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TITLE

The effectiveness of meatal cleaning in the prevention of catheter-associated urinary tract infections and bacteriuria: An updated systematic review and meta-analysis

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ABSTRACT

Introduction: Meatal cleaning prior to urinary catheterisation and post catheterisation is one element of urinary catheter care which may reduce the risk of catheter-associated urinary tract infections (CAUTIs) and bacteriuria. A systematic review on this topic was published in 2017, with further studies undertaken since this time. We present an updated systematic review on the effectiveness of antiseptic cleaning of the meatal area for the prevention of CAUTIs and bacteriuria.

Objective: To determine the effectiveness of antiseptic cleaning of the meatal area for preventing CAUTIs and bacteriuria.

Design: Systematic review

Methods: Electronic databases Cochrane Library, PubMed, Embase, CINAHL, Medline and Academic Search Complete were searched to identify randomised controlled trials and quasi-experimental studies. Odds ratios and 95% confidence intervals were calculated from the proportions of patients with CAUTI and bacteriuria in the intervention and control groups and compared between groups using Der Simonian and Laird random-effects models. Subgroup analyses were undertaken to explore effects of aspects of study design on outcomes. Heterogeneity was estimated using the I^2 statistic.

Findings: A total of 18 studies were included. Some potential benefit of using antiseptics, compared to non-antiseptics for meatal cleaning to prevent bacteriuria and or CAUTI was identified (OR 0.84, 95% CI 0.69-1.02; P=0.071). Some potential value of antiseptics prior to urinary catheterisation in reducing the incidence of bacteriuria, compared to non-antiseptic agents (OR=0.67, 95% CI 0.44-1.03; P=0.065) was also identified.

Conclusion: There is emerging evidence of the role of antiseptics prior to urinary catheterisation, in reducing CAUTIs, and some potential benefit to the role of antiseptics more generally in reducing bacteriuria.

Strengths and limitations of this study

- A summary of the latest evidence on the role of antiseptics in reducing catheter associated urinary tract infections
- Provides an update to a previous review, to include new research which impact key findings
- Heterogeneity of population groups is a limitation

INTRODUCTION

Indwelling or intermittent urinary catheter use can result in bacteriuria which may signify either colonisation (catheter-associated asymptomatic bacteriuria) or symptomatic infection (catheter-associated urinary tract infections).[1] Catheter-associated urinary tract infections (CAUTIs) are a common but preventable nosocomial infection. They account for around 70-80% of hospital-acquired UTIs, are associated with longer length of hospital stay and increased risk of morbidity and mortality.[2-5] In the UK, economic analyses of hospital inpatient costs estimated that CAUTIs caused over 45,000 excess bed days, 1,467 deaths, and a loss of 10,471 quality-adjusted life years (QALYs).[6] The burden of CAUTIs for both patients and health services highlight the importance of reducing these infections in healthcare settings.

Various strategies for reducing the risk of CAUTIs have been proposed. These include reducing unnecessary catheter use, practicing appropriate catheter insertion and maintenance, and prompt removal of urinary catheters.[7-9] A systematic review published in 2017 explored the effect of using different meatal (peri-urethral) cleaning agents prior to urinary catheter insertion on the incidence of UTIs.[10] Meatal cleaning was identified by the review as one element of urinary catheter care which may reduce CAUTI risk.[10] However, the review also identified uncertainty in the available evidence for the effectiveness of this practice. Since this publication there have been further studies published on this topic,[11 12] and the evidence base is still evolving. Moreover, some previous studies were limited by bias (e.g. selection bias, non-masking of intervention).[11 13] Given the potential importance of meatal cleaning for preventing UTIs and informing clinical practice and guidelines, we believed it was important to update the evidence base.[10] In this paper, we present findings from an updated systematic review and meta-analysis. The aim of this review is to determine the effectiveness of antiseptic cleaning of the meatal area, for preventing CAUTI and bacteriuria.

METHODS

A protocol was developed to guide the conduct of the systematic review and meta-analysis, and we have used a reporting approach consistent with the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) statement.[14] The approach used for this

update is the same as that used in the initial publication.[10] Studies included in the final synthesis from the initial publication were combined with studies identified as part of the updated search strategy.

Data sources and search strategy

The electronic databases Cochrane Library, PubMed, Embase, CINAHL, Medline and Academic Search Complete were used to undertake the search. Search parameters were adjusted to suit database requirements. A search of the databases was limited to the period between 1 January 2016 and 29 February 2020. The 1st January 2016 represents the end date of the search from the initial review.[10] Keywords and MeSH terms used were: urinary catheter and/or urinary catheterisation, urinary tract infection, meatal cleaning, periurethral cleaning, antiseptic, antimicrobial, antibacterial, antibiotic, and topical intervention. Further details on the search strategy are provided as supplementary material.

Study inclusion and exclusion criteria

Included studies were randomised controlled trials (RCTs) and quasi-experimental studies (pre-and post-test design, non RCTs) evaluating the use of antiseptic, antibacterial or non-medicated agents (such as soap and water) for cleaning the meatal, periurethral or perineal areas before indwelling catheter insertion or intermittent catheterisation or during routine meatal care. Studies were included if they involved patients requiring short- or long-term indwelling catheters or intermittent catheterisation in hospitals, community settings, and long-term/aged care facilities. Studies were excluded if they were not published in English language, focused solely on children (≤18 years), included patients with pre-existing UTIs, or were published in grey literature (conference abstracts, editorial letters, reports and guidelines). Review articles, bundle interventions, studies without available data for analysis, studies that did not evaluate the control or intervention agents, and studies for which the full-text was not available were also excluded.

The co-primary outcome measures were the difference in rates of CAUTI and bacteriuria in the intervention and control groups. While we accepted the definition of CAUTI and bacteriuria provided in the included studies, we also considered infection to be the outcome when clinical signs or symptoms of infection were present.[15]

Study selection

Database results were imported into Covidence for screening and selection.[16] Screening of abstracts of articles retrieved from electronic databases for relevance to the systematic review aim was undertaken by one researcher (CC). Ten percent of the abstracts were cross checked by a second researcher (BM). No discrepancies were found. Full-text screening was then undertaken and assessed against the inclusion and exclusion criteria by CC. A cross check of all studies deemed to meet the inclusion criteria was also undertaken by BM. A manual search of the references lists of all included articles was undertaken to identify additional studies. Where decisions were open to disagreement, this was resolved by discussion with other members of the research team (EGH and OF).

Data extraction

The data from included studies were extracted using the Cochrane Collaboration's data collection form for RCTs and non-RCTs. Data were extracted by one researcher (CC) and then checked for accuracy by a second researcher (BM). Extracted details included: age and sex distribution of the study population, study duration, sample size, study setting, type of intervention and duration, colony-forming unit (cfu/mL) count, bacteriuria and CAUTI rates (numerator/denominator data). For studies that reported the outcome at multiple time points, the outcome value closest to the end of the indwelling catheter in-situ period was extracted for analysis. Attempts were made to contact the authors of included studies where information was missing regarding the numerator or denominator data for calculating CAUTI rates, and when clarity was needed on the type of intervention used. One author was contacted regarding inaccuracies in reporting results and the author responded by sending the corrected version of the study manuscript.

Risk of bias assessment

Using Covidence and following the Cochrane Collaboration's Handbook for Systematic Reviews of Interventions (v6., 2019), the risk of bias for studies were evaluated.[17] Risk of bias was assessed as high, unclear or low. Risk of bias assessment was conducted independently by two researchers (OF and CC) and disagreements resolved by discussion with a third researcher (BM).

Data analysis

Data analyses were undertaken using Stata Version 14 (StataCorp, College Station, TX, USA). Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated from the proportions of patients with CAUTI and bacteriuria in the intervention and control groups. The pooled ORs were calculated and compared across intervention and control groups using the DerSimonian and Laird random effects meta-analysis model which considers possible heterogeneity between the studies during analysis.[18] The likelihood of clinical heterogeneity in the included studies with regards to varying meatal cleaning agents used was considered in the a-priori data synthesis strategy. Hence, the meta-analysis was stratified by the outcome and type of meatal cleaning agent used. The I^2 statistic was used to quantify between-study heterogeneity of intervention effects. Subgroup analyses were undertaken to explore effects of aspects of study methodology (antiseptic vs non-antiseptic cleaning and administration of the intervention prior to urinary catheter insertion) on the outcome. Assessment of reporting biases was by visual examination of the funnel plot. A 0.05 level of significance was used without adjustment for multiplicity (number of comparisons of meatal cleaning agents). Effect sizes and their precision, in addition to significance were considered when interpreting the results.

RESULTS

In total, 927 articles were retrieved from electronic database searches and their abstracts were screened for relevance to the systematic review aim. After evaluating these articles against the inclusion and exclusion criteria, four studies were identified for inclusion. These four studies were added to the 14 studies included in the previous review,[10] hence a total 18 studies were included in this systematic review and meta-analysis (Figure 1).

The characteristics of the included studies are presented in Table 1. The majority of studies were RCTs (n=15). There was considerable diversity in the types of interventions (meatal cleaning agent) used and whether the intervention was applied to the meatal area during ongoing meatal care, prior to catheter insertion only or a combination of both. Of the 18 studies, two compared povidone-iodine with routine (or standard) meatal care, which involved removal of debris from the catheter during bathing;[19 20] one compared green soap

with routine meatal care;[19] four compared an antibacterial agent (Neomycin-polymyxcin B, 1% silver sulfadiazine Silvadene, 2% polynoxylin) with routine meatal care;[21-24] two compared chlorhexidine (0.1% and 0.3% plus and 3% centrimide) with tap water;[25 26] three compared povidone-iodine with soap and water;[13 27 28] one compared chlorhexidine (0.1%) with saline;[11] one compared povidone-iodine with saline;[29] two compared povidone-iodine with sterile water;[12 30] one compared povidone-iodine with tap water;[31] and one compared antimicrobial cloth with chlorhexidine (2%) compared to a non-antimicrobial cloth.[32]

The term 'infection' was often referred to as the primary outcome in studies. However, the definition of 'infection' varied and for most studies, this term was used when bacteria were present in the urine with or without clinical symptoms. We recoded outcomes to be either bacteriuria or infection – where the definition of infection must have included signs/symptoms of a UTI. Two studies reported CAUTI as the only outcome, 15 studies reported bacteriuria as the only outcome and one study reported both CAUTI and bacteriuria as outcomes.

Effect of meatal cleaning on the incidence of bacteriuria and CAUTI

A forest plot displaying the results of random-effect meta-analyses for the effect of meatal cleaning on the incidence of both bacteriuria and CAUTI, stratified by meatal cleaning agent is presented in Figure 2. For the study that reported both CAUTI and bacteriuria as outcomes,[11] only data for bacteriuria were included because bacteriuria was the outcome in majority of studies.

There was no evidence of differences in the incidence of bacteriuria or CAUTI between the intervention and control groups when comparing the different agents: povidone-iodine vs routine care (OR 1.19, 95% CI 0.75-1.87; P=0.46); green soap and water vs routine care (OR 1.59, 95% CI 0.85-2.96; P=0.15), chlorhexidine vs tap water (OR 1.04, 95% CI 0.59-1.83; P=0.89); povidone-iodine vs soap and water (OR 0.88, 95% CI 0.48-1.62; P=0.69); povidone-iodine vs saline (OR 1.13, 95% CI 0.53-2.41; P=0.76); povidone-iodine vs sterile water (OR 0.42, 95% CI 0.14-1.24; P=0.12); povidone-iodine vs tap water (OR 0.80, 95% CI 0.22-2.97; P=0.74) and chlorhexidine vs antimicrobial cloths (OR 0.67, 95% CI 0.39-1.18; P=0.17).

There was potential evidence of a small difference in the incidence of bacteriuria or CAUTI between the intervention and control groups overall (pooled OR 0.84, 95% CI 0.69-1.02; P=0.071), with the CI nearly excluding 1. This also applies to the comparison of antibacterial agent vs routine care (OR 0.75, 95% CI 0.55-1.01; P=0.055). The comparison of chlorhexidine vs saline demonstrated statistical evidence of differences between the intervention and control group (OR 0.40, 95% CI 0.21-0.74; P=0.003). Overall results showed evidence of heterogeneity (I^2=13.2%; P=0.296) among the included studies.

Separate forest plots showing the effect of meatal cleaning on the incidence of bacteriuria and CAUTI are presented as supplementary material (Figure S1 and Table S1, and Figure S2, respectively). Sixteen studies were included in the meta-analysis evaluating the effect of meatal cleaning on the incidence of bacteriuria only while three studies were included in the meta-analysis evaluating the effect of meatal cleaning on the incidence of CAUTI only. [11 27 32] Both analyses showed no evidence of differences in the incidence of bacteriuria (pooled OR 0.84, 95% CI 0.68-1.04; P=0.10) and CAUTI (pooled OR 0.625, 95% CI 0.27-1.43; P=0.27) between the intervention and control groups.

Effect of antiseptic vs non-antiseptic meatal cleaning prior to urinary catheterisation on the incidence of bacteriuria and CAUTI

Six studies explored the effect of using an antiseptic meatal cleaning agent prior to catheter insertion, compared to a non-antiseptic agent, on the incidence of bacteriuria (Figure 3). [11 12 25 26 28 31] There was evidence of a potential difference in the incidence of bacteriuria when comparing the use of antiseptic and non-antiseptic agents (pooled OR=0.67, 95% CI 0.44-1.03; P=0.065) (Figure 3). Two studies explored the effect of using an antiseptic meatal cleaning agent prior to catheter insertion, compared to a non-antiseptic agent, on the incidence of CAUTI.[11 27] There was no evidence for a difference in the incidence of CAUTI when comparing the use of antiseptic and non-antiseptic agents (pooled OR=0.56, 95% CI 0.10-3.20; P=0.52) (Figure S3).

Risk of bias

Results showed that the level of risk of bias varied between the included studies (Figure 4). The majority of studies (n=15) were assessed to have a high or unclear risk of bias for

reporting of blinding processes used in the studies. The vast majority of studies were biased in the categories of allocation and performance. The studies conducted by Noto et al,[32] and Fasugba et al,[11] were deemed to be at lowest risk of bias.

Publication bias

Visual inspection of the funnel plot showed no evidence of publication bias (Figure 5).

Table 1. Characteristics of studies included in the systematic review and meta-analysis

Study author, year and design	Country	Population	Administration	Frequency of application	Outcome	Outcome definition	Intervention				Control		
							Mean age (SD)	Intervention agent	Alcohol-containing agent	Cases	Mean age (SD)	Comparator agent	Cases
Burke et al., 1981a; RCT [19]	USA	Medical and surgical patients	Daily meatal care while IDC in situ	Twice daily	Bacteriuria	$\geq 10^3$ cfu/mL	NR	10% povidone-iodine Betadine solution and ointment	Yes, pareth-25-9 as inactive ingredient	32/203	NR	Usual care; removal of debris from catheter during bathing	24/194
Burke et al., 1981a; RCT [19]	USA	Medical and surgical patients	Daily meatal care while IDC in situ	Once daily	Bacteriuria	$\geq 10^3$ cfu/mL	NR	Green soap and water	Assumed yes, 30% ethyl alcohol as solution	28/223	NR	Usual care; removal of debris from catheter during bathing	18/223
Burke et al., 1983, RCT [21]	USA	Medical and surgical patients	Daily meatal care while IDC in situ, until UTI found	Twice daily	Bacteriuria	$\geq 10^3$ cfu/mL	NR	Neomycin-polymyxcin B-bacitracin ointment	No	14/211	NR	Usual care; removal of debris from catheter during bathing	16/214
Carapeti et al., 1996; RCT [25]	UK	General surgery patients	On IDC insertion for surgery	Once for surgery	Bacteriuria (+- symptoms)	$>10^5$ cfu/mL	67.5	0.3% CHG and 3% centrimide Savlon solution	Yes, 2.84% isopropyl alcohol, 0.056% benzyl benzoate and	7/74	65.3	Tap water	9/82

Study author, year and design	Country	Population	Administration	Frequency of application	Outcome	Outcome definition	Intervention				Control			
							Mean age (SD)	Intervention agent	Alcohol-containing agent	Cases	Mean age (SD)	Comparator agent	Cases
									terpineol as excipient ingredients				
Classen et al., 1991a; RCT [22]	USA	Medical and surgical patients	Daily meatal care while IDC in situ, until UTI found	Thrice daily	Bacteriuria	$\geq 10^3$ cfu/mL	NR	Polymyxin B sulfate, neomycin sulfate, gramicidin Neosporin cream	Yes, propylene glycol as non-medicinal ingredient	26/336	NR	Routine meatal care; removal of debris from catheter during bathing	37/364
Classen et al., 1991b; RCT [20]	USA	Medical and surgical patients	Daily meatal care while IDC in situ, until UTI found	Once daily	Bacteriuria	$\geq 10^3$ cfu/mL	NR	2% Lugol's Iodine povidone-iodine solution	Unclear, assumed no	14/306	NR	Routine meatal care; removal of debris from catheter during bathing	15/306
Duffy et al., 1995; RCT [27]	USA	Male veterans in long-term care	Pre-IC and IDC	Pre-IC, ~thrice daily	Infection	$\geq 10^5$ cfu/mL + symptoms	72.6 (10.8)	10% povidone-iodine Betadine solution	Yes, pareth-25-9 as inactive ingredient	26/42	70.9 (12.1)	Soap and water	21/38
Fasugba et al., 2019; RCT [11]	Australia	Medical and surgical patients, ICU	On IDC insertion	Once, before insertion	Infection & Bacteriuria	CAUTI: CDC/ NHSN	NR	0.1% CHG solution	No	UTI: 4/94	NR	0.9% saline	UTI 13/697

Study author, year and design	Country	Population	Administration	Frequency of application	Outcome	Outcome definition	Intervention				Control		
							Mean age (SD)	Intervention agent	Alcohol-containing agent	Cases	Mean age (SD)	Comparator agent	Cases
						Bacteriuria: ≥10^5 cfu/mL				Bacteriuria 16/94			Bacteriuria 29/697
Huth et al., 1992; quasi-RCT [23]	USA	Medical and surgical patients	Daily meatal care while IDC in situ	Twice daily	Bacteriuria	Bacteriuria ≥10^3 cfu/mL	61	1% silver sulfadiazine Silvadene cream	Yes, stearyl alcohol, isopropyl myristate and propylene glycol as vehicle ingredients	38/332	63	Usual care; removal of debris from catheter during bathing	48/364
Ibrahim & Rashid, 2002; RCT [29]	Saudi Arabia	Male transurethral surgery patients	On IDC insertion, and in daily application while IDC in situ	Once daily	Bacteriuria	10^5 cfu/mL	66.7 (10.1)	Povidone-iodine solution	Unclear, assumed no	19/64	66 (10.4)	Saline	18/66
Jeong et al., 2010; quasi-RCT [13]	South Korea	Female ICU patients	On IDC insertion, and in daily meatal care while IDC in situ	Once daily	Bacteriuria+	CDC/NHSN	61.5 (17.3)	10% povidone-iodine solution	Unclear, assumed no	9/28	64.1 (13.3)	Soap and water	10/22

Study author, year and design	Country	Population	Administration	Frequency of application	Outcome	Outcome definition	Intervention				Control		
							Mean age (SD)	Intervention agent	Alcohol-containing agent	Cases	Mean age (SD)	Comparator agent	Cases
Kara & Ozyurek, 2017; RCT [30]	Turkey	ICU, surgical and medical patients	On IDC insertion, and in daily meatal care while IDC in situ	Once daily	Bacteriuria	$\geq 10^5$ cfu/mL	66.34 (14)	Sterile water	No	7/32	67.96 (12)	Sterile water	7/32
							63.5 (12)	10% povidone-iodine	No	4/33			
King et al., 1992; RCT [28]	USA	SCI rehabilitation inpatients	Pre-IC	Pre-IC, once per 4-6 hours	Bacteriuria	$\geq 10^4$ cfu/mL with symptoms	32.8 (13.7)	Povidone-iodine solution	Unclear, assumed no	13/23	27.9 (10.3)	Castile soap wipe	15/23
Lynch et al., 1991; quasi-RCT [24]	UK	Male transurethral surgery patients	On IDC insertion, and in daily meatal care while IDC in situ	Once daily	Bacteriuria	$>10^5$ cfu/mL	67 (9.7)	2% polynoxylin Anaflex spray	Yes, formaldehyde as active ingredient	6/50	68 (8.4)	No intervention	11/50
Nasiriani et al., 2009; RCT [31]	Iran	Female gynaecological surgery patients	On IDC insertion for surgery	Once for surgery	Bacteriuria	$>10^5$ cfu/mL	NR	Povidone-iodine solution	Unclear, assumed no	5/30	NR	Tap water	6/30
Noto et al., 2015; RCT [32]	USA	Surgical, medical and ICU patients	Daily bathing including meatal care	Once daily	Infection	CAUTI: CDC/NHSN	NR	2% CHG Cloths	No	20/4488	NR	Non-antimicrobial bath cloth	32/4852

Study author, year and design	Country	Population	Administration	Frequency of application	Outcome	Outcome definition	Intervention				Control		
							Mean age (SD)	Intervention agent	Alcohol-containing agent	Cases	Mean age (SD)	Comparator agent	Cases
Nugraha et al., 2019; RCT [12]	Java	Surgical and medical patients; (n=4, 12.5% aged 16-20 years)	On IDC insertion	Once, before insertion	Bacteriuria	Presence of bacteriuria; (cfu/mL level NR)	NR	10% povidone-iodine solution	Unclear, assumed no	2/16	NR	Sterile water	5/16
Webster et al., 2001; RCT [26]	Australia	Pregnant obstetrics patients	On IDC insertion for delivery	Once for delivery	Bacteriuria	$\geq 10^6$ cfu/mL	NR	0.1% CHG solution	No	20/21	NR	Tap water	18/219

Note: cfu: colony forming units; CHG: chlorhexidine gluconate; IC: intermittent catheterisation; ICU: intensive care unit; IDC: indwelling catheter; NR: not reported; RCT: randomised controlled trial; SCI: spinal cord injury; SD: standard deviation; UK: United Kingdom; USA: United States of America; UTI: urinary tract infection. Information on alcohol-containing agent ingredients assumed from research; no information on alcohol-containing agents available in included paper
* Positive UTI was assessed on following criteria: fever ≥38 degrees, suprapubic pain, dysuria, urethral erythema, purulent drainage around the catheter exit, presence of bacteria, pyuria (pus ≥3/ml in unspun urine), urine culture to stand on the presence of UTI (? $\geq 10^5$ cfu/mL, see CDC 2015), and white blood cell (WBC) count to prove presence of infection. # Table 2 results reported in the paper were incorrect. Authors were contacted for clarification, data in the table reflect clarification from authors. + Author state based "on the CDC definition of UTI, in particular, asymptomatic bacteriuria", with a reference supporting bacteriuria, therefore bacteriuria was assumed

DISCUSSION

Findings from this systematic review suggest that broadly speaking, using antiseptics for meatal cleaning may reduce the risk of bacteriuria or CAUTI. Although the odds ratios are not statistically significant at a level of 0.05,[33] the results are clinically meaningful. There are some specific subsets where the evidence is stronger and more consistent, for example prior to urinary catheterisation. There also appears to be emerging evidence that using chlorhexidine prior to urinary catheterisation may provide benefit in reducing CAUTI. Preventing CAUTI is important for a number of reasons. Prevention of CAUTI is vital, not only because of associated morbidity, mortality and increased length of stay in hospital, [2-5] but because of the added threats posed by increasing antimicrobial resistance.[34]

The meta-analysis exploring the effect of meatal cleaning in reducing the risk of bacteriuria, included studies that used antiseptics for routine meatal cleaning, for example post catheter insertion, as well as studies using antiseptics as part of the catheter insertion process (prior to urinary catheterisation) (Figure 2). The antiseptics used in studies included in this meta-analysis also varied (Table 1). When all studies were combined, the results indicated a benefit of using antiseptics, in reducing the risk bacteriuria or CAUTI (pooled OR 0.84, 95% CI 0.691-1.02; P=0.071). Although not statistically significant at an arbitrary level of 0.05, these results have clinical implications, noting it is difficult to interpret given the heterogeneity of antiseptics and timing of their use. In sub-analysis, some benefit of using an antibacterial agent vs routine (standard) care was identified (OR 0.75, 95% CI 0.55-1.01; P=0.055).

In studies specifically exploring the use of antiseptics prior to urinary catheterisation, a meta-analysis indicated some value of antiseptics in preventing bacteriuria, compared to non-antiseptic agents (pooled OR=0.67, 95% CI 0.44-1.03; P=0.065). Five of the six studies included in the meta-analysis had findings in the same direction, a benefit to antiseptics (Figure 3). The meta-analysis was largely influenced by two studies, indicating differing results, but both using chlorhexidine 0.1%. One of these two studies, a multi-centre study involving three hospitals and included all patients in each hospital, indicated a statistically significant benefit when using antiseptics (chlorhexidine 0.1%).[11] The second study, a single centre study in an obstetric population, indicated no benefit, with a non-statistically

significant result.[26] For consistency, in the meta-analysis, the outcomes presented were bacteriuria. We also present outcomes of the same meta-analysis by type of antiseptic in Table S1, with chlorhexidine 0.1% versus saline being the only statistically significant finding.

We identified two studies evaluating the use of antiseptics prior to catheterisation, with CAUTI as the primary outcome.[11 27] Fasugba and colleagues found a significant reduction in CAUTI, associated with the use of chlorhexidine 0.1% (IRR 0.06, 95% CI 0.01-0.32, p=0.00080).[11] In a follow up cost-effectiveness evaluation, the authors found that using chlorhexidine 0.1% was cost saving.[35] Duffy et al, evaluated the use of povidone-iodine prior to catheterisation, in participants who had indwelling catheters or were undertaking intermittent catheterisation.[27] Duffy and colleagues did not identify a benefit from using povidone-iodine.[27] It is worth noting other important differences. The control phase included a clean catheterisation technique, i.e. not requiring a sterile field. The intervention phase, which used povidone-iodine, also included the use of a sterile procedure. The average follow-up period for participants was 63 days. As time from catheter insertion increases, the likelihood of an infection being related to insertion practices diminishes. In contrast, participants in the study undertaken by Fasugba et al were followed up for 7 days only.[11]

This paper represents the latest evidence on the role of using antiseptics in people with urinary catheters, for the purpose of infection prevention. In turn, we hope this will inform local policy and practice, as well as infection control guidelines more generally. We acknowledge that two of the authors of this systematic review led one of the included studies.[11] To ensure there was balance, we included two authors on this paper that had no involvement in this study. Based on the evidence identified in this review and after careful consideration of the outcomes and methods used in included studies, we believe there is emerging evidence of the role of chlorhexidine 0.1% prior to urinary catheterisation, in reducing CAUTI, and potentially some benefit to the role of antiseptics more generally in reducing bacteriuria. Given the low number of included studies using CAUTI as the primary outcome, additional studies in this area are required, ensuring that important confounders are controlled for in the study design.

ETHICS APPROVAL

As this is a systematic review, ethics approval was not required.

CONFLICT OF INTEREST

Two of the authors (BM and OF) are named on one of the studies included in this systematic review. The risk of bias assessment for this study included an independent person.

FUNDING

No funding was received for this study.

AUTHORSHIP STATEMENT

OF and BM designed the study. OF conducted the search. CC conducted the primary review of the articles and data extraction. CC, OF and BM conducted the risk of bias assessment. OF, BM and EGH conducted the analysis. All authors had input into writing the paper, provided critical review and approved the final version of the paper.

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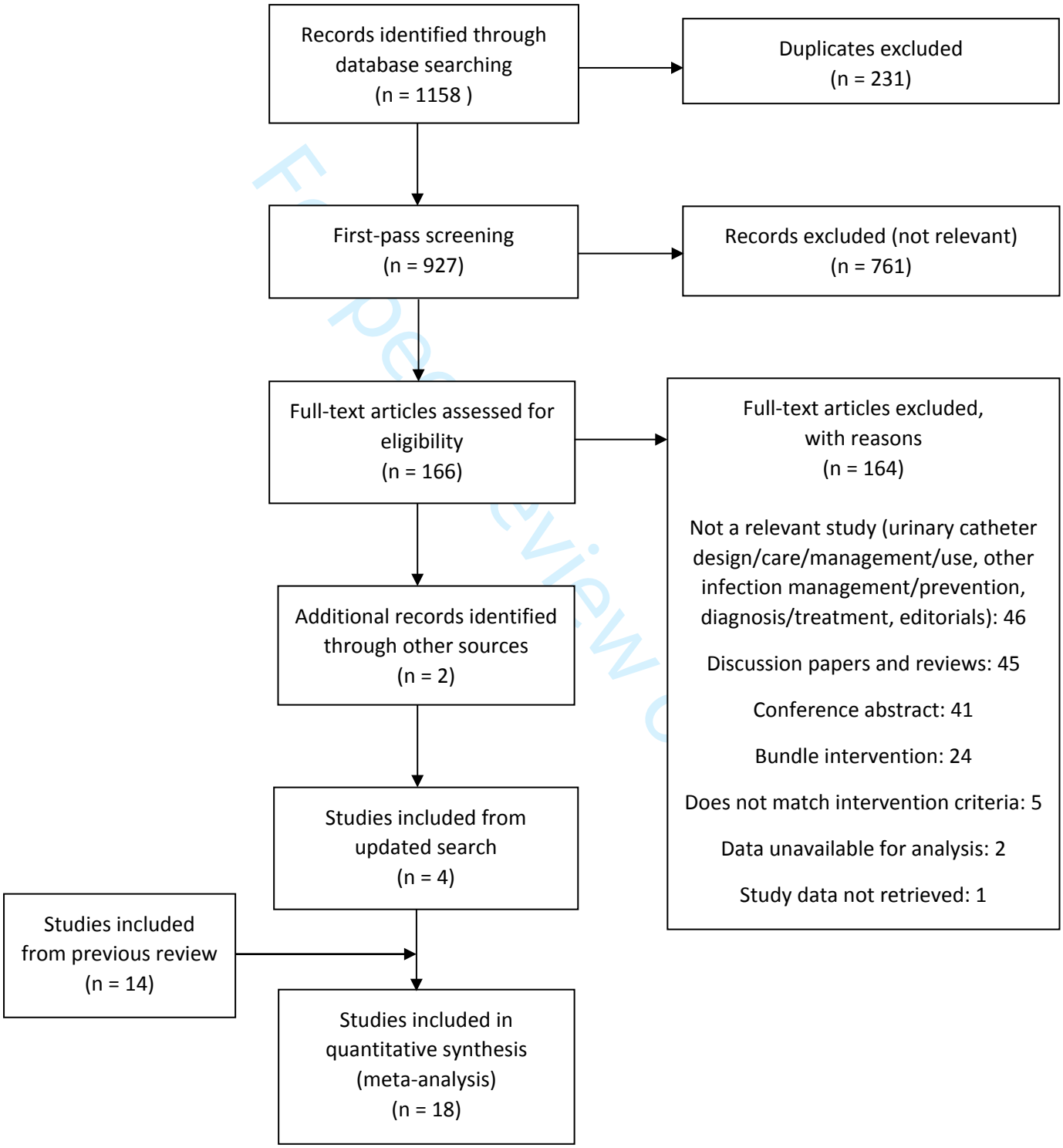

Figure 1. PRISMA flow diagram of study selection

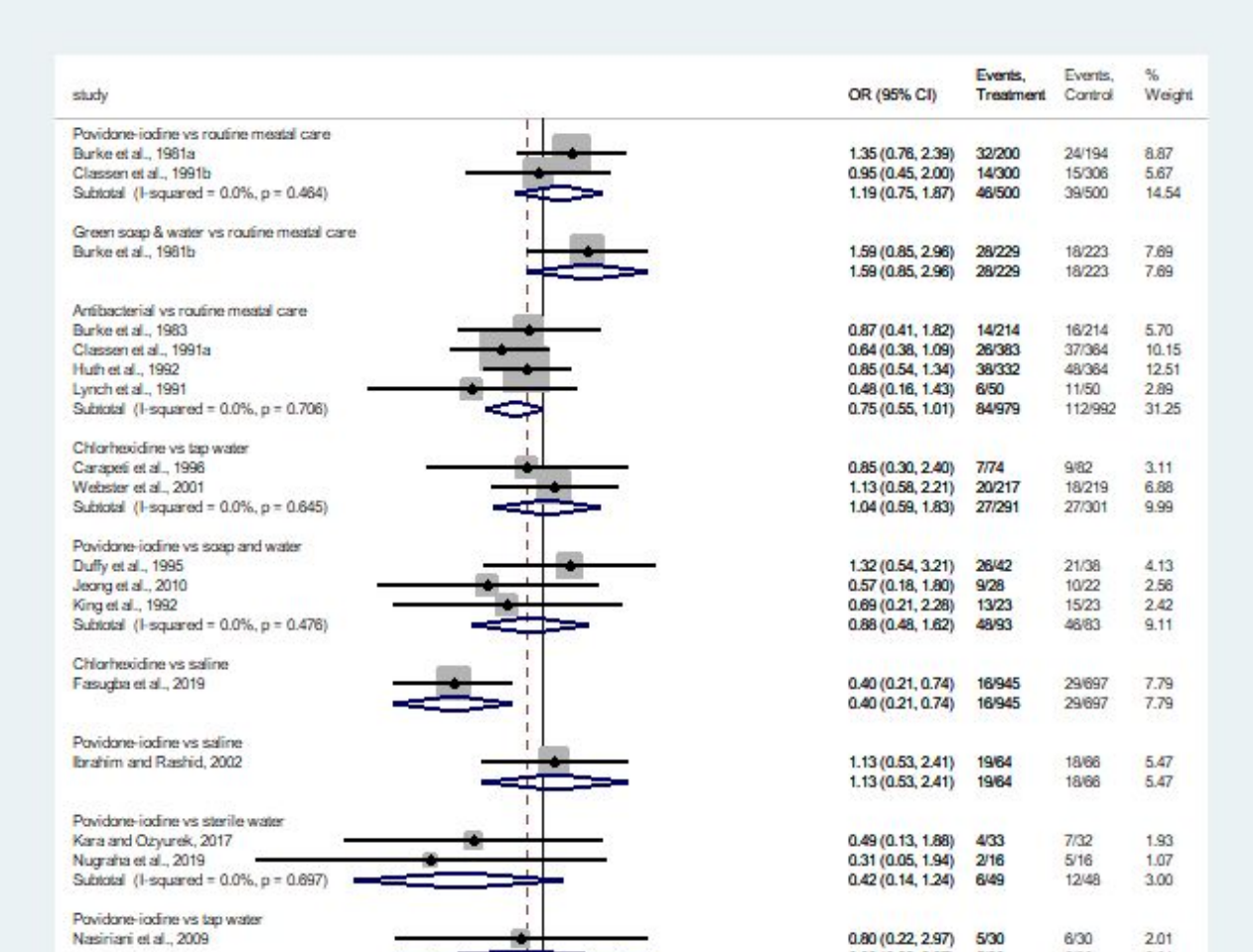

Figure 2. Forest plot displaying random-effect meta-analysis of the effect of meatal cleaning on the incidence of bacteriuria and or catheter-associated urinary tract infections (results stratified by meatal cleaning agent)

Note: Duffy et al., 1995 and Noto et al., 2015 all report CAUTI as the outcome, while Fasugba et al., 2019 report both CAUTI and bacteriuria. Bacteriuria data only from Fasugba et al, 2019 is included in this analysis.

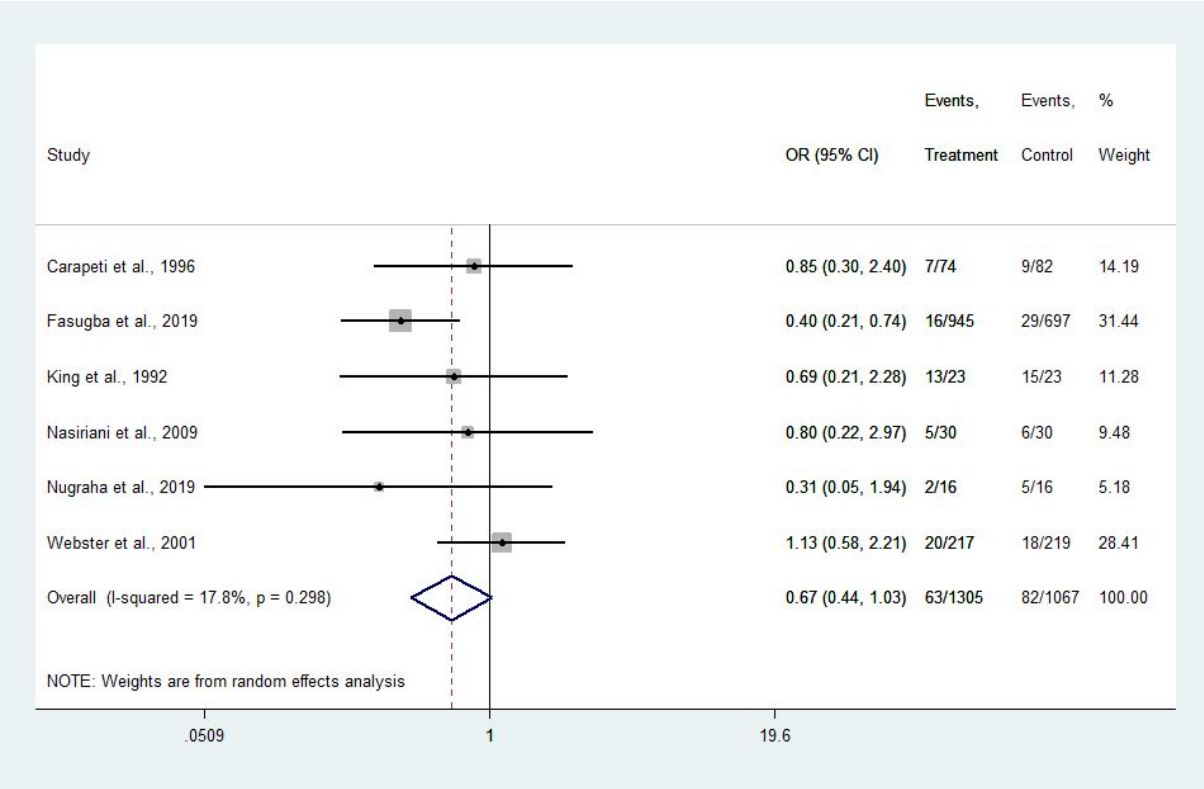

Figure 3. Random-effect meta-analysis of the effect of using an antiseptic meatal cleaning agent (povidone-iodine, chlorhexidine) vs a non-antiseptic agent (soap and water, tap water, sterile water or saline) prior to catheter insertion on the incidence of bacteriuria

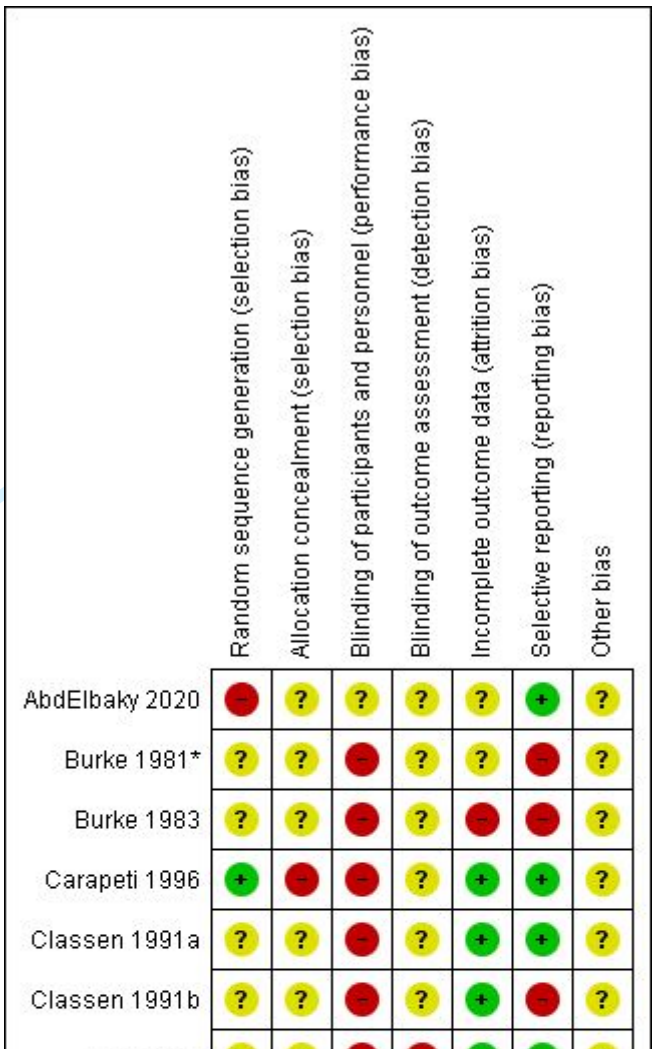

Figure 4. Risk of bias assessment

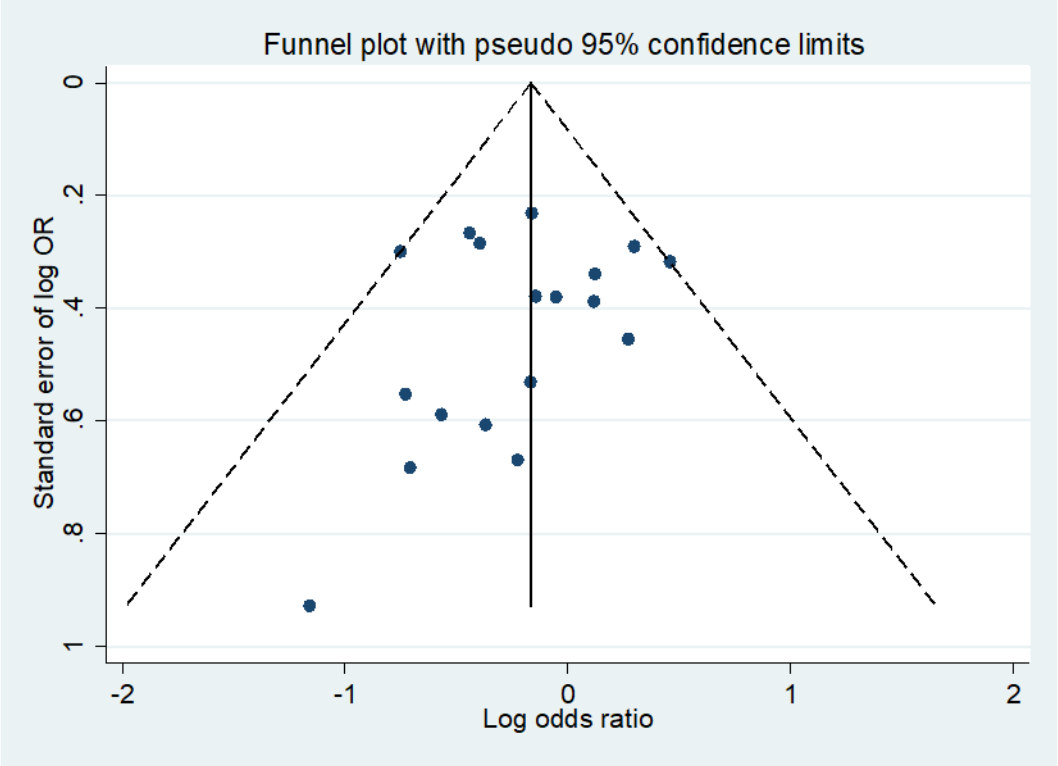

Figure 5. Funnel plot of the included studies

SUPPLEMENTARY MATERIAL

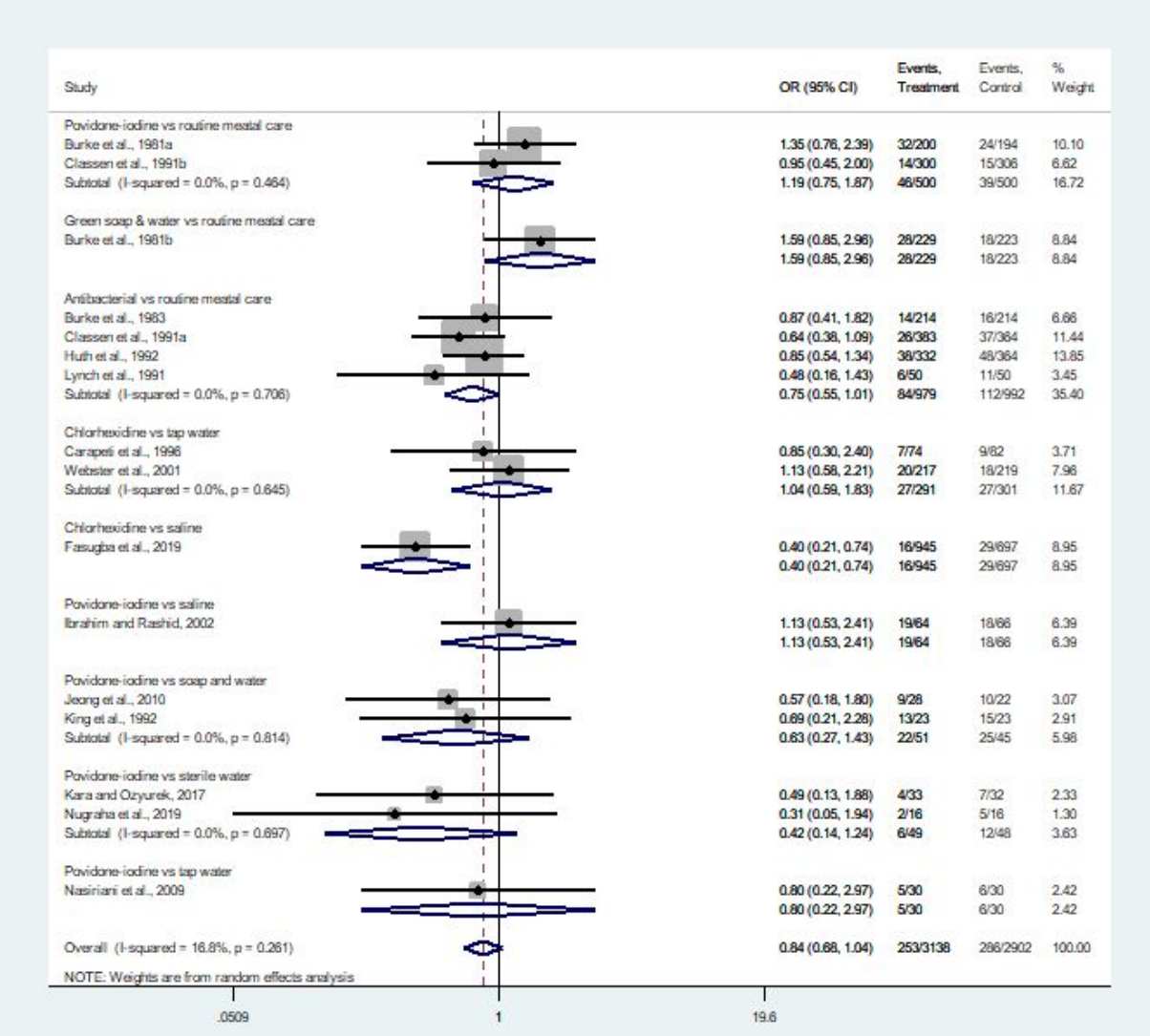

Figure S1. Forest plot displaying random-effect meta-analysis of the effect of meatal cleaning on the incidence of bacteriuria only (results stratified by meatal cleaning agent)

Table S1. Comparison of the effect of meatal cleaning on the incidence of bacteriuria only

Comparisons	**P values**
Povidone-iodine vs routine meatal care	0.462
Green soap and water vs routine meatal care	0.147
Antibacterial vs routine meatal care	0.055
Chlorhexidine vs tap water	0.886
Chlorhexidine vs saline	0.012
Povidone-iodine vs saline	0.760
Povidone-iodine vs soap and water	0.268
Povidone-iodine vs sterile water	0.116
Povidone-iodine vs tap water	0.739
Overall	**0.105**

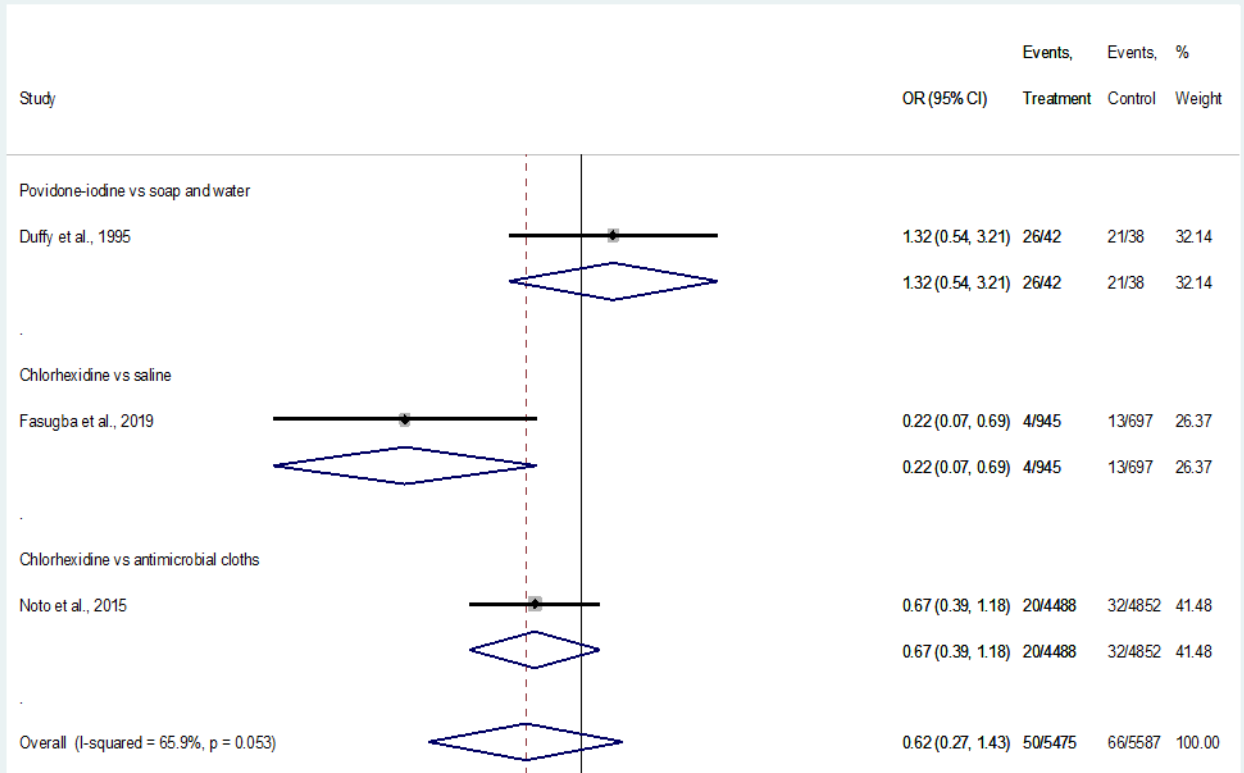

Figure S2. Forest plot displaying random-effect meta-analysis of the effect of meatal cleaning on the incidence of catheter-associated urinary tract infections only (results stratified by meatal cleaning agent)

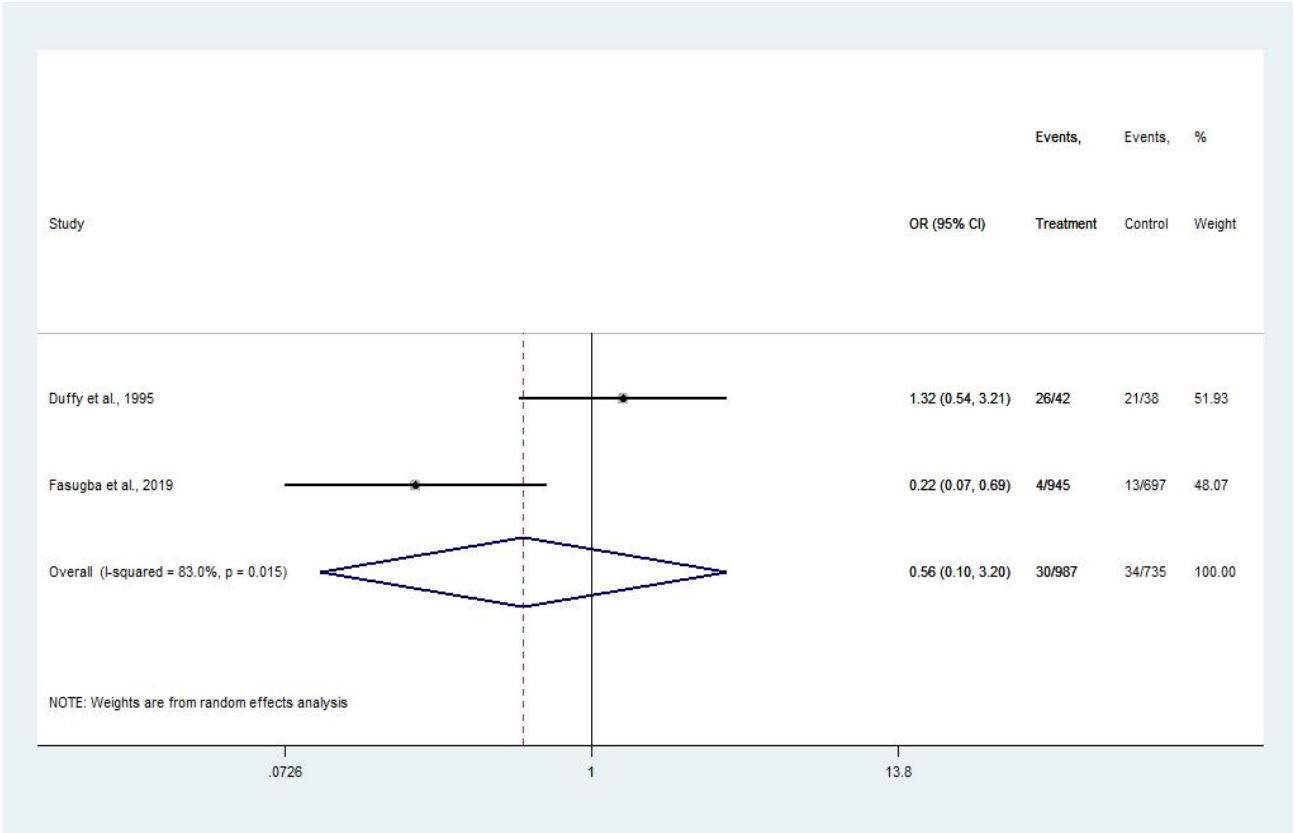

Figure S3. Random-effect meta-analysis of the effect of using an antiseptic meatal cleaning agent (povidone-iodine or chlorhexidine) vs a non-antiseptic agent (soap and water or saline) prior to catheter insertion on the incidence of catheter-associated urinary tract infections

Search strategy

#	Query	Limiters/Expanders	Last Run Via
S5	S1 AND S2 AND S3 AND S4	Expanders - Apply equivalent subjects Search modes - Find all my search terms	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - Academic Search Complete
S4	antiseptic* OR antimicrobial OR antibacterial OR anti-infective OR disinfect OR microbicide OR antibiotic OR polyantibiotic OR sterile OR "bacitracin zinc" OR betadine OR centrimide	Limiters - Published Date: 20160101-20200231 Expanders - Apply equivalent subjects Search modes - Find all my search terms	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - Academic Search Complete
S3	bath* OR hygiene OR cleans* OR cleaned OR cleaning OR topical OR apply OR applied OR application	Limiters - Published Date: 20160101-20200231 Expanders - Apply equivalent subjects Search modes - Find all my search terms	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - Academic Search Complete
S2	meatal OR meatus OR perineal OR perineum OR periurethral	Limiters - Published Date: 20160101-20200231 Expanders - Apply equivalent subjects Search modes - Find all my search terms	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - Academic Search Complete
S1	TX urinary catheter* OR TX urethral catheter* OR TX indwelling catheter* OR TX intermittent catheter	Limiters - Published Date: 20160101-20200231 Expanders - Apply equivalent subjects Search modes - Find all my search terms	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - Academic Search Complete

#	Query	Limiters/Expanders	Last Run Via
S3	S1 AND S2	Expanders - Apply equivalent subjects Search modes - Find all my search terms	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - Academic Search Complete
S2	bundle intervention OR bundle care	Limiters - Published Date: 20160101-20200231 Expanders - Apply equivalent subjects Search modes - Find all my search terms	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - Academic Search Complete
S1	TX urinary tract infection OR TX meatal OR TX meatal disinfection OR TX meatal cleaning	Limiters - Published Date: 20160101-20200231 Expanders - Apply equivalent subjects Search modes - Find all my search terms	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - Academic Search Complete

#	Query	Limiters/Expanders	Last Run Via
S6	S1 AND S2 AND S3 AND S4	Limiters - Human Expanders - Apply equivalent subjects Search modes - Find all my search terms	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Complete
S5	S1 AND S2 AND S3 AND S4	Expanders - Apply equivalent subjects Search modes - Find all my search terms	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Complete
S4	TX antiseptic* OR TX antimicrobial OR TX antibacterial OR TX	Limiters - Published Date: 20160101-20200231 Expanders - Apply equivalent subjects Search modes - Find all my search terms	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Complete

	anti-infective OR TX disinfect* OR TX microbicide OR TX antibiotic OR TX polyantibiotic OR TX sterile OR TX chlorhexidine OR TX povidone-iodine		
S3	TX bath* OR TX hygiene OR TX cleans* OR TX cleaned OR TX cleaning OR TX topical OR TX applied OR TX apply OR TX application	Limiters - Published Date: 20160101-20200231 Expanders - Apply equivalent subjects Search modes - Find all my search terms	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Complete
S2	TX meatal OR TX meatus OR TX perineal OR TX perineum OR TX periurethral	Limiters - Published Date: 20160101-20200231 Expanders - Apply equivalent subjects Search modes - Find all my search terms	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Complete
S1	TX urinary catheter* OR TX urethral catheter* OR TX indwelling catheter* OR TX intermittent catheter*	Limiters - Published Date: 20160101-20200231 Expanders - Apply equivalent subjects Search modes - Find all my search terms	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Complete

#	Query	Limiters/Expanders	Last Run Via

S3	S1 AND S2	Expanders - Apply equivalent subjects Search modes - Find all my search terms	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - MEDLINE Complete
S2	bundle OR bundle care OR bundle intervention	Limiters - Date of Publication: 20160101-20200231 Expanders - Apply equivalent subjects Search modes - Find all my search terms	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - MEDLINE Complete
S1	urinary catheter* OR urethral catheter* OR indwelling catheter* OR intermittent catheter* OR "urinary tract infection"	Limiters - Date of Publication: 20160101-20200231 Expanders - Apply equivalent subjects Search modes - Find all my search terms	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - MEDLINE Complete

#	Query	Limiters/Expanders	Last Run Via
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S4	antiseptic* OR antimicrobial OR antibacterial OR anti-infective OR disinfect* OR microbicide OR antibiotic OR polyantibiotic OR sterile OR chlorhexidine OR povidone-iodine	Limiters - Date of Publication: 20160101-20200231 Expanders - Apply equivalent subjects Search modes - Find all my search terms	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - MEDLINE Complete
S3	bath* OR hygiene OR cleans* OR cleaned OR cleaning OR topical OR applied OR apply OR application	Limiters - Date of Publication: 20160101-20200231 Expanders - Apply equivalent subjects Search modes - Find all my search terms	Interface - EBSCOhost Research Databases

			Search Screen - Advanced Search Database - MEDLINE Complete
S2	meatal OR meatus OR perineal OR perineum OR periurethral	Limiters - Date of Publication: 20160101-20200231 Expanders - Apply equivalent subjects Search modes - Find all my search terms	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - MEDLINE Complete
S1	urinary catheter* OR urethral catheter* OR indwelling catheter* OR intermittent catheter	Limiters - Date of Publication: 20160101-20200231 Expanders - Apply equivalent subjects Search modes - Find all my search terms	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - MEDLINE Complete

	EMBASE
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5	urinary tract infection.mp. or urinary tract infection/
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9	1 or 2 or 3 or 4 or 5
10	6 or 7 or 8
11	9 and 10
12	limit 11 to yr="2016 -Current"

	Cochrane Library
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#2	(meatal) OR (meatus) OR (perineal) OR (perineum) OR (periurethral)
#3	(bath) OR (hygiene) OR (clean*) OR (topical) OR (appl*)
#4	(antiseptic*) OR (antimicrobial) OR (antibacterial) OR (“anti-infective”) OR (disinfect*)
#5	(antibiotic) OR (polyantibiotic) OR (sterile)
#6	#1 AND #2 AND #3 AND #4 AND #5

	Cochrane Library

#1	(urethral catheter*) OR (intermittent catheter*) OR (indwelling catheter*) OR (urinary catheter*) OR ("urinary tract infection")
#2	(bundle) OR ("bundle care") OR ("bundle intervention")
#3	#1 AND #2

#	Query	Limiters/Expanders	Last Run Via
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S4	TX antiseptic* OR TX antimicrobial OR TX antibacterial OR TX anti-infective OR TX disinfect* OR TX microbicide OR TX antibiotic OR TX polyantibiotic OR TX sterile OR TX chlorhexidine OR TX povidone-iodine	Limiters - Published Date: 20160101-20200231 Expanders - Apply equivalent subjects Search modes - Find all my search terms	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Complete
S3	TX bath* OR TX hygiene OR TX cleans* OR TX cleaned OR TX cleaning OR TX topical OR TX applied OR TX apply OR TX application	Limiters - Published Date: 20160101-20200231 Expanders - Apply equivalent subjects Search modes - Find all my search terms	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Complete
S2	TX meatal OR TX meatus OR TX perineal OR TX perineum OR TX periurethral	Limiters - Published Date: 20160101-20200231 Expanders - Apply equivalent subjects Search modes - Find all my search terms	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Complete

S1	TX urinary catheter* OR TX urethral catheter* OR TX indwelling catheter* OR TX intermittent catheter*	Limiters - Published Date: 20160101-20200231 Expanders - Apply equivalent subjects Search modes - Find all my search terms	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Complete

#	Query	Limiters/Expanders	Last Run Via
S3	S1 AND S2	Expanders - Apply equivalent subjects Search modes - Find all my search terms	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Complete
S2	TX bundle care OR TX bundle OR TX bundle intervention	Limiters - Published Date: 20160101-20200231 Expanders - Apply equivalent subjects Search modes - Find all my search terms	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Complete
S1	TX urinary catheter* OR TX urethral catheter* OR TX indwelling catheter* OR TX intermittent catheter* OR TX urinary tract infection	Limiters - Published Date: 20160101-20200231 Expanders - Apply equivalent subjects Search modes - Find all my search terms	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Complete

PubMed	
Search	Query

#3	Search (((((((urinary catheter*) OR urethral catheter*) OR indwelling catheter*) OR intermittent catheter*) OR urinary tract infection) AND ("2016/01/01"[PDat] : "2020/02/29"[PDat]))) AND ((((("bundle care") OR "bundle intervention") OR bundle) AND ("2016/01/01"[PDat] : "2020/02/29"[PDat])) Filters: Publication date from 2016/01/01 to 2020/02/29
#2	Search (("bundle care") OR "bundle intervention") OR bundle Filters: Publication date from 2016/01/01 to 2020/02/29
#1	Search ((((urinary catheter*) OR urethral catheter*) OR indwelling catheter*) OR intermittent catheter*) OR urinary tract infection Filters: Publication date from 2016/01/01 to 2020/02/29

PubMed	
Search	Query
#8-searches 4 and 7	Search ((((((((((urinary catheter*) OR urethral catheter*) OR indwelling catheter*) OR intermittent catheter*) AND ("2016/01/01"[PDat] : "2020/02/29"[PDat]))) AND ((((((meatal) OR meatus) OR perineal) OR perineum) OR periurethral) AND ("2016/01/01"[PDat] : "2020/02/29"[PDat]))) AND ((((((((((bath*) OR hygiene) OR cleans*) OR cleaned) OR cleaning) OR topical*) OR apply) OR applied) OR application) AND ("2016/01/01"[PDat] : "2020/02/29"[PDat]))) AND ("2016/01/01"[PDat] : "2020/02/29"[PDat]))) AND ((((((((((((antiseptic) OR antimicrobial) OR antibacterial) OR "anti-infective") OR disinfect*) OR microbicide) OR polyantibiotic) OR sterile) AND ("2016/01/01"[PDat] : "2020/02/29"[PDat]))) AND ((((((((((("bacitracin zinc") OR "polymyxin b") OR "povidone-iodine") OR betadine) OR cetrimide) OR chlorhexidine) OR savlon) OR sulfadiazine) OR sulphadiazine) OR neomycin) OR gramicidin) AND ("2016/01/01"[PDat] : "2020/02/29"[PDat]))) AND ("2016/01/01"[PDat] : "2020/02/29"[PDat])) Filters: Publication date from 2016/01/01 to 2020/02/29
#7-searches 5 and 6	Search ((((((((((antiseptic) OR antimicrobial) OR antibacterial) OR "anti-infective") OR disinfect*) OR microbicide) OR polyantibiotic) OR sterile) AND ("2016/01/01"[PDat] : "2020/02/29"[PDat]))) AND ((((((((((("bacitracin zinc") OR "polymyxin b") OR "povidone-iodine") OR betadine) OR cetrimide) OR chlorhexidine) OR savlon) OR sulfadiazine) OR sulphadiazine) OR neomycin) OR gramicidin) AND ("2016/01/01"[PDat] : "2020/02/29"[PDat])) Filters: Publication date from 2016/01/01 to 2020/02/29
#6	Search ((((((((("bacitracin zinc") OR "polymyxin b") OR "povidone-iodine") OR betadine) OR cetrimide) OR chlorhexidine) OR savlon) OR sulfadiazine) OR sulphadiazine) OR neomycin) OR gramicidin Filters: Publication date from 2016/01/01 to 2020/02/29

#5	Search (((((((antiseptic) OR antimicrobial) OR antibacterial) OR "anti-infective") OR disinfect*) OR microbicide) OR polyantibiotic) OR sterile Filters: Publication date from 2016/01/01 to 2020/02/29
#4-searches 1, 2 and 3	Search (((((((urinary catheter*) OR urethral catheter*) OR indwelling catheter*) OR intermittent catheter*) AND ("2016/01/01"[PDat] : "2020/02/29"[PDat]))) AND ((((((meatal) OR meatus) OR perineal) OR perineum) OR periurethral) AND ("2016/01/01"[PDat] : "2020/02/29"[PDat]))) AND ((((((((((bath*) OR hygiene) OR cleans*) OR cleaned) OR cleaning) OR topical*) OR apply) OR applied) OR application) AND ("2016/01/01"[PDat] : "2020/02/29"[PDat])) Filters: Publication date from 2016/01/01 to 2020/02/29
#3	Search (((((((bath*) OR hygiene) OR cleans*) OR cleaned) OR cleaning) OR topical*) OR apply) OR applied) OR application Filters: Publication date from 2016/01/01 to 2020/02/29
#2	Search ((((meatal) OR meatus) OR perineal) OR perineum) OR periurethral Filters: Publication date from 2016/01/01 to 2020/02/29
#1	Search (((urinary catheter*) OR urethral catheter*) OR indwelling catheter*) OR intermittent catheter* Filters: Publication date from 2016/01/01 to 2020/02/29

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PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	3
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	4
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	N/A
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	5-6
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	5
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	4
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	6
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	6
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	6
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	6
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	6
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	7

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	6
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	7
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	7
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	7
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	9
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	7-9 + Supplementary
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	7-9 + Supplementary
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	Figure 4
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	Supplementary
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	16
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	17
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	17
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	18

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

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BMJ Open

The effectiveness of meatal cleaning in the prevention of catheter-associated urinary tract infections and bacteriuria: An updated systematic review and meta-analysis

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Primary Subject Heading:	Nursing
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Keywords:	Infection control < INFECTIOUS DISEASES, Quality in health care < HEALTH SERVICES ADMINISTRATION & MANAGEMENT, PREVENTIVE MEDICINE, Urinary tract infections < UROLOGY

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TITLE

The effectiveness of meatal cleaning in the prevention of catheter-associated urinary tract infections and bacteriuria: An updated systematic review and meta-analysis

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ABSTRACT

Objective: A systematic review on meatal cleaning prior to urinary catheterisation and post catheterisation and reduces the risk catheter-associated urinary tract infections (CAUTIs) and bacteriuria was published in 2017, with further studies undertaken since this time. The objective of this paper is to present an updated systematic review on the effectiveness of antiseptic cleaning of the meatal area for the prevention of CAUTIs and bacteriuria in patients who receive a urinary catheter.

Design: Systematic review

Data sources: Electronic databases Cochrane Library, PubMed, Embase, CINAHL, Medline and Academic Search Complete were searched from 1 January 2016 and 29 February 2020.

Eligibility criteria: Randomised controlled trials and quasi-experimental studies evaluating the use of antiseptic, antibacterial or non-medicated agents for cleaning the meatal, periurethral or perineal areas before indwelling catheter insertion or intermittent catheterisation or during routine meatal care.

Data extraction and synthesis: Dara were extracted using the Cochrane Collaboration's data collection form for RCTs and non-RCTs. Data were extracted by one researcher and then checked for accuracy by a second researcher.

Results: A total of 18 studies were included. Some potential benefit of using antiseptics, compared to non-antiseptics for meatal cleaning to prevent bacteriuria and or CAUTI was identified (OR 0.84, 95% CI 0.69-1.02; P=0.071). Antiseptics (chlorhexidine or povidine-iodine) may be of value for meatal cleaning on the incidence of CAUTI, compared to comparator agents (saline, soap or antimicrobial cloths) (OR=0.65, 95% CI 0.42-0.99; P=0.047).

Conclusion: There is emerging evidence of the role of some specific antiseptics (chlorhexidine) prior to urinary catheterisation, in reducing CAUTIs, and some potential benefit to the role of antiseptics more generally in reducing bacteriuria.

PROSPERO registration number: CRD42015023741

Strengths and limitations of this study

- A summary of the latest evidence on the role of antiseptics in reducing catheter associated urinary tract infections
- Sub-group analysis to explore effects using different antiseptics

- Heterogeneity of population groups is a limitation

INTRODUCTION

Indwelling or intermittent urinary catheter use can result in bacteriuria which may signify either colonisation (catheter-associated asymptomatic bacteriuria) or symptomatic infection (catheter-associated urinary tract infections).[1] Catheter-associated urinary tract infections (CAUTIs) are a common but preventable nosocomial infection. They account for around 70-80% of hospital-acquired UTIs, are associated with longer length of hospital stay and increased risk of morbidity and mortality.[2-5] In the UK, economic analyses of hospital inpatient costs estimated that CAUTIs caused over 45,000 excess bed days, 1,467 deaths, and a loss of 10,471 quality-adjusted life years (QALYs).[6] The burden of CAUTIs for both patients and health services highlight the importance of reducing these infections in healthcare settings.

Various strategies for reducing the risk of CAUTIs have been proposed. These include reducing unnecessary catheter use, practicing appropriate catheter insertion and maintenance, and prompt removal of urinary catheters.[7-9] A systematic review published in 2017 explored the effect of using different meatal (peri-urethral) cleaning agents prior to urinary catheter insertion on the incidence of UTIs.[10] Meatal cleaning was identified by the review as one element of urinary catheter care which may reduce CAUTI risk.[10] However, the review also identified uncertainty in the available evidence for the effectiveness of this practice. Since this publication there have been further studies published on this topic,[11 12] and the evidence base is still evolving. Moreover, some previous studies were limited by bias (e.g. selection bias, non-masking of intervention).[11 13] Given the potential importance of meatal cleaning for preventing UTIs and informing clinical practice and guidelines, we believed it was important to update the evidence base.[10] In this paper, we present findings from an updated systematic review and meta-analysis. The aim of this review is to determine the effectiveness of antiseptic cleaning of the meatal area, for preventing CAUTI and bacteriuria.

METHODS

A protocol was developed to guide the conduct of the systematic review and meta-analysis, and we have used a reporting approach consistent with the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) statement.[14] The methodological approach

used in this systematic review is the same as that used in the initial publication,[10] PROSPERO International Prospective Register of Systematic reviews (Registration No: CRD42015023741). Studies included in the final synthesis from the initial publication were combined with studies identified as part of the updated search strategy.

Data sources and search strategy

The electronic databases Cochrane Library, PubMed, Embase, CINAHL, Medline and Academic Search Complete were used to undertake the search. Search parameters were adjusted to suit database requirements. A search of the databases was limited to the period between 1 January 2016 and 29 February 2020. The 1st January 2016 represents the end date of the search from the initial review.[10] Keywords and MeSH terms used were: urinary catheter and/or urinary catheterisation, urinary tract infection, meatal cleaning, periurethral cleaning, antiseptic, antimicrobial, antibacterial, antibiotic, and topical intervention. Further details on the search strategy are provided as supplementary material.

Study inclusion and exclusion criteria

Included studies were randomised controlled trials (RCTs) and quasi-experimental studies (pre-and post-test design, non RCTs) evaluating the use of antiseptic, antibacterial or non-medicated agents (such as soap and water) for cleaning the meatal, periurethral or perineal areas before indwelling catheter insertion or intermittent catheterisation or during routine meatal care. Studies were included if they involved patients requiring short- or long-term indwelling catheters or intermittent catheterisation in hospitals, community settings, and long-term/aged care facilities. Studies were excluded if they were not published in English language, focused solely on children (≤18 years), included patients with pre-existing UTIs, or were published in grey literature (conference abstracts, editorial letters, reports and guidelines). Review articles, bundle interventions, studies without available data for analysis, studies that did not evaluate the control or intervention agents, and studies for which the full-text was not available were also excluded.

The co-primary outcome measures were the difference in rates of CAUTI and bacteriuria in the intervention and control groups. While we accepted the definition of CAUTI and

bacteriuria provided in the included studies, we also considered infection to be the outcome when clinical signs or symptoms of infection were present.[15]

Study selection

Database results were imported into Covidence for screening and selection.[16] Screening of abstracts of articles retrieved from electronic databases for relevance to the systematic review aim was undertaken by one researcher (CC). Ten percent of the abstracts were cross checked by a second researcher (BM). No discrepancies were found. Full-text screening was then undertaken and assessed against the inclusion and exclusion criteria by CC. A cross check of all studies deemed to meet the inclusion criteria was also undertaken by BM. A manual search of the references lists of all included articles was undertaken to identify additional studies. Where decisions were open to disagreement, this was resolved by discussion with other members of the research team (EGH and OF).

Data extraction

The data from included studies were extracted using the Cochrane Collaboration's data collection form for RCTs and non-RCTs. Data were extracted by one researcher (CC) and then checked for accuracy by a second researcher (BM). Extracted details included: age and sex distribution of the study population, study duration, sample size, study setting, type of intervention and duration, colony-forming unit (cfu/mL) count, bacteriuria and CAUTI rates (numerator/denominator data). For studies that reported the outcome at multiple time points, the outcome value closest to the end of the indwelling catheter in-situ period was extracted for analysis. Attempts were made to contact the authors of included studies where information was missing regarding the numerator or denominator data for calculating CAUTI rates, and when clarity was needed on the type of intervention used. One author was contacted regarding inaccuracies in reporting results and the author responded by sending the corrected version of the study manuscript.

Risk of bias assessment

Using Covidence and following the Cochrane Collaboration's Handbook for Systematic Reviews of Interventions (v6., 2019), the risk of bias for studies were evaluated.[17] Risk of bias was assessed as high, unclear or low. Risk of bias assessment was conducted

independently by two researchers (OF and CC) and disagreements resolved by discussion with a third researcher (BM).

Data analysis

Data analyses were undertaken using Stata Version 14 (StataCorp, College Station, TX, USA). Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated from the proportions of patients with CAUTI and bacteriuria in the intervention and control groups. The pooled ORs were calculated and compared across intervention and control groups using the DerSimonian and Laird random effects meta-analysis model which considers possible heterogeneity between the studies during analysis.[18] The likelihood of clinical heterogeneity in the included studies with regards to varying meatal cleaning agents used was considered in the a-priori data synthesis strategy. Hence, the meta-analysis was stratified by the outcome and type of meatal cleaning agent used. The I^2 statistic was used to quantify between-study heterogeneity of intervention effects. Subgroup analyses were undertaken to explore effects of aspects of study methodology (antiseptic vs non-antiseptic cleaning and administration of the intervention prior to urinary catheter insertion) on the outcome using a fixed effect model due to the low number of studies.[19 20] Assessment of reporting biases was by visual examination of the funnel plot. A 0.05 level of significance was used without adjustment for multiplicity (number of comparisons of meatal cleaning agents). Effect sizes and their precision, in addition to significance were considered when interpreting the results.

Patient and Public Involvement

No patient involved.

RESULTS

In total, 927 articles were retrieved from electronic database searches and their abstracts were screened for relevance to the systematic review aim. After evaluating these articles against the inclusion and exclusion criteria, four studies were identified for inclusion. These

four studies were added to the 14 studies included in the previous review,[10] hence a total 18 studies were included in this systematic review and meta-analysis (Figure 1).

The characteristics of the included studies are presented in Table 1. The majority of studies were RCTs (n=15). There was considerable diversity in the types of interventions (meatal cleaning agent) used and whether the intervention was applied to the meatal area during ongoing meatal care, prior to catheter insertion only or a combination of both. Of the 18 studies, two compared povidone-iodine with routine (or standard) meatal care, which involved removal of debris from the catheter during bathing;[21 22] one compared green soap with routine meatal care;[21] four compared an antibacterial agent (Neomycin-polymyxcin B, 1% silver sulfadiazine Silvadene, 2% polynoxylin) with routine meatal care;[23-26] two compared chlorhexidine (0.1% and 0.3% plus and 3% centrimide) with tap water;[27 28] three compared povidone-iodine with soap and water;[13 29 30] one compared chlorhexidine (0.1%) with saline;[11] one compared povidone-iodine with saline;[31] two compared povidone-iodine with sterile water;[12 32] one compared povidone-iodine with tap water;[33] and one compared antimicrobial cloth with chlorhexidine (2%) compared to a non-antimicrobial cloth.[34]

The term 'infection' was often referred to as the primary outcome in studies. However, the definition of 'infection' varied and for most studies, this term was used when bacteria were present in the urine with or without clinical symptoms. We recoded outcomes to be either bacteriuria or infection – where the definition of infection must have included signs/symptoms of a UTI. Two studies reported CAUTI as the only outcome, 15 studies reported bacteriuria as the only outcome and one study reported both CAUTI and bacteriuria as outcomes.

Effect of meatal cleaning on the incidence of bacteriuria and CAUTI

A forest plot displaying the results of random-effect meta-analyses for the effect of meatal cleaning on the incidence of both bacteriuria and CAUTI combined, stratified by meatal cleaning agent is presented in Figure 2. For the study that reported both CAUTI and bacteriuria as outcomes,[11] only data for bacteriuria were included because bacteriuria was the outcome in majority of studies. There was no evidence of differences in the incidence of bacteriuria or CAUTI between the intervention and control groups when comparing the

different agents: povidone-iodine vs routine care (OR 1.19, 95% CI 0.75-1.87; P=0.46); green soap and water vs routine care (OR 1.59, 95% CI 0.85-2.96; P=0.15), chlorhexidine vs tap water (OR 1.04, 95% CI 0.59-1.83; P=0.89); povidone-iodine vs soap and water (OR 0.88, 95% CI 0.48-1.62; P=0.69); povidone-iodine vs saline (OR 1.13, 95% CI 0.53-2.41; P=0.76); povidone-iodine vs sterile water (OR 0.42, 95% CI 0.14-1.24; P=0.12); povidone-iodine vs tap water (OR 0.80, 95% CI 0.22-2.97; P=0.74) and chlorhexidine vs antimicrobial cloths (OR 0.67, 95% CI 0.39-1.18; P=0.17).

There was potential evidence of a small difference in the incidence of bacteriuria or CAUTI between the intervention and control groups overall (pooled OR 0.84, 95% CI 0.69-1.02; P=0.071), with the CI nearly excluding 1. This also applies to the comparison of antibacterial agent vs routine care (OR 0.75, 95% CI 0.55-1.01; P=0.055). The comparison of chlorhexidine vs saline demonstrated statistical evidence of differences between the intervention and control group (OR 0.40, 95% CI 0.21-0.74; P=0.003). Overall results showed evidence of heterogeneity (I^2=13.2%; P=0.296) among the included studies.

Separate forest plots showing the effect of meatal cleaning on the incidence of bacteriuria and CAUTI are presented as supplementary material (Figure S1 and Table S1, and Figure S2, respectively). Sixteen studies were included in the meta-analysis evaluating the effect of meatal cleaning on the incidence of bacteriuria only while three studies were included in the meta-analysis evaluating the effect of meatal cleaning on the incidence of CAUTI only. [11 29 34] Analyses showed no statistically significant difference in the incidence of bacteriuria (pooled OR 0.84, 95% CI 0.70-1.01; P=0.06), noting this was close to being statistically significant. In addition, 12 of the 16 studies in this meta-analysis had findings in the same direction, a benefit to antiseptics (Figure S1). In contrast, there was a statistically significant difference in the effect of meatal cleaning using an antiseptic (chlorhexidine or povidine-iodine) versus a comparator agents (saline, soap or antimicrobial cloths)on the incidence of CAUTI (pooled OR 0.65, 95% CI 0.42-0.99; P=0.047), Figure S2.

Effect of antiseptic vs non-antiseptic meatal cleaning prior to urinary catheterisation on the incidence of bacteriuria

Six studies explored the effect of using an antiseptic meatal cleaning agent prior to catheter insertion, compared to a non-antiseptic agent, on the incidence of bacteriuria (Figure 3). [11 12 27 28 30 33] There was evidence of a potential difference in the incidence of bacteriuria when comparing the use of antiseptic and non-antiseptic agents (pooled OR=0.67, 95% CI 0.44-1.03; P=0.065) (Figure 3).

Effect of antiseptic vs non-antiseptic meatal cleaning prior to urinary catheterisation on the incidence of CAUTI

Two studies explored the effect of using an antiseptic meatal cleaning agent prior to catheter insertion, compared to a non-antiseptic agent, on the incidence of CAUTI.[11 29] One used 10% povidone-iodine and found no difference,[29] while the other study used chlorhexidine (0.1%) and identified a significant reduction in CAUTI [11] (Figure S3).

Risk of bias

Results showed that the level of risk of bias varied between the included studies (Figure 4). The majority of studies (n=15) were assessed to have a high or unclear risk of bias for reporting of blinding processes used in the studies. The vast majority of studies were biased in the categories of allocation and performance. The studies conducted by Noto et al,[34] and Fasugba et al,[11] were deemed to be at lowest risk of bias.

Publication bias

Visual inspection of the funnel plot showed no evidence of publication bias (Figure 5).

Table 1. Characteristics of studies included in the systematic review and meta-analysis

Study author, year and design	Country	Population	Administration	Frequency of application	Outcome	Outcome definition	Intervention				Control		
							Mean age (SD)	Intervention agent	Alcohol-containing agent	Cases	Mean age (SD)	Comparator agent	Cases
Burke et al., 1981a; RCT [21]	USA	Medical and surgical patients	Daily meatal care while IDC in situ	Twice daily	Bacteriuria	≥10^3 cfu/mL	NR	10% povidone-iodine Betadine solution and ointment	Yes, pareth-25-9 as inactive ingredient	32/202	NR	Usual care; removal of debris from catheter during bathing	24/194
Burke et al., 1981a; RCT [21]	USA	Medical and surgical patients	Daily meatal care while IDC in situ	Once daily	Bacteriuria	≥10^3 cfu/mL	NR	Green soap and water	Assumed yes, 30% ethyl alcohol as solution	28/223	NR	Usual care; removal of debris from catheter during bathing	18/223
Burke et al., 1983, RCT [23]	USA	Medical and surgical patients	Daily meatal care while IDC in situ, until UTI found	Twice daily	Bacteriuria	≥10^3 cfu/mL	NR	Neomycin-polymyxcin B-bacitracin ointment	No	14/211	NR	Usual care; removal of debris from catheter during bathing	16/214
Carapeti et al., 1996; RCT [27]	UK	General surgery patients	On IDC insertion for surgery	Once for surgery	Bacteriuria (+- symptoms)	>10^5 cfu/mL	67.5	0.3% CHG and 3% centrimide Savlon solution	Yes, 2.84% isopropyl alcohol, 0.056% benzyl benzoate and	7/74	65.3	Tap water	9/82

Study author, year and design	Country	Population	Administration	Frequency of application	Outcome	Outcome definition	Intervention				Control		
							Mean age (SD)	Intervention agent	Alcohol-containing agent	Cases	Mean age (SD)	Comparator agent	Cases
									terpineol as excipient ingredients				
Classen et al., 1991a; RCT [24]	USA	Medical and surgical patients	Daily meatal care while IDC in situ, until UTI found	Thrice daily	Bacteriuria	≥10^3 cfu/mL	NR	Polymyxin B sulfate, neomycin sulfate, gramicidin Neosporin cream	Yes, propylene glycol as non-medicinal ingredient	26/336	NR	Routine meatal care; removal of debris from catheter during bathing	37/364
Classen et al., 1991b; RCT [22]	USA	Medical and surgical patients	Daily meatal care while IDC in situ, until UTI found	Once daily	Bacteriuria	≥10^3 cfu/mL	NR	2% Lugol's Iodine povidone-iodine solution	Unclear, assumed no	14/306	NR	Routine meatal care; removal of debris from catheter during bathing	15/306
Duffy et al., 1995; RCT [29]	USA	Male veterans in long-term care	Pre-IC and IDC	Pre-IC, ~thrice daily	Infection	≥10^5 cfu/mL + symptoms	72.6 (10.8)	10% povidone-iodine Betadine solution	Yes, pareth-25-9 as inactive ingredient	26/42	70.9 (12.1)	Soap and water	21/38
Fasugba et al., 2019; RCT [11]	Australia	Medical and surgical patients, ICU	On IDC insertion	Once, before insertion	Infection & Bacteriuria	CAUTI: CDC/ NHSN	NR	0.1% CHG solution	No	UTI: 4/943	NR	0.9% saline	UTI 13/697

Study author, year and design	Country	Population	Administration	Frequency of application	Outcome	Outcome definition	Intervention				Control			
							Mean age (SD)	Intervention agent	Alcohol-containing agent	Cases	Mean age (SD)	Comparator agent	Cases	
						Bacteriuria: ≥10^5 cfu/mL				Bacteriuria 16/94			Bacteriuria 29/697	
Huth et al., 1992; quasi-RCT [25]	USA	Medical and surgical patients	Daily meatal care while IDC in situ	Twice daily	Bacteriuria	≥10^3 cfu/mL	61	1% silver sulfadiazine Silvadene cream	Yes, stearyl alcohol, isopropyl myristate and propylene glycol as vehicle ingredients	38/332	63	Usual care; removal of debris from catheter during bathing	48/364	
Ibrahim & Rashid, 2002; RCT [31]	Saudi Arabia	Male transurethral surgery patients	On IDC insertion, and in daily application while IDC in situ	Once daily	Bacteriuria	10^5 cfu/mL	66.7 (10.1)	Povidone-iodine solution	Unclear, assumed no	19/64	66 (10.4)	Saline	18/66	
Jeong et al., 2010; quasi-RCT [13]	South Korea	Female ICU patients	On IDC insertion, and in daily meatal care while IDC in situ	Once daily	Bacteriuria+	CDC/NHSN	61.5 (17.3)	10% povidone-iodine solution	Unclear, assumed no	9/28	64.1 (13.3)	Soap and water	10/22	

Study author, year and design	Country	Population	Administration	Frequency of application	Outcome	Outcome definition	Intervention				Control		
							Mean age (SD)	Intervention agent	Alcohol-containing agent	Cases	Mean age (SD)	Comparator agent	Cases
Kara & Ozyurek, 2017; RCT [32]	Turkey	ICU, surgical and medical patients	On IDC insertion, and in daily meatal care while IDC in situ	Once daily	Bacteriuria	$\geq 10^5$ cfu/mL	66.34 (14)	Sterile water	No	7/32	67.96 (12)	Sterile water	7/32
							63.5 (12)	10% povidone-iodine	No	4/33			
King et al., 1992; RCT [30]	USA	SCI rehabilitation inpatients	Pre-IC	Pre-IC, once per 4-6 hours	Bacteriuria	$\geq 10^4$ cfu/mL with symptoms	32.8 (13.7)	Povidone-iodine solution	Unclear, assumed no	13/23	27.9 (10.3)	Castile soap wipe	15/23
Lynch et al., 1991; quasi-RCT [26]	UK	Male transurethral surgery patients	On IDC insertion, and in daily meatal care while IDC in situ	Once daily	Bacteriuria	$>10^5$ cfu/mL	67 (9.7)	2% polynoxylin Anaflex spray	Yes, formaldehyde as active ingredient	6/50	68 (8.4)	No intervention	11/50
Nasiriani et al., 2009; RCT [33]	Iran	Female gynaecological surgery patients	On IDC insertion for surgery	Once for surgery	Bacteriuria	$>10^5$ cfu/mL	NR	Povidone-iodine solution	Unclear, assumed no	5/30	NR	Tap water	6/30
Noto et al., 2015; RCT [34]	USA	Surgical, medical and ICU patients	Daily bathing including meatal care	Once daily	Infection	CAUTI: CDC/NHSN	NR	2% CHG Cloths	No	20/4488	NR	Non-antimicrobial bath cloth	32/4852

Study author, year and design	Country	Population	Administration	Frequency of application	Outcome	Outcome definition	Intervention				Control		
							Mean age (SD)	Intervention agent	Alcohol-containing agent	Cases	Mean age (SD)	Comparator agent	Cases
Nugraha et al., 2019; RCT [12]	Java	Surgical and medical patients; (n=4, 12.5% aged 16-20 years)	On IDC insertion	Once, before insertion	Bacteriuria	Presence of bacteriuria; (cfu/mL level NR)	NR	10% povidone-iodine solution	Unclear, assumed no	2/16	NR	Sterile water	5/16
Webster et al., 2001; RCT [28]	Australia	Pregnant obstetrics patients	On IDC insertion for delivery	Once for delivery	Bacteriuria	$\geq 10^6$ cfu/mL	NR	0.1% CHG solution	No	20/21	NR	Tap water	18/219

Note: cfu: colony forming units; CHG: chlorhexidine gluconate; IC: intermittent catheterisation; ICU: intensive care unit; IDC: indwelling catheter; NR: not reported; RCT: randomised controlled trial; SCI: spinal cord injury; SD: standard deviation; UK: United Kingdom; USA: United States of America; UTI: urinary tract infection. Information on alcohol-containing agent ingredients assumed from research; no information on alcohol-containing agents available in included paper
* Positive UTI was assessed on following criteria: fever ≥38 degrees, suprapubic pain, dysuria, urethral erythema, purulent drainage around the catheter exit, presence of bacteria, pyuria (pus ≥3/ml in unspun urine), urine culture to stand on the presence of UTI (? $\geq 10^5$ cfu/mL, see CDC 2015), and white blood cell (WBC) count to prove presence of infection. # The results reported in the paper were incorrect. Authors were contacted for clarification, data in the table reflect clarification from authors. + Author state based "on the CDC definition of UTI, in particular, asymptomatic bacteriuria", with a reference supporting bacteriuria, therefore bacteriuria was assumed

DISCUSSION

Findings from this systematic review suggest that broadly speaking, using antiseptics for meatal cleaning may reduce the risk of bacteriuria or CAUTI in some instances, but uncertainty remains for antiseptics as a broad group. The uncertainly is in part driven by the diversity of antiseptics reviewed and variations in outcomes and populations. Although the odds ratios are not statistically significant at a level of 0.05,[35] the results are clinically meaningful for some specific subsets of antiseptics and or outcomes. For this reason, we discuss some important subsets below, including limitations. The evidence appears to be stronger and more consistent, for example prior to urinary catheterisation. There also appears to be emerging evidence that using chlorhexidine prior to urinary catheterisation may provide benefit in reducing CAUTI. Preventing CAUTI is important for a number of reasons. Prevention of CAUTI is vital, not only because of associated morbidity, mortality and increased length of stay in hospital, [2-5] but because of the added threats posed by increasing antimicrobial resistance.[36]

The effect of meatal cleaning in reducing the risk of bacteriuria

The meta-analysis exploring the effect of meatal cleaning in reducing the risk of bacteriuria, included studies that used antiseptics for routine meatal cleaning, for example post catheter insertion, as well as studies using antiseptics as part of the catheter insertion process (prior to urinary catheterisation) (Figure 2). The antiseptics used in studies included in this meta-analysis also varied (Table 1). When all studies were combined, the results indicated a potential benefit of using antiseptics, in reducing the risk bacteriuria or CAUTI (pooled OR 0.84, 95% CI 0.70-1.01). It is also worth noting that 13 of the 18 studies in Figure 2 had point estimates less than one i.e. direction favouring antiseptics. Although not statistically significant at an arbitrary level of 0.05, these results have clinical implications, noting it is difficult to interpret given the heterogeneity of antiseptics and timing of their use. In sub-analysis, some benefit of using an antibacterial agent vs routine (standard) care was identified (OR 0.75, 95% CI 0.55-1.01). Bacteriuria as a clinical outcome is arguably of little clinical relevance. However, studies to date have largely used this as the primary outcome. We discussion the results related to CAUTI later in this discussion. One argument in favour of bacteriuria as an outcome, is that reducing this may reduce antimicrobial use. Research

has indicated the frequency of inappropriate treatment for bacteriuria. In supplementary material, results using a random effect model are also presented (Figure S3, S4, S5 and S6).

The use of antiseptics prior to urinary catheterisation

In studies specifically exploring the use of antiseptics prior to urinary catheterisation, a meta-analysis indicated some value of antiseptics in preventing bacteriuria, compared to non-antiseptic agents (pooled OR=0.67, 95% CI 0.44-1.03; P=0.065). Five of the six studies included in the meta-analysis had findings in the same direction, a benefit to antiseptics (Figure 3). The meta-analysis was largely influenced by two studies, indicating differing results, but both using chlorhexidine 0.1%. One of these two studies, a multi-centre study involving three hospitals and included all patients in each hospital, indicated a statistically significant benefit when using antiseptics (chlorhexidine 0.1%).[11] The second study, a single centre study in an obstetric population, indicated no benefit, with a non-statistically significant result.[28] For consistency, in the meta-analysis, the outcomes presented were bacteriuria.

The use of antiseptics prior to urinary catheterisation and effect on CAUTI

Arguably the most important clinical outcome is CAUTI. We identified two studies evaluating the use of antiseptics prior to catheterisation, with CAUTI as the primary outcome.[11 29] These two studies used different antiseptics. Fasugba and colleagues found a significant reduction in CAUTI, associated with the use of chlorhexidine 0.1% (IRR 0.06, 95% CI 0.01-0.32, <p=0.001).[11] In a follow up cost-effectiveness evaluation, the authors found that using chlorhexidine 0.1% was cost saving.[37] Duffy et al, evaluated the use of povidone-iodine prior to catheterisation, in participants who had indwelling catheters or were undertaking intermittent catheterisation.[29] Duffy and colleagues did not identify a benefit from using povidone-iodine.[29] It is worth noting other important differences. The control phase included a clean catheterisation technique, i.e. not requiring a sterile field. The intervention phase, which used povidone-iodine, also included the use of a sterile procedure. The average follow-up period for participants was 63 days. As time from catheter insertion increases, the likelihood of an infection being related to insertion practices diminishes.

In contrast, participants in the study undertaken by Fasugba et al were followed up for 7 days only. Further, unlike the study by Duffy and colleagues, there were no other major changes that could potentially confound the outcome – such as a change in the procedure.[11] The risk of bias assessment also suggests less bias in the study undertake by Fasugba.

There were no report adverse events using low dose chlorhexidine prior to catheterisation.[11] Chlorhexidine prior to catheterisation is anticipated to have high acceptability noting it is already used in many clinical settings. Like most antiseptics, feasibility is unlikely to be an issue, given the relative ease of implementation, only requiring a simple product substitution. The cost-effectiveness (& cost saving) for the use of chlorhexidine 0.1% has been demonstrated and accounted for uncertainty, thus reducing equity issues. [37]

Limitations

A limitation of this review is that data extraction was undertaken by one person, noting that a second reviewer checked data extraction for accuracy. There was considerable heterogeneity in intervention and population groups, in particular those presented in Figure 2. We acknowledge that two of the authors of this systematic review led one of the included studies.[11] To ensure there was balance, we included three authors on this paper that had no involvement in this study.

Conclusion

This paper represents the latest evidence on the role of using antiseptics in people with urinary catheters, for the purpose of infection prevention. In turn, we hope this will inform local policy and practice, as well as infection control guidelines more generally. The results from this review suggest that antiseptics may be of value for meatal cleaning on the incidence of CAUTI, compared to non-antiseptic agents. In other areas of infection prevention and control, rather than a "broad brush" approach to determining the effect of antiseptics on a specific outcome, often individual agents are examined. For example in the case of prevention of surgical site infection, comparisons have been made for chlorhexidine

versus iodophor or alcoholic versus non-alcoholic based antiseptics.[38 39] The evidence to support the role of antiseptics as a broad group in reducing bacteriuria and CAUTI is challenged by variations in the diversity of antiseptics and the utility of bacteriuria as an outcome. Based on the evidence identified in this review and after careful consideration of the outcomes and methods used in included studies, we believe there is emerging but limited evidence of the role of chlorhexidine 0.1% prior to urinary catheterisation, in reducing CAUTI. However, we acknowledge this evidence is limited to one multi-centred study. Given the low number of included studies using CAUTI as the primary outcome, additional studies in this area are required, ensuring that important confounders are controlled for in the study design.

ETHICS APPROVAL

As this is a systematic review, ethics approval was not required.

CONFLICT OF INTEREST

Dr. Mitchell reports personal fees from MSD, grants from Cardinal Health, grants from Senver, outside the submitted work.

FUNDING

No funding was received for this study.

DATA AVAILABILITY STATEMENT

Please contact authors as required.

AUTHORSHIP STATEMENT

OF and BM designed the study. OF conducted the search. CC conducted the primary review of the articles and data extraction. CC, OF, and BM conducted the risk of bias assessment. OF, BM and EGH conducted the analysis. All authors (BM, OF, CC, EGH, CR) provided input into the interpretation of the data, writing the paper, provided critical review and approved the final version of the paper.

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Figure 1. PRISMA flow diagram of study selection

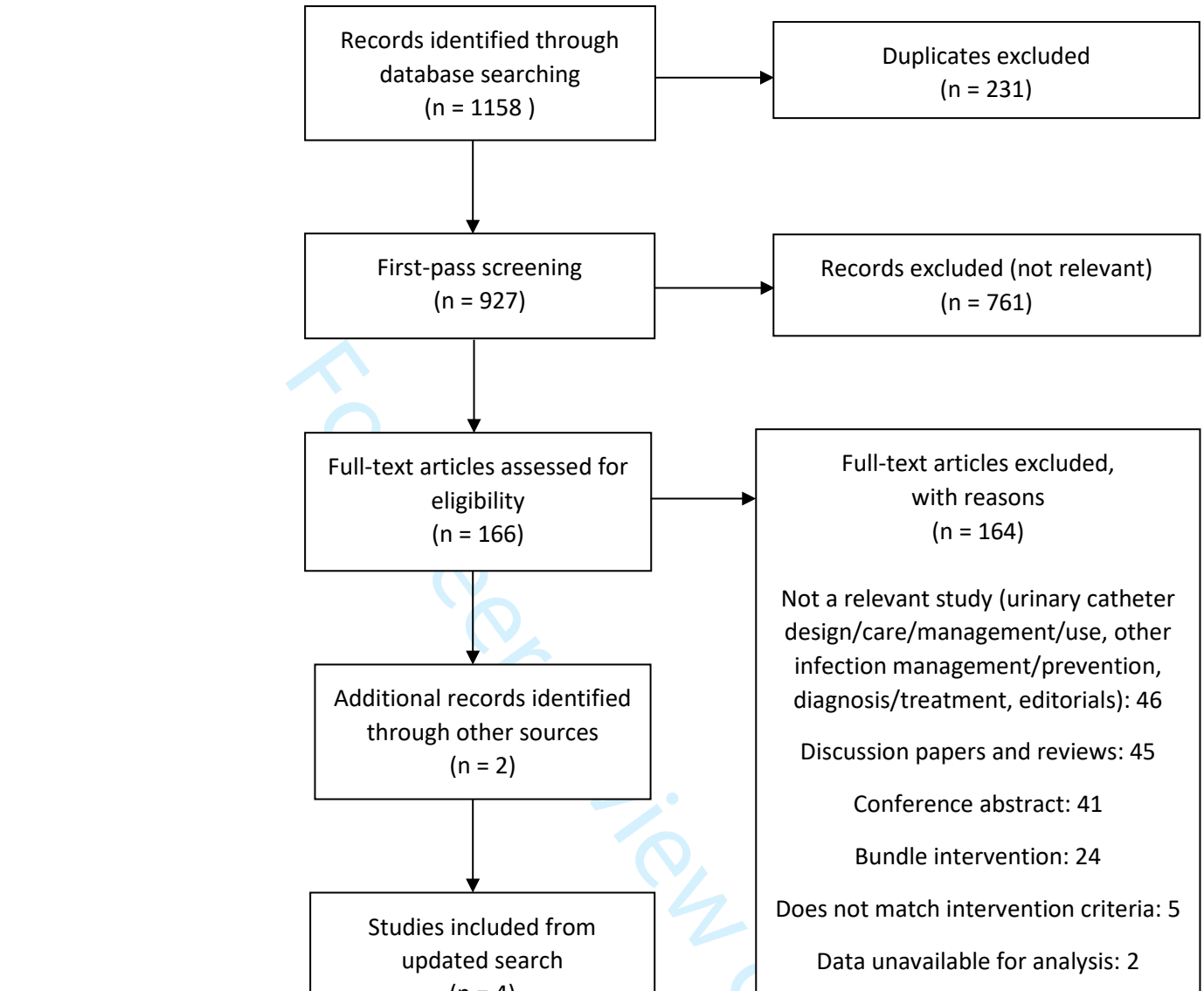
Figure 2. Forest plot displaying random-effect meta-analysis of the effect of meatal cleaning on the incidence of bacteriuria and or catheter-associated urinary tract infections (results stratified by meatal cleaning agent).

Note: Duffy et al., 1995 and Noto et al., 2015 all report CAUTI as the outcome, while Fasugba et al., 2019 report both CAUTI and bacteriuria. Bacteriuria data only from Fasugba et al, 2019 is included in this analysis.

Figure 3. Random-effect meta-analysis of the effect of using an antiseptic meatal cleaning agent (povidone-iodine, chlorhexidine) vs a non-antiseptic agent (soap and water, tap water, sterile water or saline) prior to catheter insertion on the incidence of bacteriuria

Figure 4. Risk of bias assessment

Figure 5. Funnel plot of the included studies



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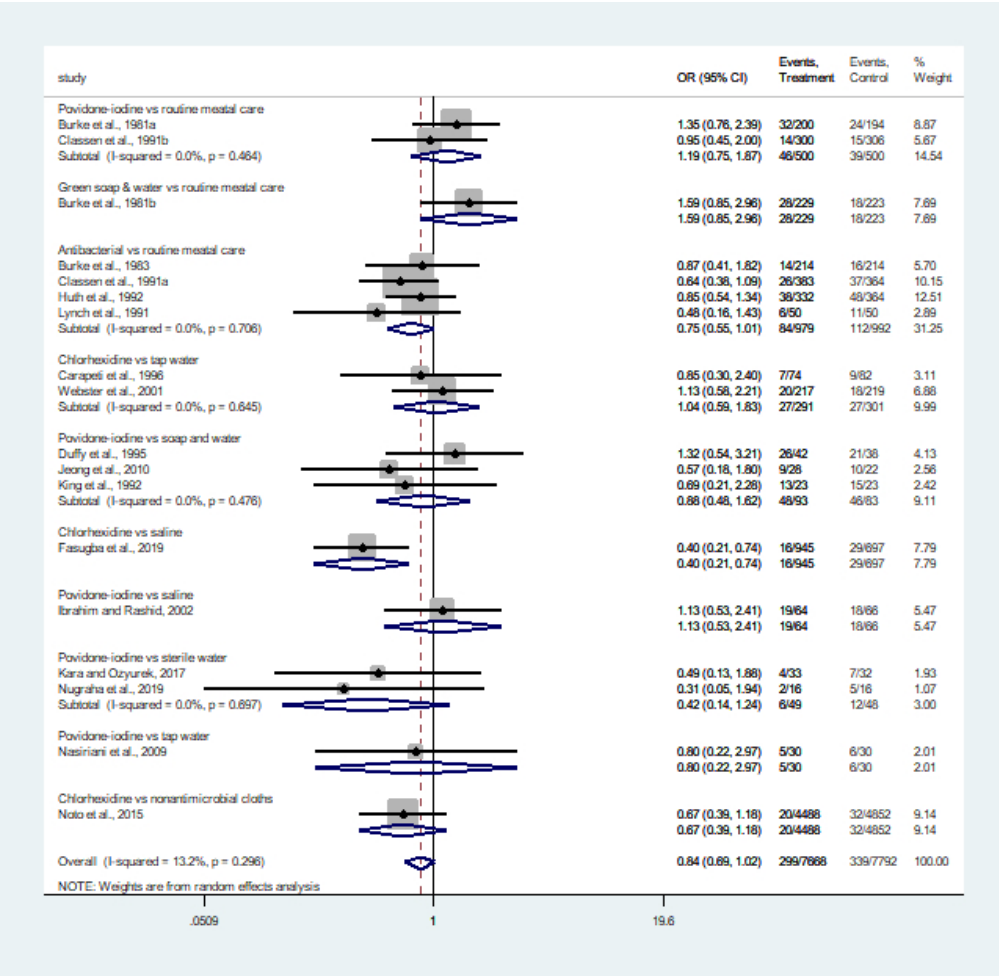

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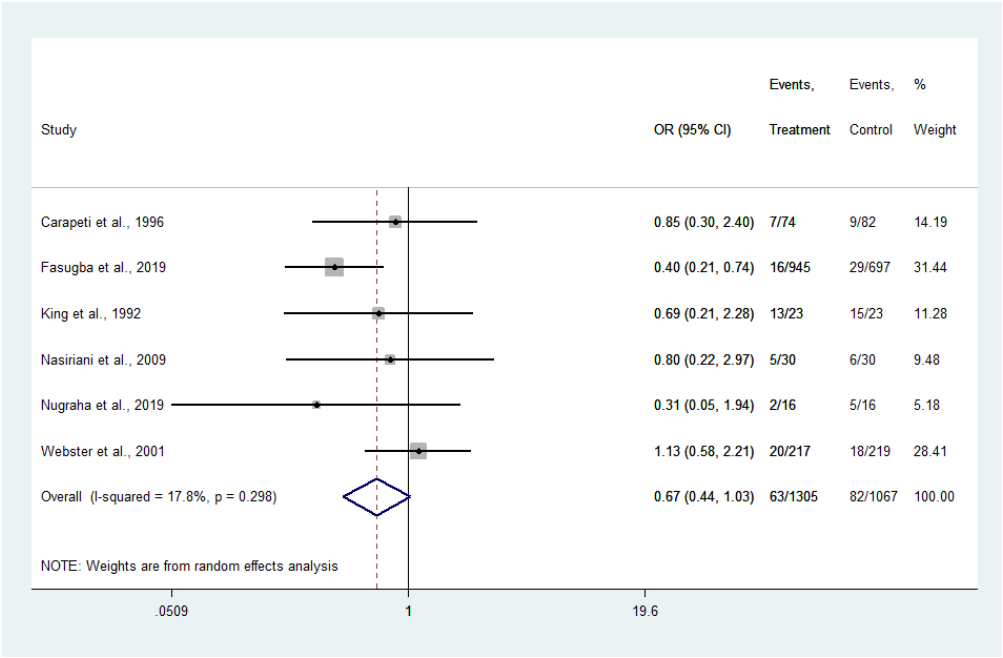

Figure 3. Random-effect meta-analysis of the effect of using an antiseptic meatal cleaning agent (povidone-iodine, chlorhexidine) vs a non-antiseptic agent (soap and water, tap water, sterile water or saline) prior to catheter insertion on the incidence of bacteriuria

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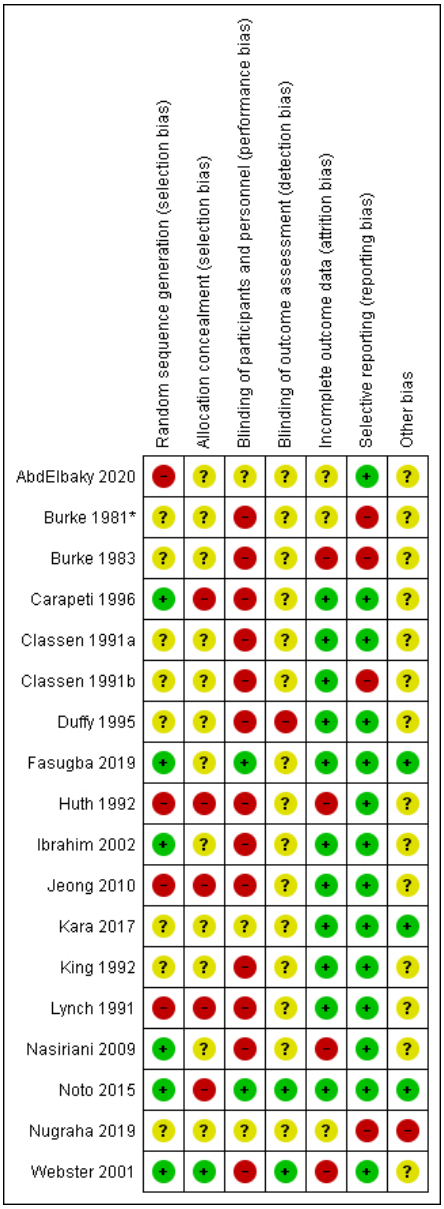

Figure 4. Risk of bias assessment

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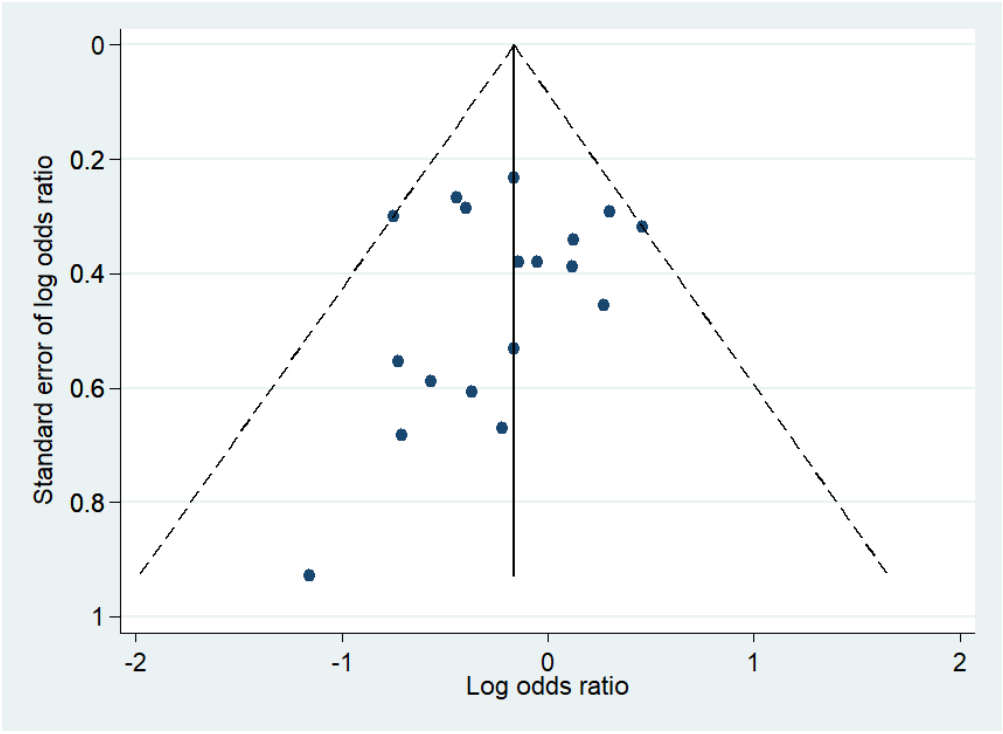

Figure 5. Funnel plot of the included studies

301x219mm (72 x 72 DPI)

SUPPLEMENTARY MATERIAL

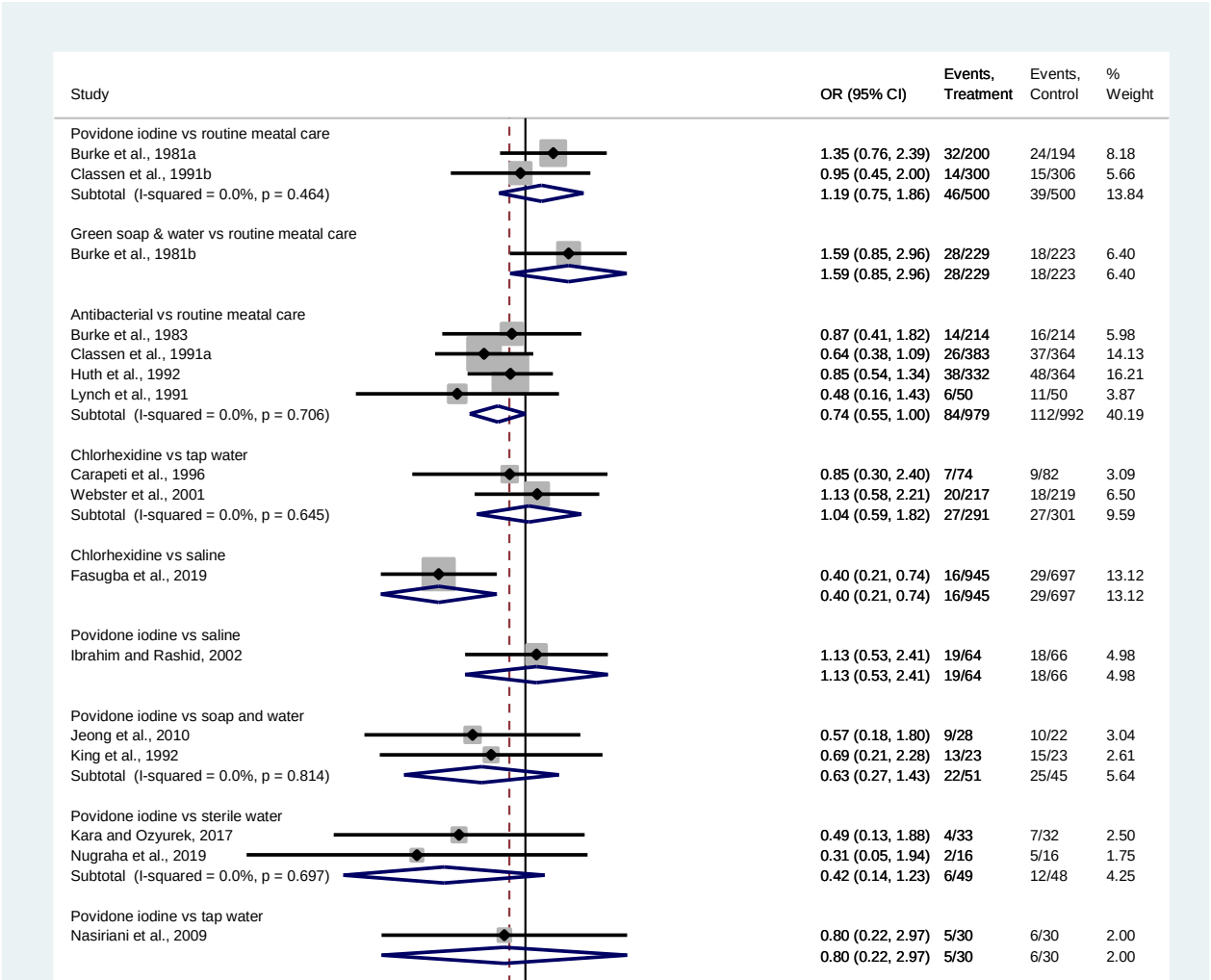

Figure S1. Forest plot displaying fixed-effect meta-analysis of the effect of meatal cleaning on the incidence of bacteriuria only (results stratified by meatal cleaning agent)

Table S1. Comparison of the effect of meatal cleaning on the incidence of bacteriuria only

Comparisons	P values (fixed effect meta-analysis)	P values (random effect meta-analysis
Povidone-iodine vs routine meatal care	0.460	0.462
Green soap and water vs routine meatal care	0.147	0.147
Antibacterial vs routine meatal care	0.053	0.055
Chlorhexidine vs tap water	0.887	0.886
Chlorhexidine vs saline	0.003	0.012
Povidone-iodine vs saline	0.760	0.760
Povidone-iodine vs soap and water	0.268	0.268
Povidone-iodine vs sterile water	0.113	0.116
Povidone-iodine vs tap water	0.739	0.739
Overall	**0.066**	**0.105**

Note: Odds ratio and confident intervals are provided in Figure S1 (fixed effect) and S4 (random-effect). P values presented are to supplement information provided in Figure S1 and Figure S4.

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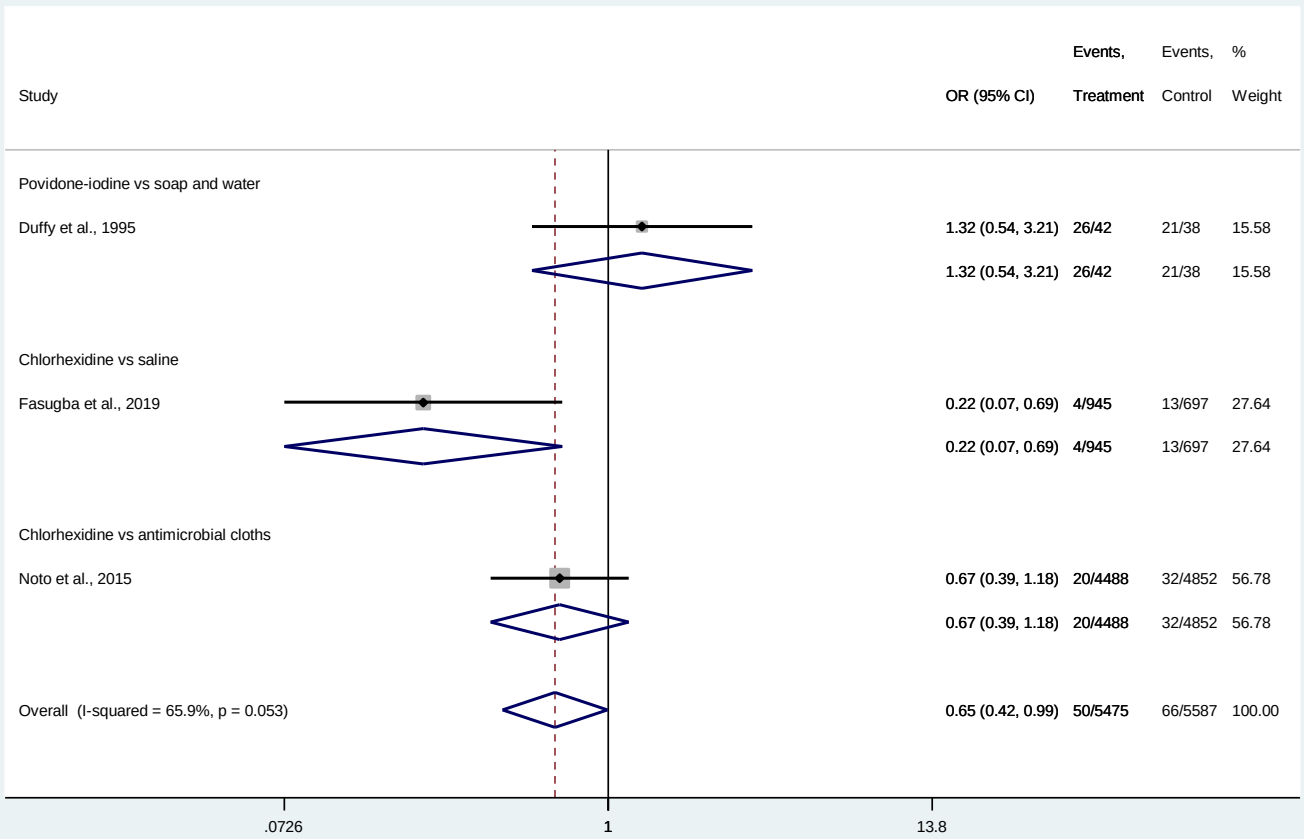

Figure S2 - Forest plot displaying fixed-effect meta-analysis of the effect of meatal cleaning on the incidence of catheter-associated urinary tract infections only (results stratified by meatal cleaning agent)

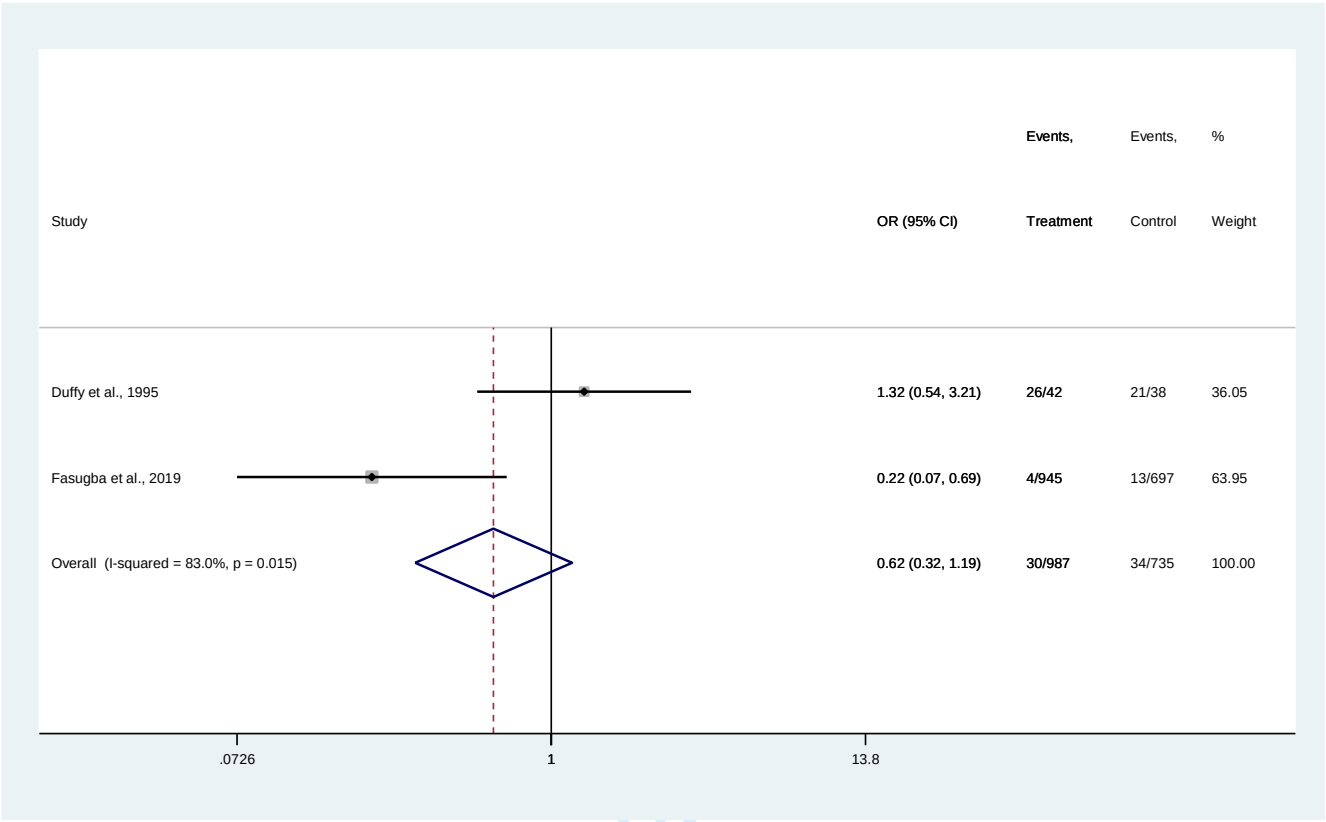

Figure S3. Fixed-effect meta-analysis of the effect of using an antiseptic meatal cleaning agent (povidone-iodine or chlorhexidine) vs a non-antiseptic agent (soap and water or saline) prior to catheter insertion on the incidence of catheter-associated urinary tract infections

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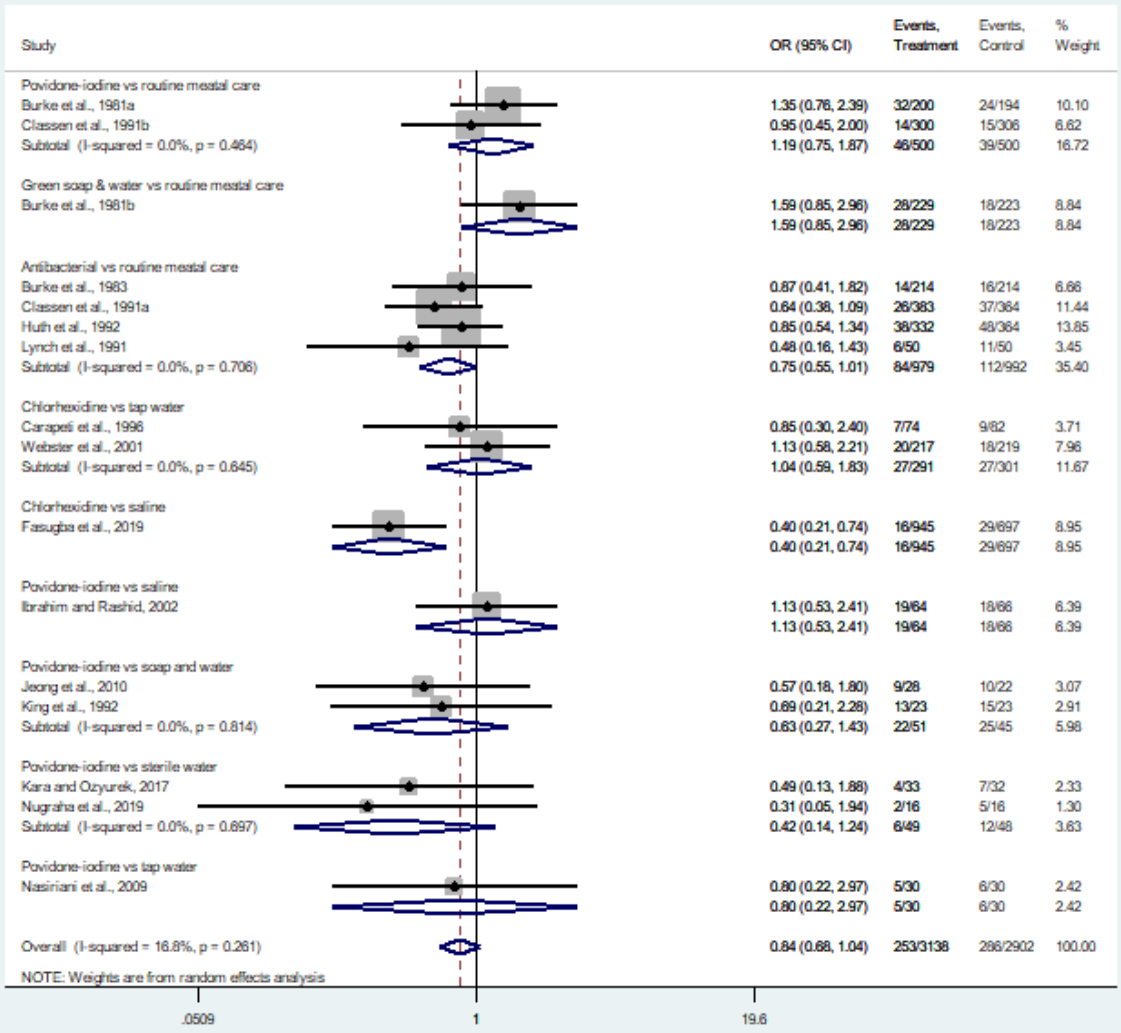

Figure S4. Forest plot displaying random-effect meta-analysis of the effect of meatal cleaning on the incidence of bacteriuria only (results stratified by meatal cleaning agent)

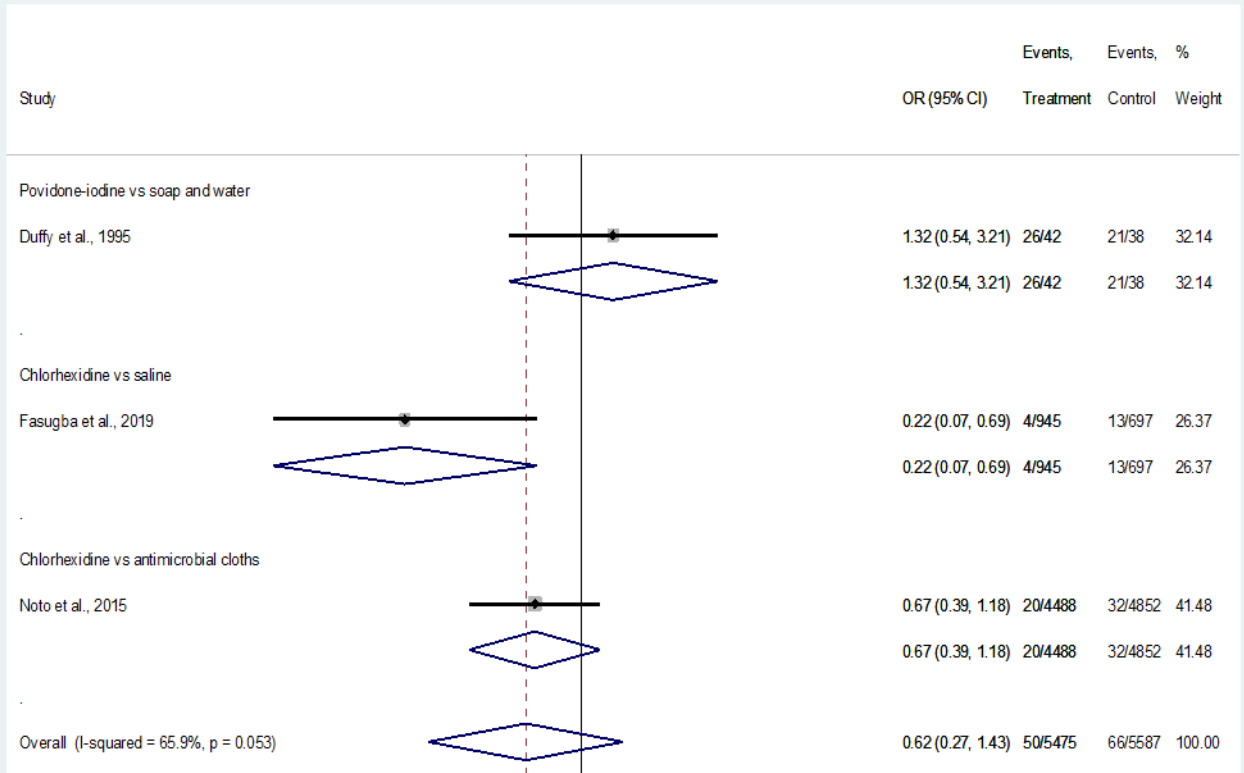

Figure S5. Forest plot displaying random-effect meta-analysis of the effect of meatal cleaning on the incidence of catheter-associated urinary tract infections only (results stratified by meatal cleaning agent)

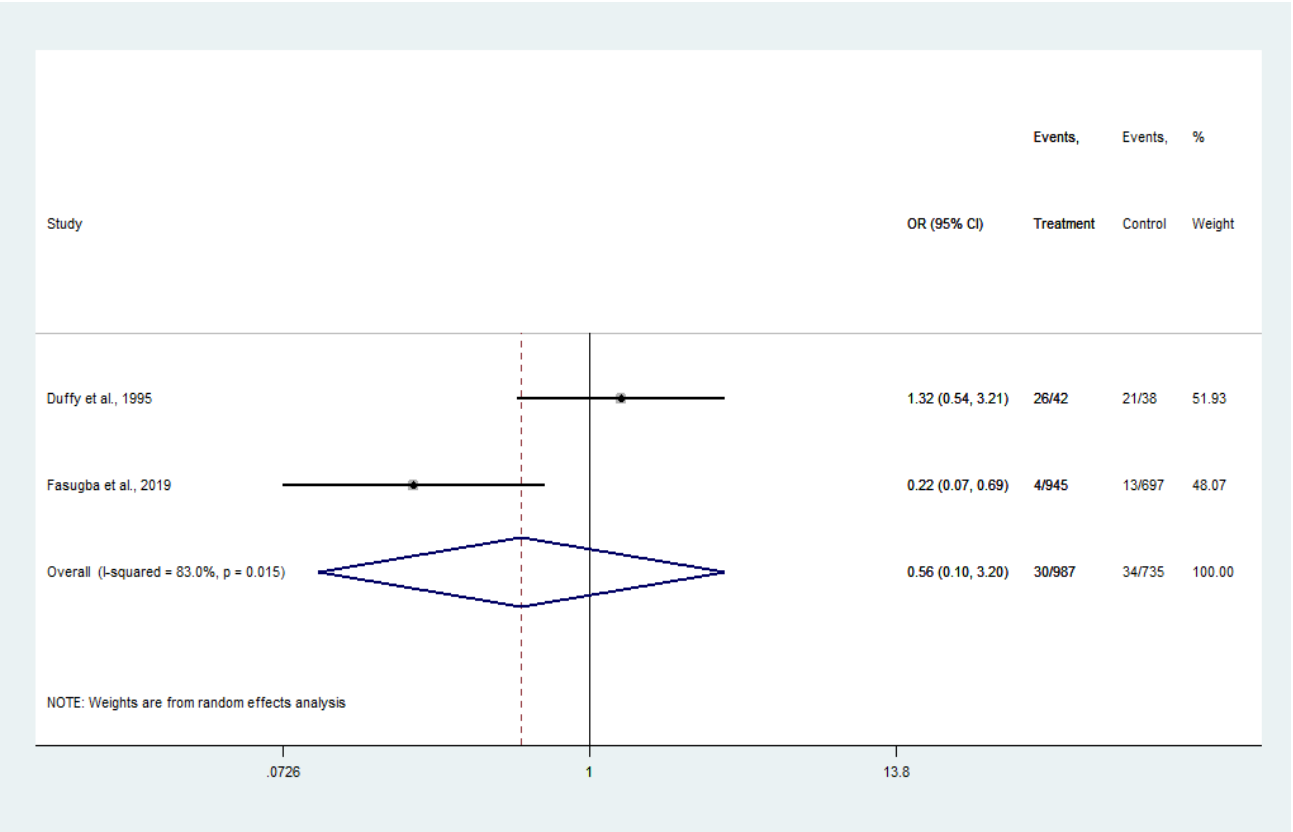

Figure S6. Random-effect meta-analysis of the effect of using an antiseptic meatal cleaning agent (povidone-iodine or chlorhexidine) vs a non-antiseptic agent (soap and water or saline) prior to catheter insertion on the incidence of catheter-associated urinary tract infections

Search strategy

#	Query	Limiters/Expanders	Last Run Via
S5	S1 AND S2 AND S3 AND S4	Expanders - Apply equivalent subjects Search modes - Find all my search terms	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - Academic Search Complete
S4	antiseptic* OR antimicrobial OR antibacterial OR anti-infective OR disinfect OR microbicide OR antibiotic OR polyantibiotic OR sterile OR "bacitracin zinc" OR betadine OR centrimide	Limiters - Published Date: 20160101-20200231 Expanders - Apply equivalent subjects Search modes - Find all my search terms	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - Academic Search Complete
S3	bath* OR hygiene OR cleans* OR cleaned OR cleaning OR topical OR apply OR applied OR application	Limiters - Published Date: 20160101-20200231 Expanders - Apply equivalent subjects Search modes - Find all my search terms	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - Academic Search Complete
S2	meatal OR meatus OR perineal OR perineum OR periurethral	Limiters - Published Date: 20160101-20200231 Expanders - Apply equivalent subjects Search modes - Find all my search terms	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - Academic Search Complete
S1	TX urinary catheter* OR TX urethral catheter* OR TX indwelling catheter* OR TX intermittent catheter	Limiters - Published Date: 20160101-20200231 Expanders - Apply equivalent subjects Search modes - Find all my search terms	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - Academic Search Complete

#	Query	Limiters/Expanders	Last Run Via
S3	S1 AND S2	Expanders - Apply equivalent subjects Search modes - Find all my search terms	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - Academic Search Complete
S2	bundle intervention OR bundle care	Limiters - Published Date: 20160101-20200231 Expanders - Apply equivalent subjects Search modes - Find all my search terms	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - Academic Search Complete
S1	TX urinary tract infection OR TX meatal OR TX meatal disinfection OR TX meatal cleaning	Limiters - Published Date: 20160101-20200231 Expanders - Apply equivalent subjects Search modes - Find all my search terms	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - Academic Search Complete

#	Query	Limiters/Expanders	Last Run Via
S6	S1 AND S2 AND S3 AND S4	Limiters - Human Expanders - Apply equivalent subjects Search modes - Find all my search terms	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Complete
S5	S1 AND S2 AND S3 AND S4	Expanders - Apply equivalent subjects Search modes - Find all my search terms	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Complete
S4	TX antiseptic* OR TX antimicrobial OR TX antibacterial OR TX	Limiters - Published Date: 20160101-20200231 Expanders - Apply equivalent subjects Search modes - Find all my search terms	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Complete

	anti-infective OR TX disinfect* OR TX microbicide OR TX antibiotic OR TX polyantibiotic OR TX sterile OR TX chlorhexidine OR TX povidone-iodine		
S3	TX bath* OR TX hygiene OR TX cleans* OR TX cleaned OR TX cleaning OR TX topical OR TX applied OR TX apply OR TX application	Limiters - Published Date: 20160101-20200231 Expanders - Apply equivalent subjects Search modes - Find all my search terms	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Complete
S2	TX meatal OR TX meatus OR TX perineal OR TX perineum OR TX periurethral	Limiters - Published Date: 20160101-20200231 Expanders - Apply equivalent subjects Search modes - Find all my search terms	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Complete
S1	TX urinary catheter* OR TX urethral catheter* OR TX indwelling catheter* OR TX intermittent catheter*	Limiters - Published Date: 20160101-20200231 Expanders - Apply equivalent subjects Search modes - Find all my search terms	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Complete

#	Query	Limiters/Expanders	Last Run Via

S3	S1 AND S2	Expanders - Apply equivalent subjects Search modes - Find all my search terms	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - MEDLINE Complete
S2	bundle OR bundle care OR bundle intervention	Limiters - Date of Publication: 20160101-20200231 Expanders - Apply equivalent subjects Search modes - Find all my search terms	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - MEDLINE Complete
S1	urinary catheter* OR urethral catheter* OR indwelling catheter* OR intermittent catheter* OR "urinary tract infection"	Limiters - Date of Publication: 20160101-20200231 Expanders - Apply equivalent subjects Search modes - Find all my search terms	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - MEDLINE Complete

#	Query	Limiters/Expanders	Last Run Via
S5	S1 AND S2 AND S3 AND S4	Expanders - Apply equivalent subjects Search modes - Find all my search terms	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - MEDLINE Complete
S4	antiseptic* OR antimicrobial OR antibacterial OR anti-infective OR disinfect* OR microbicide OR antibiotic OR polyantibiotic OR sterile OR chlorhexidine OR povidone-iodine	Limiters - Date of Publication: 20160101-20200231 Expanders - Apply equivalent subjects Search modes - Find all my search terms	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - MEDLINE Complete
S3	bath* OR hygiene OR cleans* OR cleaned OR cleaning OR topical OR applied OR apply OR application	Limiters - Date of Publication: 20160101-20200231 Expanders - Apply equivalent subjects Search modes - Find all my search terms	Interface - EBSCOhost Research Databases

			Search Screen - Advanced Search Database - MEDLINE Complete
S2	meatal OR meatus OR perineal OR perineum OR periurethral	Limiters - Date of Publication: 20160101-20200231 Expanders - Apply equivalent subjects Search modes - Find all my search terms	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - MEDLINE Complete
S1	urinary catheter* OR urethral catheter* OR indwelling catheter* OR intermittent catheter	Limiters - Date of Publication: 20160101-20200231 Expanders - Apply equivalent subjects Search modes - Find all my search terms	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - MEDLINE Complete

	EMBASE
1	urinary catheter.mp. or urinary catheter/ or indwelling catheter/
2	meatal.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word]
3	meatus.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word]
4	perineal.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word]
5	perineum.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word]
6	periurethral.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word]
7	bath*.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word]

8	hygiene.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word]
9	cleans*.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word]
10	cleaned.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word]
11	cleaning.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word]
12	topical.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word]
13	applied.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word]
14	apply.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word]
15	application.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word]
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17	antimicrobial.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word]
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21	microbicide.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word]
22	antibiotic.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word]
23	polyantibiotic.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word]
24	2 or 3 or 4 or 5 or 6
25	7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15
26	16 or 17 or 18 or 19 or 20 or 21 or 22 or 23
27	1 and 24 and 25 and 26
28	27 and 2016:2020.(sa_year).

	EMBASE
1	urinary catheter*.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word]
2	urethral catheter*.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word]
3	indwelling catheter*.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word]
4	intermittent catheter*.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word]

5	urinary tract infection.mp. or urinary tract infection/
6	bundle care.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word]
7	bundle intervention.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word]
8	bundle.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word]
9	1 or 2 or 3 or 4 or 5
10	6 or 7 or 8
11	9 and 10
12	limit 11 to yr="2016 -Current"

	Cochrane Library
#1	(urinary catheter*) OR (urethral catheter*) OR (indwelling catheter*) OR (intermittent catheter*)
#2	(meatal) OR (meatus) OR (perineal) OR (perineum) OR (periurethral)
#3	(bath) OR (hygiene) OR (clean*) OR (topical) OR (appl*)
#4	(antiseptic*) OR (antimicrobial) OR (antibacterial) OR (“anti-infective”) OR (disinfect*)
#5	(antibiotic) OR (polyantibiotic) OR (sterile)
#6	#1 AND #2 AND #3 AND #4 AND #5

	Cochrane Library

#1	(urethral catheter*) OR (intermittent catheter*) OR (indwelling catheter*) OR (urinary catheter*) OR ("urinary tract infection")
#2	(bundle) OR ("bundle care") OR ("bundle intervention")
#3	#1 AND #2

#	Query	Limiters/Expanders	Last Run Via
S5	S1 AND S2 AND S3 AND S4	Expanders - Apply equivalent subjects Search modes - Find all my search terms	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Complete
S4	TX antiseptic* OR TX antimicrobial OR TX antibacterial OR TX anti-infective OR TX disinfect* OR TX microbicide OR TX antibiotic OR TX polyantibiotic OR TX sterile OR TX chlorhexidine OR TX povidone-iodine	Limiters - Published Date: 20160101-20200231 Expanders - Apply equivalent subjects Search modes - Find all my search terms	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Complete
S3	TX bath* OR TX hygiene OR TX cleans* OR TX cleaned OR TX cleaning OR TX topical OR TX applied OR TX apply OR TX application	Limiters - Published Date: 20160101-20200231 Expanders - Apply equivalent subjects Search modes - Find all my search terms	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Complete
S2	TX meatal OR TX meatus OR TX perineal OR TX perineum OR TX periurethral	Limiters - Published Date: 20160101-20200231 Expanders - Apply equivalent subjects Search modes - Find all my search terms	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Complete

S1	TX urinary catheter* OR TX urethral catheter* OR TX indwelling catheter* OR TX intermittent catheter*	Limiters - Published Date: 20160101-20200231 Expanders - Apply equivalent subjects Search modes - Find all my search terms	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Complete

#	Query	Limiters/Expanders	Last Run Via
S3	S1 AND S2	Expanders - Apply equivalent subjects Search modes - Find all my search terms	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Complete
S2	TX bundle care OR TX bundle OR TX bundle intervention	Limiters - Published Date: 20160101-20200231 Expanders - Apply equivalent subjects Search modes - Find all my search terms	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Complete
S1	TX urinary catheter* OR TX urethral catheter* OR TX indwelling catheter* OR TX intermittent catheter* OR TX urinary tract infection	Limiters - Published Date: 20160101-20200231 Expanders - Apply equivalent subjects Search modes - Find all my search terms	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Complete

PubMed	
Search	Query

#3	Search (((((((urinary catheter*) OR urethral catheter*) OR indwelling catheter*) OR intermittent catheter*) OR urinary tract infection) AND ("2016/01/01"[PDat] : "2020/02/29"[PDat]))) AND ((((("bundle care") OR "bundle intervention") OR bundle) AND ("2016/01/01"[PDat] : "2020/02/29"[PDat])) Filters: Publication date from 2016/01/01 to 2020/02/29
#2	Search (("bundle care") OR "bundle intervention") OR bundle Filters: Publication date from 2016/01/01 to 2020/02/29
#1	Search ((((urinary catheter*) OR urethral catheter*) OR indwelling catheter*) OR intermittent catheter*) OR urinary tract infection Filters: Publication date from 2016/01/01 to 2020/02/29

PubMed	
Search	Query
#8-searches 4 and 7	Search ((((((((((urinary catheter*) OR urethral catheter*) OR indwelling catheter*) OR intermittent catheter*) AND ("2016/01/01"[PDat] : "2020/02/29"[PDat]))) AND ((((((meatal) OR meatus) OR perineal) OR perineum) OR periurethral) AND ("2016/01/01"[PDat] : "2020/02/29"[PDat]))) AND ((((((((((bath*) OR hygiene) OR cleans*) OR cleaned) OR cleaning) OR topical*) OR apply) OR applied) OR application) AND ("2016/01/01"[PDat] : "2020/02/29"[PDat]))) AND ("2016/01/01"[PDat] : "2020/02/29"[PDat]))) AND ((((((((((((antiseptic) OR antimicrobial) OR antibacterial) OR "anti-infective") OR disinfect*) OR microbicide) OR polyantibiotic) OR sterile) AND ("2016/01/01"[PDat] : "2020/02/29"[PDat]))) AND ((((((((((("bacitracin zinc") OR "polymyxin b") OR "povidone-iodine") OR betadine) OR cetrimide) OR chlorhexidine) OR savlon) OR sulfadiazine) OR sulphadiazine) OR neomycin) OR gramicidin) AND ("2016/01/01"[PDat] : "2020/02/29"[PDat]))) AND ("2016/01/01"[PDat] : "2020/02/29"[PDat])) Filters: Publication date from 2016/01/01 to 2020/02/29
#7-searches 5 and 6	Search ((((((((((antiseptic) OR antimicrobial) OR antibacterial) OR "anti-infective") OR disinfect*) OR microbicide) OR polyantibiotic) OR sterile) AND ("2016/01/01"[PDat] : "2020/02/29"[PDat]))) AND ((((((((((("bacitracin zinc") OR "polymyxin b") OR "povidone-iodine") OR betadine) OR cetrimide) OR chlorhexidine) OR savlon) OR sulfadiazine) OR sulphadiazine) OR neomycin) OR gramicidin) AND ("2016/01/01"[PDat] : "2020/02/29"[PDat])) Filters: Publication date from 2016/01/01 to 2020/02/29
#6	Search ((((((((("bacitracin zinc") OR "polymyxin b") OR "povidone-iodine") OR betadine) OR cetrimide) OR chlorhexidine) OR savlon) OR sulfadiazine) OR sulphadiazine) OR neomycin) OR gramicidin Filters: Publication date from 2016/01/01 to 2020/02/29

#5	Search (((((((antiseptic) OR antimicrobial) OR antibacterial) OR "anti-infective") OR disinfect*) OR microbicide) OR polyantibiotic) OR sterile Filters: Publication date from 2016/01/01 to 2020/02/29
#4-searches 1, 2 and 3	Search (((((((urinary catheter*) OR urethral catheter*) OR indwelling catheter*) OR intermittent catheter*) AND ("2016/01/01"[PDat] : "2020/02/29"[PDat]))) AND ((((((meatal) OR meatus) OR perineal) OR perineum) OR periurethral) AND ("2016/01/01"[PDat] : "2020/02/29"[PDat]))) AND ((((((((((bath*) OR hygiene) OR cleans*) OR cleaned) OR cleaning) OR topical*) OR apply) OR applied) OR application) AND ("2016/01/01"[PDat] : "2020/02/29"[PDat])) Filters: Publication date from 2016/01/01 to 2020/02/29
#3	Search (((((((bath*) OR hygiene) OR cleans*) OR cleaned) OR cleaning) OR topical*) OR apply) OR applied) OR application Filters: Publication date from 2016/01/01 to 2020/02/29
#2	Search ((((meatal) OR meatus) OR perineal) OR perineum) OR periurethral Filters: Publication date from 2016/01/01 to 2020/02/29
#1	Search (((urinary catheter*) OR urethral catheter*) OR indwelling catheter*) OR intermittent catheter* Filters: Publication date from 2016/01/01 to 2020/02/29

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PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	3
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	4
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	N/A
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	5-6
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	5
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	4
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	6
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	6
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	6
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	6
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	6
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	7

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	6
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	7
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	7
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	7
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	9
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	7-9 + Supplementary
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	7-9 + Supplementary
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	Figure 4
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	Supplementary
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	16
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	17
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	17
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	18

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

PRISMA 2009 Checklist