going on.” For example, one participant who was very constipated because of peritonitis threw up faeces.

Incapacitating lifestyle interference

Financial strain: Having peritonitis meant that participants were unable to work or could only work part-time. For some, their partner had to take time off work. Some could not work for more than 1 month, 1 participant shut down their business, and others were concerned about being able to pay their mortgage. The accumulating cost of frequent hospital appointments to receive treatment for peritonitis also caused financial burden.

Isolation and separation: Being in hospital meant a disruption to normal family life and some participants were placed in isolation, so they could not interact with their family. Participants with young children worried about how others such as elderly parents were coping with caring for the children and realized their children would be “missing” them.

Exacerbating burden on family: Participants had to call on others such as a parent, spouse or ex-spouse to help them when they experienced a peritonitis
episode because they were too unwell to perform normal tasks. Family members helped in a variety of ways – calling the hospital for advice when the episode first started, driving the patient to hospital, bringing home-cooked food to the hospital each evening, visiting the patient each day, caring for the patient’s children, and helping to organize treatment at home for those who did not have to be hospitalized.

**Exasperation with hospitalization**

*Dread of hospital admission:* The thought of going to hospital “depressed” participants and was described as “a big price” to pay for making a mistake. Some participants had periods when they were in hospital “nearly every second month” and once there, they would be there for “a couple of weeks again.” They saw the hospital system as an impersonal one and that they were never consistently seen by one doctor.

*Exposure to infection:* Some were concerned about the perceived lack of knowledge regarding PD among general hospital staff. For example, 1 participant had a Tenckhoff catheter inserted on an emergency basis and was told by a ward nurse post-operation that she could go for a walk but later learned from the PD nurse that this could cause leakage. Another participant who was admitted to hospital with peritonitis believed “a doctor could’ve even infected me – he didn’t even wash his hands.”

*Gruelling follow-up schedule:* Managing treatment for peritonitis was confronting for some as they had to inject antibiotics into a dialysis bag. Participants had to go to hospital every 2 days for about 2 weeks to have a blood test to find out if they needed to continue with the antibiotic treatment.
and this “took a lot of time” out of their normal routine and was “a little frustrating” and “inconvenient” but was accepted by participants as unavoidable.

Receiving inattentive care: Some felt they received inadequate care from hospital staff. Some experienced intense pain the first time they were hooked up to the APD machine, and blamed staff for a lack of monitoring. Another patient was given treatment for high blood pressure but staff left him unattended, which led to him blacking out and “even though I had buzzed no one had come.”

6.5 Discussion

Peritonitis was an ever-present concern for patients on PD as it meant they would be in pain, vomiting, possibly embarrassed, needing to go to hospital, calling on family or friends for help, and unable to go to work.

Some participants felt that family members should be informed about the process and demands involved in doing PD so that they could depend on their support in preventing and managing peritonitis. Patients found the cleaning routine around doing an exchange to be demanding, more so for those on CAPD compared with APD because of the need to connect and disconnect more often. When peritonitis occurred, patients experienced panic, incapacitating pain, and felt embarrassed because they lost bodily control and normal function. Those who were hospitalized expressed concerns about finances and placing extra responsibilities on family members. Participants who received out-of-hospital treatment felt burdened by frequent visits to the renal unit, the need to inject antibiotics into dialysis
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bags, and the costs associated with travel to and from the clinic. Many participants had difficulty identifying the symptoms of peritonitis. Changes to the management and the provision of additional support to patients could help them to cope with the challenges they encounter when they have peritonitis.

The systematic review of qualitative studies on patients’ experiences of PD found that some patients regarded PD as onerous and a disruptive intrusion. However, there were limited data specifically on peritonitis (12). More recent studies on patient and family perspectives on PD have shown that patients and family members were aware of the threat of peritonitis, took measures to prevent infection, were uncertain of how to manage a crisis, and some could not recognize the symptoms of peritonitis (15). The procedures required to prevent infection were described as “daunting and time-consuming” and peritonitis was associated with fear and uncertainty (16). Patients’ fear of PD-associated peritonitis, placing a burden on family members, and lack of confidence in their ability to maintain proper PD self-care at home have been shown to be barriers to choosing PD as a dialysis modality (17). These were identified in our study. However, our study highlights that patients want family members to be better educated about PD and its requirements, some patients are unclear about the causes of peritonitis and do not believe the treatment they receive is fully effective, patients were strongly motivated to make PD work for them, they were unprepared for the level of pain they experienced and loss of bodily control. For those who could not work and especially those who were self-employed, they were worried about finances. Patients with young children were most
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centered about the separation that hospitalization brought and many patients spoke of the added responsibility that fell on family members when they had peritonitis. We also found that patients dreaded the idea of having to go to hospital, felt they were exposed to inferior treatment and possible infection when in hospital, and found the outpatient treatment schedule to be time-consuming and inconvenient.

In our study, we achieved theoretical saturation and conducted investigator triangulation to ensure that the analysis captured the range and depth of the data collected. However, there are some potential limitations. The transferability of the findings beyond Australia is uncertain but the similarity of our results with studies conducted in the UK suggests broad relevance to other settings. We did not interview non-English speaking participants to avoid cultural and linguistic misinterpretation. In addition, we did not explicitly ask participants if they would prefer hemodialysis to PD, so it is possible that our sample was biased towards remaining on PD.

Some participants in this study could not identify the symptoms of peritonitis and some thought the treatment they were given for peritonitis did not eradicate the cause. The International Society for Peritoneal Dialysis (ISPD) guidelines recommend that retraining occur 3 months after initial training and routinely after that (at least once/year), after hospitalization, after peritonitis or catheter infection, and after change in dexterity, vision, or mental acuity (11). More frequent retraining for patients could help clear up some of the misconceptions they have, reinforce what the symptoms of peritonitis are, and check whether the patient is performing an
Chapter 6: Patients’ perspectives on the prevention and treatment of peritonitis in peritoneal dialysis: a semi-structured interview study

exchange as they were taught. A home visit by a PD nurse to see
how the patient functions in their own environment has been
recommended but only some of the participants in this study had
received a home visit (18). The desire expressed for family members
to be educated about the process of PD and the causes of peritonitis
could be accommodated by allowing family members to attend
training with the patient or if this is not practical, to perhaps attend a
day specifically designed for families of patients on PD.

Some participants had very mild symptoms when they experienced peritonitis
because the infection was detected early. Others had a very different
experience, with the peritonitis episode making a major intrusion into their
life. Being unable to work for a few weeks and travel costs to and from
hospital caused financial strain. Parents with young children in particular, had
to ask family and friends for help and some participants reported being
disappointed with the lack of family assistance that occurred. We suggest that
child care associated with the hospital be offered to patients who need to
attend clinic or be hospitalized because of peritonitis and do not have anyone
they can immediately call on. It would also help patients if access to free or
low-cost parking at the unit/hospital could be provided during the treatment
period.

We found that many participants reluctantly went to hospital when they
experienced peritonitis and the dread was intense for those patients who had
repeat episodes of peritonitis. Various reasons for this response to hospitalization
have been given and they include reality of the individual’s mortality, dealing
with an altered level of dependency, grieving for losses (self or lifestyle) and fear
of recurrent problems (19). There was a perceived lack of knowledge about PD displayed by general hospital staff and some patients felt they were potentially exposed to infection. We suggest it would be an improvement if an experienced PD nurse or physician could be on call and visit patients when they are admitted to general wards or the intensive care unit (ICU). When undergoing treatment out of hospital for peritonitis, some units gave participants the antibiotics and instructions on how to inject them into the dialysis bag.

Participants said they found this process confronting and that they were not confident of doing it correctly. More practical support for antibiotic pre-administration is needed. In addition, having to go to the hospital or renal unit every 2 days for 2 weeks was time-consuming for patients and it would be an improvement if patients who are working could attend for tests and bag collection before and after normal work hours. Table 3 outlines our suggestions for clinical practice.

Our findings have yielded insights into the perspectives of adult PD patients about peritonitis. Further research could be conducted which explores the effect of giving patient education and retraining on an ongoing basis (e.g. every 6 months) rather than in response to an event such as hospitalization, after peritonitis, or catheter infection.

**Conclusions**

Patients were highly motivated to remain on PD but many found the cleaning demands and instructions around doing an exchange to be overwhelming. Some participants were unclear about the symptoms of peritonitis and others were confused about the causes of peritonitis. Peritonitis impacted
participants physically, socially and financially as it affected their ability to work and perform normal tasks. Participants wanted to avoid hospitalization, reported suboptimal care when in hospital, and for those who were treated out of hospital for peritonitis, found the frequent trips to the renal unit or hospital to be inconvenient and time-consuming. Understanding the experiences and needs of PD patients who have had peritonitis can be used to inform strategies for patient-centered health care. Understanding the beliefs of patients about peritonitis and their knowledge of symptoms can also help inform training strategies aimed at educating patients on this topic.

Acknowledgements

We sincerely thank all of the patients who contributed their time and energy to participate in this study. We also thank the PD nurse at each of the participating units (Laraine Aw, Richard Shipton-Smith, and Francine Lynn) who provided us with the names and contact details of patients suitable for interview.
6.6 References


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Table 6.1: Participant demographic and clinical characteristics (n=29)

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Chapter 6: Patients’ perspectives on the prevention and treatment of peritonitis in peritoneal dialysis: a semi-structured interview study

Table 6.1 (continued)

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<td>HD*</td>
<td>7</td>
<td>24</td>
</tr>
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<td>Transplant*</td>
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<td>14</td>
</tr>
<tr>
<td>37-48</td>
<td>2</td>
<td>7</td>
</tr>
<tr>
<td>49-60</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>≥61</td>
<td>5</td>
<td>17</td>
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<table>
<thead>
<tr>
<th>Number of peritonitis episodes</th>
<th></th>
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</tr>
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<tbody>
<tr>
<td>0</td>
<td>8</td>
<td>27</td>
</tr>
<tr>
<td>1</td>
<td>13</td>
<td>45</td>
</tr>
<tr>
<td>2</td>
<td>4</td>
<td>14</td>
</tr>
<tr>
<td>&gt;2</td>
<td>4</td>
<td>14</td>
</tr>
</tbody>
</table>
Chapter 6: Patients’ perspectives on the prevention and treatment of peritonitis in peritoneal dialysis: a semi-structured interview study

<table>
<thead>
<tr>
<th>SD = standard deviation; APD = automated peritoneal dialysis; CAPD = continuous ambulatory peritoneal dialysis; HD = hemodialysis; PD = peritoneal dialysis; RRT = renal replacement therapy.</th>
</tr>
</thead>
<tbody>
<tr>
<td>% may not total 100 due to rounding. *Time since on PD=3-31 months; mean=11.8 months. †Not all patients have had a previous RRT and some have had more than 1.</td>
</tr>
</tbody>
</table>
Table 6.2: Illustrative quotations

<table>
<thead>
<tr>
<th>Themes</th>
<th>Quotations</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Constant vigilance for prevention</strong></td>
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</table>
| Conscious of vulnerability          | I wouldn't say I'm concerned about it, but it's in the back of your mind that you've got to make sure you're very careful. (Female, 70s, APD)  
Scared me in a sense that, at the back of my mind I was thinking I’m going to get it again. So that's what I said, when I do my bags, I'm so careful now just to make sure nothing goes wrong. (Male, 40s, CAPD) 
You were always worried you might get peritonitis because you talk to people who get three or four or five episodes a year and they appear to do everything right. I did everything as close as I could to right. That's always in the back of your mind. (Male, 60s, HD and CAPD) |
| Sharing responsibility with family  | One thing I missed that's very important is to have your partner in there. They should be educated as much as we are... Yeah because they are part of your life. They are the people who look after you away from hospital and they should have the knowledge and understanding of your sickness and what should be done. (Male, 40s, CAPD)  
But also, say for example, if they've got a carer looking after them, it doesn't help either, because the carer's got to be trained properly, or the children, because they just don't understand how important it is. (Male, 50s, Transplant and CAPD) 
See, my daughter and my grandkids - they had no idea - none whatsoever. I understand that. Maybe they should be involved with the training, to recognise something that shouldn't be there. I believe maybe they should come to the dialysis centre and speak to them. (Male, 60s, HD and CAPD) |
| Demanding attention to detail       | Well as far as doing PD the hygiene level has to be really - maybe 110 per cent, you really have to wash your hands and prepare the dialysis everything should be - we close the house in the winter we have to switch off all the heating and everything. (Male, 40s, CAPD)  
Every day and wash the hands, get it ready. Do this. Do that. Wash the hands again. Disinfect the hands. I know I've got to do it all and it's basically what's keeping me alive. But it's just doing it day after day, just drives you insane. (Male, 50s, APD)  
It's not about going home, and just putting two chords together, it's not. It's hard, you've got to open up boxes, and you got to clean your area, you got to clean [your bench], you got to attach yourself, wash your hands to [unattach] yourself. It is time consuming, it's just full on, absolutely full on. (Female, 40s, HD, CAPD and APD) |
| Ambiguity of detecting infection | I thought, I've eaten something funny maybe, I don't know. Within a couple of hours I was in crippling pain hunched over. I decided to come home from work. I drove past both Westmead and Blacktown hospital to get home. Didn't think anything of it. I got home and I just thought I'd eaten something bad or something I don't know what it was. (Male, 30s, HD and APD)
I thought it was just a tummy bug from something I ate initially because the pain from what I’d learnt about peritonitis wasn’t, the pain I had was localised and it could’ve been a lower bowel infection which my GP thought it might be as well. (Male, 40s, APD and CAPD)
The only thing is that every time my period nearly comes, I get this cloudiness of the bags. I'm not really sure if this is from the period or if I'm having peritonitis. I'm getting confused. (Female, 40s, APD and CAPD) |
| Ineradicable inhabitation | I always think that, once you've got it you never fully clear the germs out of your system. I'm not a doctor but my theory is having spent so much time on dialysis and talking to other people, if you get it once you never really completely get rid of it so you've always got that slight chance of getting it again. (Male, 30s, HD and APD)
I don't know whether I've got this right but they said, because she's had the Tenckhoff catheter in for so long when you first put that warm fluid into you because you haven't had anything in for so long, it's just the peritoneum goes, oh, oh, I can't handle this and it just, maybe, reacts to it and it gives you peritonitis. (Female, 50s, CAPD)
But I don't think I got rid of it for a long time and it was really ugly. (Male, 40s, HD, CAPD and APD) |
| Jeopardising peritoneal dialysis success | Any infection within my peritoneal cavity because that could stop me from having this style of dialysis. I don’t want to go onto hemodialysis. In conjunction with that I must admit it was the same thought I hope I don’t die and I hope I can still do dialysis this way once it's cleared up. (Male, 40s, APD and CAPD)
My most - greatest fear was that I would go off the stomach PD and onto the arm PD, because I wouldn't - I would - don't want - didn't want to go onto the arm PD. (Male, 50s, Transplant and CAPD)
No, when I first started on PD, because that first day I got it, the nurses came out and we did one bag exchange together and then my next exchange I had peritonitis. I guess that for me was a big thing because I really didn't want to go on haemo. I really wanted to make the PD work. (Female, 30s, Transplant, CAPD and APD) |
<table>
<thead>
<tr>
<th>Invading harm</th>
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<tbody>
<tr>
<td>Life-threatening</td>
<td>I was worried because they had said that people have died from peritonitis. So yeah, I was quite scared. I was thinking - well first of all I was in so much pain I just wanted it to go away, then when they confirmed I had peritonitis I was thinking, I hope I don't die. I hope it's not that bad. (Male, 30s, HD and APD) That was my first thought because I know how serious it can be. That was my first thought, I hope I don’t die from this. (Male, 40s, APD and CAPD) Yeah, I'm scared. Am I going to die? (Female, 40s, APD and CAPD)</td>
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<tr>
<td>Wreaking internal damage</td>
<td>Until you get hit with peritonitis and then everything changes. You're tender. Everything is too hard. (Male, 40s, HD, CAPD and APD) Yeah, it is not something to be taken easy. Yeah, it can cause a lot of damage to the internal lining of the… Yeah, because doctors told me what happens when the peritonitis takes place. So the internal lining is kind of scarred and all that, yeah. (Male, 50s, APD and HD)</td>
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<tr>
<td>Debilitating pain</td>
<td>Like I said I was in hospital, you're stuck to bed and can't move around and all those things and most of all the pain was enormous. (Male, 40s, CAPD and APD) I didn't know that I was going to cramp over like I was having a baby - done with labour, that's [seriously] bad pain. (Female, 40s, HD, CAPD and APD) I just remember pain. Being asleep and being in pain. Painkillers, sleeping tablets, pain. It was shocking. It was the worst feeling. (Male, 40s, HD, CAPD and APD)</td>
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<tr>
<td>Losing control and dignity</td>
<td>I was constipated which didn’t help matters much too so I was in a pretty bad way in hospital there for a while and I lost all … you lose your dignity because you’ve got no control over your body. It just does what it wants to do (Male, 60s, HD and CAPD) Then it would have been only about eight hours later I needed to go to the toilet and I threw up and it wasn't vomit. It was - so it has basically come out the other end. (Male, 50s, Transplant and CAPD) I'd come home from work because I wasn't feeling well and I had a bit of pain and then I remember doing a bag and just sitting there vomiting while I was doing my bag and waiting for the colour to see what was coming out, see if it was cloudy or not. (Female, 30s, Transplant, CAPD and APD)</td>
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</table>
### Incapacitating lifestyle interference

<table>
<thead>
<tr>
<th>Category</th>
<th>Description</th>
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</table>
| **Financial strain**      | Not great because I had to spend a lot of time at the hospital so obviously I couldn't go to work for a full day. I only had part time days or half days. (Male, 30s, HD and APD)  
But at the time I was more concerned about how long am I going to be in hospital, is this going to get worse, am I going to be able to pay the mortgage, that’s how I felt at the time. (Male, 40s, APD and CAPD)  
Didn't go to work for five weeks and what it costs you through loss of income. I had to shut down my catering business. I lost half a million dollars. (Male, 40s, HD, CAPD and APD) |
| **Isolation and separation** | Yeah the pain is really bad and then it keeps me away from my family for at least a couple of weeks in the hospital. So yeah it's a small thing and then you pay a big price. (Male, 40s, CAPD and APD)  
Well I couldn't work, or couldn't see my family for a week. The kids couldn't come in, because I was in isolation. (Female, 40s, HD, CAPD and APD)  
The children, it affected them in that if I was in hospital they'd have to go their father's. Even though we share half care anyway, but while I was in hospital they'd have to stay there more often and they're missing me and stuff like that … (Female, 30s, Transplant, CAPD and APD) |
| **Exacerbating burden on family** | Family life, yeah obviously there was a little bit of disruption because obviously I had to - again my mum was a saint at the time when she was able to help me. She would help me every morning and she'd make sure I was okay before I went to work. Or make sure I was okay after I went and saw the doctors. (Male, 30s, HD and APD)  
My mother came down and stayed with my wife to help out with my little boy a little bit … (Male, 40s, APD and CAPD)  
I was actually here by myself because my children were with their father and I ended up ringing my mum and saying mum, I think I've got peritonitis, you're going to have to come down and take me to the hospital. That's probably my worst experience of peritonitis. (Female, 30s, Transplant, CAPD and APD) |
### Exasperation with hospitalisation

<table>
<thead>
<tr>
<th>Dread of hospital admission</th>
<th>I had a very good run the last three months or so, four months, but before that it was nearly every second month I was in hospital. … I'm thinking my God, I'm back to hospital again. (Male, 40s, CAPD and APD) It's just you go in and you know you're going to end up in emergency. You know you are going to have a night with no sleep in there. Then you'll be spending a few days while they do all the stuff they have to do, to make sure that everything is alright. No-one likes being in hospital and I don't like it either. (Male, 50s, APD and CAPD) Oh my god, here we go again. (Male, 50s, APD and HD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exposure to infection</td>
<td>… somebody told me I could go for a walk while they made my bed round. Then, the one from PD ward came in and she; and what is she doing up? The nurse said, oh - you know. I said, I was told I could go for a walk. She said - because I'd just had the operation, and then they used it - because I didn't have time to have - 10 days to heal, she said you can get leakage. (Female, 70s, APD and CAPD) A doctor could've even infected me, didn't even wash his hands, and I saw how he changed me. (Female, 40s, HD, CAPD and APD)</td>
</tr>
<tr>
<td>Gruelling follow-up schedule</td>
<td>Then, I had to go into the clinic every other day I think, and had a blood test and then they'd let me know when they got the result back. They'd give me the bag with the antibiotics, and then [either they'd ring me or] I'd ring them to say, yes have that bag with the antibiotics in it until it cleared up. (Female, 70s, APD and CAPD) I'd have to break my normal routine of a morning where I'd have to get up a little bit earlier. I'd have to run around and do all the antibiotics into the bag and do the fresh bag. That took a little bit longer than normal but it wasn't too bad it was just the odd - every two or three days I'd be at the hospital for check-ups and blood tests. (Male, 30s, HD and APD) So it all depends on how - whether they can see anything or what the levels are, I'm not really up on that. But I know it was inconvenient because you had to drag in there. Even though it's not that far but you've still got to drive in there, park and - yeah. (Female, 50s, CAPD)</td>
</tr>
<tr>
<td>Receiving inattentive care</td>
<td>Within the first seven days I was in hospital after the surgery, they put me on the machine straight away and that was painful because they didn't really monitor it all that well. It's a hospital, it's new. (Male, 30s, HD and APD) Then I had a session in there where they put me up in the bed and then, because my blood pressure was really, really high, they put me on this blood pressure stuff to reduce my blood pressure. Then they walked away and they left the machine on, so my blood pressure went down to 80/20 or something. I was blacking out and I said to the patient next - even though I had buzzed and no one had come, I said, help. (Male, 50s, Transplant and CAPD)</td>
</tr>
</tbody>
</table>
Table 6.3: Suggestions for clinical practice

<table>
<thead>
<tr>
<th>Domain</th>
<th>Suggested strategies and action</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Information, education and training</strong></td>
<td>Provide more frequent retraining for patients</td>
</tr>
<tr>
<td></td>
<td>Provide a home visit by a PD nurse (e.g. in the first week of dialysis at home, 3 months after starting dialysis, following a PD-related infection)</td>
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<tr>
<td></td>
<td>Allow family members/carers to attend training with the patient</td>
</tr>
<tr>
<td></td>
<td>Develop educational materials for family members/carers</td>
</tr>
<tr>
<td></td>
<td>Educate general hospital staff about the PD method and importance of infection prevention</td>
</tr>
<tr>
<td><strong>Psychological support</strong></td>
<td>Offer referral to psychological services after a peritonitis episode</td>
</tr>
<tr>
<td><strong>Technical/clinical support</strong></td>
<td>Provide a PD nurse or nephrologist on call who can visit patients when they are admitted to a general ward or the ICU</td>
</tr>
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<td></td>
<td>Have renal unit make up the dialysis bags with antibiotics for patients to use</td>
</tr>
<tr>
<td></td>
<td>Make it possible for patients who work to attend for tests and dialysis bag collection before and after normal work hours</td>
</tr>
<tr>
<td><strong>Social support</strong></td>
<td>Offer patients access to child care associated with the hospital during the peritonitis treatment period</td>
</tr>
<tr>
<td></td>
<td>Offer patients access to free or low-cost parking at the renal unit/hospital during the peritonitis treatment period</td>
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</table>

PD = peritoneal dialysis; ICU = intensive care unit.
Figure 6.1: Thematic schema representing patient perspectives on the prevention and treatment of peritonitis in peritoneal dialysis

**Invading harm**
- Life-threatening
- Wreaking internal damage
- Debilitating pain
- Losing control and dignity

**Exasperation with hospitalisation**
- Dread of hospital admission
- Exposure to infection
- Gruelling follow-up schedule
- Receiving inattentive care

**Constant vigilance for prevention**
- Conscious of vulnerability
- Sharing responsibility with family
- Demanding attention to detail
- Ambiguity of detecting infection
- Ineradicable inhabitation
- Jeopardising PD success

**Incapacitating lifestyle interference**
- Financial strain
- Isolation and separation
- Exacerbating burden on family
Chapter 7: Discussion

7.1 Summary of findings

The prevention of peritonitis in PD patients is an important clinical activity. There has been a shift in thinking from the treatment of infection to the prevention of infection in PD patients. Peritoneal dialysis-associated peritonitis is the most acute complication of PD, is the main cause of technique failure and transfer to hemodialysis, causes significant morbidity and carries some risk of mortality. Peritonitis rates vary widely from centre to centre and from patient to patient (1,2). While some patient factors are thought to contribute to peritonitis (e.g. older age, diabetes mellitus), the quality of patient training, social factors and clinical practice patterns are also thought to play a role. It has been reported that the incidence and clinical outcomes of PD-associated peritonitis found in routine clinical audits of large unselected PD populations are not as good as those reported in a meta-analysis by the Cochrane Renal Group or in centres that have an established research and clinical interest in PD (3). The findings from the research that forms this thesis inform the discussion about: what are the main strategies in use for the reduction of PD-related infections, what are the current practice patterns in relation to the prevention of these infections in ANZ PD units, what are some of the perceived barriers to the application of relevant guideline recommendations into practice, what are effective strategies for the reduction of PD-related infections, and what is the patient perspective in relation to the prevention and treatment of peritonitis. These findings can help clinicians to develop a family- and patient-centred approach towards the management of patients going through a peritonitis episode, can also help
clinicians to assess the value of the different approaches that are suggested to reduce the chances of a PD-related infection, and can highlight the variation in practice that exists from centre to centre and pose the question as to whether or not this variation is linked to the wide variation in peritonitis outcomes that is known to exist in ANZ (4,5).

**Prevention of peritoneal dialysis-related infections**

A large number of prophylactic strategies have been used to reduce the occurrence of peritonitis. There have been previous reviews on this topic and the narrative review presented in chapter 2 is an update of the topic and summarises the existing evidence evaluating these interventions. Overall, there is a lack of RCTs for many interventions and consequently, data from less rigorous study designs such as cohort studies are the current best available evidence. In addition, systematic reviews have few RCTs that can be included in the analysis. The quality of the RCTs is also variable with some having small patient numbers, short follow-up times and an increased risk of bias because of poor or unclear randomisation and blinding processes. The quality of the evidence is strong for some aspects such as the PD connection method, the use of intravenous antibiotic administration prior to PD catheter insertion, and the use of antibiotic to prevent ESI but is weak for other areas such as the method for training patients. No advantage can be found for using different catheter designs, surgical implantation techniques, catheter placement or automated peritoneal dialysis (APD) versus chronic peritoneal dialysis (CPD). Adoption of a team-based, multifaceted approach to continuous quality improvement with regular audit of infection rates and outcomes is considered essential to improving peritonitis rates. The training
of patients is recognised as a modifiable risk factor for PD peritonitis and the review noted that research into how to best deliver this training, how often to retrain patients and how to train the trainers are an important research area.

Assessment of current practice and barriers to prophylaxis in peritoneal dialysis patients

The study described in chapter 3 presents the results of a baseline study of current practice conducted with 8 renal units located in Australia (7) and New Zealand (1). The current practice was in relation to the use of antibiotic and antifungal prophylaxis in PD patients as per current ISPD and KHA-CARI guidelines. We found that prophylactic practice varied widely between the units and the PD-related infection outcomes (exit-site infection [ESI], peritonitis) also varied widely between the units. We also found that the definitions of PD-related infections used by some units varied from those recommended by the ISPD, particularly with regard to ESI. Some units were consequently over-reporting ESI while others were under-reporting it.

Perceived barriers to the uptake of guideline recommendations included lack of knowledge of the recommendation/s, procedural lapses, lack of a centralised patient database, patients with non-English speaking background, professional concern about antibiotic resistance, medication cost, and the inability of nephrologists and infectious diseases staff to reach consensus on unit protocols.
Antimicrobial agents for preventing peritonitis in peritoneal dialysis patients (Cochrane Review)

Chapter 4 is an update to a Cochrane systematic review first conducted 10 years ago. The review assesses the evidence base for nine categories of intervention that have been used to reduce the risk of peritonitis and exit-site/tunnel infections in PD patients. Most of these comparisons are based on a small number of RCTs. Only two of the antimicrobial interventions appear to reduce the risk of peritonitis.

Infection prophylaxis in peritoneal dialysis patients: results from an Australia/New Zealand survey

Chapter 5 outlines the responses of 133 consultant nephrologists to an online survey which asked a series of questions about their use of antibiotic and antifungal prophylaxis in PD patients. There have been no recent large scale surveys of this type performed in ANZ. The findings show that practice in relation to various prophylactic measures is variable and may relate to whether the guideline recommendation is evidence- or opinion-based, leaves allowance for consideration of local conditions or reflects unawareness/disagreement with the guideline recommendations. It is possible that some of this variation contributes to the disparity in PD-related infection rates that exist between units in ANZ.
Patients’ perspectives on the prevention and treatment of peritonitis in peritoneal dialysis: a semi-structured interview study

The patient perspective in relation to the prevention and treatment of peritonitis has not been studied much. Chapter 6 is a qualitative analysis of patient beliefs, needs and experiences regarding the prevention and treatment of peritonitis. Patients perceived that peritonitis could threaten their health, treatment modality and lifestyle which motivated vigilance and attention to hygiene. A number of patients were unsure how to monitor for signs of peritonitis. The findings from this study could be used to enhance patient- and family-centred care and education strategies which could address some of the concerns patients have about the possibility of peritonitis and the impacts of a peritonitis episode.

7.2 Strengths and limitations

The studies in this thesis address the clinical problem of the need to reduce the risk of peritonitis in PD patients. The study findings have implications for clinical practice, policy making and future research. Each study was designed to be methodologically sound and reporting standards were followed. Apart from the limitations specific to each study that have already been discussed in the relevant chapters, the main limitation is that there is a lack of adequately powered and high quality RCTs to inform decision making about strategies to prevent peritonitis.

This would have affected the results of the analysis done in the Cochrane
Chapter 7: Discussion

Review. Some interventions appear to have no or very little effect on an outcome but this might only be a consequence of a lack of power and suboptimal study performance/reporting. A limitation of the survey study is that we did not think to include questions about why nephrologists choose to not adhere to guideline recommendation/s.

7.3 Clinical implications

The findings from the work comprising this thesis have implications for clinical practice in the area of the prevention of peritonitis in patients on PD. Based on the findings, it is apparent that there is considerable variation in practice between ANZ units as regards the use of prophylactic measures in PD patients. The reasons for this are not clear. Some barriers have been identified in the baseline study, which act to stop the uptake of certain guideline recommendations. The findings from the Cochrane Review call into question whether the use of nasal antibiotic to clear *S. aureus* carriage is an effective measure. It also raises questions as to whether the use of topical disinfectant at the exit site is effective in reducing the risk of PD-related infection.

Family- and patient-centred strategies are proposed in chapter 6 of this thesis to help educate and support patients, which may lead to improved treatment satisfaction and outcomes. It is accepted that patients with chronic disease should be engaged with their health care provider as a full partner in managing their disease and that this leads to better outcomes for the patient and is a prerequisite for effective and efficient health care (6). Patients can also help to set the agenda for future research, as has occurred with the inclusion of patients in the Outcome Measures in Rheumatology
(OMERACT) conferences. Patient input has influenced the scope and conduct of outcomes research in rheumatology by widening the research agenda, including patient relevant outcomes in core sets and enhancing patient reported instruments, as well as other effects (7). In the same way, the patient interview study described in chapter 6 highlighted deficiencies in patient knowledge and understanding and underlined the need for more support (psychological, technical, clinical, social) when a patient experiences a peritonitis episode. The resulting suggestions for clinical practice are an important outcome of the study and have the potential to help prevent peritonitis and make the patient experience less onerous.

The effects of employing continuous quality improvement and quality management have been investigated in a number of different clinical settings. Continuous quality improvement uses the Plan, Do, Study, Act cycle to improve the procedures followed during the care of a patient. Improvements in various important patient outcomes have been found, which include a significant decrease in the rate of catheter-related bloodstream infections in the Intensive Care Unit after the implementation of five systems interventions (over a 5 year period) (8) and a 50% reduction in overall sepsis mortality in the Emergency Departments and Inpatient Units at 11 acute care hospitals (over a 6 year period) after putting into practice the recommendations from a series of evidence-based guidelines (9). The use of various quality improvement interventions at one PD unit over 17 years also resulted in reduced infection rates in the PD patients, with the peritonitis rate and exit-site infection rate both reducing significantly (10). Another PD unit
introduced a number of changes as part of a quality improvement program, after observing consistent differences in peritonitis rates between patients using various PD connection systems. The quality improvement program resulted in a fivefold reduction in peritonitis rates at the unit (11).

The development of key performance indicators (KPIs) provides a means of measuring performance of renal services in relation to evidence-based practices and can be used to improve services. Appropriate KPIs for the prevention of PD-related infection include 100% prophylactic antibiotic administration prior to catheter insertion, achieving a PD peritonitis rate <0.36 episodes per patient per year, and 100% prescribing of antifungal agent during treatment of peritonitis (12). The development of KPIs enables a unit to determine its performance against agreed best practice parameters (13). A recent program run in Victoria by the Renal Health Clinical Network developed four KPIs relating to CKD and dialysis and two KPIs relating to transplant. One of the KPIs was ‘peritonitis rate of PD patients for each service hub’ with a target of peritonitis rate less than one episode per patient in 18 months. Nine units submitted data for this KPI. Data for the state was assessed for the 2 years that KPI use had been in place and showed that the average number of months between peritonitis episodes in Victoria had increased 2 months per year during that time (13).

It has been recognised for some time that in Australia and New Zealand, in many cases, poor peritonitis outcomes reflect significant deviations from the ISPD guidelines (14). A review of the data held by the Australian Peritonitis
Registry 2003-2006 revealed many deviations in Australian practice from the guideline recommendations. One of the conclusions of this review was that “A concerted unified approach to clinical governance with strong leadership in each unit is imperative to improve PD outcomes in ANZ.” In the US, the Medicare definition of the medical director of a dialysis centre is: “…the leader of the interdisciplinary team and the person ultimately accountable for quality, safety, and care provided in the center.” The medical director is expected to be knowledgeable about the quality assessment and performance improvement (QAPI) process and to demonstrate active leadership with a hands-on approach (15). This is considered essential in order for high quality outcomes to be achieved in a dialysis centre. The medical director is also expected to “help centers to prioritize improvement projects and direct efforts to identify and address systemic issues.” In becoming involved in quality improvement, the medical director moves from a patient care provider role to a population health management role with responsibility for facility patient care and outcome. This requires the performance of different tasks to those required with direct patient care. The medical director is in a position to set the tone and culture of the dialysis centre and can influence whether quality improvement processes become an integral part of patient care or are viewed as yet one more task that needs to be done. PD units in Australia and New Zealand need medical directors to lead the way, and drive quality improvement using process-driven KPIs that are published and socialised internally and externally.
7.4 Implications for future research

From the systematic review, it is apparent that there is a need for more well-conducted RCTs of sufficient power that investigate some of the prophylactic interventions that are commonly used in practice. For example, nasal versus exit-site application of mupirocin, pre-operative screening and elimination of nasal *S. aureus*, and the type of cleansing agent used at the exit site are suitable topics for investigation. Prospective cohort studies could also be conducted which investigate the infection and technique survival outcomes of different training methods and different retraining frequencies (e.g. proactive versus reactive).

From the survey of nephrologists, we know that current practice in ANZ as regards the use of prophylactic measures in PD patients is quite variable, as are the peritonitis rates. Research could be done which explores why nephrologists apply certain guideline recommendations in practice but not others. An investigation could also be made into the practices of those units that have good PD-related infection outcomes in order to identify practices that appear to help reduce the risk of these infections.

The data we have from the survey could be further analysed in relation to this. Some of the suggestions for clinical practice made in the qualitative study could be put into practice. It would be worthwhile to assess patient satisfaction and improvement in outcomes after implementation of the family- and patient-centred strategies for education and care that are outlined here.

These are some potential areas for research that have come out of this thesis.
Chapter 7: Discussion

7.5 Conclusion

This thesis outlines what clinical practice in relation to the use of prophylaxis in PD patients is like in ANZ and identifies some barriers to the uptake of relevant guideline recommendations. The optimal preventive strategies to reduce the occurrence of peritonitis remain unclear, with only a few interventions showing a significant effect on PD-related infection outcomes.

Studies on the prevention of PD-related infections are limited both in terms of quality and quantity, and consequently, guideline recommendations are based on a mixture of expert opinion and the available evidence.

Clinical governance with strong leadership at the unit level is essential to improve outcomes for PD patients. The use of continuous quality improvement programs and key performance indicators have the potential to reduce deviations from current best practice and improve clinical outcomes.

Patients experience ongoing anxiety about peritonitis and are impacted physically, socially and financially when they experience a peritonitis episode. Understanding the experiences and needs of PD patients who have had peritonitis can be used to inform strategies for patient-centred health care. Understanding the beliefs of patients about peritonitis and their knowledge of symptoms can help inform training strategies aimed at educating them.

Future research into the education and care strategies suggested in the qualitative interview study may help to improve PD patient outcomes.
7.6 References


Chapter 7: Discussion


Chapter 7: Discussion


Appendix A: Supporting data for chapter 2

A1. EMBASE search strategy for chapter 2

The following search strategy was used to identify randomised controlled trials, meta- analyses and systematic reviews about peritoneal dialysis-related infection in EMBASE (1980- December 2013)

1. peritoneal dialysis/

2. peritoneal dialysis.tw.

3. (PD or CAPD or CCPD).tw.

4. or/1-3

5. bacterial peritonitis/

6. peritoneal dialysis catheter/

7. catheter infection/

8. catheter$.tw.

9. (exit site$ or exit-site$).tw.

10. (tunnel$ and infection$).tw.

11. or/5-10

12. and/4,11

13. randomized controlled trial/

14. crossover procedure/
15. double-blind procedure/
16. single-blind procedure/
17. random$.tw.
18. factorial$.tw.
19. (crossover$ or cross-over$).tw.
20. placebo$.tw.
22. (singl$ adj blind$).tw.
23. assign$.tw.
24. allocat$.tw.
25. or/13-24
26. and/12,25
27. limit 12 to meta analysis
28. limit 12 to "systematic review"
29. limit 12 to "reviews (maximizes specificity)"
30. 27 or 28 or 29
A2. MEDLINE search strategy for chapter 2

The following search strategy was used to identify randomised controlled trials, meta-analyses and systematic reviews about peritoneal dialysis-related infection in MEDLINE (1950-December 2013)

1. exp Peritoneal Dialysis/
2. peritoneal dialysis.tw.
3. (PD or CAPD or CCPD).tw.
4. or/1-3
5. Peritonitis/
6. peritonitis.tw.
7. Catheters, Indwelling/
8. Catheter-Related Infections/
9. (exit site$ or exit-site$).tw.
10. (tunnel$ and infection$).tw.
11. catheter$.tw.
12. or/5-11
13. and/4,12
14. randomized controlled trial.pt.
15. controlled clinical trial.pt.
16. randomized.ab.

17. placebo.ab.

18. clinical trials as topic/

19. randomly.ab.

20. (crossover or cross-over).tw.

21. Cross-over Studies/

22. trial.ti.

23. or/14-22

24. animals/ not (humans/ and animals/)

25. 23 not 24


27. Meta-Analysis/

28. (systematic$ and (review$ or overview$)).tw.

29. meta?analy$.tw.

30. meta analy$.tw.

31. review.pt. and medline.tw.

33. or/27-32

34. and/13,33
## Appendix B: Supporting data for chapter 3

### B1. Relevant ISPD and KHA-CARI Guideline Recommendations

<table>
<thead>
<tr>
<th>Guideline Organization</th>
<th>Year of Publication</th>
<th>Guideline Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>KHA-CARI</td>
<td>2004</td>
<td>Antibiotic prophylaxis with a first generation cephalosporin should be used at peritoneal dialysis catheter insertion to reduce the incidence of peritonitis (Level II evidence). Although vancomycin prophylaxis has also been demonstrated to be effective (Level II evidence), its routine use is not recommended because of the potential development of resistant microorganisms such as vancomycin-resistant enterococci (VRE) and vancomycin-resistant Staphylococcus aureus.</td>
</tr>
<tr>
<td>KHA-CARI</td>
<td>2004</td>
<td>Prophylactic therapy using mupirocin ointment, especially for Staphylococcus aureus carriage intranasally is recommended to decrease the risk of S. aureus catheter exit site/tunnel infections and peritonitis (Level II evidence).</td>
</tr>
<tr>
<td>KHA-CARI</td>
<td>2004</td>
<td>The use of oral nystatin should be considered at the time of antibiotic administration to peritoneal dialysis patients to reduce the occurrence of fungal peritonitis (Level II evidence).</td>
</tr>
<tr>
<td>ISPD</td>
<td>2011</td>
<td>Prophylactic antibiotics administered at the time of insertion decrease the infection risk.</td>
</tr>
<tr>
<td>ISPD</td>
<td>2011</td>
<td>Prevention of catheter infections (and thus peritonitis) is the primary goal of exit site care. Antibiotic protocols against S. aureus are effective in reducing the risk of S. aureus catheter infections.</td>
</tr>
<tr>
<td>ISPD</td>
<td>2011</td>
<td>All PD patients should use topical antibiotic either at the catheter exit site or intranasally or both.</td>
</tr>
<tr>
<td>ISPD</td>
<td>2011</td>
<td>Fungal prophylaxis during antibiotic therapy may prevent some cases of Candida peritonitis in programs that have high rates of fungal peritonitis.</td>
</tr>
</tbody>
</table>
B2. Peritoneal Dialysis Implementation Project Selection Criteria

1. Unit has a problem achieving good infection control in new PD patients

2. Achieving good infection control in new PD patients is considered a priority issue by the unit

3. Belief that prevention of PD-related infections in new PD patients at the unit can be improved

4. Key staff members are willing to proactively identify barriers to achieving good infection control in new PD patients

5. A good data collection system exists at the unit

6. Unit is willing to allow the project coordinator to access the unit’s records held by the ANZDATA registry

7. Unit is willing to gain local ethical clearance if this is needed
Appendix C: Supporting data for chapter 5

Consultant nephrologist survey form, initial introductory letter, revised introductory letter, reminder survey letter

C1. Consultant nephrologist survey form

Prophylactic antibiotic use in PD patients, concurrent antifungal use, and

There are 4 parts to this survey:
- Prophylactic antibiotic use at insertion of PD catheter
- Prophylactic antibiotic use to prevent exit site/tunnel infections
- Concurrent use of antifungal agents and
- Insertion of Tenckhoff catheter

Please complete all 4 parts.

PART 1: PROPHYLACTIC ANTIBIOTIC USE AT INSERTION OF PD CATHETER

1. Does your unit routinely use antibiotics prior to Tenckhoff catheter insertion in all peritoneal dialysis (PD) patients?
   - [ ] Yes
   - [ ] No → Skip to Page 4

2. If you routinely use antibiotics at Tenckhoff catheter insertion, when are they given?
   - [ ] Prior to surgery (i.e. in the Renal Ward/Surgical Care area)
   - [ ] At time of surgery (i.e. in the Operating Theatre)
   - [ ] Other, please specify:

3. If you only routinely use antibiotics in a subset of patients, which patients receive them? (Tick all that apply)

Patients with:
- [ ] Diabetes mellitus
- [ ] Chronic lung disease
- [ ] Coronary artery disease
- [ ] Peripheral vascular disease
- [ ] Cardiac valvular disease
- [ ] BMI > 30 kg/m²
- [ ] Previous history of peritonitis
- [ ] Patient having catheter re-inserted
- [ ] Not applicable

- [ ] Other, please specify:
Appendix C: Supporting data for chapter 5

Prophylactic antibiotic use in PD patients, concurrent antifungal use, and

**8. Do you do nasal swabs to identify patients/carers/staff who are *Staphylococcus aureus* carriers?**

- Yes
- No → Skip to Page 9

**9. Do you use intranasal antibiotics to treat *Staphylococcus aureus* identified on nasal swab?**

- Yes
- No → Skip to Page 9

**10. If an individual is a carrier, how long do you give antibiotic treatment for?**

**11. Which topical antibiotic ointment do you use?**

- Mupirocin
- Other (please specify)

**12. Do you use the following to reduce *Staphylococcus aureus* colonisation at the PD catheter exit site? (Tick all that apply)**

- Mupirocin ointment
- Antibacterial wash
- Betadine wipes
- Soap and water
- Other (please specify)

**PART 3: CONCURRENT USE OF ANTIFUNGAL AGENTS**

**13. When you give an antibiotic to a PD patient, do you also routinely give an antifungal agent to prevent fungal peritonitis?**

- Yes
- No → Skip to Page 12

**14. For how long do you give antifungal treatment?**

- For the same duration as the antibiotics
- For 3 days longer than the antibiotics
Appendix C: Supporting data for chapter 5

Prophylactic antibiotic use in PD patients, concurrent antifungal use, and

*15. In which subset of patients do you use an antifungal agent when prescribing antibiotics? (Tick all that apply)

Patients with:
- Diabetes mellitus
- Chronic lung disease
- Coronary artery disease
- Peripheral vascular disease
- Geriatric/palliative diagnosis
- BMI > 30 kg/m²
- Previous history of peritonitis
- Patient having catheter re-inserted
- Other, please specify

PART 4: INSERTION OF TENCKHOFF CATHETER

*16. Are your Tenckhoff catheters inserted by: (Tick all that apply)
- A Consultant
- A Fellow
- A Registrar

*17. What kind of operator inserts the catheters, and by which technique? (Tick all that apply)
- Nephrologist (percutaneous or fluoroscopy)
- Surgeon (laparotomy)
- Surgeon (laparoscopy)
- Radiologist (percutaneous under fluoroscopy)

*18. Type of Tenckhoff catheter inserted: (Tick all that apply)
- Straight
- Cuffed

DEMOGRAPHICS

*19. Are you?
- Male
- Female
### Appendix C: Supporting data for chapter 5

#### Prophylactic antibiotic use in PD patients, concurrent antifungal use, and

**20. What age bracket do you fall into?**
- Less than 30 yrs
- 30 - 40 yrs
- 41 - 50 yrs
- 51 - 60 yrs
- 61 - 70 yrs
- Over 70 yrs

**21. How many years have you been working in the specialty of Nephrology?**
- 1 - 5 yrs
- 6 - 10 yrs
- 11 - 15 yrs
- 16 - 20 yrs
- Over 20 yrs

**22. What state/territory/country do you work in?**
- New South Wales ➔ Skip to Page 15
- Australian Capital Territory (ACT) ➔ Skip to Page 16
- Victoria ➔ Skip to Page 17
- Queensland ➔ Skip to Page 18
- Northern Territory ➔ Skip to Page 19
- South Australia ➔ Skip to Page 20
- Tasmania ➔ Skip to Page 21
- Western Australia ➔ Skip to Page 22
- New Zealand ➔ Skip to Page 23
Appendix C: Supporting data for chapter 5

Prophylactic antibiotic use in PD patients, concurrent antifungal use, and

*23. Which renal unit do you work in? (Tick all that apply)

- Coffs Harbour Hospital
- Concord Hospital
- Dubbo Base Hospital
- Gosford Hospital
- John Hunter Hospital
- Lismore Hospital
- Lismore Private Dialysis Clinic
- Liverpool Hospital
- Mackay Dialysis Centre - Kempsey
- Manning Rural Referral Hospital
- Mater Misericordiae Hospital
- Mayo Private - Tamworth
- Nepean Hospital
- Orange Hospital
- Port Macquarie Base Hospital
- Port Macquarie Private Hospital
- Prince of Wales Hospital
- Royal North Shore Hospital
- Royal Prince Alfred Hospital
- St. George Hospital
- St. Vincent's Hospital
- Sydney Adventist Hospital
- Sydney Children's Hospital
- Tamworth Hospital
- The Children's Hospital at Westmead
- The Tweed Hospital
- Westmead Hospital
- Wollongong Hospital

*24. Which renal unit do you work in?

- The Canberra Hospital
**25. Which renal unit do you work in? (Tick all that apply)**

- Alfred Hospital
- Austin Health
- Eastern Health Integrated Renal Services
- Epworth Hospital
- Forest Hill Dialysis Centre (Fresenius)
- Geelong Hospital
- Kew Private Dialysis Centre
- Melvern Dialysis Centre (Fresenius)
- Monash Medical Centre - Adult
- Monash Medical Centre - Paediatric
- North West Dialysis Service
- Royal Melbourne Hospital
- Royal Children's Hospital
- St. Vincent's Hospital
- Western Health
### Prophylactic antibiotic use in PD patients, concurrent antifungal use, and

<table>
<thead>
<tr>
<th><strong>26. Which renal unit do you work in? (Tick all that apply)</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>- Aitamanda Private Hospital (Fresenius)</td>
</tr>
<tr>
<td>- Bundaberg Base Hospital</td>
</tr>
<tr>
<td>- Cairns Base Hospital</td>
</tr>
<tr>
<td>- Caloundra Private Hospital</td>
</tr>
<tr>
<td>- Chermside Dialysis Unit (Fresenius)</td>
</tr>
<tr>
<td>- Child and Adolescent Renal Service</td>
</tr>
<tr>
<td>- Gold Coast Hospital</td>
</tr>
<tr>
<td>- Henry Daltziel Dialysis Centre (Greenioplex) (Baxter)</td>
</tr>
<tr>
<td>- Hervey Bay Hospital</td>
</tr>
<tr>
<td>- John Flynn Hospital</td>
</tr>
<tr>
<td>- Mackay Base Hospital</td>
</tr>
<tr>
<td>- Nambour General Hospital</td>
</tr>
<tr>
<td>- Nambour Selanor Private Hospital</td>
</tr>
<tr>
<td>- Princess Alexandra Hospital</td>
</tr>
<tr>
<td>- Rockhampton Base Hospital</td>
</tr>
<tr>
<td>- Royal Brisbane Hospital</td>
</tr>
<tr>
<td>- St Andrew's Dialysis Clinic (Diaverum)</td>
</tr>
<tr>
<td>- The Townsville Hospital</td>
</tr>
<tr>
<td>- Toowoomba Hospital</td>
</tr>
<tr>
<td>- Wesley Private Hospital</td>
</tr>
</tbody>
</table>

### 27. Which renal unit do you work in? (Tick all that apply)

| - Alice Springs Hospital                                     |
| - Royal Darwin Hospital                                      |

### 28. Which renal unit do you work in? (Tick all that apply)

| - Flinders Medical Centre                                    |
| - Royal Adelaide Hospital                                    |
| - The Queen Elizabeth Hospital                               |
| - Women's and Children's Hospital                            |

### 29. Which renal unit do you work in? (Tick all that apply)

| - Launceston General Hospital                                |
| - Royal Hobart Hospital                                      |
Prophylactic antibiotic use in PD patients, concurrent antifungal use, and

*30. Which renal unit do you work in? (Tick all that apply)
- Fremantle Hospital
- Hollywood Private Hospital
- Princess Margaret Hospital for Children
- Royal Perth Hospital
- Sir Charles Gairdner Hospital
- St. John of God Private Hospital

*31. Which renal unit do you work in? (Tick all that apply)
- Auckland City Hospital
- Christchurch Hospital
- Dunedin Hospital
- Hawkes Bay Hospital
- Middlemore Hospital
- Palmerston North Hospital
- Starship Children’s Hospital
- Taranaki Base Hospital
- Waikato Hospital
- Waitemata District Health Board
- Wellington Hospital
- Whangarei Area Hospital

GENERAL COMMENTS:

32. We would also be interested to receive any general comments that you think may be relevant:

Thank you for taking the time to complete this survey
C2. Initial introductory letter

Prophylactic antibiotic and antifungal use in peritoneal dialysis patients and technique used for catheter insertion: survey of consultant nephrologists

Dear All

This survey is being undertaken by the Steering Committee responsible for the current KHA-CARI Guidelines implementation project, which is looking at guideline concordant use of antibiotics and antifungal agents in incident peritoneal dialysis (PD) patients in 8 renal units. We are conducting the survey to determine if renal unit characteristics help explain the variation in peritonitis rates that is seen between the centres that report to ANZDATA. The data collected will help us to understand the variations in practice that exist. This knowledge in turn, should help us to improve the care of PD patients in Australia and New Zealand.

The survey is online and should take no more than 10-15 minutes to complete. The survey is in 4 parts with some Demographics questions and a General Comments box at the end; there are a total of 23 questions. This survey is completely confidential and anonymous and participation is voluntary. One of the questions in the survey asks for your unit name. We have requested this so that we can correlate responses to unit size, location and satellite services. Any data presented from this survey will be de-identified and all responses will be kept confidential. Your responses will only be analysed in aggregate with the responses of other respondents and at no time will your individual responses be made available to anyone. The results of the survey will be published in a peer reviewed journal and/or scientific presentation. You can reach the survey by clicking on the following link (if clicking on the link does not work, please copy and paste the link into the address bar of your internet browser)

https://www.surveymonkey.com/s/N9C5DYW

Please answer questions as they apply to the renal unit where you mainly work. You may need to ask other staff in your unit to assist you to complete some questions. If you have any questions about the survey, contact Denise Campbell on (02) 9845 1477 for more information (Email: denise.campbell@health.nsw.gov.au).

This project has been approved by The Sydney Children’s Hospital Network Human Research Ethics Committee. If you have any worries or questions about the study, please call the Research Ethics Manager (02 9845 3017), who is the Secretary of the Ethics Committee and quote the approval number 12/SCHN/194.

Please note that for each completed survey we will donate $5 to Kidney Health Australia. Thank you in advance for your time and cooperation.

Assoc. Prof David Mudge
Convenor
KHA-CARI PD Implementation Project

Denise Campbell
Project Officer
KHA-CARI PD Implementation Project
C3. Revised introductory letter

Dear All

Peritoneal Dialysis Survey of Consultant Nephrologists

This survey is being administered in Australia and New Zealand. It is intended to elicit current practice as regards prophylactic antibiotic and antifungal use in peritoneal dialysis patients. It has been developed by the Steering Committee responsible for the current KHA-CARI Guidelines implementation project.

The survey consists of 23 multiple-choice questions that can be completed in approximately 10 minutes. All responses will be kept confidential.

The information collected will be analysed to see if renal unit characteristics help explain the variation in peritonitis rates that is seen between the centres that report to ANZDATA. We will also publish the results in manuscript form.

We would very much appreciate it if you would take the time to complete the survey. You can either complete the enclosed printed copy and mail it back to the KHA-CARI office (reply paid envelope enclosed) or you can answer the survey online. The link to the survey is: https://www.surveymonkey.com/s/N9C5DYW

Please answer questions as they apply to the renal unit where you mainly work. Thank you to those who have already completed the survey.

Kind regards

Assoc. Prof David Mudge
Convenor, KHA-CARI PD Implementation
Project Tel: (07) 3176 5080
Email: David_Mudge@health.qld.gov.au

Denise Campbell
Project Officer, KHA-CARI PD Implementation
Project Tel: (02) 9845 1477
Email: denise.campbell@health.nsw.gov.au
C4. Reminder survey letter

**Reminder: Peritoneal Dialysis Survey of Consultant Nephrologists**

This survey is being administered in Australia and New Zealand. It is intended to elicit current practice as regards prophylactic antibiotic and antifungal use in peritoneal dialysis patients. It has been developed by the Steering Committee responsible for the current KHA- CARI Guidelines implementation project.

The survey consists of 23 multiple-choice questions that can be completed in **approximately 10 minutes**. All responses will be kept confidential.

The information collected will be analysed to see if renal unit characteristics help explain the variation in peritonitis rates that is seen between the centres that report to ANZDATA. We will also publish the results in manuscript form.

We would very much appreciate it if you would take the time to complete the survey. Link to the survey: [https://www.surveymonkey.com/s/N9C5DYW](https://www.surveymonkey.com/s/N9C5DYW)

Please answer questions as they apply to the renal unit where you mainly work. Thank you to those who have already completed the survey.

Kind regards

**Assoc. Prof David Mudge**

Convenor, KHA-CARI PD Implementation
Project Tel: (07) 3176 5080
Email: David_Mudge@health.qld.gov.au

**Denise Campbell**

Project Officer, KHA-CARI PD Implementation
Project Tel: (02) 9845 1477
Email: denise.campbell@health.nsw.gov.au
Appendix D: Supporting data for chapter 6
Interview guide, participant information sheets consent forms

D1. Interview guide

Patient experiences and views on peritoneal dialysis: a qualitative study

Introduction/briefing (interviewer)

How are you?
Thank you very much for agreeing to be interviewed. I am a PhD student enrolled with Sydney University and am conducting research about patients’ perspectives on peritoneal dialysis. The interviews conducted through this study, with people who have/ have had experience with peritoneal dialysis, will hopefully generate information which will help doctors provide better care and support for people receiving peritoneal dialysis.

I will be asking you questions about your experiences with peritoneal dialysis, to get a sense of what life is like on peritoneal dialysis and what impact it has had on you and your family/carers. It shouldn’t take more than one hour. I would like to record the interview with my voice recorder because this will help me later on to analyse the information generated.

The recording will be kept confidential. What you tell me will be de-identified and will not impact the care you receive. Please let me know if you want me to stop recording at any time.

Before we begin, would you like to ask me any questions?

1. Introduction
   a. Explain study information sheet and obtain informed consent
   b. What is your date of birth?
   c. Where were you born?
   d. Who lives with you? (married, single, divorced, widowed)
   e. How long have you been/ were you on peritoneal dialysis?
   f. Which type of PD are/ were you on? (APD, CAPD)
   g. Are you now on haemodialysis? Have you received a kidney transplant?
   h. Are you on the waitlist for a transplant? Do you have blood sent to the Red Cross each month?

2. General experiences and perspectives of peritoneal dialysis
   a. How did you come to be on peritoneal dialysis?
   b. What are some of the biggest challenges or difficulties you face with peritoneal dialysis and how do you cope with them?
   c. Has peritoneal dialysis made an impact on your life - how? (work, social life)
   d. Has going on peritoneal dialysis changed the way you see yourself and how you feel - how? (positive and negative impact on identity, self-esteem, emotions)
Appendix D: Supporting data for chapter 6

e. Do you think that being on peritoneal dialysis affects the people close to you - how? (family, close friends)

3. **PD technical aspects/ complications/ modality failure**
   a. What aspects of doing peritoneal dialysis are/were you most/least confident about? Why?
   b. What dialysis complications are/were you most concerned about? Why?
   c. You have been on both APD and CAPD – what do you think are the main differences between the two in terms of managing your dialysis? Do you feel one is easier to do than the other? How?
   d. Why would you switch/have you switched to haemodialysis?

4. **Perspectives on peritonitis**
   a. What is the first thought that comes to your mind when I say peritonitis?
   b. Can you describe to me your most recent episode of peritonitis? What was your initial thought/feeling when you were told you had peritonitis?
   c. How did having peritonitis impact your day to day living? (work, family, social activities)
   d. What do you think caused your peritonitis? Did your healthcare provider explain why they think you got peritonitis – what were you told?
   e. What sorts of things do you think makes a person on peritoneal dialysis have a higher chance of getting peritonitis?
   f. What do you do to prevent yourself from getting peritonitis again?
   g. What were the most difficult things to deal with when you had peritonitis? What did you do to cope with those issues?

5. **Support and education**
   a. What advice would you give to someone who was about to start peritoneal dialysis?
   b. What would you tell them about your experience of peritoneal dialysis?
   c. What programs/initiatives can you suggest that might help to improve the patient experience of PD? (education, support groups)

6. **Healthcare service provision**
   a. What aspects of care are/were most important to you? (access to PD nurses, access to nephrologists, home visits by PD staff)
   b. In an ideal world, what would be 1 or 2 things that you would do to improve peritoneal dialysis treatment? (healthcare, technical, support)

**Closing question:**

Is there anything else that you think is important about peritoneal dialysis that you want to add before we finish? Thank you for your time.
Appendix D: Supporting data for chapter 6

D2. Participant information sheet (QLD),

Patient experiences and views on peritoneal dialysis: a qualitative study

PARTICIPANT INTERVIEW INFORMATION SHEET

Dear Patient

You are invited to participate in a research study looking into the experiences, views and needs of patients on peritoneal dialysis and the effect that being on peritoneal dialysis has on a patient’s quality of life. We know that commencing dialysis has an impact on a patient’s quality of life. We also know that having an in-depth understanding of the experiences, views and needs of patients on peritoneal dialysis can be used to develop more patient-centred health care. We want to learn about your experience of being on peritoneal dialysis and hopefully, find out ways to improve the treatment and support given to patients.

The study is being conducted by all of the investigators listed above.

The study is an Australian multi-centre study coordinated by Australian researchers based at the Centre for Kidney Research, Children’s Hospital at Westmead, NSW. The study is funded by the Centre for Kidney Research, NSW.

What is the study about?

There are two main types of dialysis available for patients with end-stage kidney failure – haemodialysis and peritoneal dialysis. Quality of life is a term used to describe how you feel and how well you are able to do your usual activities. Health-related quality of life questionnaires have shown that after 1 year of dialysis, there are differences in the quality of life experienced by patients according to which type of dialysis they are on. We want to get an idea of the effect that being on peritoneal dialysis has had on
your quality of life. We also want to find out what are common experiences, needs and views of patients on peritoneal dialysis because this information can be used to improve the treatment, education and support given to patients and their families.

The purpose of this study is to investigate the experiences and views of patients who have been or are currently on peritoneal dialysis and have experienced one or more episodes of peritonitis.

**Who can participate in the study?**

You are invited to participate in this study because you have been diagnosed with end-stage kidney disease and are currently on or have been on peritoneal dialysis as your treatment. You have also experienced at least one episode of peritonitis. You will need to be able to read and communicate in English to participate.

**Do you have a choice?**

Participation in this study is voluntary. It is completely up to you whether or not you participate. If you decide not to participate, it will not affect the treatment you receive now or in the future. Whatever your decision, it will not affect your relationship with the staff caring for you. New information about the treatment being studies may become available during the course of the study. You will be kept informed of any significant new findings that may affect your willingness to continue in the study. If you wish to withdraw from the study once it has started, you can do so at any time without having to give a reason. However, it may not be possible to withdraw your data from the study results if these have already had your identifying details removed.

**What will the study involve?**

If you agree to participate in the study, you will be asked to sign the Patient Consent Form. This study will be conducted over approx. 18 months.

Participation in this project is entirely voluntary and if you decide not to take part or decide to withdraw at any time, this will not affect your care at the Hospital or that of your family in any way. The data from this study will be kept for 5 years and it is acceptable for you to withdraw from the study at any point during this time.

You will be asked to participate in a face-to-face interview with a researcher from the Centre for Kidney Research, NSW. The interview will take place either in your home or an alternative setting where you feel comfortable. If you wish, your carer may be present during the interview. Each interview will take approx. 30 minutes to 1 hour to complete and will be audio recorded. We will ask you some basic demographic questions (e.g. age, marital status, type of PD treatment) and questions about your experiences and views on peritoneal dialysis and healthcare service in general. The interview will be transcribed verbatim and if you wish, you will be sent a summary of the interview which you can give feedback on.

Please feel free to talk to the Associate Investigator at your Renal Unit if you want to discuss how you felt answering the questions. You can also call the researcher at the Centre for Kidney Research who interviewed you. The coordinating centre for this study is located at the Centre for Kidney Research, Children’s Hospital at Westmead, Westmead, NSW.

If you have any questions about the study, please call the study coordinator (Tel: (02) 9845 1477).

The information we collect during the interview will have your name and details removed and will then be analysed to identify common and uncommon themes and concepts. We will try to identify
relationships between themes and from this build a model that adequately describes the information patients have given us during the interviews. From this, we will assess what effect the peritoneal dialysis treatment and peritonitis has had on your quality of life. We will also gain insight into ways that patients on peritoneal dialysis could be better supported and clinical care improved. The results of the study will be published so that other health care professionals will benefit from our findings. Should the stored data be used for any other purpose, then Ethical Approval will need to be granted.

Are there any risks from participating in the study?

There may be risks associated with this study that are presently unknown or unforeseeable.

Are there any benefits from participating in the study?

This study aims to further medical knowledge and patient support/education and may improve future treatment of people on peritoneal dialysis, however, it may not directly benefit you.

Are there any side-effects and risks associated with this study?

There are no side-effects or risks. The questions asked during the interview are related to your dialysis treatment, episode of peritonitis and about your quality of life and are not intended to upset you.

Other information

The information we collect is kept strictly confidential. The data is accessible only to the researchers involved in this research project and it will be stored for 5 years at the Centre for Kidney Research, Children's Hospital at Westmead, Westmead, NSW.

Complaints

If you have any concerns about the conduct of this study, or your rights as a study participant, you may contact the Associate Researcher at your unit (see phone number on page 1) or the Metro South HREC Coordinator (07 3443 8049; email: PAH_Ethics_research@health.qld.gov.au) and quote HREC reference number HREC/13/QPAH/286.

Thank you for taking the time to consider this study. This Information sheet is for you to keep.
D3. Participant information sheet and consent form (VIC)

MONASH HEALTH

Participant Information
Sheet/Consent Form

Non-Interventional Study - Adult providing own consent

<table>
<thead>
<tr>
<th>Title</th>
<th>Patient experiences and views on peritoneal dialysis: a qualitative study</th>
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<tr>
<td>Short Title</td>
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<tr>
<td>Project Sponsor</td>
<td>Centre for Kidney Research</td>
</tr>
<tr>
<td>Coordinating Principal Investigator/Principal Investigator</td>
<td>Dr Fiona Brown</td>
</tr>
<tr>
<td>Associate Investigator(s)</td>
<td></td>
</tr>
<tr>
<td>Location (where CPI/PI will recruit)</td>
<td>Department of Nephrology</td>
</tr>
</tbody>
</table>

Part 1   What does my participation involve?

1 Introduction
You are invited to take part in this research project, ‘Patient experiences and views on peritoneal dialysis’. This is because we want to find out about the experiences, views and needs of patients on peritoneal dialysis and the effect that being on peritoneal dialysis has on a patient’s quality of life. The research project is aiming to learn about your experience of being on peritoneal dialysis and hopefully, find out ways to improve the treatment and support given to patients.

This Participant Information Sheet/Consent Form tells you about the research project. It explains the tests and research involved. Knowing what is involved will help you decide if you want to take part in the research.

Please read this information carefully. Ask questions about anything that you don't understand or want to know more about. Before deciding whether or not to take part, you might want to talk about it with a relative, friend or local doctor.

Participation in this research is voluntary. If you don't wish to take part, you don't have to. You will receive the best possible care whether or not you take part.

If you decide you want to take part in the research project, you will be asked to sign the consent section. By signing it you are telling us that you:

• Understand what you have read
• Consent to take part in the research project
• Consent to the tests and research that are described
Appendix D: Supporting data for chapter 6

- Consent to the use of your personal and health information as described. You will be given a copy of this Participant Information and Consent Form to keep.

2 What is the purpose of this research?

The purpose of this study is to investigate the experiences and views of patients who have been or are currently on peritoneal dialysis and have experienced one or more episodes of peritonitis.

We want to find out what are common experiences, needs and views of patients on peritoneal dialysis because this information can be used to improve the treatment, education and support given to patients and their families.

This study aims to further medical knowledge and patient support/education and may improve future treatment of people on peritoneal dialysis.

There are two main types of dialysis available for patients with end-stage kidney failure – haemodialysis and peritoneal dialysis. Quality of life is a term used to describe how you feel and how well you are able to do your usual activities. Health-related quality of life questionnaires have shown that after 1 year of dialysis, there are differences in the quality of life experienced by patients according to which type of dialysis they are on. We want to get an idea of the effect that being on peritoneal dialysis has had on your quality of life.

This research is being undertaken as part of the work being submitted for a PhD by Denise Campbell (Centre for Kidney Research, Westmead, NSW) and is funded partly by the University of Sydney and by the Centre for Kidney Research, Westmead, NSW.

This research is being conducted by Australian researchers based at the Centre for Kidney Research, Sydney Children’s Hospital Network (Westmead), NSW.

3 What does participation in this research involve?

If you agree to participate in the study, you will be asked to sign the Patient Consent Form before the interview takes place.

You will be eligible to participate in this study if you have been diagnosed with end-stage kidney disease and are currently on or have been on peritoneal dialysis as your treatment. You will have also experienced at least one episode of peritonitis. You will need to be able to read and communicate in English to participate.

You will be asked to participate in a face-to-face interview with a researcher from the Centre for Kidney Research, NSW. The interview will take place either in your home or an alternative setting where you feel comfortable. If you wish, your carer may be present during the interview. Each interview will take approx. 30 minutes to 1 hour to complete and will be audio recorded. We will ask you some basic demographic questions (e.g. age, marital status, type of PD treatment) and questions about your experiences and views on peritoneal dialysis and healthcare service in general. The interview will be audio recorded and transcribed verbatim. If you wish, you will be sent a summary of the interview which you can give feedback on.

This research project has been designed to make sure the researchers interpret the results in a fair and appropriate way and avoids study doctors or participants jumping to conclusions.
There are no costs associated with participating in this research project, nor will you be paid.

4 What do I have to do?
You will be asked to participate in a face-to-face interview with a researcher from the Centre for Kidney Research, NSW. Each interview will take approx. 30 minutes to 1 hour to complete and will be audio recorded.

5 Other relevant information about the research project
Approximately 30 people will take part in the study overall, with approximately 8 participants coming from the Monash Health site.

Interviews will take place with participants from 5 Renal Units at metropolitan hospitals – 3 Units in NSW, 1 in QLD and 1 in VIC.

Two Associate Investigators from the Centre for Kidney Research, Westmead, NSW, will conduct the face-to-face interviews.

6 Do I have to take part in this research project?
Participation in any research project is voluntary. If you do not wish to take part, you do not have to. If you decide to take part and later change your mind, you are free to withdraw from the project at any stage.

If you do decide to take part, you will be given this Participant Information and Consent Form to sign and you will be given a copy to keep.

Your decision whether to take part or not to take part, or to take part and then withdraw, will not affect your routine treatment, your relationship with those treating you or your relationship with Monash Health.

7 What are the alternatives to participation?
You do not have to take part in this research project to receive treatment at this hospital.

8 What are the possible benefits of taking part?
We cannot guarantee or promise that you will receive any benefits from this research, however possible benefits may include improved future treatment of people on peritoneal dialysis.

9 What are the possible risks and disadvantages of taking part?
There are no side-effects or risks. The questions asked during the interview are related to your dialysis treatment, episode of peritonitis and about your quality of life and are not intended to upset you.

If you become upset or distressed as a result of your participation in the research, the study doctor will be able to arrange for counselling or other appropriate support. Any counselling or support will be provided by qualified staff who are not members of the research project team. This counselling will be provided free of charge.

13 What if I withdraw from this research project?
If you decide to withdraw from this research project, please notify a member of the research team before
you withdraw. Participation in this project is entirely voluntary and if you decide not to take part or decide to withdraw at any time, this will not affect your care at the Hospital or that of your family in any way. The data from this study will be kept for 5 years and it is acceptable for you to withdraw from the study at any point during this time. You will need to complete and submit a withdrawal of consent form.

If you do withdraw your consent during the research project, the study doctor and relevant study staff will not collect additional personal information from you, although personal information already collected will be retained to ensure that the results of the research project can be measured properly and to comply with law. You should be aware that data collected by the sponsor up to the time you withdraw will form part of the research project results. If you do not want them to do this, you must tell them before you join the research project.

**15 What happens when the research project ends?**

The interview will be transcribed verbatim and if you wish, you will be sent a summary of the interview which you can give feedback on. The results of the study will be published so that other health care professionals will benefit from our findings.

**Part 2 How is the research project being conducted?**

**16 What will happen to information about me?**

The information we collect during the interview will have your name and details removed and will then be analysed to identify common and uncommon themes and concepts. You will not be individually identifiable.

The information we collect is kept strictly confidential. The data is accessible only to the researchers involved in this research project and it will be stored at the Centre for Kidney Research, Sydney Children's Hospital Network (Westmead), Westmead, NSW.

The study data will be stored for 7 years following completion of the study. The audio recordings will be stored on a computer file (external hard disk). Both electronic and paper copies of the transcripts will be stored. At the end of 7 years, both will be destroyed in a secure manner. Paper copies will be shredded. Data on electronic files will be reformatted or rewritten.

The participant is being asked to provide consent to the use of their data for this project only. The study does not involve the establishment of a databank.

By signing the consent form you consent to the study doctor and relevant research staff collecting and using personal information about you for the research project. Any information obtained in connection with this research project that can identify you will remain confidential. The interview with you will be transcribed and will have your name and details removed. You will not be individually identifiable. Your information will only be used for the purpose of this research project and it will only be disclosed with your permission, except as required by law.

It is anticipated that the results of this research project will be published and/or presented in a variety of forums. In any publication and/or presentation, information will be provided in such a way that you cannot be identified, except with your permission. The data obtained from your interview will be included with the data from other interviews and analysed to identify themes and concepts. If something you have said during interview is included in the publication/presentation, it will not include details that identify you.
In accordance with relevant Australian and/or Victorian privacy and other relevant laws, you have the right to request access to the information collected and stored by the research team about you. You also have the right to request that any information with which you disagree be corrected. Please contact the research team member named at the end of this document if you would like to access your information.

Any information obtained for the purpose of this research project that can identify you will be treated as confidential and securely stored. It will be disclosed only with your permission, or as required by law.

17 Complaints and compensation

If you suffer any injuries or complications as a result of this research project, you should contact the study team as soon as possible and you will be assisted with arranging appropriate medical treatment. If you are eligible for Medicare, you can receive any medical treatment required to treat the injury or complication, free of charge, as a public patient in any Australian public hospital.

18 Who is organising and funding the research?

The study is an Australian multi-centre study coordinated by Australian researchers based at the Centre for Kidney Research, Sydney Children’s Hospital Network (Westmead), NSW. The study is funded by the Centre for Kidney Research, Westmead, NSW.

No member of the research team will receive a personal financial benefit from your involvement in this research project (other than their ordinary wages).

19 Who has reviewed the research project?

All research in Australia involving humans is reviewed by an independent group of people called a Human Research Ethics Committee (HREC). The ethical aspects of this research project have been approved by the HREC of Monash Health.

This project will be carried out according to the National Statement on Ethical Conduct in Human Research (2007). This statement has been developed to protect the interests of people who agree to participate in human research studies.

20 Further information and who to contact

The person you may need to contact will depend on the nature of your query.

If you want any further information concerning this project or if you have any medical problems which may be related to your involvement in the project (for example, any side effects), you can contact the principal study doctor on (03) 9594 3529 or any of the following people:

**Clinical contact person**

<table>
<thead>
<tr>
<th>Name</th>
<th>Dr Fiona Brown</th>
</tr>
</thead>
<tbody>
<tr>
<td>Position</td>
<td>Consultant Nephrologist, Dept. of Nephrology</td>
</tr>
<tr>
<td>Telephone</td>
<td>(03) 9594 3529</td>
</tr>
</tbody>
</table>
Email Fiona.brown@monash.edu

For matters relating to research at the site at which you are participating, the details of the local site complaints person are:

**Complaints contact person**

<table>
<thead>
<tr>
<th>Name</th>
<th>Ms Deborah Dell</th>
</tr>
</thead>
<tbody>
<tr>
<td>Position</td>
<td>Manager, Human Research Ethics Committee</td>
</tr>
<tr>
<td>Telephone</td>
<td>(03) 9594 4605</td>
</tr>
<tr>
<td>Email</td>
<td><a href="mailto:Deborah.Dell@monashhealth.org">Deborah.Dell@monashhealth.org</a></td>
</tr>
</tbody>
</table>
**xConsent Form - Adult providing own consent**

<table>
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<tr>
<td>Coordinating Principal Investigator/</td>
<td>Dr Fiona Brown</td>
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<tr>
<td>Associate Investigator(s)</td>
<td></td>
</tr>
<tr>
<td>Location (where CPI/PI will recruit)</td>
<td>Department of Nephrology</td>
</tr>
</tbody>
</table>

**Declaration by Participant**

I have read the Participant Information Sheet or someone has read it to me in a language that I understand. I understand the purposes, procedures and risks of the research described in the project.

I have had an opportunity to ask questions and I am satisfied with the answers I have received.

I freely agree to participate in this research project as described and understand that I am free to withdraw at any time during the project without affecting my future health care.

I understand that I will be given a signed copy of this document to keep.

<table>
<thead>
<tr>
<th>Name of Participant (please print)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Signature</td>
<td>Date</td>
</tr>
</tbody>
</table>

| Name of Witness* to Participant’s |  |
| Signature (please print)         |  |
| Signature                         | Date |

* Witness is not to be the investigator, a member of the study team or their delegate. In the event that an interpreter is used, the interpreter may **not** act as a witness to the consent process. Witness must be 18 years or older.

**Declaration by Study Doctor/Senior Researcher†**

I have given a verbal explanation of the research project, its procedures and risks and I believe that the participant has understood that explanation.

<table>
<thead>
<tr>
<th>Name of Study Doctor/</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Senior Researcher† (please print)</td>
<td></td>
</tr>
<tr>
<td>Signature</td>
<td>Date</td>
</tr>
</tbody>
</table>

† A senior member of the research team must provide the explanation of, and information concerning, the research project. Note: All parties signing the consent section must date their own signature.
## Form for Withdrawal of Participation - Adult providing own consent

<table>
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<tr>
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<td></td>
</tr>
</tbody>
</table>

### Associate Investigator(s)

| Location (where CPI/PI will recruit) | Department of Nephrology |

### Declaration by Participant

I wish to withdraw from participation in the above research project and understand that such withdrawal will not affect my routine treatment, my relationship with those treating me or my relationship with Monash Health.

| Name of Participant (please print) | ______________________ |
| Signature | Date |

*In the event that the participant’s decision to withdraw is communicated verbally, the Study Doctor/Senior Researcher will need to provide a description of the circumstances below.*

### Declaration by Study Doctor/Senior Researcher†

I have given a verbal explanation of the implications of withdrawal from the research project and I believe that the participant has understood that explanation.

| Name of Study Doctor/ | |
| Senior Researcher† (please print) | |
| Signature | Date |

†A senior member of the research team must provide the explanation of and information concerning withdrawal from the research project.

Note: All parties signing the consent section must date their own signature.
D4. Participant information sheet and consent form (NSW)

PARTICIPANT INFORMATION AND CONSENT FORM

Study Title: Patient experiences and views on peritoneal dialysis: a qualitative study

Chief Investigator:
Dr Germaine Wong, Department of Renal Medicine

Introduction
We are conducting a research study into the experiences, views and needs of patients on peritoneal dialysis and the effect that being on peritoneal dialysis has on a patient’s quality of life. We know that commencing dialysis has an impact on a patient's quality of life. We also know that having an in-depth understanding of the experiences, views and needs of patients on peritoneal dialysis can be used to develop more patient-centred health care. We want to learn about your experience of being on peritoneal dialysis and hopefully, find out ways to improve the treatment and support given to patients.

The study is being conducted by the following investigators:

Associate Investigators:
Ms. Denise Campbell, Centre for Kidney Research, Sydney Children’s Hospital Network (Westmead), NSW Tel: (02) 9845 1477

Dr Allison Tong, Centre for Kidney Research, Sydney Children's Hospital Network (Westmead), NSW Tel: (02) 9845 1482

Principal Investigators:
Assoc. Prof David Mudge, Dept. of Nephrology, Princess Alexandra Hospital, QLD Tel: (07) 3176 7765

Dr John Saunders, Dept. of Renal Medicine, Royal Prince Alfred Hospital, NSW Tel: (02) 9515 6600

Dr Germaine Wong, Dept. of Renal Medicine, Westmead Hospital, NSW Tel: (02) 9845 6962

Assoc. Prof Martin Gallagher, Dept. of Nephrology, Concord Hospital, NSW Tel: (02) 9993 4552

Dr Fiona Brown, Dept. of Nephrology, Monash Medical Centre, VIC Tel: (03) 9594 3529
Before you decide whether or not you wish to participate in this study, it is important for you to understand why the research is being done and what it will involve. Please take the time to read the following information carefully and discuss it with others if you wish.

**What is the purpose of the study?**

The purpose is to investigate the experiences and views of patients who have been or are currently on peritoneal dialysis and have experienced one or more episodes of peritonitis.

There are two main types of dialysis available for patients with end-stage kidney failure – haemodialysis and peritoneal dialysis. Quality of life is a term used to describe how you feel and how well you are able to do your usual activities. Health-related quality of life questionnaires have shown that after 1 year of dialysis, there are differences in the quality of life experienced by patients according to which type of dialysis they are on. We want to get an idea of the effect that being on peritoneal dialysis has had on your quality of life. We also want to find out what are common experiences, needs and views of patients on peritoneal dialysis because this information can be used to improve the treatment, education and support given to patients and their families.

**Who will be invited to enter the study?**

You are invited to participate in this study because you have been diagnosed with end-stage kidney disease and are currently on or have been on peritoneal dialysis as your treatment.

You have also experienced at least one episode of peritonitis. You will need to be able to read and communicate in English to participate.

**Do you have a choice?**

Participation in this study is voluntary. It is completely up to you whether or not you participate. If you decide not to participate, it will not affect the treatment you receive now or in the future. Whatever your decision, it will not affect your relationship with the staff caring for you. New information about the treatment being studied may become available during the course of the study. You will be kept informed of any significant new findings that may affect your willingness to continue in the study. If you wish to withdraw from the study once it has started, you can do so at any time without having to give a reason.

However, it may not be possible to withdraw your data from the study results if these have already had your identifying details removed.

**What will happen on the study?**

If you agree to participate in this study, you will be asked to sign the Participant Information and Consent Form. This study will be conducted over approximately 18 months with individual participation of 30-60 minutes.

You will be asked to participate in a face-to-face interview with a researcher from
the Centre for Kidney Research, NSW. The interview will take place either in your home or an alternative setting where you feel comfortable. If you wish, your carer may be present during the interview. Each interview will take approx. 30 minutes to 1 hour to complete and will be audio recorded. We will ask you some basic demographic questions (e.g. age, marital status, type of peritoneal dialysis treatment) and questions about your experiences and views on peritoneal dialysis and the healthcare service in general. The interview will be recorded word for word and if you wish, you will be sent a summary of the interview which you can give feedback on.

Please feel free to talk to the Principal Investigator at your Renal Unit if you want to discuss how you felt answering the questions. You can also call the researcher at the Centre for Kidney Research who interviewed you. The coordinating centre for this study is located at the Centre for Kidney Research, Sydney Children’s Hospital Network (Westmead), Westmead, NSW.

The information we collect during the interview will have your name and personal details removed and will then be analysed to identify common and uncommon themes and concepts. We will try to identify relationships between themes and from this build a model that adequately describes the information patients have given us during the interviews. From this, we will assess what effect the peritoneal dialysis treatment and peritonitis has had on your quality of life. We will also gain insight into ways that patients on peritoneal dialysis could be better supported and clinical care improved. The results of the study will be published so that other health care professionals will benefit from our findings.

**Are there any risks?**

There may be risks associated with this study that are presently unknown or unforeseeable. There are no side-effects or risks. The questions asked during the interview are related to your dialysis treatment, episode of peritonitis and about your quality of life and are not intended to upset you. If you experience any distress as a result of participating in the interview, we will arrange for you to speak to a social worker/psychologist at the hospital.

**Are there any benefits?**

This study aims to further medical knowledge and patient support/education and may improve future treatment of people on peritoneal dialysis, however it may not directly benefit you.

**Confidentiality / Privacy**

Of the people treating you, only those named above or necessary others will know whether or not you are participating in this study. Any identifiable information that is collected about you in connection with this study will be coded by the study staff, and will not be labeled with or identified by your name, picture or any other information that can directly identify you. It will remain confidential and will be disclosed only with your permission, or except as required by law. Only the researchers named above will have access to your details and results that will be held securely at the Centre for
Kidney Research, Sydney Children’s Hospital Network (Westmead), Westmead, NSW.

**Will taking part in this study cost me anything, and will I be paid?**

Participation in this study will not cost you anything and you will not be paid for your participation. You will be reimbursed for reasonable travel expenses.

**What happens with the results?**

If you give us your permission by signing the consent document, we plan to present the results at conferences or other professional forums and publish the findings in a peer-reviewed journal. In any publication, information will be provided in such a way that you cannot be identified. Results of the study will be provided to you, if you wish.

**Complaints**

This study has been approved by Western Sydney Local Health District Human Research Ethics Committee. If you have any concerns about the conduct of the study, or your rights as a study participant, you may contact: Westmead Hospital Patient Representative, telephone 9845 7014. You should quote HREC project number HREC2013/12/4.10 (3888) AU RED HREC/13/WMEAD/419.

**Contact details**

When you have read this information, the researcher [Denise Campbell/Allison Tong] will discuss it with you and any queries you may have. If you would like to know more at any stage, please do not hesitate to contact him/her on [9845 1477/9845 1482]. If you have any problems while on the study, please contact

**Dr Germaine Wong**

Working hours Telephone No – 9845 6962

After hours Telephone No – (mobile) 0411 603 282

**Thank you for taking the time to consider this study.**

**If you wish to take part in it, please sign the attached consent form. This information sheet is for you to keep.**
CONSENT TO PARTICIPATE IN RESEARCH

Chief Investigator:

1. I understand that the researcher will conduct this study in a manner conforming to ethical and scientific principles set out by the National Health and Medical Research Council of Australia and the Good Clinical Research Practice Guidelines of the Therapeutic Goods Administration.

2. I acknowledge that I have read, or have had read to me the Participant Information Sheet relating to this study. I acknowledge that I understand the Participant Information Sheet. I acknowledge that the general purposes, methods, demands and possible risks and inconveniences which may occur to me during the study have been explained to me by ______ (“the researcher”) and I, being over the age of 18 acknowledge that I understand the general purposes, methods, demands and possible risks and inconveniences which may occur during the study.

3. I acknowledge that I have been given time to consider the information and to seek other advice.

4. I acknowledge that refusal to take part in this study will not affect the usual treatment of my condition.

5. I acknowledge that I am volunteering to take part in this study and I may withdraw at any time.

6. I acknowledge that this research has been approved by the Western Sydney Local Health District Human Research Ethics Committee.

7. I acknowledge that I have received a copy of the Participant Information, and this form which I have signed.

8. I acknowledge that any regulatory authorities may have access to my medical records relevant to this study to monitor the research in which I am agreeing to participate. However, I understand my identity will not be disclosed to anyone else or in publications or presentations.

Before signing, please read ‘IMPORTANT NOTE’ following.

IMPORTANT NOTE:
This consent should only be signed as follows:

1. Where a participant is over the age of 18 years, then by the participant personally.

Name of participant _______________________________ Date of Birth _______________________________

Address of participant _______________________________________________________________

Signature of participant _______________________________ Date: _______________________________

Signature of researcher _______________________________ Date: _______________________________

Signature of witness _______________________________ Date: _______________________________
INTERVIEW PARTICIPANT CONSENT FORM
Patient experiences and views on peritoneal dialysis: a qualitative study

Primary Investigators:
Ms. Denise Campbell, Centre for Kidney Research, The Children’s Hospital at Westmead, NSW Tel: (02) 9845 1477
Dr Allison Tong, Centre for Kidney Research, The Children’s Hospital at Westmead, NSW Tel: (02) 9845 1482

Associate Investigators:
Assoc. Prof David Mudge, Dept. of Nephrology, Princess Alexandra Hospital, QLD Tel: (07) 3176 7765
Dr John Saunders, Dept. of Renal Medicine, Royal Prince Alfred Hospital, NSW Tel: (02) 9515 6600
Dr Germaine Wong, Dept. of Renal Medicine, Westmead Hospital, NSW Tel: (02) 9845 6962
Assoc. Prof Martin Gallagher, Dept. of Nephrology, Concord Hospital, NSW Tel: (02) 9993 4552
Dr John Saunders, Dept. of Renal Medicine, Royal Prince Alfred Hospital, NSW Tel: (02) 9515 6600
Dr Germaine Wong, Dept. of Renal Medicine, Westmead Hospital, NSW Tel: (02) 9845 6962
Assoc. Prof Martin Gallagher, Dept. of Nephrology, Concord Hospital, NSW Tel: (02) 9993 4552

I have read and understand the Participant Information Sheet, and give my consent to participate in this research study, which has been explained to me by

________________________________________________________

NAME OF INDIVIDUAL: _______________________________________ (Please print)
SIGNATURE OF INDIVIDUAL: ________________________________ Date: ______

NAME OF RESEARCHER: ____________________________________ (Please print)
SIGNATURE OF RESEARCHER: ________________________________ Date: ______

I understand that I am free to withdraw from the study at any time, without having to provide a reason, and this decision will not otherwise affect my treatment at the Hospital.

I have been informed that if I wish to withdraw my consent and not be involved in the study, I need to phone, send an email or letter to:

Denise Campbell PhD student
Centre for Kidney Research, The Children’s Hospital at Westmead

Locked Bag 4001
Westmead NSW 2145
Phone: (02) 9845 1477
Email: denise.campbell@health.nsw.gov.au

I have also been advised that I may only withdraw prior to the approval of the interview transcript and that I will be asked to complete and sign a ‘Withdrawal of Consent’ form.

If I decide to leave the study, I have been told the researchers would like to keep the personal and/ health information about me that has been collected. If I do not want them to do this, I must tell them before I withdraw from the study.