

# Systematic Review: Antimicrobial Urinary Catheters To Prevent Catheter-Associated Urinary Tract Infection in Hospitalized Patients

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**Background:** The efficacy of antimicrobial urinary catheters in hospitalized patients is poorly defined.

**Purpose:** To assess currently marketed antimicrobial urinary catheters for preventing catheter-associated urinary tract infection (UTI).

**Data Sources:** Electronic databases, conference proceedings, bibliographies, trialists, and catheter manufacturers (search dates, 1966 to June 2005).

**Study Selection:** Randomized and quasi-randomized trials of nitrofurazone-coated or silver alloy-coated antimicrobial urinary catheter use for less than 30 days; no language restriction.

**Data Extraction:** Study design, study sample, inclusion and exclusion criteria, allocation, blinding, UTI definition, ascertainment methods, and proportion developing symptomatic UTI (primary end point) or bacteriuria (secondary end point) were extracted by using a structured data collection instrument.

**Data Synthesis:** Twelve qualifying trials (13 392 total participants or catheters) were identified. They compared nitrofurazone-coated silicone ( $n = 3$ ) or silver-coated latex ( $n = 9$ ) catheters with silicone or latex catheters. No study addressed symptomatic UTI. All trials suggested protection against bacteriuria with test catheter use.

However, effect size varied considerably and postrandomization exclusions were very common. Effect size was greatest in trials of nitrofurazone-coated catheters (all post-1995) and in pre-1995 silver alloy-coated catheter trials and was smallest in post-1995 silver alloy-coated catheter trials. Control group bacteriuria rate, control catheter type (latex vs. silicone), and patient sample (urology vs. other) also predicted effect size. Few studies addressed secondary bloodstream infection, mortality, costs, or microbial resistance. Short-term adverse effects were minimal.

**Limitations:** The study was limited by the number, size, and quality of studies and by lack of the following: intention-to-treat analyses, data on clinical end points, and trials comparing nitrofurazone-coated with silver alloy-coated catheters.

**Conclusions:** According to fair-quality evidence, antimicrobial urinary catheters can prevent bacteriuria in hospitalized patients during short-term catheterization, depending on antimicrobial coating and several other variables. Older data probably lack current relevance. Cost implications and effect on infectious complications remain undefined.

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Indwelling urinary catheters, which are used in 15% to 25% of short-term care patients during their hospitalization, confer a predisposition to bacteriuria (1–3). Catheter-associated urinary tract infection (UTI) is the most common type of hospital-acquired infection, accounting for approximately 40% of such infections and for most of the 900 000 patients with nosocomial bacteriuria in U.S. hospitals each year (2). Adverse consequences include local and systemic morbidity, secondary bloodstream infection, death, a reservoir of drug-resistant microorganisms, and increased health care costs (1–4).

Among catheterized patients, clinical manifestations of UTI (pain, urgency, dysuria, fever, and leukocytosis) are uncommon even when bacteriuria or funguria is present and are no more prevalent with positive urine culture results than with negative results (5). Fewer than the traditionally estimated 1% to 5% of catheter-associated bacteriuria episodes produce secondary bloodstream infection (5). However, secondary bloodstream infection almost always involves gram-negative bacilli, making catheter-associated bacteriuria the primary source for nosocomial gram-negative bacteremia (6–8).

The effect of catheter-associated bacteriuria on mortality is unclear. The 3-fold mortality increase documented in 1 study (9) was not observed in other studies (5, 10–12). Many deaths among patients with secondary bloodstream infection from catheter-associated bacteriuria are probably due to un-

derlying diseases (6, 12). Although colonized catheter systems may provide a reservoir of resistant microorganisms for transmission to other patients (3, 13), the importance of this process to nosocomial infections is undefined.

Estimated costs and length of stay attributable to catheter-associated bacteriuria vary greatly (13, 14). Only a fraction of catheter-associated bacteriuria episodes come to physicians' attention. Most that do are treated despite the absence of symptoms (5), and evidence suggests that untreated episodes do not increase costs or length of hospitalization (13). Recent data indicate that even treated episodes increase costs by a mean of only \$589 (median, \$356) without prolonging hospitalization (13). Nonetheless, the enormous aggregate numbers of episodes make catheter-associated bacteriuria a clinically significant medical problem (1–4). Preventive efforts have included reduced catheter use (15); proper catheter maintenance (16); and technical modifications, including antimicrobial catheter coatings (17, 18).

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Key Summary Points ..... 117

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Four antimicrobial urinary catheters are currently marketed in the United States. They are coated with silver alloy (3 latex- or silicone-base catheters) or nitrofurazone, a nitrofurantoin-like drug (1 silicone-base catheter). Two previous meta-analyses of randomized, controlled trials (RCTs) of antimicrobial catheters concluded that trial quality was modest, that silver oxide-coated catheters (which are no longer marketed) lack efficacy, and that silver alloy-coated catheters are protective, and no conclusions were made about the prevention of symptomatic UTI, bloodstream infection, or death (19, 20). However, these meta-analyses included only trials published through 1993 (19) or 2000 (20). Moreover, they did not address nitrofurazone-coated catheters or assess outcomes in relation to study characteristics or specific microorganisms, specifically bacteremia-associated gram-negative bacilli. Accordingly, we conducted a systematic review of clinical trials to address these important questions.

## METHODS

### Search and Selection Processes

Sources included MEDLINE (since 1966), BIOSIS (since 1998), the Cochrane Library (since 1996), [www.clinicaltrials.gov](http://www.clinicaltrials.gov) (since inception), and abstracts from meetings of relevant professional societies (as available since 1998). Search terms included *catheter* and *urinary tract infection*, limited when possible to *human* and *clinical trial* but not to English language. We contacted manufacturers of currently marketed antimicrobial catheters and experts for relevant data, and we reviewed bibliographies from these sources and from our personal files. We searched such “gray literature” (21) because of the anticipated paucity of published RCTs and because both previous meta-analyses included trials reported only as abstracts (19, 20). An author retrieved and screened publications that reported clinical trials of antimicrobial catheters. The latest search date was 5 June 2005.

We required trials to be randomized or quasi-randomized and to involve an antimicrobial urinary catheter that is currently marketed in the United States, or its equivalent, for short-term (<30 days) (2) bladder drainage. Currently marketed catheters include the Lubricath IC (silver hydrogel-coated latex) and Lubrisil IC (silver hydrogel-coated silicone) catheters (Bard Medical, Covington, Georgia), the Kendall DOVER silver Foley catheter (silver hydrogel silicone) (Tyco Healthcare, Mansfield, Massachusetts), and the RELEASE-NF catheter (nitrofurazone-coated silicone) (Rochester Medical Corp., Stewartville, Minnesota). We excluded studies if data were insufficient for outcome assessment or if the catheter system included antimicrobial modifications other than the catheter coating (20). We accepted quasi-randomized trials because of the paucity of qualifying conventional RCTs and because previous meta-analyses included them (19, 20).

### Key Summary Points

Randomized or quasi-randomized clinical trials of antimicrobial urinary catheters currently marketed in the United States (i.e., nitrofurazone-coated and silver alloy-coated catheters) provide little or no data on these devices' effect on symptomatic urinary tract infection, morbidity, secondary bloodstream infection, mortality rates, or associated health care costs.

Both nitrofurazone-coated and silver alloy-coated catheters seem to reduce the development of asymptomatic bacteriuria during short-term (<30 days) use, in comparison with latex or silicone control catheters.

The magnitude of this effect varies among studies, seemingly in relation to the type of antimicrobial catheter (nitrofurazone or silver), patient sample (urology or other), control group bacteriuria rate (high or low), and type of control catheter (latex or silicone).

No trials directly compared nitrofurazone-coated and silver alloy-coated catheters. Therefore, assessments of the comparative efficacy of nitrofurazone-coated and silver alloy-coated catheters should be made cautiously.

The clinical utility and cost-effectiveness of antimicrobial urinary catheters must be assessed in well-designed, adequately powered, randomized clinical trials.

### Data Extraction

An author assessed reports of qualifying studies for locale, funding source, study design (including allocation method, allocation concealment, and blinding), study sample (including age, sex, underlying diagnoses, reason for catheter use, and similarity of comparison groups), inclusion and exclusion criteria (before and after enrollment), definition of catheter-associated UTI, UTI ascertainment methods, duration of catheter use, and outcomes. Outcomes included proportion developing symptomatic UTI (primary outcome) or bacteriuria or funguria (secondary outcome, hereafter called “bacteriuria”), both overall and by organism type. We also sought data on secondary bloodstream infection, death, adverse events, selection for resistant microorganisms, and costs. We used a standardized data form. We sought relevant details that were not included in the primary report from previous meta-analyses, trialists, and study sponsors. We discussed disagreements about article content and quality until we reached consensus.

We assessed study quality according to Schulz and colleagues (22). In addition, we assessed whether studies were blinded or reported intention-to-treat analyses and the proportion lost to follow-up. We presumed that trials not described as blinded were nonblinded. To estimate organism-

specific outcomes when more isolates were reported than bacteriuria episodes, we assumed that episodes involved the reported microbial types in proportion to their respective prevalences. We based outcome analyses on the earliest reported result at day 5 or later to minimize the effect of patient dropout while capturing a usable number of events. For a trial that randomly assigned catheter type by ward and did not track participants (catheters) individually, we analyzed outcomes on an intention-to-treat basis as the number of catheter-associated bacteriuria episodes occurring on study wards divided by the number of study catheters used on study wards (14). For sensitivity analysis, we stratified trials by catheter coating. We further stratified silver catheter trials by publication year, with 1995 as the partition date, which divided the longest interval between any 2 trials (1993 to 1998) and yielded similar-sized comparison groups, with 1 group encompassing the past decade.

### Statistical Analysis

We estimated the risk ratio (fixed effects) and associated 95% CI for individual studies by using Review Manager (RevMan) software, version 4.2 (Cochrane Collaboration, Oxford, United Kingdom). Because of the extensive heterogeneity among studies with respect to study design, patient samples, and data reporting, we did not perform quantitative pooling of results. Absolute risk reduction was the between-group difference in outcome incidence. We assessed the effect of various study characteristics on outcomes after stratifying the studies according to the characteristics of interest. We tested 2-group comparisons involving continuous variables by using the Mann–Whitney U test.

### Role of the Funding Source

The corporate sponsor, Rochester Medical Corp. (manufacturer of the nitrofurazone-coated catheter), had no role in the design, analysis, or reporting of the study or in the decision to approve publication of the finished manuscript.

## RESULTS

### Search Results

The search identified 665 possibly relevant articles (Figure 1). We excluded 609 articles that did not describe clinical trials or that described trials other than those of antimicrobial urinary catheters. We reviewed the remaining 56 reports of clinical trials of antimicrobial catheters in detail. We excluded 28 of these reports because the trials were not randomized or quasi-randomized. We excluded another 17 reports because of nonmarketed catheter use, inclusion of patients with long-term catheterization, or insufficient outcome data. Thus, the final sample was 11 reports (14, 23–32), which described 12 trials of a currently marketed antimicrobial urinary catheter for short-term bladder drainage.

The 11 reports (1 of which described 2 trials) included

7 full articles (14, 23–27, 32), 1 letter (28), and 3 abstracts (29–31). The 12 trials provided analysis of a total of 13 319 participants or catheters. Of these, 3 trials (1 conventional RCT and 2 quasi-randomized trials [621 total participants]) assessed nitrofurazone-coated silicone catheters (27, 30, 32) and 9 trials (6 conventional RCTs, 2 quasi-randomized trials [1739 total participants] [23–26, 28, 29, 31], and 1 cluster randomized trial [11 032 catheters] [14]) assessed silver-coated latex catheters. None assessed silver-coated silicone catheters.

### Study Characteristics

The 12 studies differed considerably for several characteristics, including locale, study sample, design, methods, and definition of catheter-associated bacteriuria (Tables 1 and 2). For example, 5 studies involved primarily urologic patients, 2 other studies involved nonurologic surgery patients, 4 studies included a mixture of medical and surgical patients, and 1 study included medical patients only. Men constituted 56% to 100% of participants. Typically, patients were eligible for inclusion and were randomly assigned if they were candidates for indwelling urinary catheters. Prerandomization and postrandomization exclusion criteria varied by study. Postrandomization exclusions were common in studies that reported them, involving from 21% to 27% of randomly assigned participants. Reasons for postrandomization exclusion included bacteriuria at the time of initial catheterization (most trials), antimicrobial agent therapy during catheter use (3 trials), and catheter care violations (1 trial). Only 2 trials were double-blinded. Investigators collected urine samples daily, on alternate days, or as desired, whereas the criterion for catheter-associated bacteriuria ranged from at least  $10^5$  colony-forming units per L to at least  $10^8$  colony-forming units per L (10 trials) or involved a combination of variables (2 trials) (33). The cumulative incidence of bacteriuria was variously assessed at 1 fixed interval or more after catheter insertion or over the total duration of catheterization. Many studies either reported several of these aspects unclearly or did not report them at all. Although all 12 trials were described as randomized, 4 trials allocated treatment according to alternate patients or week.

### Prevention of Catheter-Associated UTI or Bacteriuria

No report directly addressed the primary outcome of symptomatic UTI. Accordingly, we limited our analyses to secondary outcomes. The 12 studies varied greatly in the incidence of catheter-associated bacteriuria in the control group (range, 3.4% to 53.0%) and in the estimated effect size for proportion developing catheter-associated bacteriuria, with risk ratios (for test catheter vs. control) ranging from 0.08 to 0.94 and absolute risk reduction values ranging from 0.5% to 32% (Table 2). Although point estimates consistently favored the antimicrobial catheter, the 95% CIs included 1.0 for 7 studies (including the 6 most recent studies). Of note, no trial reported an intention-to-treat analysis. Instead, patients who had bacteriuria at the

time of catheter insertion or who met various other exclusion criteria usually were ignored in efficacy estimates.

### Effect of Study Characteristics

To explore the basis for the observed heterogeneity of effect, we compared outcomes with study characteristics. The 3 nitrofurazone catheter trials, all published after 1995, yielded risk ratios ranging from 0.08 to 0.68 (median, 0.54) and absolute risk reduction values of 3% to 12% (median, 7%) (Figure 2). The 2 largest of these trials involved general medical–surgical patient samples and reported similar results for risk ratio (0.54 and 0.68, respectively) and absolute risk reduction (3% and 7%, respectively). The 9 silver catheter trials segregated naturally by publication date and locale, since the 4 pre-1995 trials were from the same institution and investigator group, whereas the 5 post-1995 trials were from diverse institutions and investigators. The pre-1995 silver catheter trials yielded lower risk ratios than the post-1995 trials (0.24 to 0.44 [median, 0.32] vs. 0.53 to 0.94 [median, 0.84];  $P = 0.002$ ) and higher absolute risk reduction values (13% to 32% [median, 28%] vs. 0.5% to 6% [median, 3%];  $P < 0.001$ ). Of note, the 3 post-1995 silver catheter trials that involved general medical–surgical patients yielded similar risk ratios (range, 0.74 to 0.85 [median, 0.84]) and absolute risk reduction values (range, 0.5% to 5% [median, 2%]).

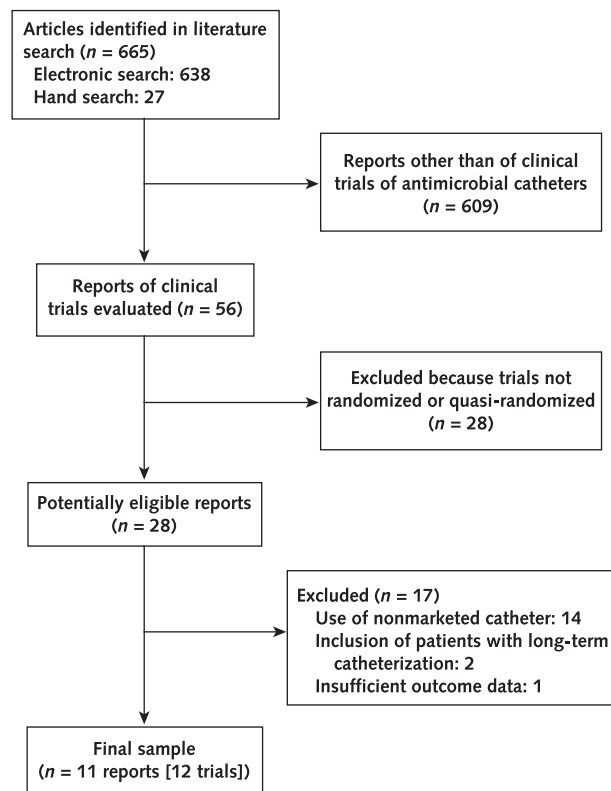
Certain additional study characteristics also predicted outcomes. The apparent protective effect of the test catheter was greater when the control catheter was latex rather than silicone. Likewise, studies involving primarily urologic patients generally yielded larger effect sizes than those involving other types of patients, as did studies that excluded patients receiving antimicrobial agent therapy. Among the silver catheter trials, control group bacteriuria rate corresponded with both effect size (positive trend) and year of publication (negative trend).

In contrast, other study characteristics were less clearly related to outcomes. Effect size did not vary consistently according to type of report, funding source, allocation method, use of blinding, duration of catheterization, bacteriuria definition, or time to outcome assessment, although the power for detecting such effects was limited. Some studies that reported outcomes at several time points had trends toward increases over time in both the risk ratio (suggesting a progressively diminishing effect of the test catheter) and absolute risk reduction (suggesting an increasing cumulative effect of the test catheter). However, these trends were inconsistent, both within and among studies.

### Specific Antimicrobial Activity

For 8 trials, available data on the distribution of microorganisms causing catheter-associated bacteriuria permitted an estimate of the effect size for preventing bacteremia-associated gram-negative bacteriuria. The 3 nitrofurazone catheter trials yielded risk ratios of 0.08 (95% CI,

Figure 1. Literature search and selection process.



0.00 to 1.33), 0.38 (CI, 0.10 to 1.42), and 1.13 (CI, 0.49 to 2.59), respectively. The latter result was derived from a study in which, exceptionally, most gram-negative isolates were nonfermenters (32), which are intrinsically resistant to nitrofurazone (34). Likewise, for silver-coated catheters, the 3 evaluable pre-1995 trials yielded risk ratios of 0.30 (CI, 0.10 to 0.93), 0.31 (CI, 0.14 to 0.74), and 0.53 (CI, 0.23 to 1.20), respectively, whereas the 2 post-1995 silver catheter trials with specific data yielded risk ratios of 0.36 (CI, 0.10 to 1.28) and 0.82 (CI, 0.61 to 1.11), respectively. A third post-1995 trial found the silver catheter to lack preventive activity against gram-negative bacilli (31).

### Adverse Effects

The 7 reports that addressed adverse effects noted few, if any, catheter-attributable complications (Table 1). Three reports stated that the test catheter (nitrofurazone catheter in 1 trial and silver catheter in 2 trials) was well-tolerated, that no urethral irritation occurred, or that both observations applied (29–31). One control participant had penile pain in 1 silver catheter trial (26), and 1 control participant and 6 test catheter participants had a burning sensation (not statistically significant) in a nitrofurazone catheter trial (32). No patient in the latter trial was considered to have UTI. The report that described an absence of urethral irritation also reported UTI as an adverse event in 5 partic-

**Table 1. Characteristics of Randomized and Quasi-Randomized Trials of Currently Marketed Antimicrobial Urinary Catheters for Prevention of Catheter-Associated Bacteriuria or Funguria during Short-Term Bladder Drainage in Hospitalized Patients\***

Study, Year (Reference)	Country	Funding Source	Test Catheter Coating (Base Catheter)	Control Catheter	Description of Participants and Inclusion and Exclusion Criteria
Lundeberg, 1986 (28)	Sweden	NR	Silver (latex)	Latex	Study sample not described (probably urologic surgery); exclusions NR
Liedberg et al., 1990 (23)	Sweden	NR	Silver hydrogel (latex)	Latex or hydrogel latex	Postoperative urologic (and other) surgery; 74% men; mean age, 58 y; excluded for antibiotics at entry, catheter use < 5 d, or other urologic procedures during catheter use
Liedberg and Lundeberg, 1990 (24)	Sweden	NR	Silver hydrogel (latex)	Teflonized latex	Postoperative urologic (and other) surgery; 69% men; mean age, 51 y; excluded for antibiotics at entry, catheter use > 6 d, other urologic procedures during catheter use, or "diabetes etc."
Liedberg and Lundeberg, 1993 (29)	Sweden	Catheter manufacturer	Silver hydrogel (latex)	Hydrogel latex	Medical surveillance and expected catheter use ≥ 21 d; 63% men; mean age, 68 y; excluded for antibiotics at entry or other urologic procedures during catheter use
Maki et al., 1997 (30)	US	Catheter manufacturer	Nitrofurazone (silicone)	Silicone	Mixed medical–surgical; 69% men; mean age, 56 y; excluded for pregnancy, inability to consent, previous catheter use, >7 d in hospital before study, or nitrofurazone allergy
Maki et al., 1998 (31)	US	Catheter manufacturer	Silver hydrogel (latex)	Silicone	Mixed medical–surgical; sex, age, and exclusions NR
Verleyen et al., 1999A (25)	Belgium	NR	Silver hydrogel (latex)	Silicone	Post-radical prostatectomy; 100% men; age NR; excluded for antibiotics during catheter use, hematuria, or violations of closed system
Verleyen et al., 1999B (25)	Belgium	NR	Silver hydrogel (latex)	Latex	Urology ward (23% radical prostatectomy); 56% men; age NR; excluded for antibiotics during catheter use or hematuria
Thibon et al., 2000 (26)	France	Public	Silver hydrogel (latex)	Silicone	Intensive care and neurosurgery (multicenter), >3 d of catheter use, >10 d in hospital; 56% men; mean age, 60 y; excluded for allergy (silver or hydrogel), antibiotics for UTI, previous catheter use (within 48 h), urology procedure, or UTI on day 0 or day 2
Karchmer et al., 2000 (14)	US	Catheter manufacturer	Silver hydrogel (latex)	Silicone-coated latex	All hospital wards (except OB-GYN, pediatrics, and psychology); sex and age NR; no exclusions (for intention-to-treat analysis)
Al-Habdan et al., 2003 (27)	Saudi Arabia	None	Nitrofurazone (silicone)	Latex	Postoperative orthopedic and trauma surgery; 75% men; mean age, 43 y; exclusions NR
Lee et al., 2004 (32)	Korea	Catheter distributor	Nitrofurazone (silicone)	Silicone	Mixed medical–surgical patients; 5 large university hospitals (40 participants each)

\* CDC = Centers for Disease Control and Prevention (33); CFU = colony-forming units; NR = not reported; OB-GYN = obstetrics and gynecology; US = United States; UTI = urinary tract infection.

† Quality of allocation concealment based on system of Schulz et al. (22), with 3 = adequate (best), 2 = uncertain (intermediate), and 1 = definitely not concealed (poor).

ipants (catheter assignment not specified) (29). The meaning of UTI in this context, and how these participants corresponded with the 110 participants who developed bacteriuria, is unclear. Finally, in another trial, approxi-

mately 5% of participants in each group developed hematuria while using a silver alloy–coated or latex catheter, although hematuria was not reported as an adverse event (25).

Table 1—Continued

Allocation Method; Quality of Allocation Concealment;† Double-Blinded	Participants Enrolled; Dropouts or Exclusions after Enrollment, <i>n</i>	Participants Included in Analysis, <i>n</i>	Test and Control Participants Well-Matched	Schedule for Urine Culture	Definition of Catheter-Associated Bacteriuria or Funguria (UTI)	Duration of Catheter Use	Time Point Used for Outcome Assessment, <i>d</i>	Adverse Events (Monitoring and Occurrence)
Randomized; 2; no	NR; NR	102	NR	Daily	$\geq 10^5$ CFU/L	NR	6	NR
Randomized; 2; no	NR; NR	90	Yes	Daily	$\geq 10^8$ CFU/L	$\geq 5$ d (all)	5	NR
Randomized; 2; no	NR; 103 excluded (unclear whether before or after enrollment)	120	Yes	Daily	$\geq 10^8$ CFU/L	Expected < 6 d (actual duration, NR)	6	NR
Randomized; 2; no	NR; NR	171	Yes	Daily	$\geq 10^8$ CFU/L	Expected > 21 d (actual duration, NR)	7	No urethral irritation; pneumonia ( <i>n</i> = 22), UTI ( <i>n</i> = 5), and sepsis ( <i>n</i> = 1) (group distribution NR)
Randomized; 2; yes (blinded assessor, patients ostensibly unaware of catheter type)	NR; NR	344	Yes	Daily	$\geq 10^6$ CFU/L	Median, 2 d (test and control) (range, 1–7 d)	7	Test catheter “well-tolerated” (assessed daily)
Randomized; 2; yes (test ostensibly indistinguishable from control)	NR; NR	850	NR	Daily	NR	NR	NR	Test catheter “well-tolerated”; urine leukocyte count not different, test vs. control
Alternate weeks; 1; no	35; 8 (23%)	27	NR	Alternate days	$\geq 10^8$ CFU/L	14 d (all participants)	14	NR (5 with hematuria; distribution by group NR)
Alternate weeks; 1; no	228; 48 (21%) (33 [14%] for early UTI)	180	Yes	Alternate days	$\geq 10^8$ CFU/L	Median, 5 d (test and control) (range, 2–14)	5	NR (4 with hematuria; distribution by group NR)
Randomized; 2 (computer-generated randomization list); yes (identical packing, “neither . . . patient nor . . . medical staff knew . . . type of catheter”)	274; 75 (27%) (22 [8%] for early UTI)	199	Yes	NR	$\geq 10^8$ CFU/L and pyuria, or $10^6$ – $10^8$ CFU/L $\times$ 2	Median, 5.9 d (test and control) (range, 2–10)	Total (mean duration, 5.9 d)	Intense burning in penis ( <i>n</i> = 1 [control]); death ( <i>n</i> = 5; distribution by group NR)
Randomized by ward, with crossover (6 mo on, 1 mo off, 6 mo on); 2; no	11 032; none	11 032	Unknown	Ad hoc (per provider)	Per CDC (urinalysis and culture not required)	NR	Total (mean duration NR)	NR
Alternate patients; 1; unclear (patients and assessors ostensibly unaware of catheter type)	NR; NR	100	Yes	Alternate days	$\geq 10^8$ CFU/L	Median, 7.9 d (test) vs. 7.2 d (control) (range, 2–30)	Total (mean duration, 7.5 d)	NR
Alternate patients; 1; no (patients ostensibly unaware of catheter type)	NR; NR	177	Percentage of men: test vs. control ( <i>P</i> = 0.003)	Daily	$\geq 10^6$ CFU/L	Median, 4.4 d (test) vs. 3.9 d (control) (range, 1–7 d) ( <i>P</i> = 0.054)	7	Burning sensation ( <i>n</i> = 6 [test] and 1 [control]); none had catheter-associated UTI

### Selection for Resistant Microorganisms

No report described the susceptibility of urine (or other) microbial isolates from participants to the test antimicrobial compound, although 1 abstract mentioned protection against catheter-associated bacteriuria without selection for resistant organisms (31). Among those studies that reported microbiological outcomes by study group, no evidence suggested that test catheter recipients experienced

an increased incidence of isolation of specific microbial types that are typically resistant to the antimicrobial compound used.

### Other Outcomes

No study directly assessed transmission of resistant microorganisms, costs, or hospital length of stay. One study, of a silver catheter, reported the frequency of presumed

**Table 2. Summary Characteristics of 12 Randomized or Quasi-Randomized Clinical Trials of Antimicrobial Urinary Catheters\***

Study Characteristic	Studies Providing Data, n	Distribution or Range of Data
Location	12	Belgium (2 studies), France (1 study), Korea (1 study), Saudi Arabia (1 study), Sweden (4 studies), and United States (3 studies)
Patient sample	12	
Urologic surgery	5	
Nonurologic surgery†	2	
Mixed medical and surgical	4	
Medical only	1	
Exclusions (enrollment or analysis)	8	
In hospital > 7 d before entry	1	
Antibiotics at entry	3	
Recent catheter use	1	
Antibiotics while in study	3	
Early UTI in study	1	
Hematuria while in study	2	
Urologic procedure during study	3	
Violations of closed system	1	
Number of participants or catheters (median by study)	12	27–11 032 participants or catheters (median among studies, 158)
Proportion of men (median by study)	9	57%–100% (median among studies, 69%)
Mean age (median by study)	7	43 y–68 y (median among studies, 56 y)
Test catheter	12	Nitrofurazone (3 studies) and silver (9 studies)
Control catheter	12	Latex (6 studies), silicone-coated latex (1 study), and silicone (5 studies)
Allocation method‡	12	
Random assignment‡	7	
Cluster randomized	1	
Quasi-randomized (systematic alternation)‡	4	By week (2 studies) and by patient (2 studies)‡
Double-blinded	3	
Frequency of urine sampling	12	Daily (8 studies), alternate days (3 studies), and ad hoc (1 study)
Definition of catheter-associated UTI	11	≥10 <sup>5</sup> CFU/L (1 study), ≥10 <sup>6</sup> CFU/L (2 studies), ≥10 <sup>8</sup> CFU/L (7 studies), and composite end point (2 studies)
Time point used for outcome assessment	11	
Fixed end point (median by study)	8	5 d–14 d (median among studies, 7 d)
Mean total duration of catheterization	3	5.9 d (1 study), 7.5 d (1 study), and NR (1 study)

\* CFU = colony-forming units; NR = not reported; UTI = urinary tract infection.

† Nonurologic surgery may have included stay in the intensive care unit.

‡ All trials were described as randomized, including the 4 trials that were quasi-randomized. Only 3 trials reported the actual method of allocation (random number list [*n* = 1]; weekly alternation of catheter type [*n* = 2]). In 2 ostensibly randomized trials, the investigators reported the actual allocation method (i.e., alternate patients). Some of the remaining ostensibly randomized trials also may have been quasi-randomized rather than randomized.

secondary bloodstream infection, which was non-statistically significantly higher in the control group (14). Mortality was reported only for the 14 patients with presumed secondary bloodstream infection, 3 of whom died in the hospital; 2 of those deaths may have been related to the bloodstream infection (14). A supplemental source reported that only 1 participant in 2 trials (of 1194 participants) had received a diagnosis of secondary bloodstream infection (5, 30, 31). Finally, 1 trial excluded a control participant and 3 participants with silver catheters from analysis because they died before day 3 (26), whereas in another trial, 22 participants developed pneumonia and 1 participant developed sepsis. Catheter assignment and the relationship (if any) of these complications to the catheter were not reported (29).

## DISCUSSION

In our systematic review of randomized and quasi-randomized clinical trials of currently marketed antimicrobial urinary catheters, we found minimal data on clinically

meaningful end points. However, we found abundant evidence that, in comparison with standard catheters, antimicrobial catheters can prevent or delay the onset of bacteriuria during short-term bladder drainage in selected hospitalized patients. This effect varied substantially among studies in relation to catheter type, year of publication, patient characteristics, and certain other variables, with recent trials of silver alloy-coated catheters suggesting substantially less effect than that observed in earlier trials of silver alloy-coated catheters or in recent nitrofurazone catheter trials. Moreover, given the highly selected study sample, several postenrollment exclusions, and absence of intention-to-treat analyses, many of these efficacy estimates probably represent idealized projections that are unlikely to be realized in practice.

The considerable heterogeneity of effect size among the 9 silver catheter trials could be largely eliminated by stratification according to various study characteristics, including publication year, patient sample, type of control catheter, and control group bacteriuria rate. Most of these

variables coalesced around the 4 earliest studies (1986 to 1993), which were from the same institution, were non-blinded, involved the same investigators, assessed mainly urology patients, were relatively small, used latex control catheters, and had high control group bacteriuria rates (23, 24, 28, 29). On the basis of these 4 trials, the authors of a previous meta-analysis and a subsequent cost-benefit analysis concluded that silver alloy-coated catheters are substantially more effective than silver oxide-coated catheters (19) and may be cost-effective (35). However, given the different results obtained in more recent RCTs of silver alloy catheters, the relevance of these 4 early studies to current practice is doubtful, especially for nonurology patients, institutions with low background rates of catheter-associated bacteriuria, and institutions already using silicone catheters or avoiding latex products because of allergy concerns (36–38).

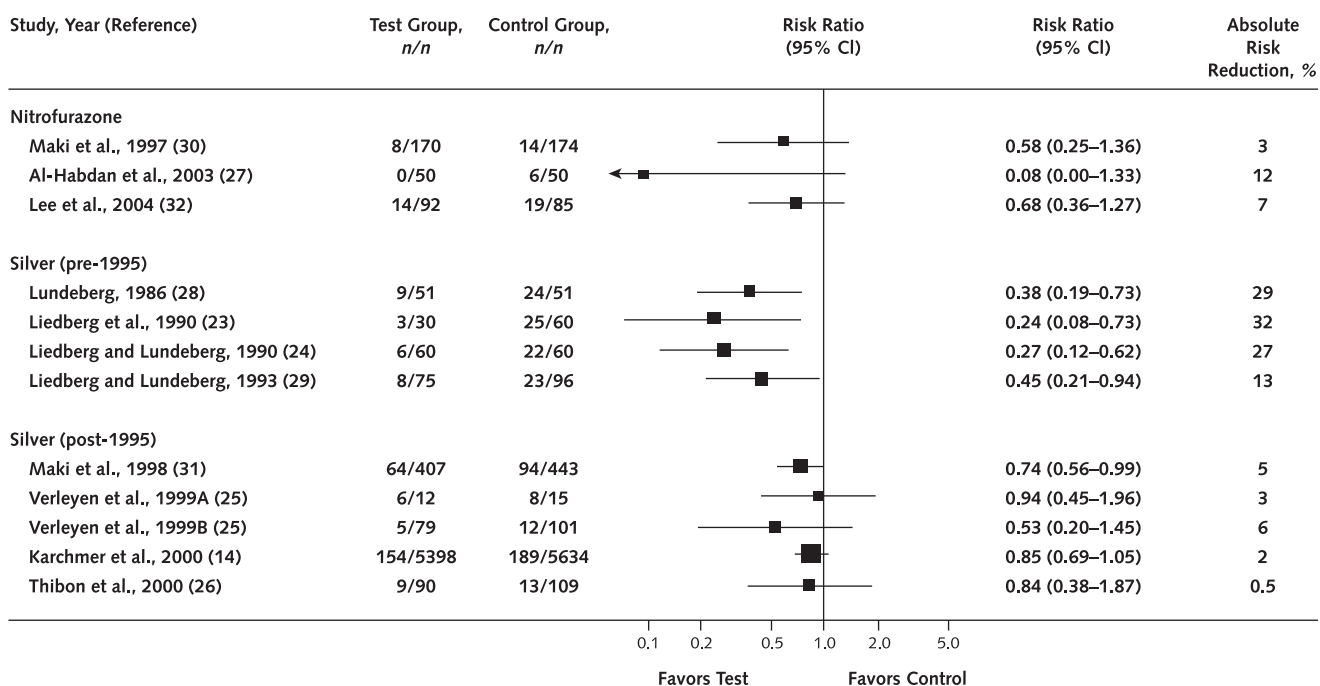
The explanation for the seemingly diminishing efficacy of silver catheters over time is not obvious. Conceivably, any study characteristic that predicted differences in effect size among the silver catheter trials, all of which corresponded with year, could be responsible. One such factor, that is, the secular trend toward decreasing background bacteriuria rates, might reflect changes in practice over time, such as increased antibiotic use or improved catheter maintenance practices. Alternatively, it could re-

fect recent trials' tendency to use silicone control catheters and to study nonurology patients.

The most recently published comparative trial of an antimicrobial urinary catheter involved more than 3000 patients, but we excluded the trial from our review because of its pre-post study design (39). It showed a non-statistically significant reduction in catheter-associated bacteriuria (risk ratio, 0.85 [CI, 0.69 to 1.06]) and a slight increase in secondary bloodstream infection with a silver-coated silicone catheter compared with a plain silicone catheter (39). These findings, which constitute the only available clinical evidence on silver-coated silicone catheters, are consistent with the results of the post-1995 RCTs of silver-coated latex catheters that we reviewed and conflict with the more favorable results typically reported from recent pre-post trials of silver-coated catheters (40, 41). Conceivably, in some pre-post studies, the silver catheter's apparent benefit was enhanced by an already improving background bacteriuria rate (12, 39, 42); concurrent co-interventions, such as nursing education (42) or replacement of preexisting catheters (43); or patient sample differences between study periods (39).

No trial we reviewed directly compared different antimicrobial catheters. Consequently, possible differences in efficacy between nitrofurazone-coated and silver alloy-coated catheters remain indeterminate, notwithstanding the seemingly superior performance of nitrofurazone cath-

**Figure 2. Outcomes (total and stratified) of randomized and quasi-randomized clinical trials of currently marketed antimicrobial urinary catheters.**



End point is proportion of participants (or catheters) developing catheter-associated bacteriuria. Three trials examined nitrofurazone catheters, 4 pre-1995 trials examined silver-alloy catheters, and 5 post-1995 trials examined silver-alloy catheters. The risk ratio is indicated by the horizontal position of the solid black squares. The 95% CIs around the risk ratios are indicated by the width of the solid lines.

eters in recent trials of either antimicrobial catheter type, separately, over control catheters. For example, for catheter-associated bacteriuria, the risk ratios from the 3 nitrofurazone catheter trials were lower than those from 4 of the 5 (post-1995) silver catheter trials. Likewise, for gram-negative bacteriuria, the median risk ratio among nitrofurazone catheter trials was 0.38, compared with 0.82 among post-1995 silver catheter trials. However, since these differences could reflect differences in study design or patient sample rather than differences between the devices, a head-to-head trial is needed to compare catheter efficacy.

Since the 4 quasi-randomized trials were described as randomized (25, 27, 32), some remaining (ostensibly randomized) trials may also not have been randomized. Nonetheless, in the 4 quasi-randomized trials, the comparison groups seemed fairly well-matched for important clinical characteristics. Exceptions included the skewed sex distribution observed by Lee and colleagues (32) (Table 1). However, sex reportedly was not a statistically significant multivariable predictor of bacteriuria, so this may have been unimportant. In contrast, duration of catheter use, which statistically significantly predicted bacteriuria, was borderline longer in the test catheter group (median, 4.4 days vs. 3.9 days;  $P = 0.054$ ) (32). This would bias against the nitrofurazone test catheter, thereby strengthening Lee and colleagues' conclusion of catheter efficacy.

Absence of or incomplete allocation concealment or blinding, which characterized most trials, also probably did not detract from validity. Comparison groups, when described, seemed well-matched, and most outcomes were objectively defined on the basis of systematically collected urine samples, largely excluding bias. However, bias could have influenced the results of the large cluster randomized trial, in which clinicians submitted urine samples on an ad hoc basis and the outcome definition incorporated clinicians' treatment decisions. Likewise, nonblinding of assessors in some trials could have biased decisions about postenrollment exclusions.

Indeed, the greatest threat to validity in most studies probably was the use of several preenrollment and postenrollment exclusions, many of which increased the likelihood of finding a treatment effect. This strategy probably led to systematic overestimation of the benefit that users could expect in clinical practice, where precatheterization exclusions would be cumbersome to apply and postcatheterization exclusions would be moot. For example, most trials excluded participants with preexisting bacteriuria from analysis, and thus these patients did not contribute to effect estimates. In practice, however, such patients would receive a catheter, thereby increasing the number needed to treat to prevent the outcome. Likewise, several trials excluded patients who received antimicrobial agent therapy from analysis. Such patients are relatively protected against catheter-associated bacteriuria, so they are less likely to benefit from the antimicrobial catheter. However, in practice, they would receive the catheter, thereby also increas-

ing the number needed to treat. Such effect size-inflating postenrollment exclusions can be dealt with by intention-to-treat analyses, in which all enrolled participants contribute to effect estimates. Likewise, careful accounting for and transparent reporting of preenrollment exclusions are needed to clarify the nature of the study sample for extrapolation to external populations.

Previous calculations of the cost-effectiveness of antimicrobial catheters have assumed greater protective activity for silver catheters, higher background bacteriuria rates, or higher per-episode costs for catheter-associated bacteriuria than recent data support (3, 14, 35, 40, 44). For example, some per-episode cost estimates have assumed 2 to 6 extra hospital days (44), whereas a recent study showed no increase in length of stay (13). Likewise, other models have required, for cost savings, a control bacteriuria rate greater than 15% and a risk ratio less than 0.75 (35), which are values observed in only some post-1995 trials (Figure 2). Revised calculations that incorporate updated cost data and efficacy estimates for both silver and nitrofurazone catheters are needed. According to manufacturers' list prices, an antimicrobial catheter costs \$3.56 to \$9.71 (that is, 80% to 130%) more than a similar noncoated catheter (\$17.14 vs. \$7.43 for nitrofurazone, \$10.70 vs. \$5.89 for Bard silver-latex, \$12.80 vs. \$7.14 for Bard silver-silicone, and \$10.00 vs. \$5.25 for Tyco silver-silicone) (actual costs may vary). Of note, the best way to reduce the cost of catheter-associated bacteriuria may be to avoid treating clinically inapparent bacteriuria episodes (12, 13, 41), whereas the best preventive measure may be to reduce unnecessary catheter use (15). Studies assessing the added benefit of antimicrobial catheters in settings that have addressed such practice-related issues are needed.

The available evidence does not allow us to make definitive recommendations for decision makers about the regulation, marketing, purchase, or clinical use of antimicrobial catheters. However, we would tentatively propose the following. First, clinical benefit (especially regarding symptomatic UTI, morbidity, secondary bloodstream infection, and infection control) and cost savings have yet to be demonstrated in a randomized trial with any of these devices and in any patient population. They can be estimated only by extrapolation, for which appropriately conservative cost and efficacy estimates should be used. Second, since clinical trial results with antimicrobial catheters are highly context-dependent, the relevance of a particular trial's results to specific institutions or patients depends greatly on the degree of correspondence between the study and the clinical setting with respect to a range of variables, including study sample characteristics, antimicrobial usage patterns, local catheter use and maintenance practices, background bacteriuria rate, year, baseline catheter type, and the local microflora. Thus, assessments of appropriateness must be individualized, and the available evidence must be scrutinized closely for its applicability. Third, researchers performing trials of antimicrobial catheters

should use, and manufacturers should report, intention-to-treat analyses to allow more realistic estimates of the number needed to treat to prevent bacteriuria or secondary bloodstream infection; these data could then be incorporated into cost–benefit analyses. Fourth, prevention of bloodstream infection should be assessed either by an adequately powered multicenter RCT, stratified by center, or, if by extrapolation from data on prevention of catheter-associated bacteriuria, with the use of appropriately conservative estimates for the proportion of bacteriuria episodes that actually produce bloodstream infection. Such estimates should take into account the types of microorganisms that cause secondary bloodstream infection compared with those that are affected by the particular test catheter. Fifth, without a head-to-head trial of nitrofurazone-coated and silver-coated catheters, recommendations about the superiority of 1 catheter are speculative. Although recent trials suggest a greater microbiological effect with the nitrofurazone catheter, particularly in mixed medical–surgical populations, and possibly against gram-negative bacilli (other than nonfermenters), this conclusion awaits direct testing. Finally, since adverse effects from antimicrobial catheters seem sufficiently uncommon, and microbial resistance to the active agents is sufficiently unlikely to emerge to a clinically important degree during catheter use, these considerations need not influence decision making.

Limitations of our analysis are largely related to the poor quality of the available evidence, including uneven study quality and reporting, paucity of studies, small study sizes and heterogeneity, absence of data on clinically meaningful end points or long-term catheter use, and extensive postrandomization exclusions. Possible publication bias could have resulted in overestimates of efficacy, if negative studies remained unpublished. We guarded against this by contacting manufacturers and screening conference proceedings for unpublished trials. Strengths of our study are the inclusion of 3 trials of nitrofurazone catheters that were not included in previous meta-analyses (27, 30, 32), comparisons of study characteristics with outcomes, and attention to organism-specific effects.

In summary, compared with control catheters, antimicrobial urinary catheters can prevent or delay the onset of catheter-associated bacteriuria in selected hospitalized patients. However, the magnitude of this effect varies greatly by catheter type, publication year, and several other variables and has been systematically overestimated in many studies because of dropouts and exclusions. The catheters' effect on morbidity, including bloodstream infection, is not known. Well-designed, adequately powered trials that assess catheter-associated bacteriuria and its associated morbidity, mortality, and costs in appropriate patient populations are needed to clarify the comparative clinical utility and economic value of currently available antimicrobial urinary catheters.

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## References

- Saint S, Chenoweth CE. Biofilms and catheter-associated urinary tract infections. *Infect Dis Clin North Am*. 2003;17:411-32. [PMID: 12848477]
- Warren JW. The catheter and urinary tract infection. *Med Clin North Am*. 1991;75:481-93. [PMID: 1996045]
- Maki DG, Tambyah PA. Engineering out the risk for infection with urinary catheters. *Emerg Infect Dis*. 2001;7:342-7. [PMID: 11294737]
- Saint S, Lipsky BA, Gould SD. Indwelling urinary catheters: a one-point restraint? [Editorial]. *Ann Intern Med*. 2002;137:125-7. [PMID: 12118969]
- Tambyah PA, Maki DG. Catheter-associated urinary tract infection is rarely symptomatic: a prospective study of 1,497 catheterized patients. *Arch Intern Med*. 2000;160:678-82. [PMID: 10724054]
- Bryan CS, Reynolds KL. Hospital-acquired bacteremic urinary tract infection: epidemiology and outcome. *J Urol*. 1984;132:494-8. [PMID: 6471184]
- Krieger JN, Kaiser DL, Wenzel RP. Urinary tract etiology of bloodstream infections in hospitalized patients. *J Infect Dis*. 1983;148:57-62. [PMID: 6350488]
- Eykyn SJ. Urinary tract infections in the elderly. *Br J Urol*. 1998;82 Suppl 1:79-84. [PMID: 9883266]
- Platt R, Polk BF, Murdock B, Rosner B. Mortality associated with nosocomial urinary-tract infection. *N Engl J Med*. 1982;307:637-42. [PMID: 7110215]
- Gross PA, Van Antwerpen C. Nosocomial infections and hospital deaths. A case-control study. *Am J Med*. 1983;75:658-62. [PMID: 6624773]
- Bueno-Cavanillas A, Delgado-Rodríguez M, López-Luque A, Schaffino-Cano S, Gálvez-Vargas R. Influence of nosocomial infection on mortality rate in an intensive care unit. *Crit Care Med*. 1994;22:55-60. [PMID: 8124975]
- Laupland KB, Bagshaw SM, Gregson DB, Kirkpatrick AW, Ross T, Church DL. Intensive care unit-acquired urinary tract infections in a regional critical care system. *Crit Care*. 2005;9:R60-5. [PMID: 15774051]
- Tambyah PA, Knasinski V, Maki DG. The direct costs of nosocomial catheter-associated urinary tract infection in the era of managed care. *Infect Control Hosp Epidemiol*. 2002;23:27-31. [PMID: 11868889]
- Karchmer TB, Giannetta ET, Muto CA, Strain BA, Farr BM. A randomized crossover study of silver-coated urinary catheters in hospitalized patients. *Arch Intern Med*. 2000;160:3294-8. [PMID: 11088092]
- Cornia PB, Amory JK, Fraser S, Saint S, Lipsky BA. Computer-based order entry decreases duration of indwelling urinary catheterization in hospitalized patients. *Am J Med*. 2003;114:404-7. [PMID: 12714131]
- Trinka D. Reductions of ICU nosocomial catheter-associated urinary tract infections [Abstract]. *Am J Infect Control*. 2004;32:E105.
- Saint S, Lipsky BA. Preventing catheter-related bacteriuria: should we? *Can*

- we? How? *Arch Intern Med.* 1999;159:800-8. [PMID: 10219925]
18. Warren J, Bakke A, Desgranchamps F, Johnson JR, Kumon H, Shah J, Tambyah P. Catheter-associated bacteriuria and the role of biomaterial in prevention. In: Naber KG, Pechere JC, Kumazawa J, Khoury S, Gerberding JL, Schaeffer AJ, eds. *Nosocomial and Health Care Associated Infections in Urology*. Plymouth, United Kingdom: Health Publication Ltd.; 2001:151-76.
  19. Saint S, Elmore JG, Sullivan SD, Emerson SS, Koepsell TD. The efficacy of silver alloy-coated urinary catheters in preventing urinary tract infection: a meta-analysis. *Am J Med.* 1998;105:236-41. [PMID: 9753027]
  20. Brosnahan J, Jull A, Tracy C. Types of urethral catheters for management of short-term voiding problems in hospitalised adults. *Cochrane Database Syst Rev.* 2004;CD004013. [PMID: 14974052]
  21. Hartling L, McAlister FA, Rowe BH, Ezekowitz J, Friesen C, Klassen TP. Challenges in systematic reviews of therapeutic devices and procedures. *Ann Intern Med.* 2005;142:1100-11. [PMID: 15968035]
  22. Schulz KF, Chalmers I, Hayes RJ, Altman DG. Empirical evidence of bias. Dimensions of methodological quality associated with estimates of treatment effects in controlled trials. *JAMA.* 1995;273:408-12. [PMID: 7823387]
  23. Liedberg H, Lundeberg T, Ekman P. Refinements in the coating of urethral catheters reduces the incidence of catheter-associated bacteriuria. An experimental and clinical study. *Eur Urol.* 1990;17:236-40. [PMID: 2190840]
  24. Liedberg H, Lundeberg T. Silver alloy coated catheters reduce catheter-associated bacteriuria. *Br J Urol.* 1990;65:379-81. [PMID: 2187551]
  25. Verleyen P, De Ridder D, Van Poppel H, Baert L. Clinical application of the Bardex IC Foley catheter. *Eur Urol.* 1999;36:240-6. [PMID: 10450010]
  26. Thibon P, Le Coutour X, Leroyer R, Fabry J. Randomized multi-centre trial of the effects of a catheter coated with hydrogel and silver salts on the incidence of hospital-acquired urinary tract infections. *J Hosp Infect.* 2000;45:117-24. [PMID: 10860688]
  27. Al-Habdan I, Sadat-Ali M, Corea JR, Al-Othman A, Kamal BA, Shriyan DS. Assessment of nosocomial urinary tract infections in orthopaedic patients: a prospective and comparative study using two different catheters. *Int Surg.* 2003;88:152-4. [PMID: 14584770]
  28. Lundeberg T. Prevention of catheter-associated urinary-tract infections by use of silver-impregnated catheters [Letter]. *Lancet.* 1986;2:1031. [PMID: 2877184]
  29. Liedberg H, Lundeberg T. Prospective study of incidence of urinary tract infection in patients catheterized with Bard hydrogel and silver-coated catheters or Bard hydrogel-coated catheters [Abstract]. *J Urol.* 1993;149:405A.
  30. Maki DG, Knasinski V, Tambyah PA. A prospective investigator-blinded trial of a novel nitrofurazone-impregnated urinary catheter [Abstract]. *Infect Control Hosp Epidemiol.* 1997;18:P50.
  31. Maki DG, Knasinski V, Halvorson KT, Tambyah PA. A novel silver-hydrogel urinary catheter reduces catheter-associated urinary tract infections. A prospective, randomized, double-blind trial [Abstract]. *Infect Control Hosp Epidemiol.* 1998;19:682.
  32. Lee SJ, Kim SW, Cho YH, Shin WS, Lee SE, Kim CS, et al. A comparative multicentre study on the incidence of catheter-associated urinary tract infection between nitrofurazone-coated and silicone catheters. *Int J Antimicrob Agents.* 2004;24 Suppl 1:S65-9. [PMID: 15364311]
  33. Garner JS, Jarvis WR, Emori TG, Horan TC, Hughes JM. CDC definitions for nosocomial infections, 1988. *Am J Infect Control.* 1988;16:128-40. [PMID: 2841893]
  34. Johnson JR, Berggren T, Conway AJ. Activity of a nitrofurazone matrix urinary catheter against catheter-associated uropathogens. *Antimicrob Agents Chemother.* 1993;37:2033-6. [PMID: 8239629]
  35. Saint S, Veenstra DL, Sullivan SD, Chenoweth C, Fendrick AM. The potential clinical and economic benefits of silver alloy urinary catheters in preventing urinary tract infection. *Arch Intern Med.* 2000;160:2670-5. [PMID: 10999983]
  36. Turjanmaa K, Alenius H, Reunala T, Palosuo T. Recent developments in latex allergy. *Curr Opin Allergy Clin Immunol.* 2002;2:407-12. [PMID: 12582324]
  37. Hepner DL, Castells MC. Latex allergy: an update. *Anesth Analg.* 2003;96:1219-29. [PMID: 12651689]
  38. Taylor JS, Erkek E. Latex allergy: diagnosis and management. *Dermatol Ther.* 2004;17:289-301. [PMID: 15327474]
  39. Srinivasan A, Karchmer T, Richards A, Sng X, Perl TM. A prospective trial of a novel, silicone based, silver coated foley catheter for the prevention of nosocomial urinary tract infections. *Infect Control Hosp Epidemiol.* 2005 [In press].
  40. Rupp ME, Fitzgerald T, Marion N, Helget V, Puumala S, Anderson JR, et al. Effect of silver-coated urinary catheters: efficacy, cost-effectiveness, and antimicrobial resistance. *Am J Infect Control.* 2004;32:445-50. [PMID: 15573050]
  41. Burt B, Pace D, Calabrese C. Reduction of healthcare-acquired urinary tract infections—a patient safety analysis [Abstract]. *Am J Infect Control.* 2004;32:E78.
  42. Lai KK, Fontecchio SA. Use of silver-hydrogel urinary catheters on the incidence of catheter-associated urinary tract infections in hospitalized patients. *Am J Infect Control.* 2002;30:221-5. [PMID: 12032497]
  43. Newton T, Still JM, Law E. A comparison of the effect of early insertion of standard latex and silver-impregnated latex foley catheters on urinary tract infections in burn patients. *Infect Control Hosp Epidemiol.* 2002;23:217-8. [PMID: 12002237]
  44. Plowman R, Graves N, Esquivel J, Roberts JA. An economic model to assess the cost and benefits of the routine use of silver alloy coated urinary catheters to reduce the risk of urinary tract infections in catheterized patients. *J Hosp Infect.* 2001;48:33-42. [PMID: 11358469]

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