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Use of non-pharmacological interventions during urinary catheter insertion for reducing urinary tract infections in non-immunocompromised adults. A systematic review

Intervenciones no farmacológicas durante la inserción de un catéter urinario permanente para reducir las infecciones en adultos inmunocompetentes. Revisión sistemática

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Abstract

Introduction: Catheter-associated urinary tract infections (CAUTI) account for up to 30% of hospital -acquired infections. In this regard, several studies have reported the use of non-pharmacological interventions during urinary catheter insertion aimed at reducing the occurrence rate of CAUTI. **Objective:** To assess the safety and effectiveness of non-pharmacological interventions during urinary catheter insertion aimed at reducing the risk of contracting infections in non-immuno-compromised adults.

Materials and methods: A literature review was conducted in the MEDLINE, Embase, and LILACS databases. Only randomized clinical trials comparing the use of non-pharmacological interventions to placebos, pharmacological interventions, or no intervention during catheter insertion were included. Results: Eight studies were retrieved (8 718 participants). Based on the evidence found in the review (low-quality and very low-quality evidence according to the GRADE system), using non-pharmacological interventions reduces the frequency of asymptomatic bacteriuria episodes (RR 0.67, 95%CI 0.48-0.94; 7 studies) or mild adverse events (RR 0.84, 95%CI 0.74-0.96; 2 studies), but does not reduce the occurrence rate of symptomatic urinary tract infections (RR 0.90, 95%CI 0.61-1.35; 4 studies) or improves quality-of-life scores (MD –0.01 EQ-5D scale; 95%CI (-0.03)-(0.01), 1 study). Conclusion: The use of non-pharmacological interventions during urinary catheter insertion does not pose any risk at all. Instead, it could help reduce the occurrence rate of infections associated with this procedure, such as asymptomatic bacteriuria and mild adverse events. However, there is very little evidence (in fact, low and very low-quality evidence) to make conclusions on the effectiveness of these interventions.

Keywords: Early Medical Intervention; Urinary Catheterization; Urinary Tract Infections; Cross Infection (MeSH).

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Resumen

Introducción. La infección asociada al catéter urinario es responsable de hasta un 30% de las infecciones nosocomiales. Al respecto, se ha descrito el uso de intervenciones no farmacológicas durante la inserción del catéter urinario para reducir la frecuencia de infecciones asociadas.

Objetivo. Evaluar la seguridad y la efectividad de intervenciones no farmacológicas durante la inserción del catéter urinario diseñadas para reducir el riesgo de infección en adultos inmunocompetentes. **Materiales y métodos.** Se realizó una búsqueda en las bases de datos MEDLINE, Embase y LILACS. Se incluyeron ensayos clínicos aleatorizados que compararan el uso de intervenciones no farmacológicas con el uso de placebos, el uso de intervenciones farmacológicas o la ausencia de intervención durante la inserción del catéter.

Resultados. Se encontraron ocho estudios (8 718 participantes). Con base en la evidencia encontrada (baja y muy baja calidad según la clasificación del sistema GRADE), el uso de intervenciones no farmacológica reduce la frecuencia de bacteriuria asintomática (RR 0.67; IC95%: 0.48-0.94; 7 estudios) o de eventos adversos menores (RR 0.84, IC95%: 0.74-0.96; 2 estudios), pero no disminuye la tasa de infecciones sintomáticas del tracto urinario (RR 0.90; IC95%: 0.61 a 1.35; 4 estudios), ni mejora las puntuaciones de calidad de vida (escala MD -0.01 EQ-5D, IC95%: (-0.03)-(0.01), 1 estudio). **Conclusión.** El uso de intervenciones no farmacológicas durante la inserción del catéter urinario no supone riesgo alguno y sí podría ayudar a disminuir la frecuencia infecciones asociadas a este procedimiento, tales como la bacteriuria asintomática y eventos adversos menores; sin embargo, hay poca evidencia, y de baja o muy baja calidad, para llegar a conclusiones sobre su efectividad. **Palabras clave:** Intervención médica temprana; Cateterismo urinario; Infecciones urinarias; Infección hospitalaria (DeCS).

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Introduction

Catheterization is a common procedure that consists of the insertion of a latex, polyurethane, or silicone tube into the bladder to drain its contents.¹ Urinary catheters can be indwelling or placed intermittently depending on the indications and the patient's condition. Intermittent catheters are inserted every 6 to 8 hours,² while indwelling catheters are inserted for a period of time greater than 24 hours, and are usually connected to a collection bag.³ Indwelling catheterization is typically used in patients with pathologies such as prostatic hyperplasia, neurogenic bladder, urinary retention, severe urinary incontinence, as well as critically ill patients⁴ and those with pressure ulcers in the sacral region, or with contaminated perineal lesions associated with incontinence.⁵

Urinary catheterization is a minor procedure undertaken in up to 25% of all hospitalized patients. It carries substantial risks and causes high morbidity and mortality secondary to bacteremia, as well as longer hospital stays and higher resource consumption. Catheter-associated urinary tract infection (CAUTI) accounts for up to 30% of health-care associated infections. In Latin America, CAUTI is the third leading cause of nosocomial infections and its incidence is estimated at 8.9 cases per 1 000 days of exposure to this device. In Colombia, the estimated prevalence is 12% to 45%, which makes it one of the top five infections reported in the country. In Bogotá, a prevalence of 16.1% was reported for the 2012-2013 period, with an incidence rate of 3.9 cases per 1 000 days of exposure.

Since urinary catheterization carries substantial risks, multiple interventions have been described with the aim of reducing the occurrence of infectious processes. Non-pharmacological interventions include staff training in catheter insertion and care.8 Access to guidelines and algorithms allows standardizing interventions that avoid variability among healthcare staff and guide the timely removal of unnecessary catheters.^{7,9} Hand washing before and after catheter insertion and manipulation reduces non-saprophytic microflora without affecting the saprophytic microflora of the skin.^{5,7} Using an aseptic technique, sterile equipment and supplies during the preparation of the catheter insertion area and during the insertion, using barrier measures such as sterile gowns and gloves; 10 and the use of antiseptics for cleaning the urinary meatus help reduce microbial load and the entrainment of microorganisms.5,11

In addition, the lubricant applied prior to insertion contributes to bladder neck relaxation, facilitating the passage of the catheter, and also prevents urethral trauma, false passages and pain. ¹⁰ Inserting a catheter of the smallest possible size can minimize urethral trauma and lead to a more effective drainage, ^{5,12} while using a closed drainage system makes it more difficult for microorganisms to colonize the urethral meatus intraluminally. ¹³

Regarding pharmacological interventions, silicone catheters are recommended for patients requiring a long-term urinary catheter and in those with frequent obstruction of the device. Antimicrobial-coated catheters are used in patients with a CAUTI that does not

decrease with the application of primary strategies. Finally, the consumption of blueberries, ¹⁴ lactobacilli¹⁵ and Chinese herbal medicines¹⁴ has also been proposed to prevent urinary infections.

Since the use of catheters in clinical practice is heterogenous and considering the frequency of adverse events and the appearance of infections associated with their insertion and use, this systematic review seeks to assess the effects of non-pharmacological interventions aimed at reducing the probability of CAUTI in the adult population. This will help develop policies designed to standardize the care of adult patients with urinary catheterization.

Materials and methods

The report was developed following the recommendations suggested by the Cochrane Handbook (CHB)¹⁶ and in accordance with the PRISMA statement.¹⁷ Review methods were established before conducting the literature search, which is detailed at http://www.crd.york.ac.uk/PROSPERO/display_record.php?ID=CRD42017051553. Ethical approval was not required because this is a secondary study.

An attempt was made to identify as many relevant randomized controlled trials (RCTs) as possible, regardless of their language of publication. To this end, the Information Specialist of The Cochrane STI Group was contacted to conduct a complete search strategy, which was constructed using controlled vocabulary and text terms. The search was conducted in the MEDLINE, EMBASE, and LILACS databases. Grey literature was also consulted through the references listed in the included studies. The search was updated to September 30, 2016 (available at: https:// www.crd.york.ac.uk/PROSPEROFILES/51553 STRAT-EGY_20161121.pdf) and citations were exported to EndNote version X6 (Thomson Reuters, New York, NY, USA). All published RCTs were included with no language restrictions.

The participants in the trials were non-immunocompromised men and non-pregnant women that required an indwelling urinary catheter as part of their inpatient or outpatient medical treatment. Indwelling urinary catheters are as those inserted for at least 24 hours in the urinary tract. The intervention of interest was the use of any non-pharmacological intervention during catheter insertion versus the use of placebo, or pharmacological interventions, or no intervention.

The primary outcomes were symptomatic urinary infection, time elapsed until the first episode of urinary infection, recurrent infection, bacteremia, asymptomatic bacteriuria, and major adverse effects associated with the intervention. The main secondary outcomes were satisfaction of participants, quality of life, mild adverse events, and cost-effectiveness of the intervention.

First, two authors (XSM and CFGA) selected the studies individually, and then, through consensus, they made the final selection of studies to be included in the systematic review. In addition, the other two authors (JAG and JLMV) assessed the risk of bias of the included RCTs using the tool suggested in the CHB:¹⁶ sequence generation and allocation concealment,

blinding of participants, incomplete outcome data, selective reporting, and other risks of bias. Disagreement was resolved by consensus among all authors. All domains were assessed as low, high, or unclear risk of bias. The GRADE system was used for rating the quality of the evidence.

Results are presented as risk ratios (RR) with 95% confidence intervals (CI) and mean differences. I^2 statistic and Chi² test values were used to assess statistical heterogeneity, which was considered relevant if the I^2 statistic was greater than 40% and if there was a low p-value (less than 0.10) in the Chi² test for consistency. Statistical analyses were performed using Rev Man, I^8 with fixed-effect meta-analysis for combining data, unless there was substantial heterogeneity, while a random-effects model was implemented if there was clinical or significant statistical heterogeneity.

Results

The searches yielded 311 references, and 214 were screened after removing duplicates. Of those, the full

texts of 30 references were reviewed. A total of 8 studies met the inclusion criteria; ¹⁹⁻²⁶ 12 papers were excluded because they were not RCTs, 6 trials implemented a different intervention and finally, 4 studies recruited a different kind of population. The following PRISMA diagram illustrates the selection process (Figure 1). For excluded RCTs and the rationale for exclusion, see Appendix A.

The selected RCTs were published from 1985 to 2012 and recruited participants from Sweden, the United Kingdom, Hong Kong, New Zealand, the USA and Belgium; 2 of those studies were funded by the industry. ^{21,25} Retrieved studies involved 8 718 men and women with an age range between 20 and 95 years, who required long-term catheterization (>24 hours) during their hospital stay due to general, ^{20,24} cardiac, ²² orthopedic or elective urologic surgery; ²⁶ 3 studies did not include information in this regard. ^{19,21,23} The studies excluded patients with current or previous urinary tract infection, recent exposure to antibiotics, history of diabetes or pelvic radiotherapy, or with a recent illness (Table 1).

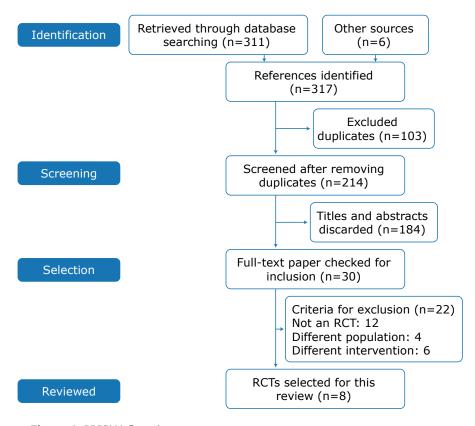


Figure 1. PRISMA flow chart. Source: Own elaboration.

The intervention most commonly implemented was silicone-coated latex catheter in 5 studies; ^{21,23-26} 2 studies described sterile catheterization as the intervention; ^{19,20} and the remaining trials used non-coated silicone catheters. ²² The comparator in 6 studies was non-coated silicone urinary catheter ²¹⁻²⁶ and in the other 2 it was clean/non-sterile catheterization technique. ^{19,20}

Sterile catheterization is the process of cleaning the urethral meatus utilizing an antiseptic aqueous solution and avoiding contact with the practitioner's gloves. The catheter is inserted following a non-touch technique and using forceps after lubrication with sterile lignocaine gel. On the other hand, participants assigned to non-sterile catheterization used sterile water and non-sterile gloves. 19,20

Table 1. Main characteristics of the studies selected.

Author	Carappetti et al.19	Cheung <i>et</i> <i>al.</i> 20	Liedberg & Lundberg et al.21	Nacey <i>et</i> <i>al.</i> 22	Pickard <i>et al.</i> 23	Riley <i>et</i> <i>al.</i> 24	Stenzelius et al.25	Verleyen et al.26
Year	1994	2008	1990	1985	2012	1995	2011	1999
Study design	RCT	RCT	RCT	RCT	RCT	RCT	RCT	RCT
Title	Randomized study of sterile versus non-sterile urethral catheterisation	Water versus antiseptic periurethral cleansing before catheterization among home care patients: a randomized controlled trial	Silver alloy coated catheters reduce catheter- associated bacteriuria	Catheter induced urethritis: a comparison between latex and silicone catheters in a prospective clinical trial	Antimicrobial catheters for reduction of symptomatic urinary tract infection in adults requiring short-term catheterisation in hospital: a multicentre randomised controlled trial	A large randomized clinical trial of a silver- impregnated urinary catheter: lack of efficacy and staphylococcal superinfection	Noble metal alloy-coated latex versus silicone Foley catheter in short-term catheterization: a randomized controlled study	Clinical application of the Bardex IC Foley catheter
Country	England	Hong Kong	Sweden	New Zealand	United Kingdom	Salt Lake City	Sweden	Belgium
Population		Elective surgery		Elective Cardiac surgery		Surgery or Internal Medicine	Elective orthopedic surgery	Elective urologic surgery
Age	22-91	mean 80.8	48-52	20-73	mean 59	mean 61.4	20-95	
Number of participants	156	20	120	100	6 394	1 309	439	180
Intervention	Sterile catheterisation	Sterile catheterization	Silver coated latex catheter	Silicone catheter	Silver alloy- coated latex catheter	Silver coated silicone catheter	Noble metal alloy coated latex catheter	Silver- coated catheter
Comparison	Clean/ non-sterile catheterisation	Sterile water	Teflonised latex catheter	Latex catheter	PTFE-coated latex catheter	Silicone elastomer- coated latex catheter	Non-coated silicone catheter	Latex catheters
Primary outcomes	Bacteriuria	Symptomatic bacteriuria	Bacteriuria	Urethritis	Symptomatic CAUTI	Bacteriuria	Bacteriuria	Bacteriuria
Secondary outcomes	Costs				- Microbiologically confirmed symptomatic CAUTI - Quality of life - Catheter-related symptoms	Catheter- related symptoms	Catheter- related symptoms	Time to develop bacteriuria

RCT: Randomized controlled trial; PTFE: Polytetrafluoroethylene; CAUTI: Catheter-Associated Urinary Tract Infection. Source: Own elaboration.

The included RCTs assessed at least one predetermined outcome, with some minor differences in the definition of the results between papers. A total of 7 studies reported bacteriuria as the primary outcome^{19-21,23-26} using as threshold 10⁵ colony-forming units (CFU) per milliliter (mL), except for one study²⁴ that defined a lower threshold (>1.000 CFU/mL). Three studies reported symptomatic urinary infection —defined as penile discomfort and purulent urethral discharge²² reported by the patient or the caregiver—, bacterial colonization in urine,²⁰ or the presence of symptoms accompanied by antibiotic prescription.²³

Urine specimens were collected at the time of catheterization, $^{19-21,25}$ at the time of catheter removal, 21,24,26 or within 7 to 14 days 20,23,25 after catheterization. The secondary outcomes reported by the trials were quality of

life (EuroQol scale; EQ-5D), ²³ mild adverse events, ²⁴⁻²⁶ and costs of the intervention. ¹⁹ For this study, data for primary outcomes (time elapsed until the first episode, recurrent urinary tract infection, bacteremia, or significant side effects), or the secondary outcome (patient satisfaction) were not collected. Finally, follow-up of participants ranged between 3 and 14 days, ^{19,21,25,26} 6 weeks, ²³ or 6 months. ²²

According to the GRADE system, publications bias should be assessed using a funnel plot and asymmetry statistical tests if 10 or more studies are included in a systematic review or a meta-analysis; therefore, since only 8 studies were included in this review, a funnel plot was not required to assess publication bias. The RCTs included (n=8) had limitations regarding the use of risk of bias tools, which are detailed in Figure 2 and Appendix B. In

this regard, 4 trials^{19,22,23,25} implemented a valid sequence generation method and 3 established an adequate allo-

cation concealment process (Figure 2), 19,22,23,25 making selection bias unclear.

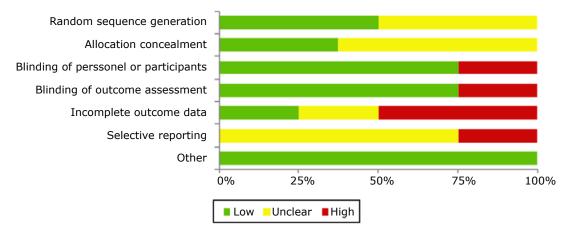


Figure 2. Risk of bias assessment of the included randomized clinical trials. Source: Own elaboration.

Regarding blinding, 5 studies 19-21,24,26 did not report the method implemented. However, the studies were considered to be at low risk of detection and performance bias since the results were objectively appraised (i.e., culture) and, therefore, the lack of blinding is unlikely to affect confidence in the results. One study 22 was masked to the allocated intervention because of the similarity of the interventions, making performance and detection bias unlikely. Finally, 23,25 the participants of 2 trials were not masked to the intervention because of the distinctive appearance of the catheters; based on the subjective nature of some outcomes (i.e., mild

adverse events of the intervention), these RCTs were considered as having high risk of performance and detection bias.

With respect to possible attrition bias, 2 RCTs^{22,24} appropriately mentioned the exclusions (<20%) and the reasons were balanced between the arms, making incomplete outcome data bias unlikely. For 6 studies, trial protocols were not available and were assessed as having unclear risk of bias. ^{19-22,24,26} Finally, all RCTs were at low risk of other potential sources of bias. Table 2 presents a detailed description of the quality of the evidence.

Table 2. Quality of the evidence regarding non-pharmacological interventions at the time of insertion of an indwelling catheter for reducing urinary tract infection in non-immunocompromised adults.

Outcomes	Abs	colute effects* (95% CI)	Relative effect	№ of participants	Quality of the evidence (GRADE)	
Outcomes	Risk without any intervention	Any non-pharmacological intervention	(95% CI)	(studies)		
Symptomatic urinary infection	136/1000	123/1000 (83-184)	RR 0.90 (0.61-1.35)	4762 (4 RCTs)	VERY LOW *,	
Asymptomatic bacteriuria	175/1000	117/1000 (84-164)	RR 0.67 (0.48-0.94)	5810 (7 RCTs)	LOW *,**	
Mild adverse events after the intervention	193/1000	162/1000 (143-186)	RR 0.84 (0.74-0.96)	4157 (2 RCTs)	LOW *,++	
Quality of life		MD - 0.01 (-0.03-0.01)	+	3672 (1 RCT)	LOW ‡,‡‡	

RR: Relative risk.

Source: Own elaboration.

Low-quality evidence showed that, compared to the control group, the use of non-pharmacological intervention does not seem to decrease the frequency of symptomatic urinary infections^{20,22,23,25} (RR 0.90, 95%CI: 0.61-1.35; 4 762 participants, 4 RCTs; I2 statistic:

63%), or improve quality-of-life scores (MD –0.01 EQ-5D scale; 95%CI: -0.03 - 0.01, 1 RCT) (Figure 3). However, there was evidence of differences between groups in terms of asymptomatic bacteriuria episodes^{19-21,23-26} (RR 0.67, 95%CI: 0.48-0.94; 5 810 participants,

^{*} Two trials have high risk of detection, attrition and reporting bias.

[†] Heterogeneity I²=63%.

[‡] CI overlaps the line of no difference and failed to exclude appreciable benefit or harm.

^{**} Relevant heterogeneity I2= 71%.

^{††} Heterogeneity I2=0%.

^{##} High risk for detection, attrition, and selective reporting.

7 studies; I2 statistic: 71%) (Figure 4) and the rate 0.96; 4 157 participants, 2 trials; I2 statistic: 0%) of mild adverse events^{23,25} (RR 0.84, 95%CI: 0.74- (Figure 5).

Non-pharmacologic	Control		Risk	Ratio		
Study or Subgroup	Events	Total	Events	Total	Weight	M-H. Random 95%CI
Cheung 2008	0	12	0	8		Not estimable
Nacey 1985	1	50	11	50	3.7%	0.99 [0.01, 0.68]
Pickard 2012	263	2097	271	2144	55.6%	0.99 [0.85, 1.16]
Stenzelius 2011	45	202	45	199	40.6%	0.99 [0.68, 1.42]

Total (95%CI)

Total events 309

Heterogeneity: Tau 2 =0.07: Chi 2 =5.47 df=2(P = 0.06): I 2 =63%

Test for overall effect: Z=0.49 (P=0.62)

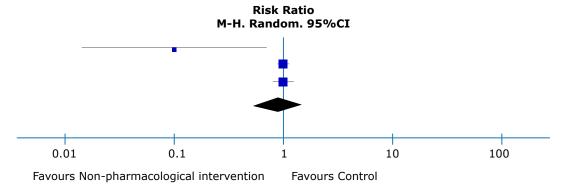


Figure 3. Symptomatic urinary infection as an outcome after performing any of the non-pharmacological interventions during catheter insertion. Source: Own elaboration.

Non-pharmacologi	Control		Risk	Ratio		
Study or Subgroup	Events	Total	Events	Total	Weight	M-H. Random 95%CI
Carapeti 1994	7	12	0	8		Not estimable
Cheung 2008	0	50	11	50	3.7%	0.99 [0.01, 0.68]
Liedberg 1990	6	2097	271	2144	55.6%	0.99 [0.85, 1.16]
Pickard 2012	310	202	45	199	40.6%	0.99 [0.68, 1.42]
Riley 1995	85	745	73	564	23.7%	0.88 [0.66, 1.18]
Stenzelius 2011	3	202	11	199	5.7%	0.27 [0.08, 0.95]
Verleyen 1999	28	79	60	101	22.4%	0.60 [0.43, 0.84]
Total (95%CI)		2957		2853	100.0%	0.67 [0.48, 0.94]
Total events	439		498			

Heterogeneity: Tau²=0.10: Chi²=20.57 df=6(P=0.002): I²=71%

Test for overall effect: Z=2.31 (P=0.02)

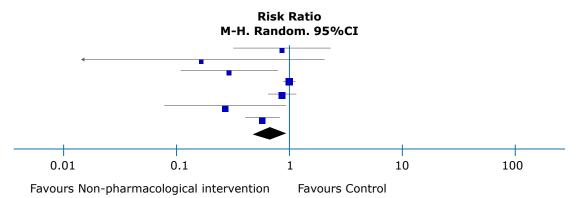


Figure 4. Asymptomatic bacteriuria as an outcome after performing any of the non-pharmacological interventions during catheter insertion. Source: Own elaboration.

Non-pharmacological intervention			Control		Risk	Ratio	
Study or Subgroup	Events	Total	Events	Total	Weight	M-H. Random 95%CI	
Pickard 2012	322	1829	396	1889	97.2%	0.84 [0.74, 0.96]	
Stenzellus 2011	9	222	11	217	2.8%	0.80 [0.34, 1.89]	
Total (95%CI)		2051		2106	100.0%	0.84 [0.74, 0.96]	
Total events	331		407				
Heterogeneity: Chi ² =0.01 df=1 (P=0.91): I^2 =0%							
Test for overall effect: Z=2.64 (P=0.008)							

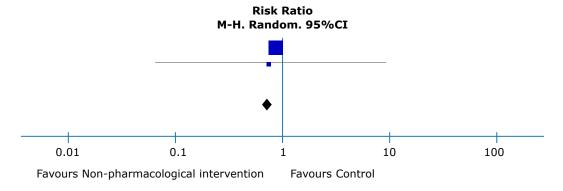


Figure 5. Mild adverse events as outcomes after performing any of the non-pharmacological interventions during catheter insertion.

Source: Own elaboration.

Carappetti *et al.* ¹⁹ measured resource and capital expenditure associated with the implementation of sterile interventions compared to clean catheterization. The recruited participants underwent preoperative urethral catheterization and the direct costs were estimated based on the supplies utilized: gloves, sterile gown, catheter pack, lignocaine gel, vaginal gel, sterile water, 10-milliliter syringes, catheter bag, Foley catheter, scrub solution, and skin preparation. Compared with clean catheterization, sterile technique doubled care-associated costs, as the total cost per participant was close to GBP 7.49 versus GBP 3.06, respectively, in 1994. This study did not assess indirect or long-term intervention-related costs.

To explore heterogeneity, a subgroup analysis was performed for the *asymptomatic bacteriuria* outcome. The tests for subgroup effect were not significantly different when the source of heterogeneity was explored (p=0.54, data not shown). Subgroup analyses did not explain the variability in the summary effect measures for the *asymptomatic bacteriuria* outcome, so these findings should be interpreted with caution. The outcomes *symptomatic urinary infection*, *time elapsed until the first episode of urinary tract infection* and *major adverse effects derived from the intervention* were not analyzed because of the sparse information provided by the RCTs included in the present review.

Discussion

This systematic review retrieved low-quality evidence to support the implementation of non-pharmacological interventions at the time of urinary catheter insertion to reduce the risk of infection in non-immunocompromised adults with indwelling catheterization. Regardless of the comparison, non-pharmacological interventions seem to reduce the frequency of asymptomatic bacteriuria episodes and the rate of mild adverse events.

One of the strengths of this systematic review is that its methodology was planned, developed and published at PROSPERO before conducting it, and all the methods that were established at that time were followed while doing the review, namely, a comprehensive literature search without language or date restrictions, two reviewers in charge of the selection of studies, data extraction and bias risk assessment using the tool suggested in the CHB; ¹⁶ evidence ranking by means of the GRADE approach; and the use of subgroup analyses and methods for statistical analysis.

One of the weaknesses of the present review is that the quality of the evidence found was very low according to the GRADE system; therefore, further research is highly likely to change the conclusions presented here. On the other hand, the RCTs included were heterogenous and publication bias was not assessed using a funnel plot due to the recommendation of the GRADE system regarding the detection of this type of bias when less than 10 studies are included in a meta-analysis or a systematic review.

There were no other systematic reviews evaluating the impact of non-pharmacological interventions for catheter insertion in cases of urinary tract infection that require long-term catheterization. Consistent with this review, a Cochrane review concludes that the use of silver-coated catheters reduces the frequency of asymptomatic bacteriuria, but the studies reviewed there only assessed short-term catheterization.²⁷

Conclusion

Very low-quality evidence shows that non-pharmacological interventions at the time of urinary catheter insertion in non-immunocompromised adults could reduce the frequency of asymptomatic bacteriuria episodes and mild adverse events, without reducing the rate of symptomatic urinary infections or improving quality-of-life scores.

Conflicts of interest

None stated by the authors.

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Appendix A. Characteristics of the excluded studies.

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Appendix B. Summary of risk of bias according to the authors of this review for each included study

