Systematic review of the effectiveness of preventing and treating Staphylococcus aureus carriage in reducing peritoneal catheter-related infections

K McCormack, K Rabindranath, M Kilonzo, L Vale, C Fraser, L McIntyre, S Thomas, H Rothnie, N Fluck, IM Gould and N Waugh

July 2007
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Systematic review of the effectiveness of preventing and treating Staphylococcus aureus carriage in reducing peritoneal catheter-related infections

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Abstract

Systematic review of the effectiveness of preventing and treating Staphylococcus aureus carriage in reducing peritoneal catheter-related infections

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Objectives: To determine the clinical effectiveness and cost-effectiveness of (1) alternative strategies for the prevention of Staphylococcus aureus carriage in patients on peritoneal dialysis (PD) and (2) alternative strategies for the eradication of S. aureus carriage in patients on PD.

Data sources: Major electronic databases were searched up to December 2005 (MEDLINE Extra up to 6 January 2006).

Review methods: Electronic searches were undertaken to identify published and unpublished reports of randomised controlled trials and systematic reviews evaluating the effectiveness of preventing and treating S. aureus carriage on peritoneal catheter-related infections. The quality of the included studies was assessed and data synthesised. Where data were not sufficient for formal meta-analysis, a qualitative narrative review looking for consistency between studies was performed.

Results: Twenty-two relevant trials were found. These fell into several groups: the first split is between prophylactic trials, aiming to prevent carriage, and trials which aimed to eradicate carriage in those who already had it; the second split is between antiseptics and antibiotics; and the third split is between those that included patients having the catheter inserted before dialysis started and people already on dialysis. Many of the trials were small or short-term. The quality was often not good by today’s standards. The body of evidence suggested a reduction in exit-site infections, but this did not seem to lead to a significant reduction in peritonitis, although to some extent this reflected insufficient power in the studies and a low incidence of peritonitis in them. The costs of interventions to prevent or treat S. aureus carriage are relatively modest. For example, the annual cost of antibiotic treatment of S. aureus carriage per identified carrier of S. aureus was estimated at £179 (£73 screening and £106 cost of antibiotic). However, without better data on the effectiveness of the interventions, it is not clear whether such costs are offset by the cost of treating infections and averting changes from peritoneal dialysis to haemodialysis. Although treatment is not expensive, the lack of convincing evidence of clinical effectiveness made cost-effectiveness analysis unrewarding at present. However, consideration was given to the factors needed in a hypothetical model describing patient pathways from methods to prevent S. aureus carriage, its detection and treatment and the detection and treatment of the consequences of S. aureus (e.g. catheter infections and peritonitis). Had data been available, the model would have compared the cost-effectiveness of alternative interventions from the perspective of the UK NHS, but as such it helped identify what future research would be needed to fill the gaps.

Conclusions: The importance of peritonitis is not in doubt. It is the main cause of people having to switch from peritoneal dialysis to haemodialysis, which then leads to reduced quality of life for patients
and increased costs to the NHS. Unfortunately, the present evidence base for the prevention of peritonitis is disappointing; it suggests that the interventions reduce exit-site infections, but not peritonitis, although this may be due to trials being in too small numbers for too short periods. Trials are needed with larger numbers of patients for longer durations.
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<th>Abbreviation</th>
<th>Description</th>
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<tbody>
<tr>
<td>CEAC</td>
<td>cost-effectiveness acceptability curve</td>
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<tr>
<td>CI</td>
<td>confidence interval</td>
</tr>
<tr>
<td>EPO</td>
<td>erythropoietin</td>
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<tr>
<td>EURODICE</td>
<td>European Dialysis and Cost Effectiveness</td>
</tr>
<tr>
<td>HCHS</td>
<td>Hospital and Community Health Services</td>
</tr>
<tr>
<td>HD</td>
<td>haemodialysis</td>
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<tr>
<td>ITT</td>
<td>intention-to-treat</td>
</tr>
<tr>
<td>MRSA</td>
<td>methicillin-resistant</td>
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<tr>
<td>MSSA</td>
<td>methicillin-sensitive</td>
</tr>
<tr>
<td>NICE</td>
<td>National Institute for Health and Clinical Excellence</td>
</tr>
<tr>
<td>PD</td>
<td>peritoneal dialysis</td>
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<tr>
<td>QALY</td>
<td>quality-adjusted life-year</td>
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<tr>
<td>RCT</td>
<td>randomised controlled trial</td>
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<tr>
<td>RR</td>
<td>relative risk</td>
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<tr>
<td>SA</td>
<td><em>Staphylococcus aureus</em></td>
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All abbreviations that have been used in this report are listed here unless the abbreviation is well known (e.g. NHS), or it has been used only once, or it is a non-standard abbreviation used only in figures/tables/appendices in which case the abbreviation is defined in the figure legend or at the end of the table.
Objectives

The objectives of this review were to determine the clinical effectiveness and cost-effectiveness of alternative strategies for the prevention and eradication of *Staphylococcus aureus* carriage in patients on peritoneal dialysis (PD). The aim was to prevent, or reduce, the frequency of peritonitis. The review does not cover treatment of peritonitis itself.

Background and intervention

In chronic renal failure, dialysis is used to replace the kidneys’ function in removing impurities and unwanted products of metabolism from the blood. Peritoneal dialysis is a form of ambulatory dialysis in which fluid is fed into the abdominal cavity via a catheter through the abdominal wall. The fluid collects the substances normally excreted by the kidney. After an interval the fluid is drained out again.

The main complication of peritoneal dialysis in the short term is infection of the peritoneal cavity, peritonitis. In the longer term, recurrent episodes of peritonitis can impair diffusion across the peritoneal membrane, so that peritoneal dialysis is no longer feasible, which means that patients have to attend hospital for haemodialysis, usually three times per week.

One of the organisms which cause peritonitis is *Staphylococcus aureus*. It can colonise parts of the body without symptoms, but may cause infection where the peritoneal catheter passes through the skin of the abdomen. These are known as exit-site infections. It may also contaminate the tip of the catheter. In both situations, peritonitis may be a consequence.

Various measures have been used to try to prevent or eradicate colonisation, in the hope that this will prevent, or reduce, the frequency of peritonitis. These include antiseptics and antibiotics. The antibiotics can be applied locally or given systemically, by mouth.

*S. aureus* can develop resistance to commonly used antibiotics, and is then known as methicillin-resistant *Staphylococcus aureus* (MRSA).

Epidemiology

End-stage renal failure can be a consequence of a number of diseases, the commonest being glomerulonephritis, diabetes, renal vascular disease, pyelonephritis and polycystic kidney disease.

Methods

Electronic searches were undertaken to identify published and unpublished reports of randomised controlled trials (RCTs) and systematic reviews evaluating the effectiveness of preventing and treating *S. aureus* carriage on peritoneal catheter-related infections. The main databases searched were MEDLINE (1966–2005), EMBASE (1980–2005), CINAHL (1982–2005), BIOSIS (1985–2005), Science Citation Index (SCI) (1980–2005), MEDLINE Extra (6 January 2006), Cochrane Library (Issue 4 2005), Database of Abstracts of Reviews of Effectiveness (December 2005) and HTA Database (December 2005). The quality of the included studies was assessed and data synthesised. Where data were not sufficient for formal meta-analysis, a qualitative narrative review looking for consistency between studies was performed.

Results

Number and quality of studies and summary of benefits

Twenty-two trials were found. These fell into several groups: the first split is between prophylactic trials, aiming to prevent carriage, and trials which aimed to eradicate carriage in those who already had it; the second split is between antiseptics and antibiotics; and the third split is between those that included patients having the catheter inserted before dialysis started and people already on dialysis. Many of the trials were small or short-term. The quality was often not good by today’s standards. The body of evidence suggested a reduction in exit-site infections but this did not seem to lead to a significant reduction in peritonitis, although to some extent this reflected insufficient power in the studies and a low incidence of peritonitis in them.
Costs
The costs of interventions to prevent or treat S. aureus carriage are relatively modest. For example, the annual cost of antibiotic treatment of S. aureus carriage per identified carrier of S. aureus was estimated at £179 (£73 screening and £106 cost of antibiotic). However, without better data on the effectiveness of the interventions, it is not clear whether such costs are offset by the cost of treating infections and averting changes from peritoneal dialysis to haemodialysis.

Cost-effectiveness
Although treatment is not expensive, the lack of convincing evidence of clinical effectiveness made cost-effectiveness analysis unrewarding at present. However, consideration was given to the factors needed in a hypothetical model describing patient pathways from methods to prevent S. aureus carriage, its detection and treatment and the detection and treatment of the consequences of S. aureus (e.g. catheter infections and peritonitis). Had data been available, the model would have compared the cost-effectiveness of alternative interventions from the perspective of the UK NHS, but as such it helped identify what future research would be needed to fill the gaps.

Conclusions
The importance of peritonitis is not in doubt. It is the main cause of people having to switch from peritoneal dialysis to haemodialysis, which leads to reduced quality of life for patients and increased costs to the NHS. Unfortunately, the present evidence base for the prevention of peritonitis is disappointing; it suggests that the interventions reduce exit-site infections but not peritonitis, although this may be due to trials being in too small numbers for too short periods.

Recommendations for research
The study identified key research questions that need to be addressed. These are given below.

- What is the natural history of carriage of S. aureus? What are the links between carriage and exit-site infection, and between exit-site infection and peritonitis? What factors predict carriage?
- Is the problem mainly with MRSA, with methicillin-sensitive Staphylococcus aureus (MSSA) being relatively harmless?
- Does decolonisation work, or is recolonisation rapid?
- Apart from antibiotic and antiseptic use, what other options for reducing peritonitis are there? Would more training help?
- Should measures to eradicate carriage be intermittent or chronic; antiseptics versus antibiotics?
- Is vaccination worth revisiting?
- Given the common use of mupirocin in renal units, research into that drug and resistance to it should be a priority.

Trials are needed with larger numbers of patients for longer durations.
The objectives of this review were to determine the clinical effectiveness and cost-effectiveness of alternative strategies for the prevention and eradication of *Staphylococcus aureus* carriage in patients on peritoneal dialysis (PD). The aim was to prevent, or reduce, the frequency of peritonitis. The review does not cover treatment of peritonitis itself.
Chapter 2

Background

**Description of the problem**

*S. aureus* is a bacterium that lives completely harmlessly on the skin and in the nose of about one-third of normal healthy people. This situation can be called colonisation or carriage. Other *S. aureus* carriage sites include the axillae, vagina, perineum and occasionally the gastrointestinal tract.

However, although colonisation of those sites may not cause any problems there, the presence of the organism means that more vulnerable parts of the body may be first contaminated and then infected. In PD, a catheter is inserted into the abdominal cavity though the skin of the abdominal wall and exits through a subcutaneous tunnel. Whenever the skin is broken, there is a risk of infection. Hence people on PD are at increased risk because of the break in the skin. Some may also be at increased risk of all infections because of the diseases which lead to renal failure, such as diabetes.

PD is used more in the UK than in other countries. Almost one-third of the dialysis population in the UK are on PD\(^1\) and 50% of PD patients are known to be *S. aureus* carriers.\(^2\) Some studies have reported that nasal carriage of *S. aureus* is more frequent in diabetic and immunosuppressed PD patients.\(^3,4\)

PD catheter-related infections are an important cause of morbidity and mortality in the PD population. Such infections are classified into exit-site, tunnel infections and peritonitis. An exit-site infection is defined as purulent drainage at the catheter exit site with or without erythema. A tunnel infection is an infection of the tissues overlying the subcutaneous portion of the catheter.\(^5\) Peritonitis is inflammation of the peritoneal membrane. Exit-site or tunnel infections cause significant morbidity as they can lead to refractory or recurrent peritonitis.\(^6\) Peritonitis is associated with several adverse consequences. It accounts for the majority of occasions when the PD catheter has to be removed, leading to transfer to haemodialysis (HD).\(^7,8\) Peritonitis is one of the most common causes for hospitalisation in PD patients.\(^9\) It contributes to the decline of peritoneal membrane function, which means that PD may become impossible. It may also lead to a more rapid decline in residual renal function (i.e. some patients still have a little function left in their kidneys) and is an important predictor of survival.\(^10\)

Although there can be many different causes of PD catheter-related infections, *S. aureus* is an important cause. It is believed to be the leading cause of PD catheter exit-site infection\(^11,12\) and one of the most frequent causes of PD-related peritonitis.\(^13\) It has been estimated that the peritonitis rates due to *S. aureus* are 0.09–0.22 per dialysis year.\(^2,14\) The cost of *S. aureus* infections in the dialysis population in the USA has been estimated to be over US$200 million annually.\(^15\)

Several studies have shown a strong link between *S. aureus* carriage and PD catheter exit-site and tunnel infections\(^16–18\) and peritonitis.\(^19,20\) *S. aureus* carriers, have a two- to six-fold higher risk of *S. aureus* peritonitis than non-carriers.\(^2,19\)

Peritonitis due to *S. aureus* tends to be more severe than that due to other organisms, with patients more likely to have fever and hypotension.\(^21\) Hospital admission may be prolonged with *S. aureus* peritonitis\(^8\) and it also increases mortality.\(^22,23\) Furthermore, removal of the PD catheter is required more often in *S. aureus* peritonitis than with peritonitis due to other bacteria, to resolve the peritonitis or prevent recurrence.\(^24\) Removal of the catheter means that PD has to be replaced by HD, requiring at least temporary attendance at hospital dialysis sessions, usually three times per week.

**Descriptions of interventions**

Studies comparing carriage and infecting *S. aureus* isolates have shown that patients are infected with their ‘own’ organism, that is, the one they carry on skin or nose.\(^2,25,26\) Although *S. aureus* is found in the body in areas other than the nose, elimination of nasal carriage also leads to loss of carriage in other sites such as hands and skin,\(^27\) implying that the other parts are being reinfected from the nose. In addition, the PD catheter exit site is reported to be most important colonising site of *S. aureus*.\(^2\)
strains that cause peritonitis. These important observations underpin strategies that aim to reduce *S. aureus*-related PD catheter infections and peritonitis.

*S. aureus* is normally susceptible to a variety of antibiotics, the most commonly used of which is mupirocin, given as an ointment.

### Recommendations according to various guidelines

Various bodies have made recommendations, although these are not necessarily followed in practice.

- **Renal Association (UK):** Peritonitis rates should be less than one episode per 18 patient months. Mupirocin should be applied to the exit site either daily or on alternate days. Nasal carriage of *S. aureus* should be treated with mupirocin twice daily for five consecutive days every 4 weeks.
- **European Renal Association–European Dialysis and Transplantation Association (ERA–EDTA):** Mupirocin should be applied either at the exit site or intranasally especially in patients who are *S. aureus* carriers.
- **International Society of Peritoneal Dialysis:** Several options are recommended: exit-site mupirocin daily in all patients or in *S. aureus* carriers only or in response to positive *S. aureus* culture; intranasal mupirocin every month in those identified as carriers or only in response to positive nose culture; exit-site gentamicin in all patients.
- **Caring for Australians with Renal Impairment (CARI guidelines):** Prophylactic therapy using mupirocin ointment, especially for *S. aureus* carriage intranasally, is recommended to decrease the risk of *S. aureus* catheter exit site/tunnel infections and peritonitis.

It is clear that although all guidelines recommend mupirocin for *S. aureus* nasal carriers, there is considerable variation with other recommendations. There has been no systematic review of evidence for the effectiveness of interventions for prevention and treatment of *S. aureus* carriage in PD patients. It was against this background that the NHS Research and Development Programme for Health Technology Assessment (HTA) commissioned this study.
Chapter 3

Efficacy and safety

Methods for reviewing effectiveness

Search strategy
Electronic searches were undertaken to identify published and unpublished reports of randomised controlled trials (RCTs) and systematic reviews evaluating the effectiveness of preventing and treating S. aureus carriage on peritoneal catheter-related infections.

The main databases searched were MEDLINE (1966–2005), EMBASE (1980–2005), CINAHL (1982–2005), BIOSIS (1985–2005), Science Citation Index (SCI) (1980–2005), MEDLINE Extra (6 January 2006), Cochrane Library (Issue 4 2005), Database of Abstracts of Reviews of Effectiveness (December 2005) and HTA Database (December 2005). Searching was restricted to English language publications only. In addition, recent conference proceedings, tables of contents of two key PD journals and reference lists of all included studies were scanned to identify additional potentially relevant studies. Full details of the search strategies used are documented in Appendix 1.

All titles and abstracts identified in these ways were assessed to identify potentially eligible studies. Two reviewers independently assessed them for inclusion, using a study eligibility form developed for this purpose (Appendix 2). Any disagreements were resolved by consensus or arbitration.

Data extraction strategy
The titles and abstracts of all papers identified by the search strategy were screened. Full text copies of all potentially relevant studies were obtained and assessed for inclusion. Reviewers were not blinded to the names of studies’ authors, institutions or sources of the reports. Any disagreements were resolved by consensus or arbitration.

A data extraction form was developed to record details of trial methods, participants, interventions, patient characteristics and outcomes (Appendix 3).

Types of participants
The trials included patients on PD for end-stage renal disease from any cause.

Types of outcomes
The following measures of outcomes were sought:

Primary outcome:
1. number of patients with peritonitis caused by S. aureus.

Secondary outcomes:
1. number of patients with S. aureus carriage
2. time to S. aureus carriage
3. peritonitis rate (number of episodes over total patient months on PD) caused by S. aureus
4. time to first peritonitis episode caused by S. aureus
5. peritonitis relapse (number and specify time to) caused by S. aureus
6. number of patients requiring catheter removal caused by S. aureus
7. number of patients requiring catheter replacement caused by S. aureus
8. number of patients switching to HD caused by S. aureus
9. number of patients with exit-site and/or tunnel infections caused by S. aureus
10. exit-site and/or tunnel infection rate caused by S. aureus
11. side-effects
12. death due to peritonitis caused by S. aureus
13. hospitalisation rates
14. quality of life
15. development of antibiotic resistance.

Inclusion and exclusion criteria

Types of studies
All published RCTs and quasi-RCTs (e.g. allocation by alternation) of patients receiving PD for end-stage renal disease in whom alternative interventions were compared for the prevention and treatment of S. aureus carriage were included. For the purposes of this review, studies comparing alternative interventions for the treatment of clinical infections and studies which did not report outcomes separately for S. aureus were excluded.

Types of participants
The trials included patients on PD for end-stage renal disease from any cause.

Types of outcomes
The following measures of outcomes were sought:

Primary outcome:
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Secondary outcomes:
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A data extraction form was developed to record details of trial methods, participants, interventions, patient characteristics and outcomes (Appendix 3).
Two reviewers independently extracted data from the included studies. Any differences that could not be resolved through discussion were referred to an arbiter.

**Quality assessment strategy**
Two reviewers, working independently, assessed the methodological quality of the included studies. Again, any disagreements were resolved by consensus or arbitration. The system for classifying methodological quality of controlled trials was based on an assessment of four principal potential sources of bias: selection bias caused by inadequate concealment of allocation of treatments; attrition bias caused by losses to follow-up without appropriate intention-to-treat (ITT) analysis; detection bias caused by biased ascertainment of outcome where knowledge of the allocation might have influenced the measurement of outcome; and selection bias in analysis (Appendix 3).

**Data synthesis**
For trials with multiple publications, only the most up-to-date data for each outcome were included. Dichotomous outcome data were combined using the Mantel–Haenszel relative risk (RR) method and 95% confidence intervals (CIs) and p-values were calculated for the estimates. The results were all reported using a fixed-effects model. χ² tests and I² statistics were used to explore statistical heterogeneity across studies and, when present, random effects methods were applied. Other possible reasons for heterogeneity were explored using sensitivity analyses. The meta-analyses were conducted using the standard Cochrane software RevMan 4.2.

Where data were not sufficient for formal meta-analysis, a qualitative narrative review looking for consistency between studies was performed.

### Results

**Quantity and quality of research available**

**Number of studies identified**
The results of the searches are summarised in Table 1. The numbers retrieved from the searches in CINAHL, SCI, Biosis and CENTRAL and screening of full text journals include only the additional reports found after excluding those identified from the MEDLINE/EMBASE multifile search.

A total of 498 titles and abstracts were identified from the various searches, of which 394 were clearly outwith the scope of this review. The remaining 104 reports (90 full text papers and 14 abstracts) were selected for full assessment. Table 2 details the numbers of these that were included and excluded.

**Number and type of studies included**

Twenty-five reports (21 full text papers and four abstracts) describing 22 RCTs met the inclusion criteria for the review and were included in the review of clinical effectiveness. The majority of these reports were identified from the MEDLINE/EMBASE search (20), with two each identified from SCI and the full text journals and one from BIOSIS. The list of included studies and associated references are listed in Appendix 4. No studies were identified only from CINAHL.

Trials fell into several groups. The first split is between prophylactic trials, aiming to prevent
carriage, and between trials which aimed to eradicate carriage in those who already had it. The second split is between antiseptics and antibiotics. The third split is between those that included patients having the catheter inserted before dialysis started and those where the people were already on dialysis.

**Number and type of studies excluded, with reasons for specific exclusions**

A total of 46 reports were obtained but subsequently were excluded because they failed to meet one or more of the inclusion criterion. Of these, 17 were not RCTs, seven were concerning the treatment of clinical infections and in 22 the authors did not report outcomes separately for participants with *S. aureus* carriage (18 primary reports and four secondary reports).

**Study quality, characteristics and evidence rating**

A summary of the quality assessment of the 22 RCTs is presented in Table 3 and the detailed quality assessment for each of the included studies is reported in Appendix 5. The method of randomisation used was stated explicitly for 11 of 22 trials: a central randomisation service was used in one study, consecutively numbered, sealed envelopes were used in one study, computer-generated random numbers were used in one study, there was consecutive allocation in two, by random numbers table in three, by date of follow-up in one, assigned by a third party in one and random selection by cards in one. By modern standards, most of these methods are unsatisfactory, but some of the trials were done some time ago. In 11 trials, the allocation was said to be ‘randomised’ but the method was not specified. Concealment of allocation was adequate in only one trial, suboptimal in four and unclear in 17.

In the majority of trials, it was unclear whether studies blinded the care provider, participant, outcome assessor or data analyst (but it is questionable if this is possible given the nature of the treatments compared). Five studies included an ITT analysis but it was unclear if this were the case for the remaining 25 studies.

Eligibility criteria were clearly specified in 21 studies. The mean or median duration of follow-up ranged from at least 48 hours to 1 year. This was not reported for three studies.

**Characteristics of included studies**

The comparisons made and characteristics of the RCTs are summarised in Table 4 and a detailed description for each of the included studies is reported in Appendix 6. Within the 22 eligible RCTs, there were 30 relevant comparisons (four trials had three arms). Three trials took place in the UK, eight in the USA, two in Hong Kong, two in Brazil and one each in Spain, Turkey, Singapore and Canada. There were two multi-centre European trials and one multi-centre Australia and New Zealand trial. Across the trials recruitment dates ranged from May 1987 to August 2003. Eleven trials failed to provide information on recruitment dates. The number of participants randomised ranged from 15 to 267. Two trials had more than 200 participants, eight more than 100 participants and 12 fewer than 100 participants. Eighteen trials gave details of the numbers of men and women in each trial group. Seventeen trials gave details of participants’ ages. One trial included children only.

**Assessment of effectiveness**

Table 5 gives a summary of the outcomes reported in the included studies.

**Prophylaxis amongst all patients**

Eighteen trials evaluated prophylaxis amongst all patients regardless of their *S. aureus* status at trial entry. Four trials evaluated prophylaxis at the time of catheter insertion and the remaining trials considered prophylaxis given once dialysis had commenced. Five trials compared antibiotic treatment with no antibiotic treatment, four trials compared two different antibiotic regimes, one three-armed trial compared two different antibiotic regimes with no antibiotic treatment, three trials compared antiseptic treatment with no antiseptic treatment, one trial compared two different types of antiseptics, one trial compared a vaccination with combined staphylococcus

---

**TABLE 3 Summary of the quality assessment of the included RCTs**

<table>
<thead>
<tr>
<th>Allocation concealment</th>
<th>Blinding of investigators</th>
<th>Blinding of participants</th>
<th>Blinding of assessor</th>
<th>Blinding of data analysis</th>
<th>ITT</th>
<th>Lost to follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adequate: 1</td>
<td>Yes: 1</td>
<td>Yes: 2</td>
<td>Yes: 1</td>
<td>Yes: 0</td>
<td>Stated: 3</td>
<td>Yes: 12</td>
</tr>
<tr>
<td>Inadequate: 4</td>
<td>No: 5</td>
<td>No: 4</td>
<td>No: 2</td>
<td>No: 1</td>
<td>Not stated: 19</td>
<td>No: 0</td>
</tr>
<tr>
<td>Unclear: 17</td>
<td>Unclear: 17</td>
<td>Unclear: 16</td>
<td>Unclear: 19</td>
<td>Unclear: 21</td>
<td></td>
<td>Unclear: 10</td>
</tr>
</tbody>
</table>

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### TABLE 4  Summary of the comparisons made and baseline characteristics

<table>
<thead>
<tr>
<th>Study</th>
<th>Comparison</th>
<th>No. of participants</th>
<th>Age (years)</th>
<th>Male/female</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Prophylaxis amongst all patients</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Antibiotic versus no antibiotic</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Catheter insertion:</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bennett-Jones, 1988&lt;sup&gt;35&lt;/sup&gt;</td>
<td>I.v. gentamicin</td>
<td>13</td>
<td>52.7 ± 18.6&lt;sup&gt;a&lt;/sup&gt;</td>
<td>8/5</td>
</tr>
<tr>
<td></td>
<td>No treatment</td>
<td>13</td>
<td>52.7 ± 18.6&lt;sup&gt;a&lt;/sup&gt;</td>
<td>9/4</td>
</tr>
<tr>
<td>Lye, 1992&lt;sup&gt;26&lt;/sup&gt;</td>
<td>I.v. cefazolin and gentamicin</td>
<td>25</td>
<td>56.0 ± 14.3</td>
<td>8/17</td>
</tr>
<tr>
<td></td>
<td>No treatment</td>
<td>25</td>
<td>52.3 ± 14.0</td>
<td>15/10</td>
</tr>
<tr>
<td><strong>During dialysis:</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sharma, 1971&lt;sup&gt;17&lt;/sup&gt;</td>
<td>Neomycin by mouth or nasogastric tube</td>
<td>48 dialysates</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td></td>
<td>Placebo</td>
<td>41 dialysates</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Lye, 1992&lt;sup&gt;36&lt;/sup&gt;</td>
<td>I.v. cefazolin and gentamicin</td>
<td>25</td>
<td>56.0 ± 14.3</td>
<td>8/17</td>
</tr>
<tr>
<td></td>
<td>No treatment</td>
<td>25</td>
<td>52.3 ± 14.0</td>
<td>15/10</td>
</tr>
<tr>
<td><strong>Antibiotic versus antibiotic</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>During dialysis:</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bernardini, 1996&lt;sup&gt;40&lt;/sup&gt;</td>
<td>Mupirocin ointment</td>
<td>41</td>
<td>–</td>
<td>49%/51%</td>
</tr>
<tr>
<td></td>
<td>Oral rifampin</td>
<td>41</td>
<td>–</td>
<td>59%/41%</td>
</tr>
<tr>
<td>Bernardini, 2005&lt;sup&gt;51,42&lt;/sup&gt;</td>
<td>Mupirocin ointment</td>
<td>66</td>
<td>51 ± 15</td>
<td>38/28</td>
</tr>
<tr>
<td></td>
<td>Gentamicin ointment</td>
<td>67</td>
<td>51 ± 15</td>
<td>34/33</td>
</tr>
<tr>
<td>Cavdar, 2004&lt;sup&gt;43&lt;/sup&gt;</td>
<td>Mupirocin ointment applied once weekly</td>
<td>18</td>
<td>55.3 ± 1.8&lt;sup&gt;c&lt;/sup&gt;</td>
<td>10/8</td>
</tr>
<tr>
<td></td>
<td>Mupirocin ointment applied thrice weekly</td>
<td>18</td>
<td>55.0 ± 2.3&lt;sup&gt;c&lt;/sup&gt;</td>
<td>11/7</td>
</tr>
<tr>
<td><strong>Antibiotic versus antibiotic versus no antibiotic</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Catheter insertion:</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gadallah, 2000&lt;sup&gt;44,45&lt;/sup&gt;</td>
<td>I.v. vancomycin</td>
<td>90 (103 procedures)</td>
<td>46 (15 to 72)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>38/52</td>
</tr>
<tr>
<td></td>
<td>I.v. cefazolin</td>
<td>88 (102 procedures)</td>
<td>47 (20 to 81)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>43/45</td>
</tr>
<tr>
<td></td>
<td>No treatment</td>
<td>87 (100 procedures)</td>
<td>45 (19 to 76)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>38/49</td>
</tr>
<tr>
<td><strong>Antiseptic versus no antiseptic</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Catheter insertion:</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Waite, 1997&lt;sup&gt;46&lt;/sup&gt;</td>
<td>Povidone–iodine ointment</td>
<td>61</td>
<td>54.4 ± 15.1</td>
<td>33/28</td>
</tr>
<tr>
<td></td>
<td>No treatment</td>
<td>56</td>
<td>53.2 ± 14.5</td>
<td>30/26</td>
</tr>
<tr>
<td><strong>During dialysis:</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Luzar, 1990&lt;sup&gt;1&lt;/sup&gt;</td>
<td>Povidone–iodine</td>
<td>74</td>
<td>–</td>
<td>63%/37%</td>
</tr>
<tr>
<td></td>
<td>Non-disinfectant soap</td>
<td>53</td>
<td>–</td>
<td>59%/41%</td>
</tr>
<tr>
<td>Sesso, 1988&lt;sup&gt;47&lt;/sup&gt;</td>
<td>Chlorhexidine</td>
<td>20</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td></td>
<td>Neutral soap</td>
<td>19</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Wilson, 1997&lt;sup&gt;48&lt;/sup&gt;</td>
<td>Povidone–iodine spray</td>
<td>77 catheters</td>
<td>53 (18–82)&lt;sup&gt;c&lt;/sup&gt;</td>
<td>55/22</td>
</tr>
<tr>
<td></td>
<td>No treatment</td>
<td>72 catheters</td>
<td>51 (21–76)&lt;sup&gt;c&lt;/sup&gt;</td>
<td>43/29</td>
</tr>
<tr>
<td>Wong, 2002&lt;sup&gt;49&lt;/sup&gt;</td>
<td>Chlorhexidine liquid soap</td>
<td>69</td>
<td>59.0 ± 11.50&lt;sup&gt;b&lt;/sup&gt;</td>
<td>34/35</td>
</tr>
<tr>
<td></td>
<td>Pure liquid soap</td>
<td>48</td>
<td>56.3 ± 11.7&lt;sup&gt;b&lt;/sup&gt;</td>
<td>23/25</td>
</tr>
<tr>
<td><strong>Antiseptic versus antiseptic</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>During dialysis:</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fuchs, 1990&lt;sup&gt;50&lt;/sup&gt;</td>
<td>Chlorhexidine</td>
<td>18</td>
<td>46&lt;sup&gt;c&lt;/sup&gt;</td>
<td>7/11</td>
</tr>
<tr>
<td></td>
<td>Sodium hypochlorite</td>
<td>13</td>
<td>47&lt;sup&gt;c&lt;/sup&gt;</td>
<td>7/6</td>
</tr>
<tr>
<td></td>
<td>Povidone–iodine swabsticks plus povidone ointment</td>
<td>20</td>
<td>55&lt;sup&gt;c&lt;/sup&gt;</td>
<td>13/7</td>
</tr>
<tr>
<td><strong>Other</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>During dialysis:</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Poole-Warren, 1991&lt;sup&gt;51&lt;/sup&gt;</td>
<td>Vaccination</td>
<td>65</td>
<td>54 ± 11</td>
<td>1.5 (ratio)</td>
</tr>
<tr>
<td></td>
<td>Placebo</td>
<td>59</td>
<td>52 ± 14</td>
<td>0.7 (ratio)</td>
</tr>
</tbody>
</table>

*continued*
toxoid/whole killed staphylococci formulation with a placebo, one three-armed trial compared a catheter immobiliser with the use of tape and non-immobilisation and one trial compared the ‘flush before fill’ technique with standard practice.

Table 6 provides details, where reported, of the results for the following outcomes: number of patients with *S. aureus* carriage (at trial entry); number of patients with peritonitis; peritonitis rate (number of episodes over total patient months on PD); number of patients requiring catheter removal; number of patients with exit-site and/or tunnel infections; and the exit-site and/or tunnel infection rate.

### Time to *S. aureus* carriage

One trial, comparing vaccination with a combined staphylococcus toxoid/whole killed staphylococci formulation (SB) given intramuscularly with placebo, also reported the number of *S. aureus*-positive nasal swabs relative to the total nasal swabs taken at each time point (Table 7).

### Time to the first peritonitis episode

One trial comparing intravenous vancomycin approximately 12 hours before catheter placement with intravenous cefazolin approximately 3 hours before catheter placement with no antibiotics for at least 1 week before procedure, reported the time to the first peritonitis episode. There was one case of peritonitis at 6 days in the intravenous cefazolin and two cases of peritonitis at 1 and 4 days in the group allocated to receive no antibiotics at least 1 week before surgery.

### Side-effects

Three trials reported side-effects of antibiotic prophylaxis: Bernardini and colleagues reported that four out of 41 patients experienced nausea and vomiting in the oral rifampin group and one other required liver function tests. There were no reported side-effects in the mupirocin group. Bernardini and colleagues reported exit-site irritation in seven out of 66 patients in the mupirocin group and seven out of 67 patients in the gentamicin group. Wilson and colleagues reported...

---

### TABLE 4  Summary of the comparisons made and baseline characteristics (cont’d)

<table>
<thead>
<tr>
<th>Study</th>
<th>Comparison</th>
<th>No. of participants</th>
<th>Age (years)</th>
<th>Male/female</th>
</tr>
</thead>
<tbody>
<tr>
<td>Turner, 1992</td>
<td>Catheter immobiliser</td>
<td>22</td>
<td>45 ± 15.5</td>
<td>–</td>
</tr>
<tr>
<td></td>
<td>Tape</td>
<td>23</td>
<td>40 ± 14.2</td>
<td>–</td>
</tr>
<tr>
<td></td>
<td>Non-immobilisation</td>
<td>21</td>
<td>43 ± 15.8</td>
<td>–</td>
</tr>
<tr>
<td>Warady, 2003</td>
<td>‘Flush before fill’</td>
<td>62</td>
<td>11.4 ± 5.6</td>
<td>54.8%/45.2%</td>
</tr>
<tr>
<td></td>
<td>Flushing with 15 ml of sterile dialysate</td>
<td>59</td>
<td>11.2 ± 6.0</td>
<td>59.3%/40.7%</td>
</tr>
</tbody>
</table>

#### Treatment of *S. aureus* carriage

**Antibiotic versus no antibiotic**

**During dialysis:**

- Blowey, 1994
  - Oral rifampin plus bacitracin: 7 participants
  - No treatment: 8 participants

- Mupirocin Study Group, 1996
  - Mupirocin ointment: 134 participants
  - Placebo ointment: 133 participants

**Antibiotic versus antibiotic**

**During dialysis:**

- Perez-Fontan, 1992
  - Mupirocin nasal ointment: 12 participants
  - Neomycin sulphate ointment: 10 participants

- Sesso, 1994
  - Sodium fusidate ointment: 9 participants
  - Oral ofloxacin: 9 participants
  - Placebo tablets: 13 participants

---

* Data are expressed as mean ± standard deviation (SD) unless stated otherwise.
* Measure unclear.
* Mean.
* Mean ± standard error of the mean (SEM).
* Mean ± standard error (range).
### TABLE 5  Summary of outcomes reported in the included studies

<table>
<thead>
<tr>
<th>Study ID</th>
<th>Prophylaxis amongst all patients</th>
<th>Treatment of S. aureus carriage</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. of patients with S. aureus carriage</td>
<td>Time to S. aureus carriage</td>
</tr>
<tr>
<td>Bennett-Jones, 1988</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Bernardini, 1996</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Bernardini, 2005</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Cavdar, 2004</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Fuchs, 1990</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Gadallah, 2000</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Luzar, 1990</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Lye, 1992</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Poole-Warren, 1991</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Sesso, 1988</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Sharma, 1971</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Turner, 1992</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Waite, 1997</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Warady, 2003</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Wilson, 1997</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Wong, 2002</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Wong, 2003</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Zimmerman, 1999</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Blower, 1994</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Muriprocin Study Group, 1996</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Perez-Fontan, 1992</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Sesso, 1994</td>
<td>✓</td>
<td>✓</td>
</tr>
</tbody>
</table>
### TABLE 6  Outcomes results for prophylaxis amongst all patients

<table>
<thead>
<tr>
<th>Study</th>
<th>Comparison</th>
<th>S. aureus carriage at trial entry (no.)</th>
<th>Peritonitis (no.)</th>
<th>Peritonitis rate</th>
<th>Catheter removal (no.)</th>
<th>ESI and/or T1 (no.)</th>
<th>ESI and/or T1 rate</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Antibiotic versus no antibiotic</strong></td>
<td>Catheter insertion:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bennett-Jones, 198835</td>
<td>I.v. gentamicin – No treatment</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>0/13</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Wong, 200338</td>
<td>I.v. cefazolin and gentamicin – No treatment</td>
<td>16/73</td>
<td>1/78 (MSSA)</td>
<td>–</td>
<td>0/78</td>
<td>0/78</td>
<td>–</td>
</tr>
<tr>
<td>Wong, 200338</td>
<td>Neomycin – Placebo</td>
<td>–</td>
<td>0/48</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Wong, 200338</td>
<td>Mupirocin ointment – Placebo</td>
<td>1/81</td>
<td>1/88 (MRSA)</td>
<td>–</td>
<td>0/88</td>
<td>10/88</td>
<td>–</td>
</tr>
<tr>
<td>Zimmerman, 199139</td>
<td>Rifampin – No treatment</td>
<td>9/32</td>
<td>3/32</td>
<td>0.11 mean episodes/patient year</td>
<td>3/32</td>
<td>0.22 mean infections/patient year</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Antibiotic versus antibiotic</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bernardini, 199640</td>
<td>Mupirocin ointment – Oral rifampin</td>
<td>44%</td>
<td>–</td>
<td>0.04 episodes/dialysis year</td>
<td>–</td>
<td>–</td>
<td>0.13 episodes/dialysis year</td>
</tr>
<tr>
<td>Bernardini, 200541</td>
<td>Mupirocin ointment – Gentamicin ointment</td>
<td>9/66</td>
<td>0/66</td>
<td>0 episodes/patient year</td>
<td>3/66</td>
<td>0.06 episodes/patient year</td>
<td></td>
</tr>
<tr>
<td>Cavdar, 200443</td>
<td>Mupirocin ointment once weekly – Mupirocin ointment thrice weekly</td>
<td>3/18</td>
<td>0/18</td>
<td>–</td>
<td>0/18</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td></td>
<td>Antibiotic versus antibiotic versus no antibiotic</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gadallah, 2000445</td>
<td>I.v. vancomycin – No treatment</td>
<td>–</td>
<td>0/90</td>
<td>–</td>
<td>0/90</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td></td>
<td>I.v. cefazolin – No treatment</td>
<td>–</td>
<td>1/88</td>
<td>–</td>
<td>1/88</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td></td>
<td>No treatment</td>
<td>–</td>
<td>2/87</td>
<td>–</td>
<td>1/87</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td></td>
<td>Antiseptic versus no antiseptic</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Whate, 199746</td>
<td>Povidone-iodine ointment – No treatment</td>
<td>22/61</td>
<td>0/61</td>
<td>–</td>
<td>1/61</td>
<td>2/61</td>
<td>–</td>
</tr>
<tr>
<td></td>
<td></td>
<td>14/56</td>
<td>2/56</td>
<td>–</td>
<td>2/56</td>
<td>8/56</td>
<td>–</td>
</tr>
</tbody>
</table>

Continued
### TABLE 6 Outcomes results for prophylaxis amongst all patients (cont’d)

<table>
<thead>
<tr>
<th>Study</th>
<th>Comparison</th>
<th>S. aureus carriage at trial entry (no.)</th>
<th>Peritonitis (no.)</th>
<th>Peritonitis rate</th>
<th>Catheter removal (no.)</th>
<th>ESI and/or TI (no.)</th>
<th>ESI and/or TI rate</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>During dialysis:</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Luzar, 19903</td>
<td>Povidone iodine</td>
<td>–</td>
<td>8/74</td>
<td>–</td>
<td>–</td>
<td>15/74</td>
<td>–</td>
</tr>
<tr>
<td></td>
<td>Non-disinfectant soap</td>
<td>–</td>
<td>3/53</td>
<td>–</td>
<td>16/53</td>
<td>–</td>
<td></td>
</tr>
<tr>
<td>Sesso, 198847</td>
<td>Chlorhexidine</td>
<td>–</td>
<td>6/19</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Neutral soap</td>
<td>–</td>
<td>4/16</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td></td>
</tr>
<tr>
<td>Wilson, 199748</td>
<td>Povidone–iodine spray</td>
<td>–</td>
<td>2/77</td>
<td>–</td>
<td>9/77</td>
<td>–</td>
<td></td>
</tr>
<tr>
<td></td>
<td>No treatment</td>
<td>–</td>
<td>3/72</td>
<td>–</td>
<td>22/72</td>
<td>–</td>
<td></td>
</tr>
<tr>
<td>Wong, 200249</td>
<td>Chlorhexidine liquid soap</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>0/69</td>
<td>–</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Pure liquid soap</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>4/48</td>
<td>–</td>
<td></td>
</tr>
<tr>
<td><strong>Antiseptic versus antiseptic</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fuchs, 199050</td>
<td>Chlorhexidine</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>1/18</td>
<td>1/134 per patient month</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Sodium hypochlorite</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>2/13</td>
<td>1/41 per patient month</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Povidone–iodine/povidone ointment</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>0/20</td>
<td>–</td>
<td></td>
</tr>
<tr>
<td><strong>Other</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Poole-Warren, 199151</td>
<td>Vaccination</td>
<td>13/40</td>
<td>8/60</td>
<td>–</td>
<td>29/44</td>
<td>–</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Placebo</td>
<td>11/36</td>
<td>8/51</td>
<td>–</td>
<td>25/25</td>
<td>–</td>
<td></td>
</tr>
<tr>
<td>Turner, 199252</td>
<td>Catheter immobiliser</td>
<td>10/22</td>
<td>–</td>
<td>–</td>
<td>4/22</td>
<td>–</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Tape</td>
<td>11/23</td>
<td>–</td>
<td>–</td>
<td>4/23</td>
<td>–</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Non-immobilisation</td>
<td>6/21</td>
<td>–</td>
<td>–</td>
<td>4/21</td>
<td>–</td>
<td></td>
</tr>
<tr>
<td>Warady, 200353</td>
<td>‘Flush before fill’</td>
<td>–</td>
<td>7/62</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Flushing with 15 ml of sterile dialysate</td>
<td>–</td>
<td>15/59</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td></td>
</tr>
</tbody>
</table>

ESI, exit-site infection; MRSA, methicillin-resistant *Staphylococcus aureus*; MSSA, methicillin-sensitive *Staphylococcus aureus*; TI, timed infection.

a Denominators are unclear therefore numbers randomised are reported.

b 5 × MSSA; 5 × MRSA.

c Catheter infections.

d Episodes.

e Microorganisms.
reported a rash and pruritus at the catheter exit site in five patients allocated to use the povidone–iodine spray. There were no reported side-effects in the group which received no treatment.

**Death due to peritonitis caused by *S. aureus***

Only one trial reported this outcome. Only one trial compared neomycin 0.5 g by mouth or nasogastric tube every 6 hours with a placebo and reported that there were no deaths due to peritonitis caused by *S. aureus*.

**Development of antibiotic resistance**

One trial comparing mupirocin applied to the exit site once weekly with mupirocin applied three times weekly reported no difference between the groups (one out of seven isolations were resistant to mupirocin in the group applying mupirocin once weekly and one isolation resistant to mupirocin and methicillin in the group applying mupirocin three times weekly).

No data were reported for the following outcomes: peritonitis relapse, number of patients requiring catheter replacement, hospitalisation rates and quality of life.

**Oral antibiotics versus no antibiotics**

Four trials compared an oral antibiotic with no antibiotics and one trial compared two different types of oral antibiotics with no antibiotic. When considering all oral antibiotics together, there were fewer cases of peritonitis caused by *S. aureus* in the groups which received antibiotics (Figure 1: 6/283 versus 7/185: RR 0.69, 95% CI 0.28 to 1.72; \( p = 0.43 \)), but this was not a statistically significant difference. There were also fewer cases of exit-site and/or tunnel infections caused by *S. aureus* (Figure 2, 5/70 versus 20/70: RR 0.27, 95% CI 0.11 to 0.65; \( p = 0.003 \)). The direction of effect was similar when considering subcategories (catheter insertion and during dialysis).

**Topical antibiotics versus no antibiotics**

Only one trial compared the use of a topical antibiotic with no antibiotics. There was no difference in the number of patients with peritonitis caused by *S. aureus*. However, there were 0/78 cases of exit-site and/or tunnel infections caused by *S. aureus*.

### TABLE 7  *S. aureus* nasal carriage versus weeks following vaccination, expressed as number of carriers/group total

<table>
<thead>
<tr>
<th>No. of weeks</th>
<th>Vaccination</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-study</td>
<td>13/40</td>
<td>11/36</td>
</tr>
<tr>
<td>7</td>
<td>19/50</td>
<td>14/44</td>
</tr>
<tr>
<td>19</td>
<td>11/51</td>
<td>14/46</td>
</tr>
<tr>
<td>32</td>
<td>9/29</td>
<td>5/20</td>
</tr>
<tr>
<td>44</td>
<td>2/22</td>
<td>6/25</td>
</tr>
<tr>
<td>57</td>
<td>10/20</td>
<td>6/22</td>
</tr>
</tbody>
</table>

![FIGURE 1](https://example.com) Oral antibiotic prophylaxis amongst all patients: number of patients with peritonitis caused by *S. aureus*
infections in the group allocated to use a topical antibiotic compared with 10/88 cases in the no treatment group [five of which were methicillin-resistant Staphylococcus aureus (MRSA) and five were methicillin-sensitive Staphylococcus aureus (MSSA)].

Antiseptic versus no antiseptic

When considering all antiseptics together, there were more cases of peritonitis caused by S. aureus in the groups allocated to antiseptic use (Figure 3: 16/231 versus 12/197: RR 1.08, 95% CI 0.54 to 2.16; p = 0.84), but this was not statistically significant.
However, when considering antiseptic use at the time of catheter insertion, there were fewer cases of peritonitis (one trial). There were fewer cases of exit-site and/or tunnel infections caused by *S. aureus* (Figure 4, 26/281 versus 50/229: RR 0.43, 95% CI 0.28 to 0.66; *p* = 0.0001). The direction of effect was similar when considering subcategories (catheter insertion and during dialysis).

### Treatment of *S. aureus* carriage

Four trials evaluated treatment of *S. aureus* carriage, all during dialysis. Two compared antibiotic treatment with no antibiotic treatment, one trial compared two different antibiotic regimes and one three-armed trial compared two different antibiotic regimes with no antibiotic treatment.

<table>
<thead>
<tr>
<th>Study or subcategory</th>
<th>Antiseptic n/N</th>
<th>No antiseptic n/N</th>
<th>RR (fixed)</th>
<th>Weight %</th>
<th>RR (fixed)</th>
</tr>
</thead>
<tbody>
<tr>
<td>01 Catheter insertion Waite 1997</td>
<td>2/61</td>
<td>8/56</td>
<td>-</td>
<td>15.16</td>
<td>0.23 (0.05 to 1.04)</td>
</tr>
<tr>
<td></td>
<td>Subtotal (95% CI)</td>
<td></td>
<td>61</td>
<td>56</td>
<td>15.16</td>
</tr>
<tr>
<td></td>
<td>Total events: 2 (Antiseptic), 8 (No antiseptic)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Test for heterogeneity: not applicable</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Test for overall effect: z = 1.91 (p = 0.06)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>02 During dialysis Luzar 1990</td>
<td>15/74</td>
<td>16/53</td>
<td>-</td>
<td>33.89</td>
<td>0.67 (0.36 to 1.24)</td>
</tr>
<tr>
<td>Wilson 1997</td>
<td>9/77</td>
<td>22/72</td>
<td>-</td>
<td>41.33</td>
<td>0.38 (0.19 to 0.77)</td>
</tr>
<tr>
<td>Wong 2002</td>
<td>0/69</td>
<td>4/48</td>
<td>-</td>
<td>9.62</td>
<td>0.08 (0.00 to 1.41)</td>
</tr>
<tr>
<td></td>
<td>Subtotal (95% CI)</td>
<td></td>
<td>220</td>
<td>173</td>
<td>84.84</td>
</tr>
<tr>
<td></td>
<td>Total events: 24 (Antiseptic), 42 (No antiseptic)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Test for heterogeneity: $\chi^2 = 3.16, df = 2 (p = 0.21), I^2 = 36.7%$</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Test for overall effect: z = 3.36 (p = 0.0008)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Total (95% CI)</td>
<td></td>
<td>261</td>
<td>229</td>
<td>100.00</td>
</tr>
<tr>
<td></td>
<td>Total events: 26 (Antiseptic), 50 (No antiseptic)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Test for heterogeneity: $\chi^2 = 4.18, df = 3 (p = 0.24), I^2 = 28.2%$</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Test for overall effect: z = 3.87 (p = 0.0001)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**FIGURE 4** Antiseptic prophylaxis amongst all patients: number of patients with exit-site and/or tunnel infections caused by *S. aureus*

### Side-effects

Two trials reported side-effects: the Mupirocin Study Group reported six episodes of side-effects in six patients (one withdrew due to rhinitis) using mupirocin ointment and eight episodes in seven patients (one withdrew due to rhinorrhea and sneezing) using the placebo ointment; and Sesso and colleagues reported that one patient using sodium fusidate ointment discontinued use due to nasal irritation.

### Death due to peritonitis caused by *S. aureus*

One trial reporting this outcome reported that there were no deaths due to peritonitis caused by *S. aureus*.

### Development of antibiotic resistance

One trial reported that no patient developed ofloxacin-resistant organisms.

There were no data reported for the following outcomes: time to first peritonitis episode; peritonitis relapse; number of patients requiring catheter replacement; hospitalisation rates; and quality of life.

### Oral antibiotics versus no antibiotics

Two trials compared oral antibiotics with no antibiotics. When considering all oral antibiotics together, there were fewer cases of peritonitis caused by *S. aureus* in the groups which received...
### TABLE 8  Outcomes results for treatment of S. aureus carriage

<table>
<thead>
<tr>
<th>Study</th>
<th>Comparison</th>
<th>S. aureus carriage (no.)</th>
<th>Peritonitis (no.)</th>
<th>Peritonitis rate</th>
<th>Catheter removal (no.)</th>
<th>ESI and/or TI (no.)</th>
<th>ESI and/or TI rate</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Antibiotic versus no antibiotic</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>During dialysis: Blowey, 1994</td>
<td>Oral rifampin plus bacitracin</td>
<td>0/7</td>
<td>0/7</td>
<td>–</td>
<td>0/7</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td></td>
<td>No treatment</td>
<td>2/8</td>
<td>2/8</td>
<td>–</td>
<td>2/8</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Mupirocin Study, Group, 1996</td>
<td>Mupirocin ointment</td>
<td>18/134&lt;sup&gt;a&lt;/sup&gt;</td>
<td>18/134&lt;sup&gt;a,b&lt;/sup&gt;</td>
<td>1 in 81.8 patient months</td>
<td>3/134&lt;sup&gt;a,b&lt;/sup&gt;</td>
<td>9/134</td>
<td>1 in 99.3 patient months</td>
</tr>
<tr>
<td></td>
<td>Placebo ointment</td>
<td>24/133&lt;sup&gt;a&lt;/sup&gt;</td>
<td>24/133&lt;sup&gt;a,b&lt;/sup&gt;</td>
<td>1 in 53.8 patient months</td>
<td>5/133&lt;sup&gt;a,b&lt;/sup&gt;</td>
<td>20/133</td>
<td>1 in 28.1 patient months</td>
</tr>
<tr>
<td><strong>Antibiotic versus antibiotic</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>During dialysis: Perez-Fontan, 1992</td>
<td>Mupirocin nasal ointment</td>
<td>0/12&lt;sup&gt;b&lt;/sup&gt;</td>
<td>0/12&lt;sup&gt;b&lt;/sup&gt;</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td></td>
<td>Neomycin sulphate ointment</td>
<td>1/10&lt;sup&gt;b&lt;/sup&gt;</td>
<td>1/10&lt;sup&gt;b&lt;/sup&gt;</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td><strong>Antibiotic versus antibiotic versus no antibiotic</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>During dialysis: Sesso, 1994</td>
<td>Sodium fusidate ointment</td>
<td>1/9</td>
<td>1/9</td>
<td>0.16</td>
<td>4/9</td>
<td>5/9</td>
<td>0.97</td>
</tr>
<tr>
<td></td>
<td>Oral ofloxacin</td>
<td>4/9</td>
<td>4/9</td>
<td>0.83</td>
<td>3/9</td>
<td>2/9</td>
<td>0.33</td>
</tr>
<tr>
<td></td>
<td>Placebo tablets</td>
<td>5/13</td>
<td>5/13</td>
<td>0.75</td>
<td>6/9</td>
<td>3/13</td>
<td>0.50</td>
</tr>
</tbody>
</table>

<sup>a</sup> Denominators are unclear, therefore numbers randomised are reported.

<sup>b</sup> Episodes.

<sup>c</sup> Catheter infections.

### TABLE 9  Response to treatment and time to recolonisation (months, M)

<table>
<thead>
<tr>
<th>Study ID</th>
<th>Comparison</th>
<th>Eradication: +1M no. (%)</th>
<th>+1M</th>
<th>+2M</th>
<th>+3M</th>
<th>+4M</th>
<th>+6M</th>
<th>+10M</th>
</tr>
</thead>
<tbody>
<tr>
<td>Perez-Fontan, 1992&lt;sup&gt;57&lt;/sup&gt;</td>
<td>Mupirocin</td>
<td>12 (100)</td>
<td>12 (0)</td>
<td>12 (8)</td>
<td>12 (41)</td>
<td>11 (55)</td>
<td>11 (55)</td>
<td>3 (66)</td>
</tr>
<tr>
<td></td>
<td>Neomycin</td>
<td>10 (40)</td>
<td>4 (0)</td>
<td>4 (25)</td>
<td>4 (75)</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
</tbody>
</table>
antibiotics (Figure 5: 1/16 versus 7/21: RR 0.27, 95% CI 0.05 to 1.35; p = 0.11) and fewer cases of exit site and/or tunnel infections caused by S. aureus (Figure 6, 2/16 versus 5/21: RR 0.60, 95% CI 0.16 to 2.28; p = 0.46). However, these results were not statistically significant.

Topical antibiotics versus no antibiotics
Two trials compared topical antibiotics with no antibiotics. When considering all topical antibiotics together, there were fewer cases of peritonitis caused by S. aureus in the groups which received antibiotics (Figure 7: 22/143 versus 29/146: RR 0.80, 95% CI 0.49 to 1.32; p = 0.39), fewer patients requiring catheter removal (Figure 8, 7/143 versus 11/142: RR 0.63, 95% CI 0.29 to 1.39; p = 0.26), and fewer cases of exit site and/or tunnel infections caused by S. aureus (Figure 9, 14/143 versus 23/146: RR 0.66, 95% CI 0.36 to 1.20; p = 0.17). However, these results were not statistically significant.
### TABLE 10 Summary of the clinical effect size

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Prophylaxis amongst all</th>
<th>Treatment of S. aureus carriage</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td><strong>n/N</strong></td>
<td><strong>RR (95% CI)</strong></td>
</tr>
<tr>
<td><strong>Oral antibiotic versus no antibiotic</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peritonitis (no.)</td>
<td>6/283 vs 7/185</td>
<td>0.75 (0.29 to 1.93)</td>
</tr>
<tr>
<td>ESI and/or TI (no.)</td>
<td>(5/70 vs 20/70)</td>
<td>0.27 (0.11 to 0.65)</td>
</tr>
<tr>
<td><strong>Topical antibiotic versus no antibiotic</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peritonitis (no.)</td>
<td>ND</td>
<td>ND</td>
</tr>
<tr>
<td>Catheter removal (no.)</td>
<td>ND</td>
<td>ND</td>
</tr>
<tr>
<td>ESI and/or TI (no.)</td>
<td>ND</td>
<td>ND</td>
</tr>
<tr>
<td><strong>Antiseptic versus no antiseptic</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peritonitis (no.)</td>
<td>16/231 vs 12/197</td>
<td>1.08 (0.54 to 2.16)</td>
</tr>
<tr>
<td>ESI and/or TI (no.)</td>
<td>26/281 vs 50/229</td>
<td>0.43 (0.28 to 0.66)</td>
</tr>
</tbody>
</table>

ND, no data.
**Clinical effect size**
When considering trials comparing antibiotics with no antibiotics, a summary of the clinical effect size for all outcomes where data were available are given in Table 10.

When considering prophylaxis amongst all patients, there is a consistent finding that exit-site and/or tunnel infections are statistically significantly reduced with the use of antibiotics (oral or topical) and antiseptics. However, these findings do not appear to translate into a reduction in peritonitis. To some extent this may reflect the greater frequency of exit-site and/or tunnel infections than peritonitis, and hence lower power for peritonitis, but it does raise the question of how carriage leads to peritonitis.
Chapter 4

Economic evaluation

Introduction

In this chapter, the approach taken to consider the relative cost-effectiveness of interventions to prevent and treat *S. aureus* carriage is presented. A review of previous economic evaluations has not been conducted but one economic evaluation conducted alongside an RCT was identified. This economic evaluation compared prophylactic nasal mupirocin with placebo in patients either starting or established on continuous ambulatory PD. Although this study was generally well conducted and reported, it did not consider the full range of interventions for the prevention and treatment of *S. aureus* carriage. As reported in Table 8, the use of the antibiotics reduced the rate of a catheter infection caused by *S. aureus* from one every 28.1 months to one every 99.3 months. The incremental cost per *S. aureus*-related catheter infection prevented in 1994 prices was £187. The costs included the cost of screening and prophylaxis for 1 year and the cost savings arising from the reduced use of therapeutic antibiotics and hospitalisations avoided. Quality-adjusted life-years (QALYs) were not reported as part of this study. Nevertheless, the gain in QALYs required to provide an incremental cost per QALY that society might consider worthwhile (between £20,000 and £30,000 per QALY) would be between 0.0019 and 0.0029. This would be equivalent to between an additional 0.7–1.1 days in full health over 1 year (1 day in full health is equal to 0.00274 QALYs). From this particular study, a judgement would be required as to whether the gains in QALYs estimated could be realised in practice and, even if they can be realised, whether society would be willing to pay for these additional benefits.

The usefulness of the study by Davey and colleagues is that the results indicate that it is not implausible that interventions to prevent or treat *S. aureus* carriage might be cost-effective. Ideally, an economic evaluation comparing all relevant interventions (including the use of a no treatment arm) and utilising the best available evidence would be performed.

The first part of this chapter outlines the framework provided by economic evaluation for informing decision-making. As described in this section, there is insufficient evidence to determine the relative efficiency of the alternative interventions. In response to the limited evidence available, no economic evaluation was performed. However, a hypothetical model is outlined. If sufficient data were available from future research to populate this model, then it would provide an explicit framework to estimate cost-effectiveness.

The economic approach

Relationship between benefits and cost

The objective of economic evaluation is to provide information to assist decision-makers in the allocation of available scarce resources so that benefits can be maximised. The decision to use resources in one way means that the opportunity to use them in other desirable ways is given up. The cost of this decision is the benefits (health gains, etc.) that could have been obtained had the resources been used in another way. The ‘opportunity cost’ of a decision to use resources in one way is equivalent to the benefits foregone in the best alternative use of these resources. One of the goals of healthcare decision-making is to maximise benefits and minimise opportunity costs. To achieve this, information is required on both resource use (i.e. costs) and benefits (i.e. effectiveness) from alternative courses of action.

Data on effectiveness and costs can be brought together in a matrix format (Figure 10) to aid in the judgement about whether a new procedure is preferable to a comparator. In Figure 10, it can be seen that, relative to a comparator, the new procedure could achieve (1) greater effectiveness, (2) the same level of effectiveness or (3) less effectiveness. Of course, a fourth option is possible whereby there is not enough evidence to make a judgement on whether the new procedure is more or less effective. In terms of cost, a new procedure could (A) be less costly, (B) result in no difference in costs or (C) be more costly (again, there is the possibility of there being not enough evidence to judge, as represented by row D).

Figure 10 is adapted from that which appeared in early editions of the Cochrane Collaboration Handbook. For any procedure to prevent or treat
S. aureus carriage or infection, the optimum position on the matrix is square A1, where an experimental treatment would both save costs and have greater effectiveness relative to current treatment. In squares A1, A2 and B1, the new procedure is more efficient and is assigned a ✓ response to the question of whether it is to be preferred to current practice. In squares B3, C2, and C3 the new procedure is less efficient and thus receives a ✗ response. In squares A3 and C1, a judgement would be required as to whether the more costly procedure is worthwhile in terms of the additional effectiveness gained. Square B2 is neutral, as there is no difference in either costs or effectiveness and other reasons may be needed to justify the adoption of treatment. The areas marked with a ? response represent situations in which there is not enough evidence on effectiveness, costs or both to judge whether the new procedure is to be preferred.

**Consideration of the available evidence**

As reported in Chapter 3, the evidence available on relative effectiveness of the alternative methods of preventing or treating S. aureus carriage as a means of preventing peritonitis was limited. In terms of the matrix set out in Figure 10 there is insufficient evidence to draw any conclusions about relative effectiveness (column 4 of the matrix), and hence about the relative cost-effectiveness of any of the interventions (square D4 of the matrix). Additional data collection is required to conduct a formal economic evaluation. The structure for a hypothetical economic model is presented in the next section.

---

**FIGURE 10 Matrix combining costs and effectiveness**

<table>
<thead>
<tr>
<th>A</th>
<th>✓</th>
<th>✓</th>
<th>?</th>
</tr>
</thead>
<tbody>
<tr>
<td>B</td>
<td>✓</td>
<td>✗</td>
<td>✗</td>
</tr>
<tr>
<td>C</td>
<td>✗</td>
<td>✗</td>
<td>?</td>
</tr>
<tr>
<td>D</td>
<td>?</td>
<td>?</td>
<td>?</td>
</tr>
</tbody>
</table>

✓ = recommended experimental treatment
✗ = recommended control
✓ ✗ = neutral
? = judgement required
? = not enough evidence

Compared with control treatment, experimental treatment is:
1. more effective
2. of equal effectiveness
3. less effective
4. insufficient evidence to judge

A. less costly
B. of equal cost
C. more costly
D. insufficient evidence to judge

**Hypothetical economic model**

The methods for a model and its use are illustrated below, and this helps to highlight the areas where additional data would be required before a robust evaluation could be conducted. A Markov model is used to display the temporal and logical sequence of prevention and treatment events. This approach adopted as a Markov model has the ability to represent repetitive events, and the time dependence of both probabilities and utilities which allows for more accurate representation of clinical settings that involve these issues. The model would be designed to estimate costs from the UK NHS perspective and outcomes in terms of QALYs.

This study focuses on patients who receive PD as the initial modality of treatment. A patient who elects or receives PD could over time either die, receive a transplant or transfer to HD. The hypothetical model does not include transplantation and hence may be considered applicable to the majority of patients who, for whatever reason (usually lack of donor organs), do not receive a transplant. As part of the process of developing the model, the parameters needed to assess the cost-effectiveness of alternative interventions were identified. The systematic review of effectiveness reported in Chapter 3, secondary data sources and consultation with clinical experts would provide the parameter estimates. Where such data were likely to be deficient, this has been indicated in the text, to aid future research. The model structure was based on
detailed discussions with clinical members of the review team about the care pathways that patients might follow while on PD and further discussion about how these pathways (and transitions between different modalities of treatment and clinical events) would be influenced by the prevention or treatment of *S. aureus* carriage. The model was then presented to the clinicians and other members of the review team and any relevant changes made to the structure.

**Description of the model**

The model is made up of a set of health states between which a patient can move over specified periods of time (Figure 11). On entry into the model, all patients receive PD. The patient will spend 4 weeks in each state (the cycle length) before facing the possibility of making a transition to another state.

Within the model patients could move into any one of the following states:

1. ‘*Catheter insertion*’. In this initial state a patient has their peritoneal catheter inserted and begins PD. At the time of their peritoneal catheter insertion the patient may receive a prophylactic intervention or a treatment of *S. aureus* carriage. Following the first 4 weeks after insertion of the catheter, a patient may remain on PD with or without carriage of *S. aureus*. Patients in this state could potentially also develop an infection, transfer to HD or die.

2. ‘*On PD without SA carriage*’. In this state, the patient receives PD and may also receive routine checks for the development of *S. aureus* carriage. The risk of developing carriage and hence the probability of moving to ‘*On PD with SA carriage*’ may be affected by the use of some form of prophylactic preventive treatment either at the time of catheter insertion (the first initial state of the model) or while on dialysis. Patients in this state could potentially also develop an infection, transfer to HD or die.

3. ‘*On PD with SA carriage*’. Patients in this state are still on PD but are carriers of *S. aureus*. If *S. aureus* carriage were eradicated, the patient would move back to the state ‘*On PD without SA carriage*’. The patient could suffer some form of infection although the risk of this happening may be affected by any of the methods of treating *S. aureus* carriage (antibiotic sprays, ointment or powders). Patients in this state could potentially also transfer to HD or die.

4. ‘*Infection*’. While on PD, a patient may suffer an exit-site infection, isolated tunnel infection or peritonitis. The infections may occur either separately or sequentially: exit site infection leading to tunnel infection leading to peritonitis. While in this state, patients face the risk of losing their PD tube and moving into temporary or permanent HD. Factors that could make a person move from PD are clearance failure, technique failure or recurrent peritonitis. The types of infection and their effects are:

   (a) Exit-site infection, which is treated with using a local treatment, systemic treatment or catheter change.

   (b) Isolated tunnel infections, which are treated using systemic treatments and/or catheter removal.

   (c) Peritonitis infection, which is mainly due to contamination and is treated with 2 weeks of antibiotics administered peritoneally, intravenously or orally.

   *S. aureus* infection can be cured without the patient moving from PD (i.e. move to ‘*On PD without SA carriage*’). If *S. aureus* infection is not resolved, the catheter can be removed and the treatment modality switched to ‘Temporary HD’. Non-resolution of *S. aureus* infection can be attributed to failure of antibiotics to clear the infection (relapsing peritonitis) or it may arise from an entirely new infection. Relapsing peritonitis can be defined as the recurrence of peritonitis caused by the same organism as the immediately preceding episode of peritonitis within 4 weeks of completion of antibiotic treatment. The model would allow a patient to have a maximum of between two and four infections (i.e. to stay in the state of infection for between two and four cycles) before the PD catheter is removed, in which case the patient would move to the state of ‘Temporary HD’.

5. ‘*Temporary HD*’. As briefly described above, there are several factors that could make a person move from PD, such as clearance failure, technique failure or recurrent peritonitis. Once these factors are resolved some patients may elect to move back to PD. If they are not resolved, a patient may have to stay in HD until they die (and hence move to the state of ‘Permanent HD’).

6. ‘*Permanent HD*’. Once a patient enters this state, they do not leave it until they die.

7. ‘*Dead*’ (included as all-cause mortality). This state can be entered from all preceding states.

While the model allows for variation in the parameters of the prevention and treatment of peritonitis across each intervention (either prophylactic prevention of *S. aureus* carriage or
FIGURE 11 Draft model structure for the estimation of the relative cost-effectiveness of alternative methods to prevent and treat S. aureus (SA) carriage
treatment of *S. aureus* carriage), it is necessary to assume that many parameters will be the same across the different branches. The following section identifies the data required to populate the model. To illustrate this description, the data available for the comparison of the prophylactic use of antibiotics at the time of catheter insertion compared with no treatment have been used.

**Estimation of model parameters**

A detailed description of the methods that might be used to derive parameters for this model are described in Appendix 7. In brief, this description covers the derivation of transition probabilities, costs and health state utilities.

**Assessment of cost-effectiveness**

The results of the base-case analysis would be based on the costs and outcomes faced by male and female patients who initially started on PD. If the National Institute for Health and Clinical Excellence (NICE) HTA guidelines were followed, discount rates of 3.5% per annum would be applied to both costs and health benefits. The central outcomes of the analysis and the systematic review would first be presented in terms of a balance sheet. In the balance sheet the incremental differences between the alternative interventions would be presented in their natural units, such as the number of patients with exit-site and/or tunnel infections caused by *S. aureus* and number of patients with peritonitis. The purpose of the balance sheet is to illustrate the trade-offs that would exist when choosing amongst interventions.

Within the economic model, the different outcomes would be combined into a single measure of relative efficiency measured in terms of the incremental cost per QALY. Data on the incremental cost per QALY would be presented in two ways. First, mean costs and QALYs for the alternative interventions could be presented and incremental cost per QALYs calculated where appropriate. The second way in which the cost-effectiveness of the alternative interventions might be presented would be by cost-effectiveness acceptability curves (CEACs). CEACs can be used to illustrate the uncertainty caused by the combined statistical variability in the model’s parameter estimates. These curves illustrate the likelihood that a strategy is cost-effective at various threshold values for society’s willingness to pay for an additional QALY. It should be noted that in order to be able to perform the probabilistic sensitivity analysis underpinning the estimation of CEACs, all the parameters required for the model should be described by an appropriate statistical distribution that reflects the statistical imprecision surrounding the point estimates (which has not been attempted within this chapter).

**Additional analyses**

The results of any economic evaluation will be surrounded by uncertainty. In part, this will be reflected by the probabilistic analysis that is proposed above. However, other sensitivity analyses would be required to address the uncertainty around the available data or about the way in which it would be used in the model. In addition to the sensitivity analyses described above, another potential sensitivity analysis might focus on establishing at what point preventing or treating carriage ceases to be cost-effective. Examples of other potential sensitivity analyses are described below.

**Risks of *S. aureus* carriage, risks of progression to infection and other transition probabilities**

Data on the prevalence of *S. aureus* carriage are not available, yet it is likely that the cost-effectiveness will be dependent on the proportion of people starting PD who are carriers of *S. aureus* and the risks of developing carriage and the consequences of carriage in terms of the development of infections and transitions to other modalities of dialysis.

**Costs**

The costs of antibiotics identified varied greatly. The most expensive and least expensive costs could be used in the sensitivity analysis. These costs could be varied by increasing/reducing them to establish at what cost prevention or treatment of *S. aureus* carriage and infection ceased to be cost-effective. Similarly, the costs of dialysis would also be varied. This is because costs that would be used in the base-case analysis although coming from a very detailed costing exercise are derived from a small number of centres and so might not be generalisable to the rest of the NHS. The impact of using other relevant costs such as those reported in the NHS reference costs would be explored.

**Utilities**

The utility data used in the model were based on non-randomised data. These data were based on patient responses to the EQ-5D questionnaire weighted using UK population tariffs. Further analyses could be performed using the utility data from other sources.

**Results**

Although no formal attempt to conduct the proposed modelling exercise has been made, an
illustration of the limitations of the evidence base is provided by presenting a balance sheet for the comparison of the use of antibiotic versus no antibiotic at catheter insertion (Table 11). As can be seen, the data available are very limited and due to the paucity of data no further analyses were carried out.

**Summary**

In this chapter, a hypothetical model for the comparison of alternative methods to prevent or treat *S. aureus* carriage has been presented. The purpose of this exercise was to consider what information would be required for an economic evaluation and where the main information gaps are. There is insufficient information on the effectiveness and relative effectiveness of the interventions that might be considered. Better data are available for costs and utilities but further data collection would be helpful. In particular, evidence on the utility value for those experiencing any of the infections would be useful.

As the model is hypothetical, the structure outlined in this chapter may need to be adapted to reflect either new knowledge of the care pathways, restrictions imposed by the data available or the nature of the comparisons considered.

<table>
<thead>
<tr>
<th>Favours antibiotic</th>
<th>Favours no intervention</th>
<th>Trials contributing data</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trends towards fewer exit-site and/or tunnel infections (OR 0.15, 95% CI 0.06 to 0.3)</td>
<td>Lower costs</td>
<td>4</td>
</tr>
<tr>
<td>No statistically significant difference in number of patients with peritonitis (RR 0.73, 95% CI 0.31 to 1.72)</td>
<td></td>
<td>8</td>
</tr>
</tbody>
</table>

No information on:
- Numbers of *S. aureus* carriage
- Number of *S. aureus* cured
- Number with relapse
- Modality change rates

OR, odds ratio; RR, relative risk.
Volume of evidence

There is a good number of trials but, as discussed in Chapter 3, the quality of design, or at least of reporting, is not good by today’s standards. The first priority is to determine whether treatments are effective, and this requires placebo controls. Many of the trials were of one antibiotic or antiseptic against another. Table 12 shows those in which there was a placebo arm. The number falls to 13. Some of these were very small, for example those by Bennett-Jones and colleagues with 26 patients, Blowey and colleagues with 15 and Sesso and colleagues with 31 amongst three arms.

A number of the trials show a reduction in exit-site infections but not in the incidence of peritonitis. This may just be a power problem (exit-site infections being much commoner than peritonitis, plus the relatively small numbers involved), but raises the question of the relationship between carriage, infection and peritonitis. It is likely that infection is introduced mainly at exchange via contamination of the tip of the catheter, rather than tracking along the tunnel. Better technique might reduce the risk.

In an observational study, the Scottish Renal Registry Group noted that peritonitis was 15% (95% CI 4 to 26%) less common in units using nasal mupirocin than those not, although this did not apply to S. aureus peritonitis (one episode every 106 months in user units versus one every 96 months in non-users; p = 0.52).

Other reviews

Our findings are similar to those of the Cochrane Review by Strippoli and colleagues, who also concluded that nasal mupirocin reduces exit-site and tunnel infections, but not peritonitis.

Guideline 31 of the European Guidelines states that, “Use of mupirocin or gentamicin cream at the exit site is recommended to reduce exit site infections”, but cites no evidence that this reduces peritonitis. Like the other guidelines, they have to extrapolate from reduction in exit-site infections to reduction in peritonitis.

One issue of concern has been the emergence of resistance to mupirocin, especially in MRSA. Mupirocin became available in 1985 and some laboratories have reported increasing numbers of mupirocin-resistant S. aureus, especially MRSA. Particularly high resistance rates have been reported from New Zealand, but that may be related to its availability over the counter without prescription. In some European studies, high-level mupirocin resistance was seen in only 2–3% of S. aureus isolates, but there was variation amongst countries, from 0% in most up to 6% in Belgium and 5% in the UK. Much higher rates have been reported in units with high mupirocin use. In one neonatal intensive care unit, which applied mupirocin routinely to insertion sites of central venous catheters, resistance rates rose over 5 years to 42% of coagulase-negative staphylococci (no results for S. aureus were reported), falling again once the routine use was stopped.

### Table 12 Summary list of trials of active agents against placebo

<table>
<thead>
<tr>
<th>I.v. antibiotics</th>
<th>Oral antibiotics</th>
<th>Topical antibiotics</th>
<th>Antiseptics</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Prophylaxis</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>At first insertion</td>
<td>Bennett-Jones, 1988(^{35})</td>
<td></td>
<td>Waite, 1997(^{46})</td>
</tr>
<tr>
<td></td>
<td>Lye, 1992(^{36})</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Gadallah, 2000(^{45})</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>During later dialysis</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Zimmerman, 1991(^{29})</td>
<td>Wong, 2003(^{28})</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Sharma, 1971(^{37})</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Eradication</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Blowey, 1994(^{44})</td>
<td>Sesso, 1994(^{58})</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Sesso, 1994(^{48})</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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Research needs

As the Cochrane Review said:63

“Given the large number of patients on PD and the importance of peritonitis, the lack of adequately powered RCTs to inform decision-making about strategies to prevent peritonitis is striking.”

This is echoed in the UK guidelines:69

“We recommend that a large double-blind placebo controlled study is now needed to confirm whether mupirocin remains useful in clearing carriage in patients or staff when low-level mupirocin resistance is present.”

One of their concerns was that eradication of carriage was lower in resistant strains, whether they had high or low level resistance.

The key questions include:

1. What is the natural history and biology of carriage? What are the links between carriage and exit-site infection, and between exit-site infection and peritonitis? How long does carriage last for without treatment? How often is it temporary rather than permanent? The natural history of MRSA carriage suggests that up to half of those colonised will clear spontaneously within 1 year.70

2. How do we define carriage? Some centres take swabs from multiple sites. But there is evidence that eradication from the nose reduces carriage elsewhere. Other sites include throat, groin, gut, any wounds and the catheter. Site of carriage seems to be important.

3. Treatment of carriage. Is MSSA relatively harmless? MRSA carriage seems to be a much stronger predictor of infection than MSSA (about 50% by 18 months versus 2% with MSSA).71 Should the focus be on those with MRSA? Is decolonisation of proven effectiveness, or is recolonisation rapid? Typing of strains could separate relapse from reinfection. Most decolonisation efforts are directed to the nose, which is the most common site of carriage, and to the catheter insertion site, but topical application of antibiotic or antiseptic to these sites will not affect carriage elsewhere, unless carriage elsewhere requires repeated spread of the organism from its more favoured sites. Individual strain type may also be important.

4. What other options for reducing peritonitis might be tried? Would more training help?

5. What factors predict carriage – home contacts, smoking, recent antibiotic treatment, recent hospital admissions? The underlying disease, such as diabetes, may affect susceptibility to infection.

Eradication topics include:

- intermittent versus chronic
- antiseptics versus antibiotics
- the choice of drug
- is vaccination worth revisiting?

The design of any intervention trial should consider confounding factors such as type of catheter, training and automated PD versus ambulatory PD.

The choice of antibiotic(s) to be tested in trials should take into account susceptibility of individual strains, and these may vary amongst different dialysis centres. MRSA rates also vary, and its presence is likely to compromise the benefits of any β-lactam antibiotic. MRSA strains also vary in their susceptibility to other key antibiotics such as gentamicin, rifampicin, fucidin, neomycin and mupirocin, though probably not to antiseptics. Long-term studies would be needed to monitor the emergence of resistance – this is high risk for agents such as mupirocin and rifampicin. Some agents such as mupirocin, rifampicin and fucidin are active mainly against Gram-positive infections.

The widespread use of mupirocin, and the concerns about resistance, make it a high priority for research.

The key outcomes of research into prevention would be:

- Episodes of peritonitis – average number per patient per annum in population on PD in each unit.
- Patient-based data – number of patients having one or more episodes per annum, or over a longer period; time from first insertion of catheter to first episode of peritonitis. Even if the number of infections was the same, delaying infection would be a useful outcome.
- Numbers of temporary transfers to HD.
- Duration of successful treatment on PD. Repeated episodes of peritonitis will shorten the life of the peritoneal membrane as a dialysis membrane.
Chapter 6
Conclusions

The importance of peritonitis in PD is not in doubt, and it remains the main cause of transfer to HD. The evidence on prevention is disappointing: exit-site infections are reduced but not peritonitis, although this may be because the studies were too small or too short, or because the incidence of peritonitis was low. There is also some concern about the development of resistance to mupirocin amongst MRSA strains. More research is required.
Acknowledgements

We thank our peer reviewers, Dr Chris Isles, Dumfries, Dr Conal Daly, Glasgow, and Dr Andrew Lloyd, London, for commenting on a near final draft, and Professor Peter Davey, Dundee, for commenting on an earlier one, but we absolve them from any deficiencies in the final document, responsibility for which rests with the Aberdeen HTA Group.

Contribution of authors
Kirsty McCormack (Research Fellow), Linda McIntyre (Systematic Reviewer), Sian Thomas (Systematic Reviewer) and Helen Rothnie (Systematic Reviewer) carried out the assessment of studies for inclusion and data extraction. Kirsty McCormack completed the review of effectiveness. Mary Kilonzo (Research Fellow) conducted the economic evaluation under supervision by Luke Vale (Senior Research Fellow). Cynthia Fraser (Information Officer) developed and ran the search strategies, and was responsible for obtaining papers and for reference management. Kannaiyan Rabindranath (Specialist Registrar in Nephrology) drafted the protocol and the introduction and provided specialist renal advice. Nick Fluck (Consultant Nephrologist) and Ian Gould (Consultant Microbiologist) provided expert advice on renal and microbiological aspects, respectively. Norman Waugh (Professor of Public Health; methodology adviser) provided clinical and methodological advice and commented on drafts of the review.
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77. The EuroQol Group. EQ-5D user guide: a measure of health related quality of life. Rotterdam: Rotterdam Centre for Health Policy and Law, Erasmus University; 1996.


Appendix 1

Search strategies

The following search strategies were used to identify reports of RCTs and systematic reviews evaluating the effectiveness of preventing and treating *Staphylococcus aureus* carriage on peritoneal catheter-related infections.


Ovid Multifile Search. URL: 
http://gateway.ovid.com/athens

1. exp peritoneal dialysis/
2. continuous ambulatory peritoneal dialysis/ use emez
3. peritoneal dialysis.tw.
4. (capd or ccpd or apd).tw.
5. or/1-4
6. staphylococcal infections/pc
7. peritonitis/pc
8. bacterial peritonitis/pc use emez
9. catheterization/ae use mesz
10. catheterization/ use emez
11. catheters, indwelling/ae use mesz
12. indwelling catheter/ use emez
13. surgical wound infection/ use mesz
14. surgical infection/ use emez
15. catheter exit$.tw.
16. exit site$.tw.
17. (catheter adj3 infect$).tw.
18. (catheter adj3 infect$).tw.
20. or/13-19
21. (prevent$ or prophyla$ or reduc$ or limit$).tw.
22. 20 and 21
23. or/6-12,22
24. 5 and 23
25. staphylococcus aureus/
26. bacterium carrier/ use emez
27. bacterial colonization/ use emez
28. methicillin resistance/ use mesz
29. vancomycin resistance/ use mesz
30. methicillin resistant staphylococcus aureus/ use emez
31. aureus.tw.
32. (msra or mssa or visa or vrsa).tw.
33. (carriage or carrier$ or host$).tw.
34. (colony or coloni?ation).tw.
35. 33 or 34
36. or/25,28-32
37. 35 and 36
38. or/26-27,37
39. 5 and 38
40. antibiotic prophylaxis/
41. exp anti-infective agents/
42. or/40-41
43. 5 and (25 or 31) and 42
44. 24 or 39 or 43
45. animal/ not human/ use mesz
46. (animal/ or nonhuman/) not human/ use emez
47. 44 not (45 or 46)
48. clinical trial.pt. use mesz
49. exp controlled clinical trials/ use mesz
50. randomised controlled trial/ use emez
51. clinical trial/ use emez
52. random allocation/ use mesz
53. randomization/ use emez
54. placebo effect/ use mesz
55. placebo/ use emez
56. random$.tw.
57. placebo$.tw.
58. or/48-57
59. meta analysis.tw.
60. meta analysis.pt. use mesz
61. meta analysis/ use emez
62. review.ab.
63. review.pt. use mesz
64. systematic review/ use emez
65. or/60-65
66. 47 and (59 or 66)
67. 67 and eng.la.
68. remove duplicates from 68

**CINAHL (1982–December Week 2 2005)**

Ovid Multifile Search. URL: 
http://gateway.ovid.com/athens

1. exp peritoneal dialysis/
2. peritoneal dialysis.tw.
3. (capd or ccpd or apd).tw.
4. or/1-3
5. staphylococcal infections/pc
6. peritonitis/pc
7. catheterization/ae
8. catheters, dialysis/ae
9. catheter-related infections/
10. catheter exit$.tw.
11. exit site$.tw.
Appendix 1

14 or/9-13
15 prevent$ or prophyla$ or reduc$ or
limit$).tw.
16 14 and 15
17 or/5-8,16
18 4 and 17
19 Staphylococcus Aureus/
20 methicillin resistance/
21 vancomycin resistance/
22 aureus.tw.
23 (msra or mssa or visa or vrsa).tw.
24 bacterial colonization/
25 carrier state/
26 (carriage or carrier$ or host$).tw.
27 (colony or coloni?ation).tw.
28 or/25-27
29 or/19-23
30 28 and 29
31 24 or 30
32 4 and 31
33 antibiotic prophylaxis/
34 exp antiinfective agents/
35 or/33-34
36 4 and (19 or 22) and 35
37 18 or 32 or 36
38 37 and eng.lg.

Science Citation Index (1985–7 January 2006)
Web of Knowledge URL: http://wok.mimas.ac.uk/

#1 TS=(capd OR ccpd OR apd)
#2 TS=(peritoneal SAME dialysis)
#3 #1 OR #2
#4 TS=(coloni* SAME (aureus OR msra OR
mssa OR visa OR vrsa))
#5 TS=(colony SAME (aureus OR msra OR
mssa OR visa OR vrsa))
#6 TS=(host* SAME (aureus OR msra OR mssa
OR visa OR vrsa))
#7 TS=(carrier* SAME (aureus OR msra OR mssa
OR visa OR vrsa))
#8 TS=(carriage SAME (aureus OR msra OR
mssa OR visa OR vrsa))
#9 TS=((methicillin OR vancomycin) SAME
resist*)
#10 #4 OR #5 OR #6 OR #7 OR #8 OR #9
#11 #3 AND #10
#12 TS=((prevent* OR prophyla* OR reduc* OR
limit*) SAME staphylococcal)
#13 TS=((prevent* OR prophyla* OR reduc* OR
limit*) SAME aureus)
#14 TS=((prevent* OR prophyla* OR reduc* OR
limit*) SAME peritonitis)
#15 TS=(catheter* SAME infect*)
#16 TS=(tunnel SAME infect*)
#17 TS=(exit* SAME (catheter* OR site*))
#18 #12 OR #13 OR #14 OR #15 OR #16 OR
#17
#19 #3 AND #18
#20 #11 OR #19
#21 TS=randomized
#22 TS=randomised
#23 TS=random
#24 TS= randomly
#25 TS=random* assign*
#26 TS=random* alloc*
#27 TS=(control* SAME trial*)
#28 TS=meta analysis
#29 TS=systematic review*
#30 #20 AND (#21 OR #22 OR #23 OR #24
OR #25 OR #26 OR #27 OR #28 OR #29)

DocType=All document types; Language=All

BIOSIS (1985–3 January 2006)
Edina URL: http://edina.ac.uk/biosis/

((( (((al: (meta analysis) or al: (systemtic review*))
and () or ((al: (random or randomly) or al:
(control* n3 trial*)) and ())) or ((al: (randomized
or randomised) or al: (random* alloc*) or al:
(random* assign*)) and ()))) and (((((((al: (exit*
n3 catheter*) or al: (exit* n3 site*)) and ())) or ((al:
catheter* n3 infect*) or al: (tunnel n3 infect*))
and ())) or ((al: (prevent* or prophyla* or reduc*
or limit*) and al: (staphylococcal or aureus or
peritonitis)) and ()))) and (((((al: (peritoneal n3
dialysis)) and ())) or ((al: (capd) or al: (ccpd) or al:
(apd)) and ())))))))) and (((((((al: (methicillin n3 resist*)
or al: (vancomycin n3 resist*)) and ())) or (al:
(aureus or msra or mssa or visa or vrsa) and al:
carriage or carrier* or host* or colony or
coloni*)))) and (((al: (peritoneal n3 dialysis)) and
(18 or 32 or 36)
37 and eng.lg.

Clinical Trials (December 2005)
URL: http://clinicaltrials.gov/ct/gui/c/r

Current Controlled Trials (December 2005)
URL: http://www.controlled-trials.com/

Cochrane Library Issue 4, 2005
URL: http://www3.interscience.wiley.com/cgi-bin/mrwhome/106568753/HOME

National Research Register (Issue 4, 2005)
URL: http://www.update-software.com/National/

#1 MeSH descriptor Peritoneal Dialysis explode
all trees in MeSH products
#2 peritoneal dialysis in All Fields in all products
#3 capd in All Fields or ccpd in All Fields or apd in All Fields in all products
#4 (#1 OR #2 OR #3)
#5 MeSH descriptor Staphylococcal Infections explode all trees with qualifier: PC in MeSH products
#6 MeSH descriptor Peritonitis explode all trees with qualifier: PC in MeSH products
#7 MeSH descriptor Catheterization explode all trees with qualifier: AE in MeSH products
#8 MeSH descriptor Catheters, Indwelling explode all trees with qualifier: AE in MeSH products
#9 MeSH descriptor Surgical Wound Infection explode all trees in MeSH products
#10 exit site* in All Fields or catheter NEAR/3 infect* in All Fields or tunnel NEAR/3 infect* in All Fields or catheter exit* in All Fields in all products
#11 (#9 OR #10)
#12 prevent* in All Fields or prophyla* in All Fields or reduc* in All Fields or limit* in All Fields in all products
#13 (#11 AND #12)
#14 (#5 OR #6 OR #7 OR #8 OR #13)
#15 (#4 AND #14)
#16 MeSH descriptor Staphylococcus aureus explode all trees in MeSH products
#17 aureus in All Fields in all products
#18 mrsa in All Fields or mssa in All Fields or visa in All Fields or vrsa in All Fields in all products
#19 MeSH descriptor Methicillin Resistance explode all trees in MeSH products
#20 MeSH descriptor Vancomycin Resistance explode all trees in MeSH products
#21 carriage in All Fields or carrier* in All Fields or host* in All Fields in all products

#22 colony in All Fields or colonization in All Fields or colonisation in All Fields in all products
#23 (#16 OR #17 OR #18 OR #19 OR #20)
#24 (#21 OR #22)
#25 (#23 AND #24)
#26 (#4 AND #25)
#27 MeSH descriptor Antimicrobial Prophylaxis explode all trees in MeSH products
#28 MeSH descriptor Anti-Infective Agents explode all trees in MeSH products
#29 (#27 OR #28)
#30 (#16 OR #17)
#31 (#4 AND #29 AND #30)
#32 (#15 OR #26 OR #31)

DARE and HTA Databases (December 2005)
NHS Centre for Reviews and Dissemination
URL: http://nhscrd.york.ac.uk/welcome.htm

Peritoneal-dialysis (exploded) or capd and aureus

Conference proceedings abstracts screened
1st Asian Chapter Meeting ISPD, Hong Kong, December 2002, Perit Dial Int 2003;23(Suppl 2).

Journals full text screened
Appendix 2
Study eligibility form

Effectiveness of preventing and treating *Staphylococcus aureus* carriage on peritoneal catheter-related infections

Study ID: __________________________ Refman ID: __________________________

**Type of study**
Q1. Is the study a randomised controlled trial or a quasi-randomised controlled trial?

<table>
<thead>
<tr>
<th>Yes</th>
<th>Unclear</th>
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</tr>
</thead>
<tbody>
<tr>
<td>🔽</td>
<td>🔽</td>
<td>🔽</td>
</tr>
</tbody>
</table>

Go to Next question

**Participants in the study**
Q2. Were the participants in the study adult or paediatric patients undergoing peritoneal dialysis or about to undergo a peritoneal catheter placement procedure?

<table>
<thead>
<tr>
<th>Yes</th>
<th>Unclear</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>🔽</td>
<td>🔽</td>
<td>🔽</td>
</tr>
</tbody>
</table>

Go to Next question

**Interventions in the study**
Q3. Did one group receive antimicrobial treatment, antiseptic medication or other intervention to prevent or treat *S. aureus* carriage?

<table>
<thead>
<tr>
<th>Yes</th>
<th>Unclear</th>
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</tr>
</thead>
<tbody>
<tr>
<td>🔽</td>
<td>🔽</td>
<td>🔽</td>
</tr>
</tbody>
</table>

Go to Next question

Q4. Did another group receive a different intervention or no treatment to prevent or treat *S. aureus* carriage?

<table>
<thead>
<tr>
<th>Yes</th>
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<th>No</th>
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</thead>
<tbody>
<tr>
<td>🔽</td>
<td>🔽</td>
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</tr>
</tbody>
</table>

Go to Next question

**Outcomes in the study**
Q5. Did the study report any of the pre-specified outcomes (refer to data abstraction and quality assessment form)

<table>
<thead>
<tr>
<th>Yes</th>
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<th>No</th>
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</thead>
<tbody>
<tr>
<td>🔽</td>
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<td>🔽</td>
</tr>
</tbody>
</table>

Include, subject to clarification of ‘unclear’ points

**Final decision:**

Include trial  □  Background information  □  Economic data  □  Systematic review  □

Unclear  □  Exclude  □
### Appendix 3

Data abstraction and quality assessment form

**Effectiveness of preventing and treating *Staphylococcus aureus* carriage on peritoneal catheter-related infections**

Reviewer ID: ______________________

<table>
<thead>
<tr>
<th>Study Details</th>
</tr>
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<tbody>
<tr>
<td><strong>Study ID:</strong></td>
</tr>
<tr>
<td><strong>Authors:</strong></td>
</tr>
<tr>
<td><strong>Title:</strong></td>
</tr>
<tr>
<td><strong>Publication year or date of interim data collection:</strong></td>
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</table>

<table>
<thead>
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<th>Study Design</th>
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<tr>
<td><strong>RCT</strong></td>
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<tr>
<td><strong>Quasi RCT</strong></td>
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<tr>
<td><strong>Randomisation details</strong></td>
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</table>

<table>
<thead>
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<th>Quality assessment</th>
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<tr>
<td><strong>Allocation concealment:</strong> Adequate □</td>
</tr>
<tr>
<td><strong>Blinding:</strong></td>
</tr>
<tr>
<td><strong>Blinding of investigators:</strong> Yes □</td>
</tr>
<tr>
<td><strong>Blinding of participants:</strong> Yes □</td>
</tr>
<tr>
<td><strong>Blinding of outcome assessor:</strong> Yes □</td>
</tr>
<tr>
<td><strong>Blinding of data analysis:</strong> Yes □</td>
</tr>
<tr>
<td><strong>Intention to treat analysis:</strong></td>
</tr>
<tr>
<td>Stated &amp; confirmed ITT □</td>
</tr>
<tr>
<td>Not stated but confirmed not ITT □</td>
</tr>
<tr>
<td><strong>Participants lost to follow-up:</strong> Yes □</td>
</tr>
<tr>
<td><strong>Percent of participants excluded or lost to follow-up:</strong></td>
</tr>
</tbody>
</table>
### Participants

<table>
<thead>
<tr>
<th>Number of participants randomised or included in trial:</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Proportion of numbers in clinic included in trial:</td>
<td></td>
</tr>
<tr>
<td>Criteria for inclusion:</td>
<td>Criteria for exclusion:</td>
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</table>

### Setting and Timing

<table>
<thead>
<tr>
<th>Setting of study:</th>
<th></th>
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</thead>
<tbody>
<tr>
<td>Recruitment period:</td>
<td></td>
</tr>
<tr>
<td>Follow-up period:</td>
<td></td>
</tr>
</tbody>
</table>

### Screening and treatment of nasal *S. aureus*

<table>
<thead>
<tr>
<th>Screening:</th>
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</thead>
<tbody>
<tr>
<td>Treatment</td>
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</tr>
</tbody>
</table>

### Interventions

<table>
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<tr>
<th>Interventions</th>
<th>Treatment/Prevention</th>
<th>No of patients</th>
</tr>
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<tbody>
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<td>Intervention 1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intervention 2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intervention 3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patient Characteristics</td>
<td>Intervention 1</td>
<td>Intervention 2</td>
</tr>
<tr>
<td>--------------------------------------------------------------</td>
<td>---------------------------------</td>
<td>---------------------------------</td>
</tr>
<tr>
<td>Age (years)</td>
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<td></td>
</tr>
<tr>
<td>Sex (M/F)</td>
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<td></td>
</tr>
<tr>
<td>Adults (No)</td>
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<td></td>
</tr>
<tr>
<td>Paediatrics (No)</td>
<td></td>
<td></td>
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<tr>
<td>Diabetic Nephropathy (No)</td>
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<td></td>
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<tr>
<td>Hypertension and Renovascular Disease (No)</td>
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<td></td>
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<tr>
<td>Glomerulonephritis (No)</td>
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<tr>
<td>Adult Polycystic Kidney Disease (No)</td>
<td></td>
<td></td>
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<tr>
<td>Reflux Nephropathy (No)</td>
<td></td>
<td></td>
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<tr>
<td>E coli 0157 (No)</td>
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<td></td>
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<tr>
<td>Other aetiology (No &amp; specify)</td>
<td></td>
<td></td>
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<tr>
<td>Time on PD before treatment</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Indications of infirmity (specify)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hygiene measures taken (specify)</td>
<td></td>
<td></td>
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<tr>
<td>Outcomes</td>
<td>Intervention 1</td>
<td>Intervention 2</td>
</tr>
<tr>
<td>----------------------------------------------</td>
<td>----------------</td>
<td>----------------</td>
</tr>
<tr>
<td>No of patients with <em>S. aureus</em> carriage</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Time to <em>S. aureus</em> carriage</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No of patients with peritonitis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peritonitis rate (no of episodes over total pt months on PD)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Time to first peritonitis episode</td>
<td></td>
<td></td>
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<tr>
<td>Peritonitis relapse (No &amp; specify time to)</td>
<td></td>
<td></td>
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<tr>
<td>No of patients requiring catheter removal</td>
<td></td>
<td></td>
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<tr>
<td>No of patients switching to haemodialysis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No of patients requiring catheter replacement</td>
<td></td>
<td></td>
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<tr>
<td>No of patients with exit-site and tunnel infections</td>
<td></td>
<td></td>
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<tr>
<td>Exit-site and tunnel infection rate</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Side effects of antibiotics</td>
<td></td>
<td></td>
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<tr>
<td>Death due to peritonitis</td>
<td></td>
<td></td>
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<tr>
<td>Hospitalisation rates</td>
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<tr>
<td>Quality of life</td>
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<tr>
<td>Development of antibiotic resistance</td>
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Appendix 4

List of included studies

Bennett-Jones, 1988

Bernardini, 1996

Bernardini, 2005
Primary reference

Secondary reference

Blowey, 1994

Cavdar, 2004

Fuchs, 1990

Gadallah, 2000
Primary reference

Secondary reference

Lazar, 1990

Lye, 1992

Mupirocin Study Group, 1996
Primary reference

Secondary reference

Perez-Fontan, 1992

Poole-Warren, 1991

Sesso, 1988

Sesso, 1994

Sharma, 1971
Turner, 1992

Waite, 1997

Warady, 2003

Wilson, 1997

Wong, 2002

Wong, 2003

Zimmerman, 1991
Appendix 5

Detailed quality assessment results for included trials
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<tr>
<th>Study ID</th>
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<th>Blinding of investigators</th>
<th>Blinding of participants</th>
<th>Blinding of assessor</th>
<th>Blinding of data analysis</th>
<th>ITT</th>
<th>Lost to follow-up</th>
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<tbody>
<tr>
<td>Bennett-Jones, 1988</td>
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<td>Unclear</td>
<td>Unclear</td>
<td>Undear</td>
<td>Unclear</td>
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<td>Bernardini, 1996</td>
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<td>Unclear</td>
<td>Undear</td>
<td>Unclear</td>
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<tr>
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<td>Sharma, 1971</td>
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<td>Wilson, 1997</td>
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<td>Undear</td>
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<td>No</td>
<td>Undear</td>
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</table>
Appendix 6

Detailed description of included studies
<table>
<thead>
<tr>
<th>Study</th>
<th>Study details</th>
<th>Intervention/comparator</th>
<th>Intervention 1 population characteristics</th>
<th>Intervention 2 population characteristics</th>
<th>Intervention 3 population characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bennett-Jones, 1988</td>
<td>Single-centre RCT</td>
<td>Gentamicin 1.5 mg/kg body weight given i.v. by anaesthetist at time of induction of anaesthesia in anaesthetic room (n = 13) versus no treatment (n = 13; 1 withdrawn)</td>
<td>Age mean ± SD 52.7 ± 18.6 years 8 male/5 female</td>
<td>Age mean ± SD 53.1 ± 13.0 years 9 male/4 female</td>
<td></td>
</tr>
<tr>
<td>Bernardini, 1996</td>
<td>Single-centre RCT</td>
<td>Mupirocin calcium ointment 2%, applied daily to catheter exit site (n = 41) versus 300 mg oral rifampin twice per day for 5 days once every 3 months (n = 41)</td>
<td>49% male/51% female 41/41 adult Time on PD mean (range) 1.3 ± 1.8 (0.0–57) years 44% S. aureus carriage</td>
<td>59% male/41% female 41/41 adult Time on PD mean (range) 1.1 ± 1.7 (0.0–9.1) years 44% S. aureus carriage</td>
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<tr>
<td>Bernardini, 2005</td>
<td>Multicentre RCT</td>
<td>Mupirocin 2% cream daily to catheter exit site (n = 66) versus gentamicin cream 0.1% daily to exit site (n = 67)</td>
<td>Age mean ± SD 51 ± 15 years 38 male/28 female 66/66 adult 9/66 S. aureus carriage</td>
<td>Age mean ± SD 54 ± 15 years 34 male/33 female 67/67 adult 9/67 S. aureus carriage</td>
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<tr>
<td>Blowey, 1994</td>
<td>Single-centre RCT</td>
<td>Oral rifampin (20 mg/kg/day in 2 doses for 5 days) and bacitracin (topical to anterior nares 2 times per day for 7 days) (n = 7) versus no treatment (n = 8)</td>
<td>7/7 S. aureus carriage</td>
<td>8/8 S. aureus carriage</td>
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<tr>
<td>Cavdar, 2004</td>
<td>Single-centre RCT</td>
<td>Mupirocin to exit site once weekly (n = 18) versus mupirocin to exit site 3 times weekly (n = 18)</td>
<td>Age mean 55.3 ± 1.8 years 10 male/8 female 3/18 S. aureus carriage</td>
<td>Age mean 55.0 ± 2.3 years 11 male/7 female 0/18 S. aureus carriage</td>
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<td>Study</td>
<td>Study details</td>
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<tr>
<td>Fuchs, 1990&lt;sup&gt;50&lt;/sup&gt;</td>
<td>RCT</td>
<td>Washing exit site with chlorhexidine, then rinsing well, no dressing applied (n = 18), versus cleaning the exit site once daily with 0.005% sodium hypochlorite no dressing applied (n = 13), versus daily cleansing of exit site with 10% povidone-iodine swabsticks, followed by application of povidone ointment and a dry sterile dressing (n = 20)</td>
<td>Age mean 46 years  7 male/11 female  66/66 adult  Time on PD mean ± SD 14.3 ± 12.9 months</td>
<td>Age mean 47 years  7 male/6 female  67/67 adult  Time on PD mean ± SD 21.2 ± 28.6 months</td>
<td>Age mean 55 years  13 male/7 female  67/67 adult  Time on PD mean ± SD 23.6 ± 19.0 months</td>
</tr>
<tr>
<td>Gadallah, 2000&lt;sup&gt;44,45&lt;/sup&gt;</td>
<td>Quasi-RCT</td>
<td>I.v. vancomycin 1 000 mg ~12 hours before PD catheter placement (n = 90; 103 catheters) versus i.v. cefazolin 1 000 mg ~3 hours before PD catheter placement (n = 88, 102 catheters) versus no antibiotics for at least 1 week before procedure (n = 87, 100 catheters)</td>
<td>Age 46 (15–72) years  38 male/52 female  90/90 adult  32/90 diabetic nephropathy  42/90 hypertension and renovascular disease  4/90 glomerulonephritis  3/90 APKD  4/90 lupus nephritis  5/90 HIV nephropathy</td>
<td>Age 47 (20–81) years  43 male/45 female  88/88 adult  30/88 diabetic nephropathy  38/88 hypertension and renovascular disease  5/88 glomerulonephritis  4/88 APKD  4/88 lupus nephritis  7/88 HIV nephropathy</td>
<td>Age 45 (19–76) years  38 male/49 female  87/87 adult  28/87 diabetic nephropathy  41/87 hypertension and renovascular disease  6/87 glomerulonephritis  2/87 APKD  5/87 lupus nephritis  5/87 HIV nephropathy</td>
</tr>
<tr>
<td>Luzar, 1990&lt;sup&gt;3&lt;/sup&gt;</td>
<td>Multicentre RCT</td>
<td>Povidone-iodine (concentration 20 g/l) applied to exit site with sterile gauze (n = 74) versus cleaning of exit site daily with non-disinfectant soap on sterile gauze (simple soap in UK or savon de Marseilles in France) (n = 53)</td>
<td>63% male/37% female  74/74 adult  17% diabetic glomerulonephritis</td>
<td>59% male/41% female  53/53 adult  11% diabetic glomerulonephritis</td>
<td>59% male/41% female  53/53 adult  11% diabetic glomerulonephritis</td>
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<tr>
<td>Lye, 199236</td>
<td>Single-centre quasi-RCT</td>
<td>Preoperative antibiotics: cefazolin (300 mg) and gentamicin (80 mg) as rapid i.v. infusion no more than 60 minutes before surgery ( (n = 25) ) versus no treatment ( (n = 25) )</td>
<td>Age mean ± SD 56.0 ± 14.3 years ( 8 ) male/17 female ( 1/25 ) diabetic nephropathy 4/25 glomerulonephritis 1/25 urolithiasis 3/25 other 3/25 S. aureus carriage 6/25 MRSA</td>
<td>Age mean ± SD 52.3 ± 14.0 years 15 male/10 female 13/25 diabetic nephropathy 7/25 glomerulonephritis 1/25 urolithiasis 4/25 other 6/25 S. aureus carriage 4/25 MRSA</td>
<td></td>
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<tr>
<td>Mupirocin Study Group, 1996</td>
<td>Multicentre RCT 267 participants</td>
<td>Calcium mupirocin 2%, 2 × daily for 5 consecutive days every 4 weeks ( (n = 134) ) versus placebo ointment ( (n = 133) )</td>
<td>Age mean 60.3 years 60.4% male/39.6% female 16.4% hypertension and renovascular disease 26.1% glomerulonephritis 10.4% polycystic disease 5.2% pylonephritis 24.6% other 134/134 S. aureus carriage 133/133 S. aureus carriage</td>
<td>Age mean 60.3 years 60.2% male/39.8% female 8.3% hypertension and renovascular disease 19.5% glomerulonephritis 5.3% polycystic disease 7.5% pylonephritis 36.8% other</td>
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<tr>
<td>Perez-Fontan, 1992</td>
<td>Single-centre RCT 22 participants</td>
<td>2% mupirocin nasal ointment t.d.s. for 7 days ( (n = 12) ) versus 0.1% neomycin sulphate ointment t.d.s. for 7 days ( (n = 10) )</td>
<td>Age mean ± SD 51 ± 15 years 5 male/7 female Time on PD 32 ± 16 months 12/12 S. aureus carriage</td>
<td>Age mean ± SD 48 ± 21 years 5 male/3 female Time on PD 32 ± 15 months 10/10 S. aureus carriage</td>
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<tr>
<td>Poole-Warren, 1991</td>
<td>Multicentre RCT 124 participants</td>
<td>Vaccinated with combined staphylococcus toxoid/whole killed staphylococci formulation (SB). Given i.m. Six injections given in increasing concentrations ( (1, 5, 10, 20, 50% and undiluted) ) over 6 weeks. Four booster injections (each 1 ml of undiluted SB) given every 12 weeks (weeks 17, 29, 41 and 53) ( (n = 65) ) versus placebo (normal saline injections given i.m. on same schedule) ( (n = 59) )</td>
<td>Age mean ± SD 54 ± 11 years 1.5 [ratio] 12/65 diabetic nephropathy 11/65 hypertension and renovascular disease 16/65 glomerulonephritis 5/65 reflux nephropathy 7/65 analgesic nephropathy 8/65 other Time on PD mean ± SD 1.5 ± 1.3 years 13/40 S. aureus carriage</td>
<td>Age mean ± SD 52 ± 14 years 0.7 [ratio] 9/59 diabetic nephropathy 5/59 hypertension and renovascular disease 18/59 glomerulonephritis 2/59 reflux nephropathy 9/59 analgesic nephropathy 6/59 other Time on PD mean ± SD 1.7 ± 1.9 years 11/36 S. aureus carriage</td>
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<td>Study</td>
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<tr>
<td>Sesso, 1988</td>
<td>RCT</td>
<td>4% chlorhexidine gluconate ((n = 20)) versus neutral soap ((n = 19))</td>
<td>Age mean ± SE 46.1 ± 3.8 (33–69) years</td>
<td>Age mean ± SE 36.6 ± 4.6 (22–61) years</td>
<td>Age mean ± SE 42.1 ± 4.6 (17–68) years</td>
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<td></td>
<td>150 patient months; Group B 133</td>
<td>Follow-up = Group A150 patient months; Group B 133 patient months Correspondence</td>
<td>Time on PD mean ± SE 16.1 ± 6.2 months</td>
<td>Time on PD mean ± SE 16.1 ± 6.2 months</td>
<td>Time on PD mean ± SE 15.0 ± 4.5 months</td>
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<td></td>
<td>patient months</td>
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<td>S. aureus carriage: all = 9/9; nares = 2/9; exit site = 2/9; nares + exit site = 5/9</td>
<td>S. aureus carriage: all = 9/9; nares = 0/9; exit site = 4/9; nares + exit site = 5/9</td>
<td>S. aureus carriage: all = 13/13; nares = 4/9; exit site = 4/13; nares + exit site = 5/13</td>
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<td>patient months</td>
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<td>Age mean ± SE 46.1 ± 3.8 (33–69) years</td>
<td>Age mean ± SE 36.6 ± 4.6 (22–61) years</td>
<td>Age mean ± SE 42.1 ± 4.6 (17–68) years</td>
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<tr>
<td>Sesso, 1994</td>
<td>Single-centre RCT</td>
<td>2% sodium fusidate (ointment as applied to anterior nares and catheter exit site × 2 daily for 5 days) ((n = 9)) versus 200 mg ofloxacin orally every 48 hours for 5 days ((n = 9)) versus placebo tablets ((n = 13))</td>
<td>Age mean ± SE 46.1 ± 3.8 (33–69) years</td>
<td>Age mean ± SE 36.6 ± 4.6 (22–61) years</td>
<td>Age mean ± SE 42.1 ± 4.6 (17–68) years</td>
</tr>
<tr>
<td></td>
<td>31 participants Follow-up = mean ± SE 7.8 ± 0.6 months</td>
<td>6 male/3 female 9/9 adult 1/9 diabetic nephropathy 0/9 glomerulonephritis 8/9 other</td>
<td>6 male/3 female 9/9 adult 3/9 diabetic nephropathy 1/9 glomerulonephritis 5/9 other</td>
<td>9 male/4 female 13/13 adult 1/13 diabetic nephropathy 3/13 glomerulonephritis 6/13 other</td>
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<td>Follow-up = at least 48 hours</td>
<td>Time on PD mean ± SE 16.1 ± 6.2 months</td>
<td>Time on PD mean ± SE 16.1 ± 6.2 months</td>
<td>Time on PD mean ± SE 16.1 ± 6.2 months</td>
<td>Time on PD mean ± SE 15.0 ± 4.5 months</td>
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<tr>
<td></td>
<td>Full text</td>
<td>S. aureus carriage: all = 9/9; nares = 2/9; exit site = 2/9; nares + exit site = 5/9</td>
<td>S. aureus carriage: all = 9/9; nares = 0/9; exit site = 4/9; nares + exit site = 5/9</td>
<td>S. aureus carriage: all = 13/13; nares = 4/9; exit site = 4/13; nares + exit site = 5/13</td>
<td>S. aureus carriage: all = 13/13; nares = 4/9; exit site = 4/13; nares + exit site = 5/13</td>
</tr>
<tr>
<td>Sharma, 1971</td>
<td>RCT</td>
<td>Neomycin (0.5 g by mouth or nasogastric tube every 6 hours) ((n = 48) dialysates) versus placebo ((n = 41) dialysates)</td>
<td>Age mean ± SE 46.1 ± 3.8 (33–69) years</td>
<td>Age mean ± SE 36.6 ± 4.6 (22–61) years</td>
<td>Age mean ± SE 42.1 ± 4.6 (17–68) years</td>
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<td></td>
<td>41 participants (95 dialysates)</td>
<td>6 male/3 female 9/9 adult 1/9 diabetic nephropathy 0/9 glomerulonephritis 8/9 other</td>
<td>6 male/3 female 9/9 adult 3/9 diabetic nephropathy 1/9 glomerulonephritis 5/9 other</td>
<td>9 male/4 female 13/13 adult 1/13 diabetic nephropathy 3/13 glomerulonephritis 6/13 other</td>
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<td></td>
<td>Follow-up = at least 48 hours</td>
<td>Time on PD mean ± SE 16.1 ± 6.2 months</td>
<td>Time on PD mean ± SE 16.1 ± 6.2 months</td>
<td>Time on PD mean ± SE 15.0 ± 4.5 months</td>
<td>Time on PD mean ± SE 15.0 ± 4.5 months</td>
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<tr>
<td></td>
<td>Full text</td>
<td>S. aureus carriage: all = 9/9; nares = 2/9; exit site = 2/9; nares + exit site = 5/9</td>
<td>S. aureus carriage: all = 9/9; nares = 0/9; exit site = 4/9; nares + exit site = 5/9</td>
<td>S. aureus carriage: all = 13/13; nares = 4/9; exit site = 4/13; nares + exit site = 5/13</td>
<td>S. aureus carriage: all = 13/13; nares = 4/9; exit site = 4/13; nares + exit site = 5/13</td>
</tr>
<tr>
<td>Turner, 1992</td>
<td>Single-centre RCT</td>
<td>Immobiliser ((n = 22)) versus tape ((n = 23)) versus non-immobilised ((n = 21))</td>
<td>Age mean ± SD 45 ± 15.51 years</td>
<td>Age mean ± SD 40 ± 14.26 years</td>
<td>Age mean ± SD 43 ± 15.8 years</td>
</tr>
<tr>
<td></td>
<td>66 participants Follow-up = mean (range) 20 ± 17 (2–49) versus 21 ± 17 (2–54) versus 23 ± 20 (1–60) weeks</td>
<td>10/22 S. aureus carriage</td>
<td>11/23 S. aureus carriage</td>
<td>6/21 S. aureus carriage</td>
<td>6/21 S. aureus carriage</td>
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<td>Follow-up = mean (range) 20 ± 17 (2–49) versus 21 ± 17 (2–54) versus 23 ± 20 (1–60) weeks</td>
<td>Full text</td>
<td>S. aureus carriage: all = 9/9; nares = 2/9; exit site = 2/9; nares + exit site = 5/9</td>
<td>S. aureus carriage: all = 9/9; nares = 0/9; exit site = 4/9; nares + exit site = 5/9</td>
<td>S. aureus carriage: all = 13/13; nares = 4/9; exit site = 4/13; nares + exit site = 5/13</td>
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<tr>
<td>Waite, 1997</td>
<td>Single-centre RCT 120 participants (117 analysed) Follow-up = mean 14.6 vs 13.2 months Full text</td>
<td>3.5 g (10%) povidone–iodine ointment (n = 61) versus no intervention (n = 56)</td>
<td>Age mean ± SD 54.4 ± 15.1 years 33 male/28 female 22/61 S. aureus carriage</td>
<td>Age mean ± SD 53.2 ± 14.5 years 30 male/26 female 14/56 S. aureus carriage</td>
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<tr>
<td>Warady, 2003</td>
<td>Multicentre RCT 121 participants Follow-up = mean 305.3 ± 22.2 vs 313.0 ± 26.5 days Abstract</td>
<td>‘Flush before fill’ flushing of 100 ml of sterile dialysate from each bag of dialysate through the cycler tubing and into the drain bag following drainage of effluent from the patient and before the infusion of sterile dialysate into the patient (n = 62) versus 15 ml of sterile dialysate flushed through the tubing originating only from the heater bag into the drain bag prior to infusion (n = 59)</td>
<td>Age mean 11.4 ± 5.6 years 54.8% male/45.2% female 62/62 paediatrics 3.2% reflux nephropathy 41.9% other Time on PD 24.6 (3.8) months</td>
<td>Age mean 11.2 ± 6.0 year 59.3% male/40.7% female 59/59 paediatrics 1.7% reflux nephropathy 50.8% other Time on PD 18.9 (2.9) months</td>
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<td>Wilson, 1997</td>
<td>RCT 130 participants (149 catheters) Follow-up = 1 year or until a significant difference was present Full text</td>
<td>Sterile povidone iodine (2.5%) dry powder spray to exit site every time dressing changed (every other day) (n = 77 catheters) versus no intervention (n = 72 catheters)</td>
<td>Age mean (range) 53 (18–82) years 77/77 adults 3.2% reflux nephropathy 41.9% other Time on PD median (range) 422 (52–1280) days</td>
<td>Age mean (range) 51 (21–76) years 72 adults 1.7% reflux nephropathy 50.8% other Time on PD median (range) 512 (42–1572) days</td>
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<tr>
<td>Wong, 2002</td>
<td>Single-centre quasi-RCT 124 participants (117 analysed) Follow-up = 6 months Full text</td>
<td>4% chlorhexidine liquid soap used in cleansing of exit site (n = 69) versus pure liquid soap used in cleansing of exit site (n = 48)</td>
<td>Age mean 59.0 ± 11.50 years 34 male/35 female</td>
<td>Age mean 56.3 ± 11.7 years 23 male/25 female</td>
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<th>Study</th>
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<th>Intervention 2 population characteristics</th>
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<tr>
<td>Wong, 200338</td>
<td>Single-centre RCT</td>
<td>Mupirocin applied using cotton-tipped applicator to apply ointment round skin around catheter exit site daily (n = 78, 73 analysed) versus no intervention (n = 88, 81 analysed)</td>
<td>Age mean 60 ± 12 years 32 male/41 female Time on PD 41 ± 37 months 16/73 S. aureus carriage</td>
<td>Age mean 59 ± 13 years 47 male/34 female Time on PD 39 ± 25 months 14/81 S. aureus carriage</td>
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<tr>
<td>Zimmerman, 1991</td>
<td>Single-centre RCT</td>
<td>Rifampin 300 mg 2 times daily for 5 days at the start of each 12-week interval (n = 32) versus no treatment (n = 32)</td>
<td>Age mean ± SEM 53 ± 3 years 17 male/15 female 32/32 adults Time on PD 41 ± 37 months 9/32 S. aureus carriage</td>
<td>Age mean ± SEM 55 ± 4 years 24 male/8 female 32/32 adults Time on PD 39 ± 25 months 8/32 S. aureus carriage</td>
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APKD, adult polycystic kidney disease; SD, standard deviation; SE, standard error; SEM, standard error of the mean.
Appendix 7

Proposed methods for parameterising the economic model

Probabilities

As mentioned before, the main source of effectiveness data that would be used to populate the model is the review of effectiveness (Chapter 3). However, as described below, other sources such as existing datasets and population cohort studies may be required. The outcomes of the systematic review of effectiveness were primarily presented in terms of relative effect sizes (RRs) for the comparison of prophylactic antibiotic with no treatments. By identifying the relevant transition probabilities for the ‘no treatment’ intervention and combining with relevant relative effect sizes for the prophylactic antibiotic intervention, the transition probabilities for this intervention can be derived.

Estimation of baselines comparator transition probabilities

One source of data on the relevant transition probabilities for this is the control arms of studies that compared an active treatment with no treatment. Table 13 describes the parameters used to determine transitions between the states of the model. The data that might be used for these parameters are described below.

Transition probabilities from ‘Catheter insertion’

Following the initial insertion of the PD catheter a person would receive PD, although they may have a risk of being a carrier of S. aureus. Ideally, the risk of S. aureus carriage would come from a large population based survey of patients pre-dialysis. Some data on the risk of S. aureus carriage at the time of catheter insertion could be obtained from systematic review of effectiveness36,46 (see Table 6). These sources provide rates of S. aureus carriage of between 18.0 and 30.8% and a crude mean of 27.0% (46 cases out of 167 trial participants). In the model, it would be assumed that 27% of those who do not die less those who experience an infection (see below) would transfer into the state of ‘On PD with SA carriage’.

The risk of infections caused by S. aureus following catheter insertion could also be provided by review of effectiveness data. The systematic review of effectiveness sought to identify the number of patients with peritonitis, peritonitis rates, peritonitis relapses, exit-site and tunnel infection rates. Although the aim was to identify exit-site, tunnel and peritonitis infections separately, most of the studies reported exit-site/tunnel infections together (Chapter 3). Table 6 provides details on the number of patients without S. aureus carriage who develop peritonitis and also the mean number of episodes per patient year. The data from the no treatment arms of these studies can

<table>
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<th>State</th>
<th>Parameter</th>
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<tr>
<td>‘Catheter insertion’</td>
<td>On PD without SA carriage</td>
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<td></td>
<td>On PD with SA carriage</td>
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<tr>
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<td>On PD with an infection</td>
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<tr>
<td>‘On PD without SA’</td>
<td>Remain on PD without SA carriage</td>
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<tr>
<td></td>
<td>On PD with SA carriage</td>
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<tr>
<td></td>
<td>On PD with an infection</td>
</tr>
<tr>
<td></td>
<td>Transfer to HD</td>
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<tr>
<td></td>
<td>Die</td>
</tr>
<tr>
<td>‘On PD with SA’</td>
<td>Go back to PD without SA carriage</td>
</tr>
<tr>
<td></td>
<td>Remain on PD with SA carriage</td>
</tr>
<tr>
<td></td>
<td>On PD with an infection</td>
</tr>
<tr>
<td></td>
<td>Transfer to HD</td>
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<tr>
<td></td>
<td>Die</td>
</tr>
<tr>
<td>‘Infection’</td>
<td>Infection cured, return to PD without SA carriage</td>
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<tr>
<td></td>
<td>Relapsing infection</td>
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<td></td>
<td>Temporary HD</td>
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<tr>
<td></td>
<td>HD</td>
</tr>
<tr>
<td></td>
<td>Die</td>
</tr>
<tr>
<td>‘Temporary HD’</td>
<td>Infection cured, return to PD without SA carriage</td>
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<tr>
<td></td>
<td>HD</td>
</tr>
<tr>
<td></td>
<td>Die</td>
</tr>
<tr>
<td>‘Permanent HD’</td>
<td>Remain on HD</td>
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<td>Die</td>
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In the hypothetical model, ‘infection’ is defined as a single state. In a full model, the different types of infection might be defined as individual states that would allow them to occur either singularly or in sequence.
be used to provide some information of the risks of infection (and types of infection) per year. However, very few data are available.\textsuperscript{39} A crude estimate of the risk of peritonitis per patient per month would be 1.3%. A similar estimate for the risk of exit-site or tunnel infections would be 5.4%. Such data come from a small study and hence are imprecise and unreliable.\textsuperscript{39} Ideally, such data would be replaced by data from a larger study. Data are also required on the risk of infections for those with \textit{S. aureus} carriage. Data from the no treatment arms for comparisons of alternative methods to treat \textit{S. aureus} carriage provided by the systematic review are one source of data\textsuperscript{55} (Table 8). However, such data are not comparable to the risks of infections for those without \textit{S. aureus} carriage. For example, from the data available, the risk of peritonitis per patient per month can be calculated as 1.9% and the risk of exit-site and tunnel infections as 3.6%. It might be expected that the infections caused by \textit{S. aureus} would be greater in the group that were known carriers of \textit{S. aureus}. Ideally, the information on infection rates amongst those who are and are not carriers of \textit{S. aureus} would come from a single study of sufficient size to provide reasonably precise and reliable data for a UK setting.

Survival rates or death rates for patients on PD would also be needed. The Renal Registry has published survival rates derived from data on 3-year survival rates using Kaplan–Meier survival analysis.\textsuperscript{1} To use such data would require that the proportion of people dying from \textit{S. aureus} infection while on PD is only a small proportion of the total risk of death on PD.

**Transition probabilities from ‘On PD without SA carriage’**

Patients who are \textit{S. aureus} free can remain on PD until they die either free of \textit{S. aureus} carriage or become carriers of \textit{S. aureus}. These is insufficient information on the risk that a patient might develop \textit{S. aureus} carriage from the review of effectiveness, but one study reported how the risk of \textit{S. aureus} nasal carriage changes over time.\textsuperscript{51} This study is small and even though such data could be used in the model, they are likely be both imprecise and unreliable. Ideally, such data should come from the control arm of a large RCT or from a large cohort study relevant to a UK setting.

As indicated in Table 10, a patient on PD but free of \textit{S. aureus} also faces the probability of developing an infection or dying. The data required to derive the relevant transition probabilities could be derived using similar methods to those outlined for the transitions from ‘Catheter insertion’.

The remaining transition probability required from the state ‘On PD without SA carriage’ is the transition to HD. The review of effectiveness sought to establish the number of patients requiring catheter replacement/removal (and hence requiring temporary HD, a clinically possible transition but not one allowed for this state in this hypothetical model) and the number of patients permanently switching to HD (unclear whether this included both permanent and temporary transfers). Although some data were reported on catheter removal for those with \textit{S. aureus} carriage (see Table 6), no data were identified on the number of patients switching modality. A search of the Renal Registry indicated that the sequential annual risk of switching from PD to HD permanently was 11% at the end of the first year, 18% at the end of the second year and 23% at the end of the third year (based on data for patients established on PD in 1998–9, the most recent years for which data are available).\textsuperscript{1} From such data, monthly transition probabilities might be estimated.

**Transition probabilities from ‘On PD with SA carriage’**

Similar methods and data sources would be required to estimate the transition probabilities from this state as those described for transitions from ‘Catheter insertion’ and ‘On PD without SA carriage’.

**Transition probabilities from ‘Infection’**

Ideally, the likelihood that an infection is cured would be derived by consideration of the data on the effectiveness of interventions to treat \textit{S. aureus} interventions. The most appropriate source of such data would not be the review of effectiveness reported in Chapter 3 but a new review of studies looking at alternative treatments of infections (the data from such a review are presented in Appendix 8). From such a review, data would be extracted on the likelihood of infections that do not resolve and the risk of death or transferring modality. Following consultation with the clinical co-reviewers, it has been assumed in the model that should a patient suffer three consecutive months (cycles) of infection that they would automatically transfer to the state of temporary HD.

**Transition probabilities from ‘Temporary HD’**

Patients who enter this state will remain in it for only one cycle; at the end of that cycle, they may...
either transfer to the state ‘On PD without SA carriage’, transfer to the state of ‘Permanent HD’ or die. The risk of death is not likely to be greatly different to the rates used for earlier states. However, there is no evidence available on the likelihood of returning to PD or moving to permanent HD. Data from the Renal Registry suggest that patients rarely switch from HD to PD (approximately 3% per annum), but these numbers may not be applicable for the group of patients who switch to HD only until their symptoms resolve. Ideally, data from a well-designed study would be useful but, as this is only a transitory state, sensitivity analysis could be conducted over a range of plausible values.

**Transitions from ‘Permanent HD’**

In the model, it is assumed that once patients are transferred to HD they will stay in this state until they die. The Renal Registry has published survival rates using Kaplan–Meier survival analysis and these data could be used to establish the relevant transition probabilities.

**Estimation of relative effect sizes**

Data on relative effect sizes for an active treatment compared with no treatment (e.g. antibiotics versus no antibiotics for the prevention of carriage) can, when combined with the transition probabilities for no treatment, be used to estimate the transition probabilities for the an active treatment, e.g. prophylactic antibiotics. The various relative effect sizes estimated as part of the review of effectiveness are presented in Figures 1–7. Although such relative effect sizes could be used in a model, they are limited as they are based on sparse data, and a full evaluation comparing all relevant interventions would rely on indirect comparisons. Details of the data available for comparison of antibiotics provided at the time of catheter insertion compared with no treatment are provided below.

**S. aureus carriage cure rates**

This relative effect size is needed to estimate the probability of entering ‘PD without SA carriage’ and ‘PD with SA carriage’ states following prophylactic use of antibiotics at the time of catheter insertion. From the review of effectiveness, no data were available on the ability of prophylactic antibiotics at the time of catheter insertion to prevent infection with *S. aureus*. Some estimate could be obtained by considering the effectiveness of antibiotics at curing those with known *S. aureus* carriage. Table 8 reports the results on the number of people treated for *S. aureus* carriage during dialysis. The number of patients cured (those who did not have *S. aureus* at the end of the treatment) could therefore be derived from these data.

**S. aureus infection rates**

These relative effect sizes would be used to estimate the likelihood of developing an infection. Data are not available split by whether the infections occurred in those who were *S. aureus* carriers and those who were not. Although consideration of data provided in Figures 1, 2, 5 and 6 might provide some information with which plausible estimates could be derived. Nevertheless, ideally such data would be more usefully derived from the participant-level data from a large controlled study.

**Exit site/tunnel and peritonitis cure rates**

Once an infection has occurred, the assumption would be made that the probability of cure would be independent of the intervention used to prevent or treat *S. aureus* carriage. Thus, the transition probabilities from the state of ‘Infection’ following the use of prophylactic antibiotics would be the same as those following no treatment. What would vary between the two interventions would be the probability of an infection.

**Modality changes**

Few studies provided any data on the number of patients switching modality from PD or the number of patients requiring catheter removal (and at least a move to temporary HD). The studies identified in Chapter 3 were not designed to provide such data and provided, at best, only proxy indicators. Such data as are available are presented in Tables 6 and 8 but are both imprecise and potentially unreliable due to the small size of the studies. Furthermore, such data would ideally be split by those who were *S. aureus* carriers and those who were not carriers. Ideally, such data would be more usefully derived from the participant-level data from a large controlled study.

Relative effect sizes for the risk of modality changes from the states of ‘Infection’, ‘Temporary HD’ and ‘Permanent HD’ would not be required as these transition probabilities are assumed to be independent of the method used to prevent or treat *S. aureus* carriage.

**Death or survival rates**

Exactly the same situation arises for relative effect sizes associated with the risk of death as those
noted above for changes in modality. Again, data from a large controlled study would be useful. Such a study would need to have sufficiently long enough follow-up to capture differences in survival (and other relevant effects).

Cost data

The perspective of the assessment of costs would be that of the NHS and Personal Social Services. Resource use data would be identified from published studies, healthcare service utilisation data and advice from experts in this field. Cost data used to illustrate this part of the hypothetical model were mainly extracted from the literature published in 1999 and were inflated to 2005 using the Hospital and Community Health Services (HCHS) pay and price inflation indices and the currency used is pounds sterling (£). The main cost components were the costs of the interventions themselves and the costs of treating an infection or the consequences of an infection (e.g. a change in modality or the replacement of a catheter). Details of the cost values used are reported in Table 14 and the methods used to derive these values are described below.

Estimation of the cost of catheter insertion

The cost of inserting a peritoneal catheter was derived from Kirby and Vale. These costs were calculated by identifying items of resource use from studies and by consulting the renal administrator at NHS Grampian. Local prices were then attached to each item and drug costs obtained from nationally available sources. The cost of access was estimated at £1955 in 1999 (£2235 in 2004 prices). The same cost would be used for patients who required a replacement of a PD catheter (following a period on temporary HD).

Estimation of the cost of interventions to prevent or treat S. aureus carriage

Data on patients who received antibiotics were derived from a published study. The cost data reported were based on the consideration of the unit dose, route of administration, doses per day and duration of therapy. The total cost of 1 year’s treatment per identified carrier of S. aureus was £137 (£157 at 1994 prices) and this comprised costs of £64 for screening and £93 for antibiotics. These costs were based on one antibiotic (mupirocin). The inflated annual cost per identified carrier of S. aureus is £179 (£73 for screening and £106 for antibiotic).

Estimation of the costs of treating infections

Data on patients who received antibiotics were derived from a published study and the costs of treatment were comprised of unit dose, route of administration, doses per day and duration. The study indicated that the mean costs of treating infections were highly skewed. The mean costs of treating all infections (exit-site infections and other infections) was £178 for the prophylaxis group and £379 for the placebo group at 1994 prices. The difference between the means was not statistically significant (–£201 (–£493 to £90). The cost data inflated to 2005 prices were £203 for the prophylaxis group and £433 for the placebo group.

Estimation of the costs of providing dialysis

The cost data for these interventions included consumables such as catheters and prophylactic treatments, staff costs, capital costs of providing HD, overheads and transport where necessary. These data were based on data provided by the EURODICE study (Wordsworth S, Health Economist, Oxford: personal communication, 2005). This study was an observational study investigating the costs, effects and cost-effectiveness of PD and HD in 10 European centres, two of which were in the UK. Costs in each centre were detailed data on the use of resources required for the different dialysis modalities in use. These were collected between 1999 and 2001 during site visits, detailed examination of records and the completion of questionnaires by manager, healthcare professionals and patients. In this review, data from the two UK centres (Aberdeen and Dundee) would be used as they are most likely to be applicable to the UK. The five main categories included in the estimation of costs were consumables, staff, capital, overheads and patient transport. The consumables were composed mainly of disposable items such as dialysers, line and recombinant human erythropoietin (EPO). Staff costs were based on weekly work rosters from the units which detailed the time devoted to the provision of HD and PD. The capital costs for HD were composed of building costs, dialysis machine, repairs, water treatment and computers. Although PD typically takes place outwith the hospital, some hospital costs would normally be incurred. The capital costs of PD were based on building costs, weighing scales, bag warmers, drip stand and blood pressure monitor. Staff costs were derived by identifying the salary grades of those who spent time with the patients (both medical and nursing).
and the amount of time they spent with the patients. Overhead costs included floor space allocation that was composed of cleaning, building, engineering, local government authority taxation on buildings (rates), water, energy and occupied bed days allocation that were composed of medical records, linen and catering. The total cost of HD for 1 month was £2458 and for PD £1603 at 2005 prices.

**Estimation of costs of change in modality**

One of the main effects of infections is the need to remove and replace the catheter and the cost of change in modality of treatment. The cost of loss of catheter/catheter replacement is based on the cost of a catheter, which is £2235 as reported above. The cost of switch in modality is the cost of HD, including creation of the access fistula. These data were also derived from Kirby and Vale and were estimated using the same methods as described for the cost of catheter insertion.73 The cost was £1959 (1999 prices), which was inflated to £2240 (2005 prices).

**Estimation of quality of life**

The main measure of effectiveness that would be used within the economic evaluation is QALYs. QALYs would be estimated by multiplying the length of time spent in each health state by a quality of life weight (a utility value) for that state. A search for studies on quality of life identified one study.74 The data came from 165 dialysis patients and were elicited using the EQ-5D instrument. Their results indicated that patients undergoing hospital HD had a utility score of 0.66, satellite HD patients had a value of 0.81, continuous ambulatory PD patients had a value of 0.71 and continuous cycling PD patients had a value of 0.81. As these do not come from an RCT, these utility scores are influenced by the choice of modality for each patient (i.e. there may be a selection bias). Although the utility scores for patients with end-stage renal disease were identified, there were no data on utilities of people on dialysis with infections.

Another further source of utility values was the data collected by the European Dialysis and Cost Effectiveness (EURODICE) study. This study prospectively identified cohorts of patients starting on HD and PD and collected EQ-5D data from patients on 1 July 1998 and 31 October 1999 every 6 months for a period of 2–3 years. Health state utilities were collected from all study participants including those from two UK centres (Aberdeen and Dundee). These data had not been previously reported but were obtained from the study researchers (Caskey F, Consultant Nephrologist, Bristol: personal communication, 2005)75,76 and the utilities were derived using the UK population tariffs.77

The modality of first treatment was assumed to be the method the patient was receiving at 90 days and not the initial dialysis method, as many patients, especially those being referred late to renal units, undergo a brief period of HD before being established on PD. Utility scores for this and three other time points (collected every 6 months) were estimated from the data provided. Secondary analysis was also carried out on the scores of patients who transferred from PD to HD. However, the numbers of patients changing treatment modality from PD to HD were very low, so the estimates were not reliable. Although there is not much detail on what type of HD and PD was being administered by the 12th month, EQ-5D values are similar to these reported by de Wit and colleagues.74 The utility value for patients receiving PD was 0.84 and for those receiving HD it was 0.69. These scores could therefore be used as the utility scores associated with ‘PD without SA carriage’, ‘PD with SA carriage’, ‘Temporary HD’,

**TABLE 14** Cost parameters available for use in the hypothetical model

<table>
<thead>
<tr>
<th>Cost element</th>
<th>Value (£)</th>
<th>Unit</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peritoneal dialysis</td>
<td>1603</td>
<td>Cost per month</td>
</tr>
<tr>
<td>Permanent and temporary haemodialysis</td>
<td>2458</td>
<td>Cost per month</td>
</tr>
<tr>
<td>Prophylaxis for <em>S. aureus</em> carriage</td>
<td>15</td>
<td>Cost</td>
</tr>
<tr>
<td>Treatment for <em>S. aureus</em> carriage</td>
<td>15</td>
<td>Cost per course</td>
</tr>
<tr>
<td>Treatment of exit-site infection</td>
<td>192</td>
<td>Cost per treatment</td>
</tr>
<tr>
<td>Treatment of tunnel infection</td>
<td>1035</td>
<td>Cost per treatment complication; may require removal of catheter</td>
</tr>
<tr>
<td>Catheter replacement</td>
<td>2235</td>
<td>Cost per procedure</td>
</tr>
<tr>
<td>Cost of creating access for haemodialysis</td>
<td>2240</td>
<td>Cost per access</td>
</tr>
<tr>
<td>Treatment of peritonitis</td>
<td>203</td>
<td>Cost per treatment</td>
</tr>
</tbody>
</table>

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and ‘Permanent HD’ in the model, as they are more representative of the UK population than those available from de Wit and colleagues. These data, however, should be treated with great caution as they are associated with considerable imprecision (which, although reported here, would need to be incorporated into the economic evaluation) derived from a non-randomised study and, like the data from de Wit and colleagues, will suffer from patient selection bias.

The EURODICE data provided no information with which to inform estimates of the utility associated with infections. Ideally, primary data collection would be performed to inform this. In the absence of such data, one approach would be to perform a sensitivity analysis using a range of values to explore the impact of this uncertainty on the results. A second approach would be to explore the use of other data sets such as the Health Outcomes Data Repository (eHODAR) (http://www.crc-limited.co.uk), although it is unlikely that such sources will contain sufficient information on the utilities relevant to this study.
Eight trials evaluated different antibiotic regimes for the treatment of PD-related infections and one trial compared intraperitoneal urokinase with a placebo.

Table 15 provides details, where reported, of the results for the following outcomes: number of patients with peritonitis caused by *S. aureus*; number of patients to have a primary response or successful treatment; number of patients for whom the treatment has failed; peritonitis relapse (number and specify time to) caused by *S. aureus*; and number of patients requiring catheter removal.

**Number of patients with exit-site and/or tunnel infections caused by *S. aureus***

Plum and colleagues\(^7^8\) reported the number of exit sites with *S. aureus* carriage as 6/8 versus 4/8; tunnel erythema before treatment 2/6 versus 1/4 and after treatment 0/6 versus 0/4; and tunnel drainage before treatment 6/6 versus 4/4 and after treatment 2/6 versus 1/4.

**Side-effects**

One trial\(^7^9\) reported one pseudo-obstruction and one hypotension as a result of antibiotic use in the intraperitoneal vancomycin plus gentamicin group and three nausea and one abdominal swelling in the oral ciproflaxin group.

**Death due to peritonitis caused by *S. aureus***

Tong and colleagues\(^8^6\) reported that one death in the placebo group was due to peritonitis.

No data were reported for the following outcomes: number of patients requiring catheter replacement caused by *S. aureus*; number of patients switching to HD; hospitalisation rates; quality of life; and development of antibiotic resistance.
<table>
<thead>
<tr>
<th>Study</th>
<th>Comparison</th>
<th>S. aureus peritonitis (no.)</th>
<th>Primary response/ treatment success (no.)</th>
<th>Treatment failure (no.)</th>
<th>Peritonitis relapse (no.)</th>
<th>Catheter removal (no.)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Antibiotic vs antibiotic</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bennett-Jones, 1990&lt;sup&gt;79&lt;/sup&gt;</td>
<td>Lp. vancomycin + gentamicin</td>
<td>5/26</td>
<td>2/5</td>
<td>3/5</td>
<td>1/5 (14 days)</td>
<td>–</td>
</tr>
<tr>
<td></td>
<td>Oral ciprofloxin</td>
<td>5/22</td>
<td>4/5</td>
<td>1/5</td>
<td>1/5 (14 days)</td>
<td>–</td>
</tr>
<tr>
<td>Cheng, 1991&lt;sup&gt;80&lt;/sup&gt;</td>
<td>Oral ofloxacin</td>
<td>3/23&lt;sup&gt;a&lt;/sup&gt;</td>
<td>3/3</td>
<td>0/3</td>
<td>0/3</td>
<td>–</td>
</tr>
<tr>
<td></td>
<td>Lp. vancomycin/aztreonam</td>
<td>5/25&lt;sup&gt;a&lt;/sup&gt;</td>
<td>5/5</td>
<td>0/5</td>
<td>1/5</td>
<td>–</td>
</tr>
<tr>
<td>Flanigan, 1991&lt;sup&gt;81&lt;/sup&gt;</td>
<td>Lp. vancomycin</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>4/30</td>
</tr>
<tr>
<td></td>
<td>Lp. cefazolin</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>5/15</td>
</tr>
<tr>
<td>Gucek, 1994&lt;sup&gt;82&lt;/sup&gt;</td>
<td>Lp. cefazolin</td>
<td>15%</td>
<td>1/3</td>
<td>2/3</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td></td>
<td>Oral ofloxacin</td>
<td>0%</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Gucek, 1997&lt;sup&gt;83&lt;/sup&gt;</td>
<td>Cefazolin/netilmicin</td>
<td>3/26&lt;sup&gt;a&lt;/sup&gt;</td>
<td>2/3</td>
<td>1/3</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td></td>
<td>Vancomycin/cefazidime</td>
<td>2/26&lt;sup&gt;a&lt;/sup&gt;</td>
<td>2/2</td>
<td>0/2</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Leung, 2004&lt;sup&gt;84&lt;/sup&gt;</td>
<td>Lp. imipenem/cilastatin</td>
<td>2/51</td>
<td>0/2</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td></td>
<td>Lp. cefazolin/cefazidime</td>
<td>13/51</td>
<td>4/13</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Merchant, 1992&lt;sup&gt;85&lt;/sup&gt;</td>
<td>Lp. imipenem/cilastatin</td>
<td>2/21</td>
<td>1/2</td>
<td>1/2</td>
<td>–</td>
<td>1/2</td>
</tr>
<tr>
<td></td>
<td>Lp. netilmicin/vancomycin</td>
<td>1/20</td>
<td>1/1</td>
<td>0/1</td>
<td>–</td>
<td>0/1</td>
</tr>
<tr>
<td>Plum, 1997&lt;sup&gt;86&lt;/sup&gt;</td>
<td>Oral clindamycin</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td></td>
<td>Lp. clindamycin</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td><strong>Other</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tong, 2005&lt;sup&gt;87&lt;/sup&gt;</td>
<td>Lp. urokinase</td>
<td>7/44 (3 MRSA)</td>
<td>3/4</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td></td>
<td>Placebo</td>
<td>11/44 (4 MRSA)</td>
<td>3/7</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
</tbody>
</table>

<sup>a</sup> Episodes.
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<td><strong>Ms Norma Armston</strong>, Freelance Consumer Advocate, Bolton</td>
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<td><strong>Professor Rudy Bilous</strong>, Professor of Clinical Medicine &amp; Consultant Physician, The Academic Centre, South Tees Hospitals NHS Trust</td>
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<td><strong>Ms Dea Birkett</strong>, Service User Representative, London</td>
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<tr>
<td><strong>Dr Paul Cockcroft</strong>, Consultant Medical Microbiologist and Clinical Director of Pathology, University Hospital of Radiology, University of Cambridge Clinical School</td>
</tr>
<tr>
<td><strong>Professor Adrian K Dixon</strong>, Professor of Radiology, University of Cambridge, Department of Radiology, University of Cambridge</td>
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<tr>
<td><strong>Dr David Elliman</strong>, Consultant in Community Child Health, Islington PCT &amp; Great Ormond Street Hospital, London</td>
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<td><strong>Professor Glyn Ewlyn</strong>, Research Chair, Centre for Health Sciences Research, Cardiff University, Department of General Practice, Cardiff</td>
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<td><strong>Professor Paul Glaziov</strong>, Director, Centre for Evidence-Based Practice, University of Oxford</td>
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<tr>
<td><strong>Dr Jennifer J Kurinczuk</strong>, Consultant Epidemiologist, National Perinatal Epidemiology Unit, Oxford</td>
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<td><strong>Dr Susanne M Ludgate</strong>, Clinical Director, Medicines &amp; Healthcare Products Regulatory Agency, London</td>
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<tr>
<td><strong>Mr Stephen Pilling</strong>, Director, Centre for Outcomes, Research &amp; Effectiveness, Joint Director, National Collaborating Centre for Mental Health, University College London</td>
</tr>
<tr>
<td><strong>Mrs Una Rennard</strong>, Service User Representative, Oxford</td>
</tr>
<tr>
<td><strong>Dr Phil Shackley</strong>, Senior Lecturer in Health Economics, Academic Vascular Unit, University of Sheffield</td>
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<tr>
<td><strong>Dr Margaret Somerville</strong>, Director of Public Health Learning, Peninsula Medical School, University of Plymouth</td>
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<tr>
<td><strong>Dr Graham Taylor</strong>, Scientific Director &amp; Senior Lecturer, Regional DNA Laboratory, The Leeds Teaching Hospitals</td>
</tr>
<tr>
<td><strong>Professor Lindsay Wilson Turnbull</strong>, Scientific Director, Centre for MR Investigations &amp; YCR Professor of Radiology, University of Hull</td>
</tr>
<tr>
<td><strong>Professor Martin J Whittle</strong>, Clinical Co-director, National Co-ordinating Centre for Women’s and Child Health</td>
</tr>
<tr>
<td><strong>Dr Dennis Wright</strong>, Consultant Biochemist &amp; Clinical Director, The North West London Hospitals NHS Trust, Middlesex</td>
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</tbody>
</table>

### Pharmaceuticals Panel

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<thead>
<tr>
<th>Members</th>
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<tbody>
<tr>
<td><strong>Chair</strong></td>
</tr>
<tr>
<td><strong>Ms Anne Baileff</strong>, Consultant Nurse in First Contact Care, Southampton City Primary Care Trust, University of Southampton</td>
</tr>
<tr>
<td><strong>Professor Imti Choonara</strong>, Professor in Child Health, Academic Division of Child Health, University of Nottingham</td>
</tr>
<tr>
<td><strong>Professor John Geddes</strong>, Professor of Epidemiological Psychiatry, University of Oxford</td>
</tr>
<tr>
<td><strong>Mrs Barbara Greggains</strong>, Non-Executive Director, Greggains Management Ltd</td>
</tr>
<tr>
<td><strong>Dr Bill Gutteridge</strong>, Medical Adviser, National Specialist Commissioning Advisory Group (NSCAG), London</td>
</tr>
<tr>
<td><strong>Dr Jonathan Karnon</strong>, Senior Research Fellow, Health Economics and Decision Science, University of Sheffield</td>
</tr>
<tr>
<td><strong>Dr Yoon Loke</strong>, Senior Lecturer in Clinical Pharmacology, University of East Anglia</td>
</tr>
<tr>
<td><strong>Ms Barbara Meredith</strong>, Lay Member, Epsom</td>
</tr>
<tr>
<td><strong>Dr Andrew Prentice</strong>, Senior Lecturer and Consultant Obstetrician &amp; Gynaecologist, Department of Obstetrics &amp; Gynaecology, University of Cambridge</td>
</tr>
<tr>
<td><strong>Dr Frances Rothblat</strong>, CPMP Delegate, Medicines &amp; Healthcare Products Regulatory Agency, London</td>
</tr>
<tr>
<td><strong>Dr Martin Shelly</strong>, General Practitioner, Leeds</td>
</tr>
<tr>
<td><strong>Mrs Katrina Simister</strong>, Assistant Director New Medicines, National Prescribing Centre, Liverpool</td>
</tr>
<tr>
<td><strong>Dr Richard Tiner</strong>, Medical Director, Medical Department, Association of the British Pharmaceutical Industry, London</td>
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(NSCAG), London

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West London Mental Health 
Trust, Middlesex

Ms Jeanett Martin, 
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Dr John Jackson, 
General Practitioner, 
Newcastle upon Tyne

Dr Chris McCall, General 
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Mrs Veronica James, Chief 
Officer, Horsham District Age 
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## Expert Advisory Network

### Members

<table>
<thead>
<tr>
<th>Name</th>
<th>Position &amp; Affiliation</th>
</tr>
</thead>
<tbody>
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<td>Professor Douglas Altman,</td>
<td>Professor of Statistics in Medicine, Centre for Statistics in Medicine, University of Oxford</td>
</tr>
<tr>
<td>Professor John Bond,</td>
<td>Director, Centre for Health Services Research, University of Newcastle upon Tyne, School of Population &amp; Health Sciences, Newcastle upon Tyne</td>
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<td>Professor Andrew Bradbury,</td>
<td>Professor of Vascular Surgery, Solihull Hospital, Birmingham</td>
</tr>
<tr>
<td>Mr Shaun Brogan,</td>
<td>Chief Executive, Ridgeway Primary Care Group, Aylesbury</td>
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<td>Mrs Stella Burnside OBE,</td>
<td>Chief Executive, Regulation and Improvement Authority, Belfast</td>
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<tr>
<td>Ms Tracy Bury,</td>
<td>Project Manager, World Confederation for Physical Therapy, London</td>
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<td>Professor Iain T Cameron,</td>
<td>Professor of Obstetrics and Gynaecology and Head of the School of Medicine, University of Southampton</td>
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<td>Dr Christine Clark,</td>
<td>Medical Writer &amp; Consultant Pharmacist, Rossendale</td>
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<td>Professor Collette Clifford,</td>
<td>Professor of Nursing &amp; Head of Research, School of Health Sciences, University of Birmingham, Edgbaston, Birmingham</td>
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<td>Professor Barry Cookson,</td>
<td>Director, Laboratory of Healthcare Associated Infection, Health Protection Agency, London</td>
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<td>Clinical Senior Lecturer in Neurology, Department of Medicine &amp; Therapeutics, University of Aberdeen</td>
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<td>Professor Howard Cuckle,</td>
<td>Professor of Reproductive Epidemiology, Department of Paediatrics, Obstetrics &amp; Gynaecology, University of Leeds</td>
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<td>Dr Katherine Darton,</td>
<td>Information Unit, MIND – The Mental Health Charity, London</td>
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<tr>
<td>Professor Carol Dezateux,</td>
<td>Professor of Paediatric Epidemiology, London</td>
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<td>Dr Keith Dodd,</td>
<td>Consultant Paediatrician, Derby</td>
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<td>Mr John Dunning,</td>
<td>Consultant Cardiothoracic Surgeon, Cardiothoracic Surgical Unit, Papworth Hospital NHS Trust, Cambridge</td>
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<td>Mr Jonathan Earnshaw,</td>
<td>Consultant Vascular Surgeon, Gloucestershire Royal Hospital, Gloucester</td>
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<td>Professor of Clinical Effectiveness, Centre for Health Services Research, University of Newcastle upon Tyne</td>
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<td>Professor of Community Rehabilitation, Institute of General Practice and Primary Care, University of Sheffield</td>
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<td>Professor of Primary Care Research &amp; Development, Centre for Health Sciences, Barts &amp; The London</td>
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<td>Queen Mary’s School of Medicine &amp; Dentistry, London</td>
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<td>Mr Leonard R Fenwick,</td>
<td>Chief Executive, Newcastle upon Tyne Hospitals NHS Trust</td>
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<td>Antenatal Teacher &amp; Tutor and President, National Childbirth Trust, Henfield</td>
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<td>Professor of Psychiatry, University of Cambridge, Cambridge</td>
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<td>Professor Stan Kaye,</td>
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<td>Dr Duncan Keeley,</td>
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<td>Dr Donna Lamping,</td>
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<td>Mr George Levy,</td>
<td>Chief Executive, Motor Neurone Disease Association, Northampton</td>
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<td>Professor James Lindesay,</td>
<td>Professor of Psychiatry for the Elderly, University of Leicester, Leicester General Hospital</td>
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<td>Professor Julian Little,</td>
<td>Professor of Human Genome Epidemiology, Department of Epidemiology &amp; Community Medicine, University of Ottawa</td>
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<td>Consultant in Public Health, South Manchester Primary Care Trust, Manchester</td>
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<td>Professor Alexander Markham,</td>
<td>Director, Molecular Medicine Unit, St James’s University Hospital, Leeds</td>
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<td>Professor Alistaire McGuire,</td>
<td>Professor of Health Economics, London School of Economics</td>
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<td>Director, NHS Cancer Screening Programmes, Sheffield</td>
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<tr>
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Systematic review of the effectiveness of preventing and treating *Staphylococcus aureus* carriage in reducing peritoneal catheter-related infections

K McCormack, K Rabindranath, M Kilonzo, L Vale, C Fraser, L McIntyre, S Thomas, H Rothnie, N Fluck, IM Gould and N Waugh

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We look forward to hearing from you.