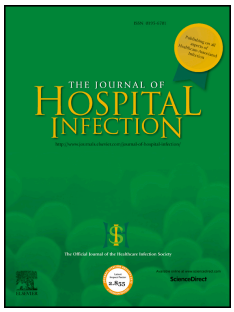
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A systematic review and meta-analysis of the effectiveness of antiseptics for meatal cleaning in the prevention of catheter associated urinary tract infections

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Title

A systematic review and meta-analysis of the effectiveness of antiseptics for meatal cleaning in the prevention of catheter associated urinary tract infections

Running title: Meatal cleaning for prevention of CAUTIs

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Summary

Background: Catheter associated urinary tract infections (CAUTI) are one of the most frequent healthcare associated infections. Antiseptic cleaning of the meatal area before and during catheter use may have the potential to reduce CAUTI risk.

Aim: To systematically review the literature and meta-analyse studies investigating the effectiveness of antiseptic cleaning before urinary catheter insertion and during catheter use for prevention of CAUTI.

Methods: Electronic databases were searched to identify randomised controlled trials. Pooled odds ratios (ORs) and 95% confidence intervals (CI) were calculated and compared across intervention and control groups using DerSimonian-Laird random effects model. Subgroup analyses were performed. Heterogeneity was estimated using the I^2 statistic.

Findings: We identified 2665 potential papers, of which 14 studies were eligible for inclusion. There was no difference in CAUTI incidence when comparing an antiseptic and non-antiseptic agent (pooled OR=0.90, 95% CI=0.73-1.10; *P*=0.31) and for different agents compared: povidone-iodine versus routine care; povidone-iodine versus soap and water; chlorhexidine versus water; povidone-iodine versus saline; povidone-iodine versus water; and green soap and water versus routine care (*P*>0.05 for all). Comparison of an antibacterial with routine care indicated near significance (*P*=0.06). There was no evidence of heterogeneity (I^2=0%; *P*>0.05). Subgroup analyses showed no difference in CAUTI incidence regarding country, setting, risk of bias, sex and frequency of administration.

Conclusions: There were no differences in CAUTI rates although methodological issues hamper generalisability of this finding. Antibacterials might be significant in a well conducted study. Results provide good evidence to inform infection control guidelines in catheter management.

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Keywords: antiseptic; meatal cleaning; urinary catheter; urinary tract infection; systematic review; meta-analysis

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Introduction

Indwelling urinary catheters (IDC) are commonly used in hospital settings, and their use is implicated in hospital acquired infections (HAIs) which are costly and largely preventable. Recent estimates from 183 American hospitals found 23.6% of patients had an IDC,[1] with a rate of 17.5% reported from 66 European hospitals,[2] and 26% of Australian acute care patients.[3] Infections associated with IDCs are one of the most frequent HAIs and are referred to as catheter associated urinary tract infections (CAUTIs) .[4] A survey of adult patients in acute hospitals across England, Wales, Northern Ireland and the Republic of Ireland found urinary tract infections (UTIs) to be the second most common cause of HAIs.[5] CAUTI rates from 82 Australian hospitals were estimated to be 0.2%.[6] Catheter use and CAUTIs have been associated with increased length of stay, higher hospital costs, antibiotic use, morbidity and mortality,[7,8] providing a strong rationale for the implementation of effective interventions to reduce the risk of infection.

Recent interventions to prevent HAIs include the implementation of bundle interventions. CAUTI prevention bundles include staff training on CAUTI prevention measures, audits on catheter insertion, and implementation of more detailed catheter related record keeping.[9-11] Evaluation of CAUTI bundles has found significant reductions in catheter utilisation and CAUTI rates.[11] Recent data from 603 hospitals in the United States showed that following implementation of the national Comprehensive Unit-based Safety Program to reduce CAUTIs, CAUTI rates decreased by 22.3% from 2.82 to 2.19 infections per 1000 catheter-days.[11] Given that bundle interventions have been shown to be effective in reducing CAUTIs, there is a need to explore other strategies that may further contribute to decreasing CAUTIs.

Periurethral colonisation is strongly associated with bacteriuria and CAUTIs,[12] hence reducing bacterial colonisation around the meatal area may have the potential to reduce CAUTI risk. Reviews conducted to date have been inconclusive about the benefits of antiseptic cleaning or periurethral area before and during IDC use to prevent CAUTIs.[13,14] Although the guidelines of the Infectious Diseases Society of America do not recommend the use of antiseptics, they state that data are insufficient to make recommendations on the effectiveness of meatal cleaning prior to catheter insertion in preventing CAUTIs.[15] Similarly, United Kingdom guidelines also do not recommend using antiseptics, advising cleaning of the urethral meatus with sterile normal saline prior to catheter insertion.[16] These recommendations are based on single studies with limited number of participants.[14] Australian guidelines also acknowledge that the benefits of using antiseptic versus sterile saline for meatal cleaning before IDC insertion are unresolved.[17] The most recent systematic review with meta-analysis reported that there was evidence to suggest cleaning with water or saline as opposed to disinfection may reduce CAUTI rates.[18] These findings need to be treated with caution in that although the authors claim that the meta-analysed studies were comparable due to the lack of statistical heterogeneity, there was considerable clinical heterogeneity in the included studies.

There is a strong rationale to undertake this current study given inconclusive evidence. We systematically reviewed the literature and conducted a meta-analysis of studies investigating the effectiveness of antiseptic cleaning before IDC insertion and during catheter use for prevention of CAUTI. The findings will inform clinical practice, contribute to future guideline development and inform the development of well-designed intervention studies in the future.

Methods

A protocol was developed to guide the conduct of the systematic review and meta-analysis and the protocol was registered on the PROSPERO International Prospective Register of Systematic reviews (registration number: CRD42015023741). The format for reporting this review followed the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) statement.[19]

Data sources and search strategy

Electronic databases specifically: Cochrane Library, PubMed, Embase, CINAHL, Medline, Joanna Briggs Institute EBP database, Ovid, Science Direct, EBSCO, Scopus, Academic Search Complete and Health Source, were searched from inception to December 2015. Search parameters were adapted to database requirements. Text words and MeSH terms used included urinary catheter, urinary tract infection, meatal cleaning, periurethral cleaning, antiseptic, antimicrobial, antibacterial, antibiotic, topical, and bundle intervention. Details of the search strategy are provided in Appendix A. Furthermore, reference lists of relevant articles were manually searched for relevant papers.

Study inclusion and exclusion criteria

Randomised control trials (RCTs) and quasi-experimental studies (pre- and post-test design, non-randomised trials) which evaluated the use of an antiseptic, antibacterial or non-medicated agents for cleaning the meatal, periurethral, or perineal area before IDC insertion or intermittent catheterisation, and during routine meatal care were included. Studies involving patients requiring short or long term IDC or intermittent catheterisation in hospital, community settings and long term care facilities were included. Studies from all countries and published in English language were considered. Studies where participants were children

only were excluded. Excluded studies were those of patients with pre-existing UTIs, grey literature such as conference abstracts, letters to editors, reports and guidelines, studies with data unavailable for analysis, studies that did not evaluate the intervention or control agents and studies for which the full text article was not held in an Australian library.

The primary outcome measure under investigation was the difference in the rates of CAUTI in the intervention and control groups. This systematic review accepted the definition of CAUTI provided in included studies.

Study selection

Preliminary selection involved two reviewers (JK and AG) who independently examined the titles and abstracts of all articles retrieved from electronic databases and hand searches for relevance and appropriateness to the review question. Second, full texts of the potentially relevant papers were assessed against the inclusion and exclusion criteria. Articles deemed to have relevant data were included in the systematic review and meta-analysis. Assessment was performed independently by two reviewers (JK and AG). Agreement between reviewers was assessed using Cohen's Kappa coefficient and differences were resolved by discussion with the third and fourth reviewers (OF and BM).

Data extraction

The Cochrane Collaboration's data collection form for randomised and non-randomised controlled trials was used to extract data for the systematic review and meta-analysis.[20] Data were extracted by one reviewer (JK) and checked for accuracy by a second reviewer (AG). Data extracted included: age and sex distribution of the study population, study duration, sample size, study setting, type of intervention, intervention duration, colony forming unit

(cfu) count, CAUTI rates (numerator and denominator data). For studies that reported the outcome at multiple time points, the outcome closest to the end of IDC in situ period was extracted for analysis. Attempts were made to contact the authors of included studies where there was missing information on the numerator or denominator data for calculating the CAUTI rate, and when clarity was needed on type of intervention used.

Risk of bias assessment

The Cochrane Collaboration's tool for assessing risk of bias was used to evaluate included studies following the summary method outlined in Cochrane Handbook for Systematic Reviews of Interventions.[21] Risk of bias was assessed as high, unclear or low. Risk of bias assessment was conducted independently by two reviewers (JK and AG) and disagreements were resolved by discussion with OF and BM.

Data Analysis

All included studies reported the proportions of CAUTI in the intervention and control groups; hence, odds ratios (ORs) and 95% confidence intervals (CI) were calculated from the proportions. The pooled ORs were calculated and compared across both intervention and control groups using a random-effects meta-analysis model. This is based on the DerSimonian and Laird method which incorporates an estimate of the between-study variance into the study weights and standard error of the estimate.[22] A random-effects model was chosen as opposed to a fixed-effects model as the random-effects model takes into account possible heterogeneity between the studies during analysis.[21] Given the clinical heterogeneity between studies in regards to varying meatal cleaning agents used, data from all included studies could not be pooled in a single meta-analysis and were therefore stratified by type of meatal cleaning agent. Assessment of heterogeneity among the studies was by the

I^2 statistic.[23] Subgroup analyses were undertaken to explore effects of aspects of study methodology (country of study, study setting, sex of participants, frequency of intervention, cfu count and risk of bias) on the outcome. Assessment of reporting biases was by visual examination of funnel plots. Statistical analyses were undertaken using Stata (Statacorp, Texas) software version 14.

Results

Study characteristics

A total of 2665 articles were retrieved from electronic database searches and manual searching of reference lists. Following assessment against the inclusion and exclusion criteria, thirteen papers were identified for inclusion in the systematic review and meta-analysis. Agreement between reviewers for assessment of articles against the inclusion and exclusion criteria was 96% (Kappa (95% CI) = 0.75 (0.51-0.99), $P \leq 0.001$). One paper described two studies,[24] hence there were a total of fourteen studies (3 quasi-RCTs; 11 RCTs) (Figure 1). Of the fourteen studies, two compared povidone-iodine with the routine meatal care, which involved removal of debris from the catheter during bathing;[24,25] three compared povidone-iodine with soap and water;[26-28] two compared chlorhexidine with water;[29,30] four compared an antibacterial agent with routine meatal care;[31-34] one compared povidone-iodine with saline;[35] one compared povidone-iodine with water;[36] and the last study compared green soap with routine meatal care.[24] Over half (57.1%) of studies were undertaken in the United States and the majority (71.4%) included medical and/or surgical patients. Eight studies included patients of both sexes, three studies included only women and three studies included only men. Demographic data on age of participants was not stated in the majority of papers. There was considerable diversity in the types of interventions used, frequency of

administration of the intervention and laboratory definition of UTI. Further details on characteristics of the included studies are provided in Table I.

Effect of meatal cleaning on the incidence of catheter-associated UTI

Data from 255 patients in the intervention group and 266 patients in the control group were included in the meta-analysis. Given the variability in the types of intervention agents used, the meta-analyses were stratified by meatal cleaning agent. The forest plot of pooled ORs (Figure 2) showed no significant differences in the incidence of CAUTI between the intervention and control groups overall (OR=0.95, 95% CI=0.78-1.15; *P*=0.60) and for the different agents compared: povidone-iodine versus routine care (*P*=0.46); povidone-iodine versus soap and water (*P*=0.69); chlorhexidine versus water (*P*=0.89); povidone-iodine versus saline (*P*=0.76); povidone-iodine versus water (*P*=0.74); and green soap and water versus routine care (*P*=0.15). Comparison of an antibacterial agent versus routine care indicated near significance (*P*=0.055). Results showed no evidence of heterogeneity (I^2=0%; *P*>0.05) among the included studies within each subgroup and overall.

Effect of antiseptic versus non-antiseptic meatal cleaning agents on the incidence of catheter-associated UTI

Studies were further grouped based on the type of intervention into antiseptic (povidone-iodine, chlorhexidine or antibacterial) versus non-antiseptic (water, saline, soap and water or routine care). There was no difference in the CAUTI incidence when comparing the use of an antiseptic and non-antiseptic agent (pooled OR=0.90, 95% CI=0.73-1.10; *P*=0.31) (Figure 3). One study was excluded from this analysis as the authors compared a non-antiseptic solution of green soap and water with a potential non-antiseptic (routine care).[24]

Subgroup analysis

Subgroup analysis was undertaken for trials comparing povidone-iodine versus routine care; povidone-iodine versus soap and water; chlorhexidine versus water; and an antibacterial versus routine care, as these categories included more than one trial. We found no significant difference in incidence of CAUTIs with regards to country of study, study setting, cfu count, risk of bias, sex and frequency of administration of the intervention (P>0.05, for all).

Effect of alcohol-containing antiseptics on the incidence of catheter-associated UTI

Although no specific information was provided on the presence of alcohol in the intervention agents in the included studies, 6 (42.9%) antiseptic interventions may have potentially included alcohol as an agent to deliver the ointment, cream or liquid.[24,26,29,32-34] Given the difficulty in ascertaining the level of alcohol that intervention agents might contain, further analysis on this potential confounder was not possible.

Risk of bias

Results showed that the level of risk of bias varied among the included studies (Figure 4). Five (35.7%) of the fourteen studies were summarised as having low risk of bias, and 9 (64.3%) as having high risk of bias. The most common limitation identified in the risk of bias assessment was poor reporting of blinding processes used in individual studies.

Publication bias

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

Discussion

This systematic review and meta-analysis provides the most recent and comprehensive analysis of the effectiveness of meatal cleaning for prevention of CAUTI. The results of the meta-analysis indicate there is no difference in the effect of meatal cleaning with antiseptics such as povidone-iodine or chlorhexidine on the incidence of CAUTI as opposed to using non-antiseptic agents. However, near significance was reached for the use of antibacterial agents. Our findings are consistent with other published reviews,[13,14] and individual studies,[24,37] that have shown no benefit in regards to prevention of CAUTI when using an antiseptic agent compared to a non-antiseptic agent for meatal cleaning prior to catheter insertion or while the catheter is in situ. Current guidelines for the prevention of CAUTIs recommend using an aseptic approach for insertion of indwelling urinary catheters although the use of antiseptics for daily meatal care is not recommended.[15,16] However, the guidelines also highlight that there is currently insufficient information available to make recommendations on the benefit of different types of meatal cleaning agents in reducing the risk of CAUTI.[15] Possible reasons that have been proposed for the lack of beneficial effect of meatal cleaning in reducing CAUTI include the negative effect of increased manipulation of the catheter and insufficient residual activity of the agent, among others.[15] Although these factors were not assessed in the current review due to the absence of information in the individual studies, other potential confounders taken into account did not alter the outcome.

A factor that may have influenced the effectiveness of interventions was the presence of alcohol in the intervention agents. A review evaluating the efficacy of the antiseptic chlorhexidine on skin antisepsis suggested that alcohol may be a possible confounding factor in the efficacy of alcohol-containing antiseptics.[38] The inclusion of alcohol is said to create an enhanced antiseptic as there are now two active components and perceived efficacy of antiseptics may be based on the combination agent.[38] Included studies did not state the exact

quantity and effect of alcohol, although further investigation of the intervention agents by the authors suggests the alcohol content was low. The potentially low dose and difficulty confirming exact alcohol content prevented sub-analyses of studies using alcohol. Although the alcohol content in the various intervention agents was potentially not at therapeutic levels to contribute to the antiseptic effect of the interventions, they may have an effect on the outcome and this issue needs to be explored further to explain the effect of alcohol's inclusion in antiseptics in regards to CAUTI prevention.

The meta-analysis of specific intervention agents showed a near statistically significant effect for antibacterial agents for prevention of CAUTI in reference to the pre-specified and widely accepted significance level of 0.05. A recent evaluation study identified benefits from using an antimicrobial solution for cleaning prior to catheter insertion instead of saline with reductions in CAUTI rates including catheterisation related trauma.[39] Burke et al. also found a significant reduction in bacteriuria rates with the use of a polyantibiotic ointment for daily meatal care in a group of high risk females and suggested that there may be small benefits from using this agent.[31] The study authors acknowledge that the low overall bacteriuria rates and sample size may have limited the ability of their study to detect a reduction in infection rates. This suggests that the near significance we found for the effect of an antibacterial agent may have been affected by the rarity of the outcome which will require a large sample size to detect a small effect size. To detect very small clinically significant differences between interventions, extremely precise estimates of the true population value are required for each intervention group.[40] This emphasizes the need for well-designed, rigorous and sufficiently powered RCTs to further evaluate the effect of an antibacterial agent for meatal cleaning on CAUTI reduction.

There are a several limitations in our review. Although there was no evidence of statistical heterogeneity in the meta-analysis, the studies were clinically heterogeneous with regards to the diversity in the patient groups, intervention types and microbiological definitions of the outcome. To overcome for this limitation, meta-analyses were stratified by meatal cleaning agent. Also, the majority of the included studies were assessed to have a high risk of bias indicating the poor quality of the conduct and reporting of published studies. This review is strengthened by the development of a protocol which aided the design and conduct of the systematic review and meta-analysis.

Our review provides the most up to date analysis to inform infection prevention practice and guidelines. The prevalence of CAUTIs provide an imperative to provide evidence based hospital infection control guidelines, including information on appropriate catheter insertion and maintenance procedures, with education of staff on these procedures.[15,16] The overall results of this rigorously conducted study showed no benefits of using an antiseptic over a non-antiseptic for meatal cleaning in the prevention of CAUTIs, however there are two main implications from our findings. First, given that non-antiseptic agents such as water or saline are less expensive than antiseptics and also that antiseptics are allergenic for some patients, the findings from this review have potential cost effectiveness and patient care implications. One may therefore argue in favour of using non-antiseptics. Second, based on our findings which suggest a possible beneficial effect from using antibacterials; it may be worthwhile investing financially into undertaking well conducted RCTs to determine an appropriate sample size to detect a clinically significant difference. This may prove highly beneficial given the complications of UTI with potential to spread to the bloodstream. The implications of our findings are definitely worth further consideration.

Conflict of interest statement

None declared.

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Figure Legend

Figure 1. PRISMA flow diagram of study selection

* One paper described two studies

Figure 2. Forest plot displaying random-effect meta-analysis of the effect of meatal cleaning on incidence of CAUTI (results stratified by meatal cleaning agent)

Figure 3. Random-effect meta-analysis of the effect of using an antiseptic meatal cleaning agent (povidone-iodine, chlorhexidine or antibacterial) versus non-antiseptic agent (no treatment/usual care, soap and water, water or saline) on the incidence of CAUTI

Figure 4. Risk of bias assessment for studies included in the systematic review

***** Paper described two studies

Figure 5. Funnel plot of the included studies

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

Study author, year and design	Country	Population	Administration	Frequency of application	UTI definition	Intervention				Control		
						Mean age (SD)	Intervention agent	Alcohol-containing agent	UTI rates	Mean age (SD)	Comparator agent	UTI rates
Burke *et al*, 1981a; RCT	USA	Medical and surgical patients	Daily meatal care while IDC in situ	Twice daily	$\geq 10^3$ cfu/mL	NR	10% povidone-iodine Betadine solution and ointment	Yes, pareth-25-9 as inactive ingredient	32/200	NR	Usual care; removal of debris from catheter during bathing	24/194
Burke *et al*, 1981b; RCT	USA	Medical and surgical patients	Daily meatal care while IDC in situ	Once daily	$\geq 10^3$ cfu/mL	NR	Green soap and water	Assumed yes, 30% ethyl alcohol as solution	28/229	NR	Usual care; removal of debris from catheter during bathing	18/223
Burke *et al*, 1983, RCT	USA	Medical and surgical patients	Daily meatal care while IDC in situ, until UTI found	Twice daily	$\geq 10^3$ cfu/mL	NR	Neomycin-polymyxcin B-bacitracin ointment	No	14/214	NR	Usual care; removal of debris from catheter during bathing	16/214
Carapeti *et al*, 1996;	UK	General surgery patients	On IDC insertion for surgery	Once for surgery	$>10^5$ cfu/mL	67.5	0.3% CHG and 3% centrimide	Yes, 2.84% isopropyl	7/74	65.3	Tap water	9/82

Study author, year and design	Country	Population	Administration	Frequency of application	UTI definition	Intervention				Control		
						Mean age (SD)	Intervention agent	Alcohol-containing agent	UTI rates	Mean age (SD)	Comparator agent	UTI rates
RCT							Savlon solution	alcohol, 0.056% benzyl benzoate and terpineol as excipient ingredients				
Classen et al., 1991a; RCT	USA	Medical and surgical patients	Daily meatal care while IDC in situ, until UTI found	Thrice daily	$\geq 10^3$ cfu/mL	NR	Polymyxin B sulfate, neomycin sulfate, gramicidin Neosporin cream	Yes, propylene glycol as non-medicinal ingredient	26/383	NR	Routine meatal care; removal of debris from catheter during bathing	37/364
Classen et al., 1991b;	USA	Medical and surgical patients	Daily meatal care while IDC in situ,	Once daily	$\geq 10^3$ cfu/mL	NR	2% Lugol's Iodine	Unclear, assumed no	14/300	NR	Routine meatal care; removal of debris	15/306

Study author, year and design	Country	Population	Administration	Frequency of application	UTI definition	Intervention				Control			
						Mean age (SD)	Intervention agent	Alcohol-containing agent	UTI rates	Mean age (SD)	Comparator agent	UTI rates
RCT			until UTI found				povidone-iodine solution				from catheter during bathing	
Duffy *et al*, 1995; RCT	USA	Male veterans in long-term care	Pre-IC	Pre-IC, ~thrice daily	$\geq 10^5$ cfu/mL	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
Huth *et al*, 1992; quasi-RCT	USA	Medical and surgical patients	Daily meatal care while IDC in situ	Twice daily	$\geq 10^3$ 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,	Saudi Arabia	Male transurethral	On IDC insertion, and in daily	Once daily	10^5 cfu/mL	66.7 (10.1)	Povidone-iodine solution	Unclear, assumed no	19/64	66 (10.4)	Saline	18/66

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Study author, year and design	Country	Population	Administration	Frequency of application	UTI definition	Intervention				Control		
						Mean age (SD)	Intervention agent	Alcohol-containing agent	UTI rates	Mean age (SD)	Comparator agent	UTI rates
2002; RCT		surgery patients	application while IDC in situ									
Jeong *et al*, 2010; quasi-RCT	South Korea	Female ICU patients	On IDC insertion, and in daily meatal care while IDC in situ	Once daily	$\geq 10^5$ cfu/mL	61.5 (17.3)	10% povidone-iodine solution	Unclear, assumed no	9/28	64.1 (13.3)	Soap and water	10/22
King *et al*, 1992; RCT	USA	SCI rehabilitation inpatients	Pre-IC	Pre-IC, once per 4-6 hours	$\geq 10^4$ 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	UK	Male transurethral surgery patients	On IDC insertion, and in daily meatal care while IDC in situ	Once daily	$>10^5$ 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*	Iran	Female	On IDC insertion	Once for	$>10^5$	NR	Povidone-iodine	Unclear,	5/30	NR	Tap water	6/30

Study author, year and design	Country	Population	Administration	Frequency of application	UTI definition	Intervention				Control		
						Mean age (SD)	Intervention agent	Alcohol-containing agent	UTI rates	Mean age (SD)	Comparator agent	UTI rates
al, 2009; RCT		gynaecological surgery patients	for surgery	surgery	cfu/mL		solution	assumed no				
Webster *et al*, 2001; RCT	Australia	Pregnant obstetrics patients	On IDC insertion for delivery	Once for delivery	$\geq 10^3$ cfu/mL	NR	0.1% CHG solution	No	20/217	NR	Tap water	18/219

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

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Search strategy

	Academic Search Complete (via EBSCOhost search interface): Keyword search strategy
1	TX (urinary catheter*) OR (urethral catheter*) OR (dwelling catheter*) OR (intermittent catheter*)
2	TX meatal OR meatus OR perineal OR perineum OR periurethral
3	TX bath* OR hygiene OR cleans* OR cleaned OR cleaning OR topical OR applied OR apply OR application
4	TX 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 OR chlorhexidine OR "polymyxin b" OR povidone-iodine OR savlon OR sulfadiazine OR sulphadiazine OR neomycin OR gramicidin
5	#1 AND #2 AND #3 AND #4
6	#5 AND Source Type: Academic Journals

* denotes truncation

[TX] Performs a keyword search across all searchable citation fields and in the full text.

#	**Academic Search Complete (via EBSCOhost search interface): Keyword search strategy**
1	TX (urinary tract infection) OR (meatal) OR (meatal disinfection) OR (meatal cleaning)
2	TX (bundle intervention) OR (bundle care)
3	#1 AND #2

#	**ACU Full Text Journals@Ovid (via Ovid search interface): Keyword search strategy**
1	(urinary catheter* or urethral catheter* or dwelling catheter* or intermittent catheter*).mp. [mp=title, abstract, full text, caption text]
2	(meatal or meatus or perineal or perineum or periurethral).mp. [mp=title, abstract, full text, caption text]
3	(bath* or hygiene or cleans* or cleaned or cleaning or topical or applied or apply or application).mp. [mp=title, abstract, full text, caption text]
4	(antiseptic* or antimicrobial or antibacterial or anti-infective or disinfect* or microbicide or antibiotic or polyantibiotic or "bacitracin zinc" or betadine or centrimide or chlorhexidine or "polymyxin b" or povidone-iodine or savlon or sulfadiazine or sulphadiazine or neomycin or gramicidin).mp. [mp=title, abstract, full text, caption text]
5	#1 AND #2 AND #3 AND #4

* denotes truncation

[mp] Searches title, abstract, full text, and caption text.

#	**ACU Full Text Journals@Ovid (via Ovid search interface): Keyword search strategy**
1	(urinary tract infection or meatal cleaning or meatal disinfection or meatal).mp. [mp=title, abstract, full text, caption text]
2	(bundle care or bundle intervention or bundle).mp. [mp=title, abstract, full text, caption text]
3	#1 AND #2

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#	**CINAHL Complete (via EBSCOhost search interface): Keyword search strategy**
1	TX (urinary catheter*) OR (urethral catheter*) OR (dwelling catheter*) OR (intermittent catheter*)
2	TX meatal OR meatus OR perineal OR perineum OR periurethral
3	TX bath* OR hygiene OR cleans* OR cleaned OR cleaning OR topical OR applied OR apply OR application
4	TX 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 OR chlorhexidine OR "polymyxin b" OR povidone-iodine OR savlon OR sulfadiazine OR sulphadiazine OR neomycin OR gramicidin
5	#1 AND #2 AND #3 AND #4
6	#5 AND Human
7	#6 AND Source Type: Academic Journals

* denotes truncation.

[TX] Performs a keyword search across all searchable citation fields and in the full text.

#	**CINAHL Complete (via EBSCOhost search interface): Keyword search strategy**
1	TX (urinary catheter*) OR (urethral catheter*) OR (dwelling catheter*) OR (intermittent catheter*) OR (urinary tract infection)
2	TX bundle care OR bundle OR bundle intervention
3	#1 AND #2

#	**Cochrane Collection (via Wiley Online Library): Keywords search strategy**
1	(dwelling next catheter*) or (urinary next catheter*) or (urethral next catheter*) or (intermittent next catheter*)
2	meatal* or "meatus" or perineal* or "perineum" or periurethral*
3	bath* or "hygiene" or cleans* or cleaned or cleaning or topical or apply or application or applied
4	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 or chlorhexidine or "polymyxin b" or povidone or savlon or sulfadiazine or sulphadiazine or neomycin or gramicidin
5	#1 AND #2 AND #3 AND #4

#	**Cochrane Collection (via Wiley Online Library): Keywords search strategy**
1	(urethral cather*) or (intermittent catheter*) or (*dwelling catheter) or "urinary tract infection"
2	bundle or “bundle care” or “bundle intervention”
3	#1 AND #2

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#	**EMBASE: Excerpta Medica (Embase Classic+Embase 1947 to current (via Ovid search interface): Keyword Search Strategy**
1	(urinary catheter* or urethral catheter* or dwelling catheter* or intermittent catheter*).mp. [mp=title, abstract, full text, caption text]
2	(meatal or meatus or perineal or perineum or periurethral).mp. [mp=title, abstract, full text, caption text]
3	(bath* or hygiene or cleans* or cleaned or cleaning or topical or applied or apply or application).mp. [mp=title, abstract, full text, caption text]
4	(antiseptic* or antimicrobial or antibacterial or anti-infective or disinfect* or microbicide or antibiotic or polyantibiotic or "bacitracin zinc" or betadine or centrimide or chlorhexidine or "polymyxin b" or povidone-iodine or savlon or sulfadiazine or sulphadiazine or neomycin or gramicidin).mp. [mp=title, abstract, full text, caption text]
5	#1 AND #2 AND #3 AND #4

#	**EMBASE: Excerpta Medica (Embase Classic+Embase 1947 to current (via Ovid search interface): Keyword Search Strategy**
1	(urinary catheter* or urethral catheter* or dwelling catheter* or intermittent catheter* or "urinary tract infection").mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]
2	(bundle care or bundle intervention or bundle).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword)
3	#1 AND #2
4	Limit #3 to English language
5	Limit #4 to human

#	**Health Source: Nursing/Academic Edition: Keyword Search Strategy (via EBSCOhost search interface)**
1	TX (urinary catheter*) OR (urethral catheter*) OR (dwelling catheter*) OR (intermittent catheter*)
2	TX meatal OR meatus OR perineal OR perineum OR periurethral
3	TX bath* OR hygiene OR cleans* OR cleaned OR cleaning OR topical OR applied OR apply OR application
4	TX 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 OR chlorhexidine OR "polymyxin b" OR povidone-iodine OR savlon OR sulfadiazine OR sulphadiazine OR neomycin OR gramicidin
5	#1 AND #2 AND #3 AND #4
6	#5 AND Source Type: Academic Journals

* denotes truncation.

[TX] Performs a keyword search across all searchable citation fields and in the full text.

#	**Health Source: Nursing/Academic Edition: Keyword Search Strategy (via EBSCOhost search interface)**
1	TX (urinary catheter*) OR (urethral catheter*) OR (dwelling catheter*) OR (intermittent catheter*) OR (“urinary tract infection”)
2	TX (bundle) OR (bundle care) OR (bundle intervention)
3	#1 AND #2

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#	**The Joanna Briggs Institute EBP Database (via Ovid search interface): Keyword search strategy**
1	(urinary catheter* or urethral catheter* or dwelling catheter* or intermittent catheter*).mp. [mp=title, abstract, full text, caption text]
2	(meatal or meatus or perineal or perineum or periurethral).mp. [mp=title, abstract, full text, caption text]
3	(bath* or hygiene or cleans* or cleaned or cleaning or topical or applied or apply or application).mp. [mp=title, abstract, full text, caption text]
4	(antiseptic* or antimicrobial or antibacterial or anti-infective or disinfect* or microbicide or antibiotic or polyantibiotic or "bacitracin zinc" or betadine or centrimide or chlorhexidine or "polymyxin b" or povidone-iodine or savlon or sulfadiazine or sulphadiazine or neomycin or gramicidin).mp. [mp=title, abstract, full text, caption text]
5	#1 AND #2 AND #3 AND #4

[mp=text, heading word, subject area node, title]

#	**The Joanna Briggs Institute EBP Database (via Ovid search interface): Keyword search strategy**
1	(urinary catheter* or urethral catheter* or dwelling catheter* or intermittent catheter* or “urinary tract infection”).mp. [mp=text, heading word, subject area node, title]
2	(bundle or “bundle care” or “bundle intervention”).mp. [mp=title, abstract, full text, caption text]
3	#1 AND #2

#	**MEDLINE Complete (via EBSCOhost search interface): Keyword search strategy**
1	TX (urinary catheter*) OR (urethral catheter*) OR (dwelling catheter*) OR (intermittent catheter*)
2	TX meatal OR meatus OR perineal OR perineum OR periurethral
3	TX bath* OR hygiene OR cleans* OR cleaned OR cleaning OR topical OR applied OR apply OR application
4	TX 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 OR chlorhexidine OR "polymyxin b" OR povidone-iodine OR savlon OR sulfadiazine OR sulphadiazine OR neomycin OR gramicidin
5	#1 AND #2 AND #3 AND #4
6	#5 AND Human
7	#6 AND Source Type: Academic Journals AND Guidelines

* denotes truncation.

[TX] Searches for keyword(s) in all indexed citation fields as well as in the full text (word indexed).

#	**MEDLINE Complete (via EBSCOhost search interface): Keyword search strategy**
1	TX (urinary catheter*) OR (urethral catheter*) OR (dwelling catheter*) OR (intermittent catheter*) OR (“urinary tract infection”)
2	TX (bundle) OR (bundle care) OR (bundle intervention)
3	#1 AND #2

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#	**PubMed: Keyword search strategy**
1	Search (urinary catheter*) OR urethral catheter*) OR dwelling catheter*) OR intermittent catheter*[All Fields]
2	Search (meatal OR meatus OR perineal OR perineum OR periurethral)[All Fields]
3	Search (bath* OR hygiene OR cleans* OR cleaned OR cleaning OR topical* OR apply OR applied OR application)[All Fields]
4	#1 AND #2 AND #3 Search (urinary catheter*) OR urethral catheter*) OR dwelling catheter*) OR intermittent catheter*) AND (meatal OR meatus OR perineal OR perineum OR periurethral) AND (bath* OR hygiene OR cleans* OR cleaned OR cleaning OR topical* OR apply OR applied OR application)
5	Search (antiseptic OR antimicrobial OR antibacterial OR "anti-infective" OR disinfect* OR microbicide OR polyantibiotic OR sterile)[All Fields]
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)[All Fields]
7	#5 OR #6 Search (antiseptic OR antimicrobial OR antibacterial OR "anti-infective" OR disinfect* OR microbicide OR polyantibiotic OR sterile) OR ("bacitracin zinc" OR "polymyxin b" OR "povidone-iodine" OR betadine OR cetrimide OR chlorhexidine OR savlon OR sulfadiazine OR sulphadiazine OR neomycin OR gramicidin)[All Fields]
8	#4 AND #7 Search (urinary catheter*) OR urethral catheter*) OR dwelling catheter*) OR intermittent catheter*) AND (meatal OR meatus OR perineal OR perineum OR periurethral) AND (bath* OR hygiene OR cleans* OR cleaned OR cleaning OR topical* OR apply OR applied OR application) AND (antiseptic OR antimicrobial OR antibacterial OR "anti-infective" OR disinfect* OR microbicide OR polyantibiotic OR sterile) OR ("bacitracin zinc" OR "polymyxin b" OR "povidone-iodine" OR betadine OR cetrimide OR chlorhexidine OR savlon OR sulfadiazine OR sulphadiazine OR neomycin OR gramicidin)[All Fields]
9	#8 AND Filter: Humans

#	**PubMed: Mesh Terms**
1	Search (urinary catheter*) OR urethral catheter*) OR dwelling catheter*) OR intermittent catheter*) OR "urinary tract infection" [All Fields]
2	Search (("bundle care") OR "bundle intervention") OR bundle [All Fields]
3	#1 and #2

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#	**Science Direct: Keyword search strategy**
1	("urinary catheter*" OR "urethral catheter*" OR "dwelling catheter*" OR "intermittent catheter*")
2	(meatal OR meatus OR perineal OR perineum OR periurethral)
3	(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 or chlorhexidine or “polymyxin b” or povidone-iodine or savlon) or (sulfadiazine or sulphadiazine or neomycin or gramicidin)
4	(bath* or hygiene or cleans* or cleaned or cleaning or topical or applied or apply or application)
5	#1 AND #2 AND #3 AND #4 ("urinary catheter*" OR "urethral catheter*" OR "dwelling catheter*" OR "intermittent catheter*") AND (meatal OR meatus OR perineal OR perineum OR periurethral) AND (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 or chlorhexidine or “polymyxin b” or povidone-iodine or savlon) or (sulfadiazine or sulphadiazine or neomycin or gramicidin) AND (bath* or hygiene or cleans* or cleaned or cleaning or topical or applied or apply or application)

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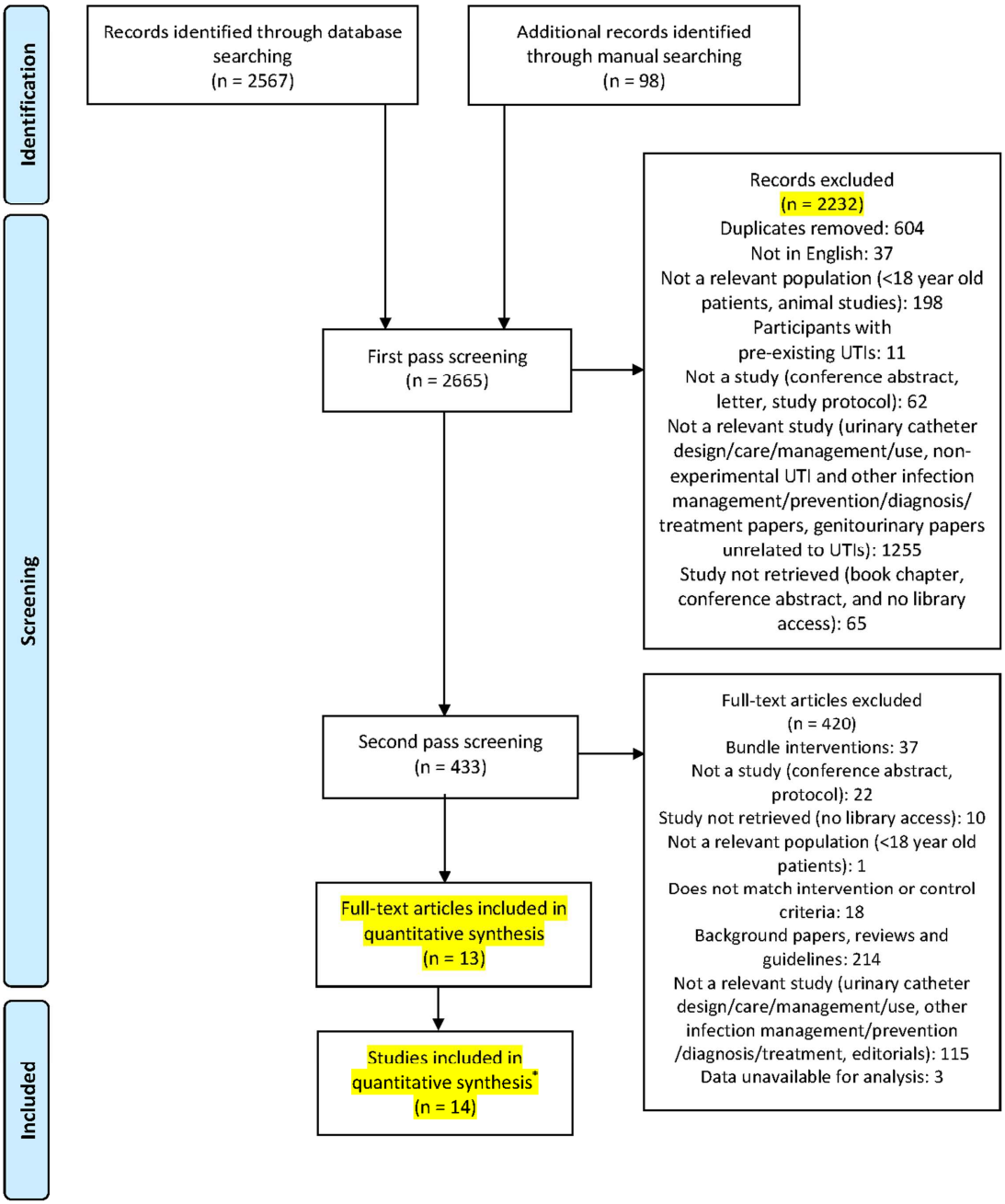
#	**Science Direct: Keyword search strategy**
1	("urinary catheter*" OR "urethral catheter*" OR "dwelling catheter*" OR "intermittent catheter*")
2	(“bundle care” OR “bundle intervention” OR bundle)
3	#1 AND #2
4	Limit to Sciences: ‘Nursing and Health Professions’
5	Limit to 1981 to present

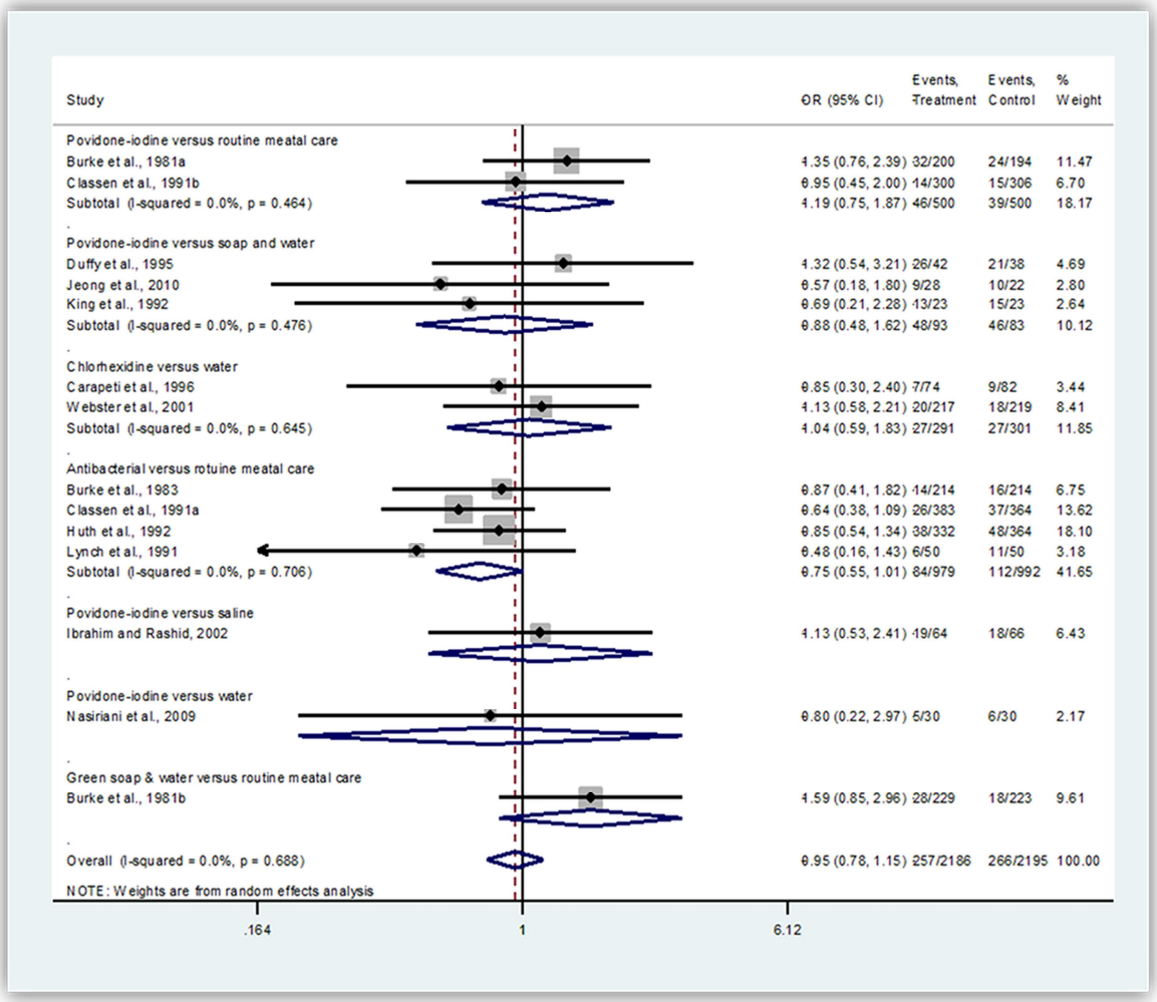
#	**Scopus: Keyword Search Strategy**
1	(TITLE-ABS-KEY (urinary catheter*) OR TITLE-ABS-KEY (urethral catheter*) OR TITLE-ABS-KEY (dwelling catheter*) OR TITLE-ABS-KEY (intermittent catheter*) OR TITLE-ABS-KEY ("urinary tract infection"))
2	(TITLE-ABS-KEY (bundle) OR TITLE-ABS-KEY (“bundle care”) OR TITLE-ABS-KEY (“bundle intervention”))
3	(TITLE-ABS-KEY (bath*) OR TITLE-ABS-KEY (hygiene) OR TITLE-ABS-KEY (cleans*) OR TITLE-ABS-KEY (cleaned) OR TITLE-ABS-KEY (cleaning) OR TITLE-ABS-KEY (topical) OR TITLE-ABS-KEY (applied) OR TITLE-ABS-KEY (apply) OR TITLE-ABS-KEY (application))
4	(TITLE-ABS-KEY (antiseptic*) OR TITLE-ABS-KEY (antimicrobial) OR TITLE-ABS-KEY (antibacterial) OR TITLE-ABS-KEY (anti-infective) OR TITLE-ABS-KEY (disinfect*) OR TITLE-ABS-KEY (microbicide) OR TITLE-ABS-KEY (antibiotic) OR TITLE-ABS-KEY (polyantibiotic) OR TITLE-ABS-KEY (sterile) OR TITLE-ABS-KEY ("bacitracin zinc") OR TITLE-ABS-KEY (betadine) OR TITLE-ABS-KEY (centrimide) OR TITLE-ABS-KEY (chlorhexidine) OR TITLE-ABS-KEY ("polymyxin b") OR TITLE-ABS-KEY (povidone-iodine) OR TITLE-ABS-KEY (savlon) OR TITLE-ABS-KEY (sulfadiazine) OR TITLE-ABS-KEY (sulphadiazine) OR TITLE-ABS-KEY (neomycin) OR TITLE-ABS-KEY (gramicidin))
5	#1 AND #2 AND #3 AND #4
6	#5 AND PUBYEAR > 1980
7	#6 AND EXCLUDE (SUBJAREA , "VETE")

[TITLE-ABS-KEY] A combined field that searches article titles, abstracts, and keywords (AUTHKEY, INDEXTERMS, TRADENAME, and CHEMNAME fields).
[PUBYEAR] Publication Year.
[SUBJAREA] Subject Area
[VETE] Veterinary

#	**Scopus: Keyword Search Strategy**
1	(TITLE-ABS-KEY (urinary catheter*) OR TITLE-ABS-KEY (urethral catheter*) OR TITLE-ABS-KEY (dwelling catheter*) OR TITLE-ABS-KEY (intermittent catheter*) OR TITLE-ABS-KEY ("urinary tract infection"))
2	(TITLE-ABS-KEY (bundle) OR TITLE-ABS-KEY (“bundle care”) OR TITLE-ABS-KEY (“bundle intervention”))
3	#1 and #2

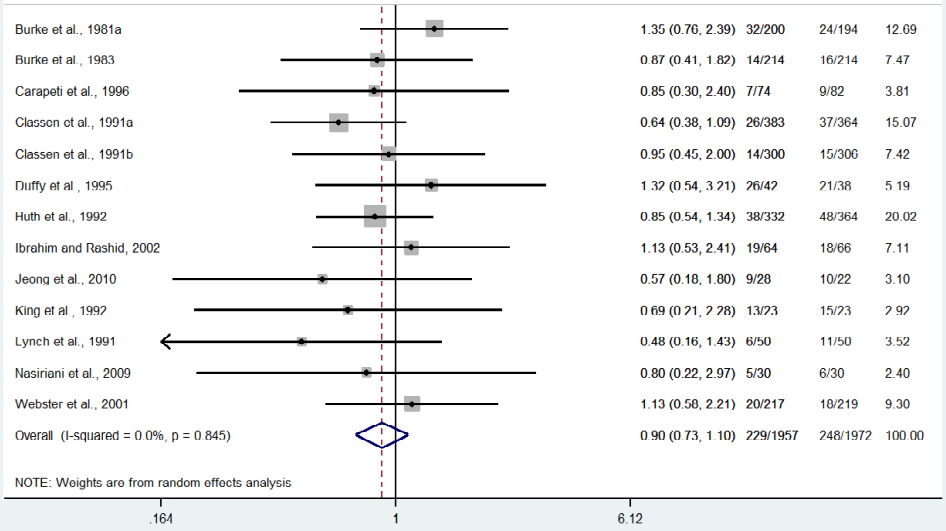
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Identification
Screening
Included
Records identified through database searching (n = 2567)
Additional records identified through manual searching (n = 98)
First pass screening (n = 2665)
Records excluded (n = 2232)
Duplicates removed: 604
Not in English: 37
Not a relevant population (<18 year old patients, animal studies): 198
Participants with pre-existing UTIs: 11
Not a study (conference abstract, letter, study protocol): 62
Not a relevant study (urinary catheter design/care/management/use, non-experimental UTI and other infection management/prevention/diagnosis/ treatment papers, genitourinary papers unrelated to UTIs): 1255
Study not retrieved (book chapter, conference abstract, and no library access): 65
Second pass screening (n = 433)
Full-text articles excluded (n = 420)
Bundle interventions: 37
Not a study (conference abstract, protocol): 22
Study not retrieved (no library access): 10
Not a relevant population (<18 year old patients): 1
Does not match intervention or control criteria: 18
Background papers, reviews and guidelines: 214
Not a relevant study (urinary catheter design/care/management/use, other infection management/prevention /diagnosis/treatment, editorials): 115
Data unavailable for analysis: 3
Full-text articles included in quantitative synthesis (n = 13)
Studies included in quantitative synthesis* (n = 14)

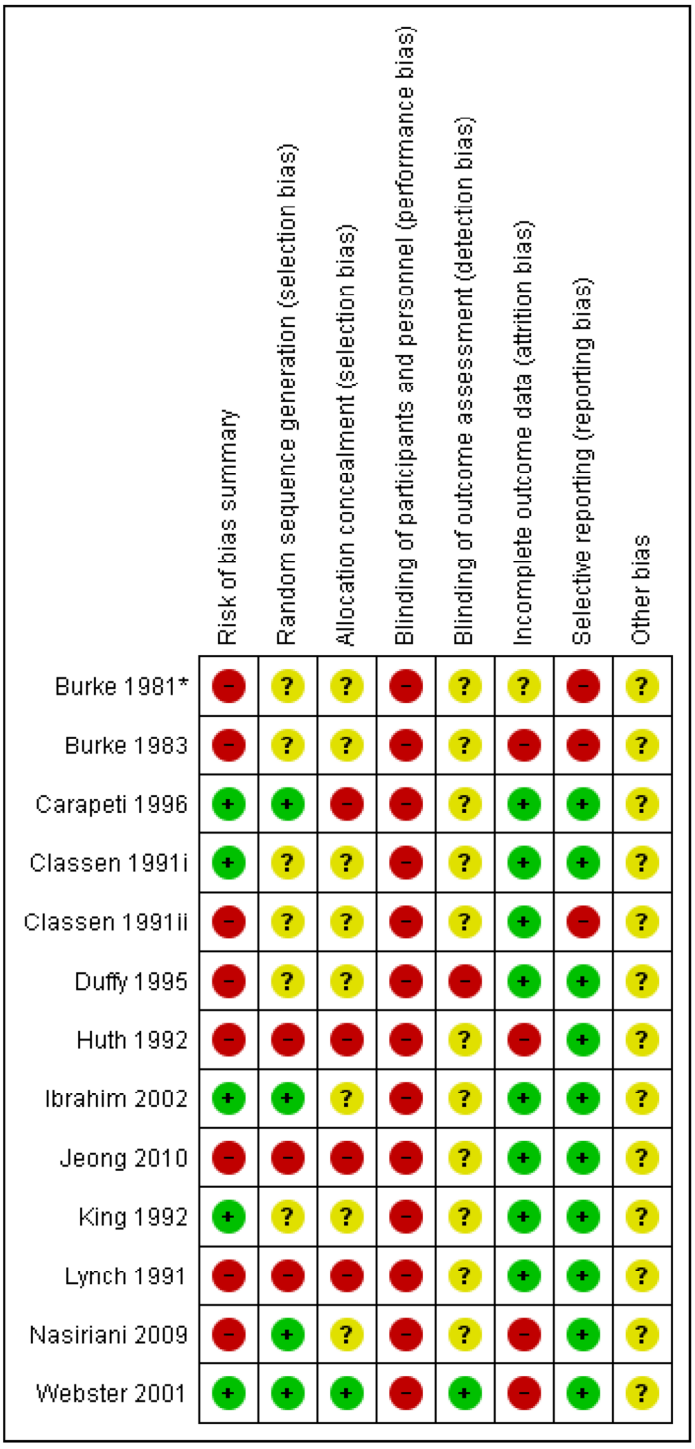

Study
OR (95% CI)
Events, Treatment
Events, Control
% Weight
Povidone-iodine versus routine meatal care
Burke et al., 1981a 1.35 (0.76, 2.39) 32/200 24/194 11.47
Classen et al., 1991b 0.95 (0.45, 2.00) 14/300 15/306 6.70
Subtotal (I-squared = 0.0%, p = 0.464) 1.19 (0.75, 1.87) 46/500 39/500 18.17
Povidone-iodine versus soap and water
Duffy et al., 1995 1.32 (0.54, 3.21) 26/42 21/38 4.69
Jeong et al., 2010 0.57 (0.18, 1.80) 9/28 10/22 2.80
King et al., 1992 0.69 (0.21, 2.28) 13/23 15/23 2.64
Subtotal (I-squared = 0.0%, p = 0.476) 0.88 (0.48, 1.62) 48/93 46/83 10.12
Chlorhexidine versus water
Carapeti et al., 1996 0.85 (0.30, 2.40) 7/74 9/82 3.44
Webster et al., 2001 1.13 (0.58, 2.21) 20/217 18/219 8.41
Subtotal (I-squared = 0.0%, p = 0.645) 1.04 (0.59, 1.83) 27/291 27/301 11.85
Antibacterial versus rotuine meatal care
Burke et al., 1983 0.87 (0.41, 1.82) 14/214 16/214 6.75
Classen et al., 1991a 0.64 (0.38, 1.09) 26/383 37/364 13.62
Huth et al., 1992 0.85 (0.54, 1.34) 38/332 48/364 18.10
Lynch et al., 1991 0.48 (0.16, 1.43) 6/50 11/50 3.18
Subtotal (I-squared = 0.0%, p = 0.706) 0.75 (0.55, 1.01) 84/979 112/992 41.65
Povidone-iodine versus saline
Ibrahim and Rashid, 2002 1.13 (0.53, 2.41) 19/64 18/66 6.43
Povidone-iodine versus water
Nasiriani et al., 2009 0.80 (0.22, 2.97) 5/30 6/30 2.17
Green soap & water versus routine meatal care
Burke et al., 1981b 1.59 (0.85, 2.96) 28/229 18/223 9.61
Overall (I-squared = 0.0%, p = 0.688) 0.95 (0.78, 1.15) 257/2186 266/2195 100.00
NOTE: Weights are from random effects analysis
.164
1
6.12

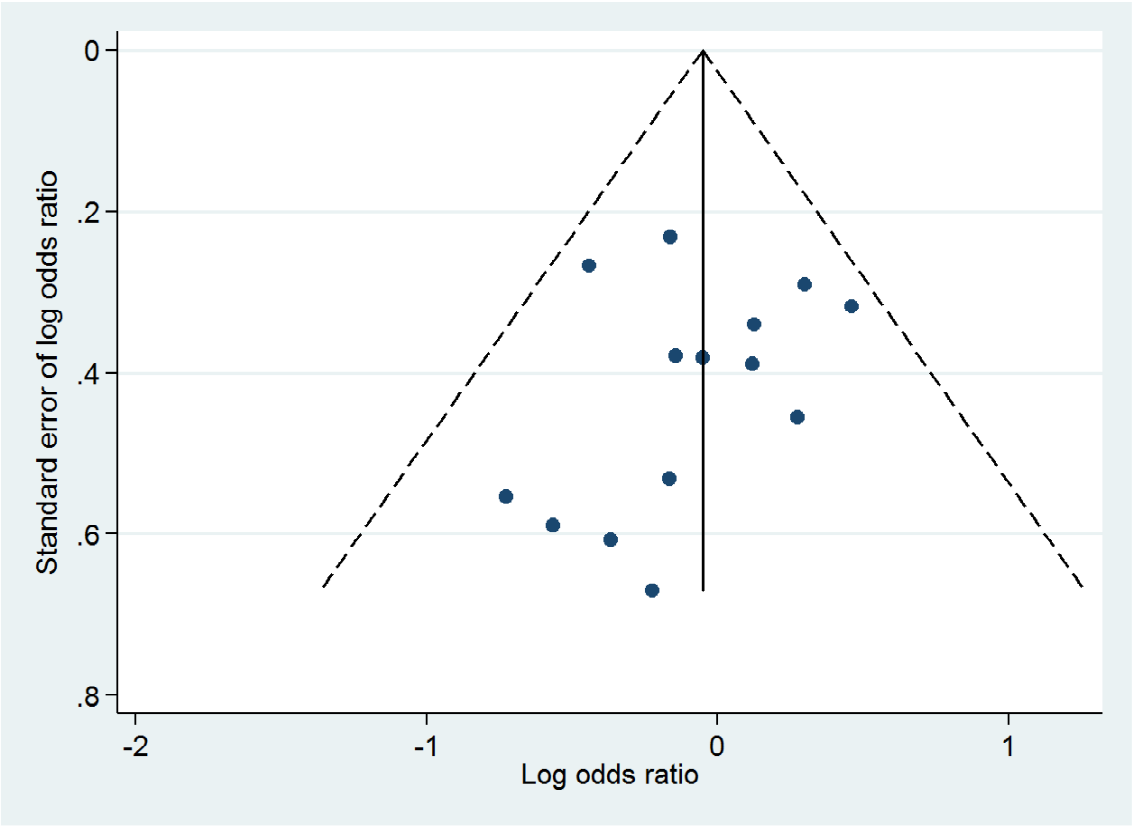
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Risk of bias summary
Random sequence generation (selection bias)
Allocation concealment (selection bias)
Blinding of participants and personnel (performance bias)
Blinding of outcome assessment (detection bias)
Incomplete outcome data (attrition bias)
Selective reporting (reporting bias)
Other bias
Burke 1981*
Burke 1983
Carapeti 1996
Classen 1991i
Classen 1991ii
Duffy 1995
Huth 1992
Ibrahim 2002
Jeong 2010
King 1992
Lynch 1991
Nasiriani 2009
Webster 2001
Low risk of bias
High risk of bias
Unclear risk of bias



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