Antimicrobial catheters for reduction of symptomatic urinary tract infection in adults requiring short-term catheterisation in hospital: a multicentre randomised controlled trial

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Summary

Background Catheter-associated urinary tract infection (CAUTI) is a major preventable cause of harm for patients in hospital. We aimed to establish whether short-term routine use of antimicrobial catheters reduced risk of CAUTI compared with standard polytetrafluoroethylene (PTFE) catheterisation.

Methods In our parallel, three group, multicentre, randomised controlled superiority trial, we enrolled adults (aged ≥16 years) requiring short-term (≤14 days) catheterisation at 24 hospitals in the UK. Participants were randomly allocated 1:1:1 with a remote computer allocation to receive a silver alloy-coated catheter, a nitrofural-impregnated catheter, or a PTFE-coated catheter (control group). Patients undergoing unplanned catheterisation were also included and consent for participation was obtained retrospectively. Participants and trial staff were unmasked to treatment assignment. Data were collected by trial staff and by patient-reported questionnaires for 6 weeks after randomisation. The primary outcome was incidence of symptomatic urinary tract infection for which an antibiotic was prescribed by 6 weeks. We postulated that a 3·3% absolute reduction in CAUTI would represent sufficient benefit to recommend routine use of antimicrobial catheters. This study is registered, number ISRCTN75198618.

Findings 708 (10%) of 7102 randomly allocated participants were not catheterised, did not confirm consent, or withdrew, and were not included in the primary analyses. Compared with 271 (12·6%) of 2144 participants in the control group, 263 (12·5%) of 2097 participants allocated a silver alloy catheter had the primary outcome (difference –0·1% [95% CI –2·4 to 2·2]), as did 228 (10·6%) of 2153 participants allocated a nitrofural catheter (–2·1% [–4·2 to 0·1]). Rates of catheter-related discomfort were higher in the nitrofural group than they were in the other groups.

Interpretation Silver alloy-coated catheters were not effective for reduction of incidence of symptomatic CAUTI. The reduction we noted in CAUTI associated with nitrofural-impregnated catheters was less than that regarded as clinically important. Routine use of antimicrobial-impregnated catheters is not supported by this trial.

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Introduction

Urinary tract infection associated with indwelling catheters that drain urine during and after surgery or critical illness is the second most common cause of hospital-acquired infection worldwide. Conservative estimates suggest 145 000 adults were affected in the USA in 2010[1–3] and 47% of newly catheterised patients in the Philippines develop such an infection.[4] Catheter-associated urinary tract infection (CAUTI) causes avoidable morbidity and increased health-care costs in high-income and developing countries.[5,6] Implementation of evidence-based prevention strategies such as avoidance of catheter use, aseptic catheter insertion, and shortened duration of catheterisation[7,8] have been associated with a 50% reduction in CAUTI in hospitals.[3,9] Alternatively, catheters can be made with antimicrobial coatings that delay bacterial colonisation; two widely available examples are a silver alloy-coated latex catheter and a nitrofural-impregnated silicone catheter, which both inhibit urinary pathogens.[10] A Cochrane Review[11] reported that, although these devices can reduce bacterial contamination of urine, their usefulness against symptomatic CAUTI and thus avoidance of the need for antibiotic treatment was uncertain. Recent guidance[8] called for more evidence of effectiveness before routine implementation and emphasised the need to focus on clinical outcomes such as symptomatic urinary tract infection. We aimed to establish whether short-term use of antimicrobial catheters reduced the risk of clinical CAUTI compared with equivalent use of standard catheters.

Methods

Study design and participants

In our multicentre, randomised, controlled trial, we enrolled adults (aged ≥16 years) undergoing urethral catheterisation for an anticipated duration of up to 14 days from 24 UK National Health Service (NHS) hospitals that provide surgical care in various specialties

See Online for appendix

(appendix).[12] Participants who needed planned catheterisation as part of standard care were identified by local researchers. Instances of unplanned catheterisation with an anticipated short duration were identified by hospital ward staff. We used wide eligibility criteria, including people with diabetes and individuals treated with immunosuppressive drugs. Ineligible patients were those who had symptomatic urinary tract infection at baseline, had undergone urological procedures in the previous 7 days, or had allergies to catheter materials. Participants provided written, informed consent before randomisation apart from cases of unplanned catheterisation, in which participants were randomised and then invited to consent when recovered sufficiently; if individuals declined to participate they were excluded from the analyses. The trial was approved by a UK NHS research ethics committee and overseen by trial steering and data monitoring committees.

Randomisation and masking

Participants were allocated through simple randomisation in a 1:1:1 ratio to a silver alloy-coated latex catheter (Bardex IC, Bard Medical, Crawley, UK), a nitrofural-impregnated silicone catheter (ReleaseNF, Rochester Medical, Lancing, UK), or a standard polytetrafluoroethylene (PTFE)-coated latex catheter (Bard PTFE, Bard

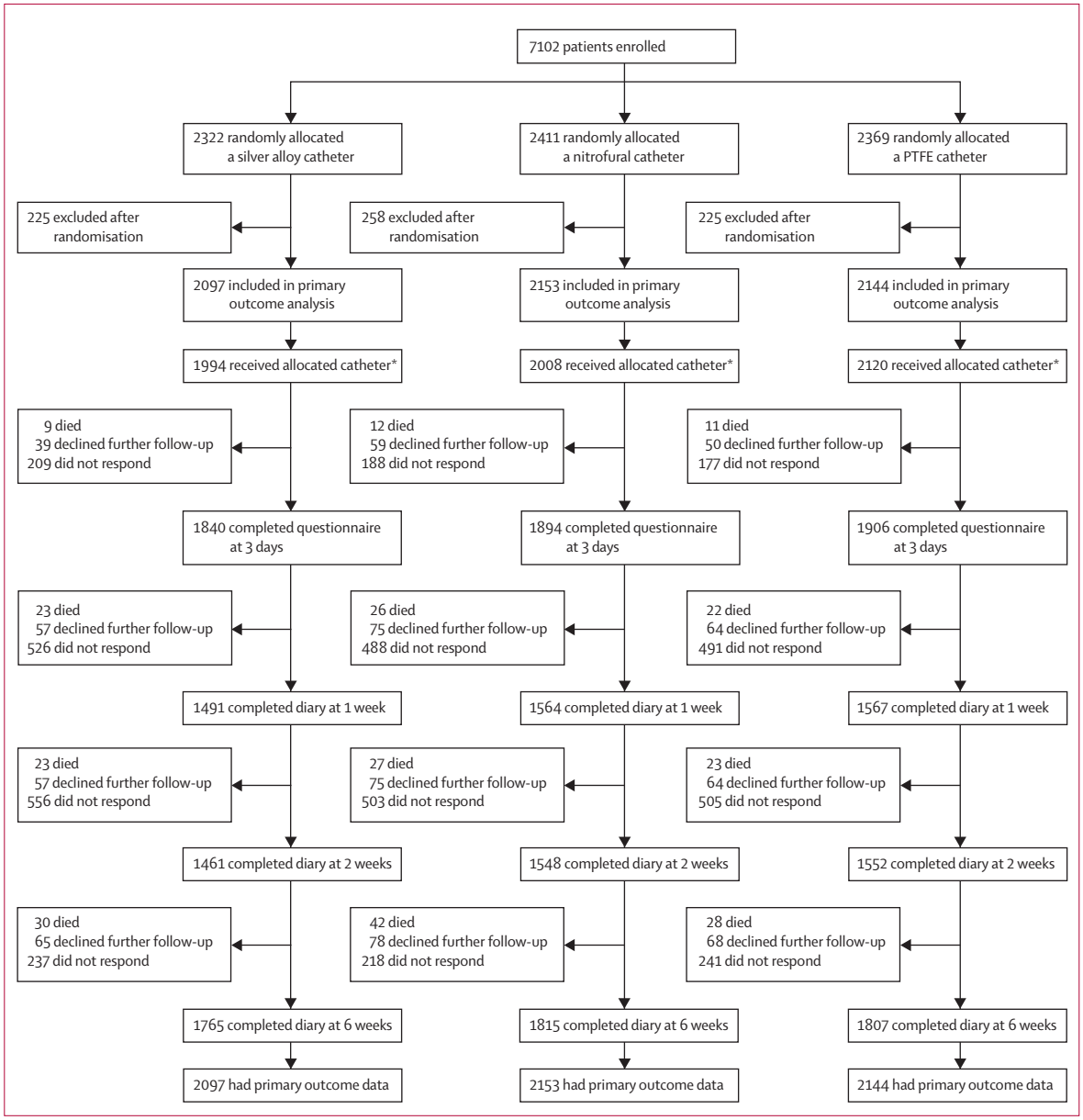


Figure 1: **Trial profile**
Numbers of participants dying, declining further follow-up, or not responding are cumulative in direction of participant flow.

Medical; control group). The randomisation was implemented with a computer generated system, which users accessed via an automated telephone service or secure website to obtain the allocation sequence. We recorded compliance with the allocated intervention. Participants, clinicians, and the trial team were not masked to the allocated intervention because of the distinctive appearances of each catheter. When the period of catheterisation was unexpectedly longer than 14 days, we recorded trial data as if the catheter had been removed on day 14.

Procedures

The primary outcome was incidence of symptomatic CAUTI, defined as the presence of participant-reported symptoms of urinary tract infection and clinician prescription of antibiotic for a urinary tract infection at any time up to 6 weeks after randomisation. Secondary outcomes included incidence of microbiologically confirmed symptomatic CAUTI, which was defined as the primary outcome and a positive urine culture; incidence of bacteriuria up to 3 days after catheter removal; changes in health-related quality of life during the 6 weeks of trial participation; and urethral discomfort related to catheterisation.

Local trial staff collected outcomes data from clinical records during hospitalisation and from self-completed participant questionnaires or diaries 3 days after catheter removal, 1–2 weeks after catheter removal, and 6 weeks after randomisation. Participant questionnaires included questions about symptoms of urinary tract infection, catheter discomfort (mild, moderate, or severe), use of antibiotics, and a generic health-related quality of life measure, EQ-5D.[13] This scale divides health status into five dimensions (mobility, self care, usual activities, pain and comfort, and anxiety and depression).[13] Each of these dimensions has three levels and therefore there are 243 possible health states. We used utility scores to calculate quality-adjusted life-years by multiplying the time spent in each health state by the utility score for that state.[14] We verified participant reports of an episode of CAUTI after the end of hospital visits by contacting their primary care physician to confirm prescription of an antibiotic for urinary tract infection. Midstream voided urine samples or samples of urine taken directly from the catheter were collected at baseline, up to 3 days after catheter removal, and if feasible at the time of CAUTI. Samples were analysed according to microbiology laboratory protocols in UK NHS hospitals with a positive result defined as bacterial counts of 10 000 colony-forming units (cfu) per mL or more of no more than two microorganisms.

Statistical analysis

Because a high degree of benefit would be needed to change routine clinical practice, we specified a 3·3% absolute reduction on the basis of estimated incidence in the control group of 11% (30% relative reduction; odds ratio [OR] 0·67). With 90% power and 2·5% significance level to account for the two comparisons, and allowing for an attrition rate of 15%, we needed to recruit 2345 participants in each group (7035 participants overall). Two comparisons of equal importance were tested in the trial: silver alloy catheters versus PTFE catheters and nitrofural catheters versus PTFE catheters. We assessed urinary tract infection outcomes with logistic regression and summarised findings as absolute percentage risk differences and ORs, both with 95% CIs calculated as 97·5% confidence intervals to adjust for the two comparisons. For the primary analysis, p=0·025 was regarded as significant. We analysed all included participants in their allocated group irrespective of the catheter received, according to intention-to-treat principles, and assumed participants did not have a symptomatic CAUTI unless they met the primary outcome criteria. We report outcomes from an unadjusted model and an adjusted model that corrected for age, sex, comorbidities, indication for catheterisation, and antibiotic use before catheterisation. We did a sensitivity analysis with the recruiting hospital as a random effect. We examined the influence of factors that affect the risk of CAUTI on the reported effectiveness of the experimental catheters compared with control with tests for

	Silver alloy catheter (n=2097)	Nitrofural catheter (n=2153)	PTFE catheter control (n=2144)
Age, years	59 (16)	59 (16)	59 (16)
Sex, female	1319 (63%)	1333 (62%)	1325 (62%)
Unplanned catheterisation	94 (5%)	94 (4%)	89 (4%)
Comorbidity associated with increased CAUTI risk			
Urological disorder	196/2084 (9%)	214/2138 (10%)	214/2136 (10%)
Diabetes	207/2084 (10%)	197/2138 (9%)	216/2136 (10%)
Immunosuppression*	144/2084 (7%)	135/2138 (6%)	151/2136 (7%)
Antibiotics ≤7 days before randomisation	370 (18%)	396 (18%)	385 (18%)
Prophylactic antibiotics before surgical procedure	1529 (73%)	1537 (71%)	1547 (72%)
Antibiotics during period of catheterisation (unrelated to CAUTI)	533 (25%)	511 (24%)	474 (22%)
Antibiotics after catheter removal (unrelated to CAUTI)	193 (9%)	178 (8%)	204 (10%)
Baseline urine sample			
Midstream urine specimen	1709/2002 (85%)	1735/2074 (84%)	1721/2057 (84%)
Catheter urine specimen	293/2002 (15%)	339/2074 (16%)	336/2057 (16%)
Baseline bacterial growth			
No reported growth	1830/1998 (92%)	1923/2071 (93%)	1901/2054 (93%)
≥10 000 cfu per mL	168/1998 (8%)	148/2071 (7%)	153/2054 (7%)
Duration of catheterisation, days	2 (1–3)	2 (1–3)	2 (1–3)
Prolonged catheterisation >14 days	73 (3%)	79 (4%)	67 (3%)
Duration of hospital admission, days	6 (3–8)	6 (3–9)	6 (3–9)

Data are mean (SD), n (%), n/number with available data (%), or median (IQR). PTFE=polytetrafluoroethylene. CAUTI=catheter-associated urinary tract infection. cfu=colony-forming unit. *Immunosuppression was defined as current receipt of immunosuppressive therapy with corticosteroids, methotrexate, or chemotherapy drugs.

Table 1: **Baseline characteristics**

	Silver alloy catheter	Nitrofural catheter	PTFE catheter control
Symptomatic antibiotic-treated UTI within 6 weeks of randomisation (primary outcome)			
Incidence	263/2097 (12·5%)	228/2153 (10·6%)	271/2144 (12·6%)
Absolute risk difference (95% CI) *vs* control	–0·1% (–2·4 to 2·2)	–2·1% (–4·2 to 0·1)	..
Unadjusted odds ratio (95% CI)	0·99 (0·81 to 1·22; p=0·92)	0·82 (0·66 to 1·01; p=0·037)	..
Adjusted odds ratio (95% CI)	0·96 (0·78 to 1·19; p=0·69)	0·81 (0·65 to 1·01; p=0·031)	..
Symptomatic antibiotic-treated UTI up to 6 weeks after randomisation associated with positive urine culture (≥10 000 cfu per mL)			
Incidence n (%)	105/2097 (5·0%)	69/2153 (3·2%)	99/2144 (4·6%)
Absolute risk difference (95% CI) *vs* control	0·4% (–1·2 to 1·9)	–1·4% (–2·7 to –0·1)	..
Unadjusted odds ratio (95% CI)	1·08 (0·78 to 1·52; p=0·55)	0·68 (0·48 to 0·99; p=0·017)	..
Adjusted odds ratio (95% CI)	1·09 (0·78 to 1·51; p=0·58)	0·68 (0·47 to 0·98; p=0·019)	..
Symptomatic or asymptomatic bacteriuria detected by urine culture up to 3 days after catheter removal (≥10 000 cfu per mL)			
Incidence n (%)	310/1785 (17·4%)	249/1846 (13·5%)	321/1839 (17·5%)
Absolute risk difference (95% CI) *vs* control	–0·1% (–3·2 to 2·8)	–4·0% (–6·7 to –1·2)	..
Unadjusted odds ratio (95% CI)	0·99 (0·82 to 1·21; p=0·94)	0·74 (0·60 to 0·91; p=0·001)	..
Adjusted odds ratio (95% CI)	0·99 (0·81 to 1·21; p=0·89)	0·73 (0·59 to 0·90; p=0·001)	..
Self-reported participant discomfort ratings with catheter in place			
Incidence of any discomfort	322/1829 (17·6%)	496/1879 (26·4%)	396/1889 (21·0%)
Absolute risk difference (95% CI) *vs* control	–3·4% (–6·4 to –0·4)	5·4% (2·2 to 8·7)	..
Odds ratio of experiencing discomfort (95% CI)	0·81 (0·67 to 0·98)	1·35 (1·13 to 1·62)	..
Self-reported participant discomfort ratings for catheter removal			
Incidence of any discomfort	521/1817 (28·7%)	707/1867 (38·9%)	499/1881 (26·5%)
Absolute risk difference (95% CI) *vs* control	2·2% (–1·3 to 5·6)	11·3% (7·8 to 14·9)	..
Odds ratio of experiencing discomfort (95% CI)	1·11 (0·94 to 1·31)	1·69 (1·44 to 1·97)	..

Absolute risk differences derived from logistic regression models with the δ method. Adjusted models were corrected for age, sex, comorbidity, indication for catheterisation, and antibiotic use before catheterisation. cfu=colony-forming unit. PTFE=polytetrafluoroethylene. UTI=urinary tract infection.

Table 2: **Primary and secondary trial outcomes**

	Fixed effects	Random effects
Silver alloy *vs* PTFE control		
Unadjusted odds ratio	0·99 (0·81–1·22; p=0·92)	1·00 (0·84–1·22; p=0·88)
Adjusted odds ratio	0·96 (0·78–1·19; p=0·69)	0·99; (0·81–1·20; p=0·88)
Nitrofural *vs* PTFE control		
Unadjusted odds ratio	0·82 (0·66–1·01; p=0·037)	0·83 (0·69–1·02; p=0·039)
Adjusted odds ratio	0·81 (0·65–1·01; p=0·031)	0·83 (0·68–1·02; p=0·045)

Data are odds ratio (95% CI; p value). PTFE=polytetrafluoroethylene.

Table 3: **Sensitivity analysis of interaction between recruiting hospital and primary outcome**

interaction at the 1% significance level because of their exploratory nature. We did a post-hoc effect modification sensitivity analysis to explore any potential effects of duration of catheterisation on reported effectiveness. All subgroup and treatment-effect modification analyses were done with the same generalised linear modelling framework as the main analyses. Responses to the EQ-5D were plotted as mean (SD) at 3 days, 1 week, and 2 weeks after catheter removal, and at 6 weeks after randomisation, and we assessed changes by calculating the area under the curve. We explored sensitivity to missing data with the missing at random assumption, but did not impute data. We analysed all outcomes related to symptoms and catheter-associated discomfort with ordered logit models suitable for ordinal outcome data. Analyses were done with SAS version 9.2 and Stata version 11.

This study is registered, number ISRCTN75198618.

Role of the funding source

The sponsor of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report. RP, TL, GM, MK, GMc, CB, LV, and JN'D had full access to data collected for the trial, and JN'D and RP had final responsibility for the decision to submit for publication.

Results

Between July 23, 2007, and Oct 15, 2010, we enrolled 7102 patients. 430 of these patients did not provide retrospective consent or withdrew their consent before catheterisation and were excluded from the primary analysis. 278 other participants who were randomly allocated a catheter and consented to study inclusion became ineligible predominantly because they did not undergo urethral catheterisation owing to changed clinical care decisions. We included 6394 (90%) of 7102 enrolled participants in the main analyses, including 520 (8%) who provided retrospective consent after unplanned

catheterisation. 272 (4%) of 6394 participants included in the analysis did not receive the allocated catheter because clinical staff substituted an alternative catheter (figure 1). Reasons for catheterisation were recorded for 6296 participants; 5966 (95%) required perioperative monitoring of urine output and 277 (5%) had urinary retention. The proportion of participants in the care of different specialties recruiting to the trial was balanced across the three groups (appendix). Baseline characteristics (table 1) and response rates to postal questionnaires (figure 1) were much the same between groups. We obtained primary outcome data for the main analyses for all but one non-responder (in the control group) for whom we assumed that no CAUTI occurred.

Incidence of symptomatic CAUTI up to 6 weeks after randomisation did not differ significantly between groups (table 2). A sensitivity analysis incorporating recruiting hospital gave almost the same results (table 3). No patients were reported to have been admitted to intensive care or died because of a CAUTI. Patients in the three groups did not differ in terms of duration of catheter use and length of hospital stay (table 1). We did not note any interactions between effectiveness of the antimicrobial catheters and presence of risk factors for CAUTI (figure 2). Longer catheter duration was associated with increased rate of CAUTI in all three trial groups but the statistical model showed no significant interaction between catheter duration and the silver alloy versus control comparison (p=0·83) and the nitrofural versus control comparison (p=0·19; figure 3). Table 4 shows the time of occurrence of CAUTI relative to catheter removal. The nitrofural catheter used in the trial was associated with a reduced incidence of microbiologically proven symptomatic CAUTI (p=0·02) and a lower rate of bacteriuria (p=0·001), but also greater participant-reported discomfort during use and at removal (table 2). Health statuses did not differ between trial groups during follow-up (table 5).

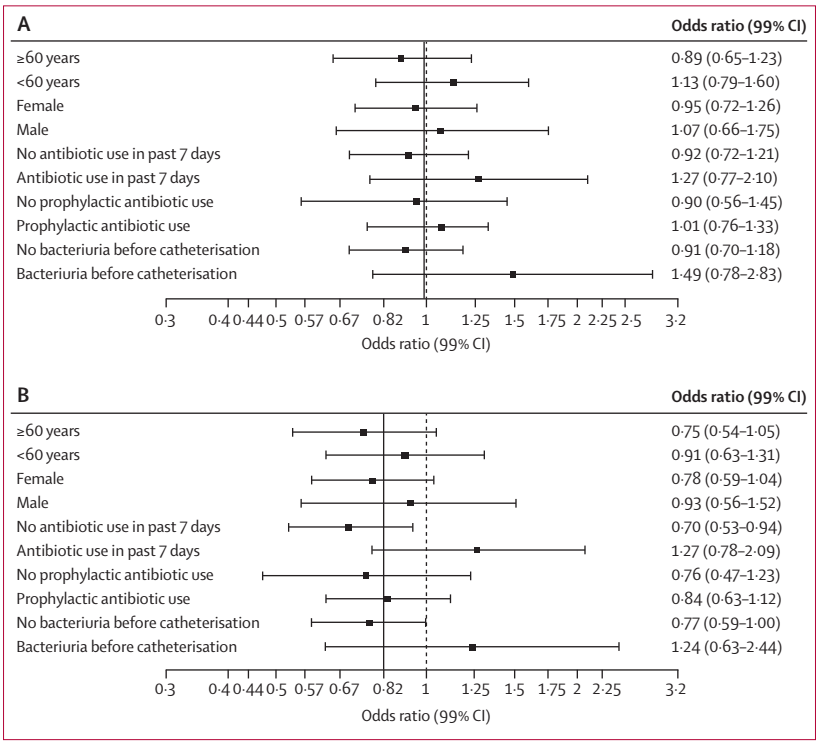
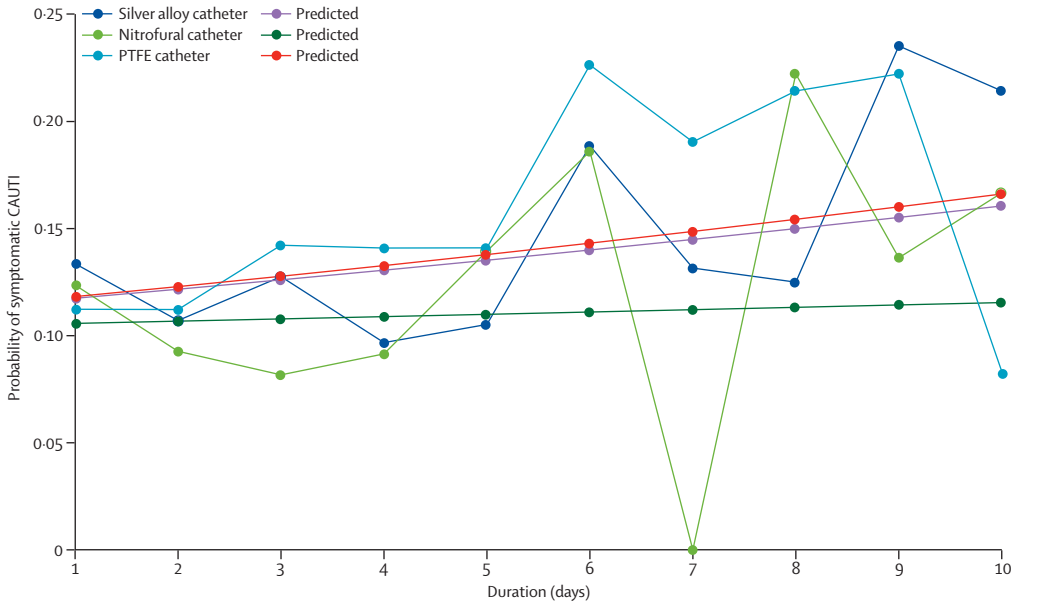


Figure 2: **Catheter-associated urinary tract infection up to 6 weeks after randomisation for the silver alloy catheter versus control (A) and nitrofural catheter versus control (B)**

Discussion

We aimed to establish whether short-term use of either of two available antimicrobial catheters was clinically effective in reducing CAUTI compared with the PTFE control (panel). Interpretation of our findings depends on the level of benefit thought sufficient to justify changes in practice. From a clinical perspective and taking into account previously reported effect sizes,[15–17] we regarded avoidance of one CAUTI in 30 people (3·3% absolute reduction) to be of benefit and powered our trial accordingly. Other groups, such as patients needing short-term catheterisation or the health-care funders with a restricted budget, might have required lesser or greater degrees of benefit.

Our best estimate of the effectiveness of the silver alloy catheter compared with control suggested almost no difference. The results suggest that 1000 people would need to receive a silver alloy catheter to prevent one CAUTI, with the true effect lying between one infection prevented in 42 people and one infection caused in 45 people. Because the 95% CI of the absolute risk difference did not include the prestated effect size but did include zero, we conclude that the silver alloy catheter is not effective for prevention of CAUTI. Nevertheless, hospitals in the USA and UK have implemented silver alloy-coated catheters for routine short-term use as part of prevention strategies against CAUTI.[17–19] This use began after a meta-analysis of previous trials suggested a relative risk of 0·54 (95% CI 0·43–0·67) for bacteriuria compared with standard catheters,[11] which was not changed substantially after accounting for possible bias.[20] We felt that bacteriuria did not match closely with the clinical diagnosis of urinary tract infection and therefore used a primary patient-reported urinary tract infection outcome backed by clinician action of antibiotic prescription without requirement for microbiological proof, assessed for at least 4 weeks after catheter removal. This analysis was designed to reflect usual clinical care and experience of patients, with an adequate observation period to capture relevant events, and to fulfil research priorities set out in international public health policy guidelines.[7,21,22] Our secondary outcomes of microbiologically proven symptomatic CAUTI and bacteriuria at up to 3 days after catheter removal were more closely matched to previous trials than was our primary analysis, but also suggested that the silver alloy catheter was



Silver alloy catheter	89/666 (13%)	74/691 (11%)	31/243 (13%)	15/155 (10%)	8/76 (11%)	10/53 (19%)	5/38 (13%)	2/16 (13%)	4/17 (24%)	3/14 (21%)
Nitrofural catheter	90/728 (12%)	65/701 (9%)	21/257 (8%)	14/153 (9%)	12/86 (14%)	8/43 (19%)	0/28	4/18 (22%)	3/22 (14%)	1/6 (17%)
PTFE catheter	81/721 (11%)	79/704 (11%)	33/232 (14%)	21/149 (14%)	11/78 (14%)	12/53 (23%)	8/42 (19%)	6/28 (21%)	4/18 (22%)	1/12 (8%)

Figure 3: **Observed and fitted incidence of catheter-associated urinary tract infection up to 6 weeks after randomisation versus duration of catheterisation**

Data are n/N (%). n=number of participants with episode of CAUTI within 6 weeks of randomisation. N=number of participants with catheter duration of specified number of days. PTFE=polytetrafluoroethylene (control group). CAUTI=catheter-associated urinary tract infection.

	Silver alloy catheter (n=2097)	Nitrofural catheter (n=2153)	PTFE catheter control (n=2144)
No CAUTI	1834 (87%)	1925 (89%)	1873 (87%)
CAUTI during catheterisation	34 (2%)	28 (1%)	33 (2%)
CAUTI reported before completion of week 1 diary	99 (5%)	77 (4%)	92 (4%)
CAUTI reported in week 1 or week 2 diary or on 6 week questionnaire	127 (6%)	122 (6%)	144 (7%)
Missing*	3 (<1%)	1 (<1%)	2 (<1%)

CAUTI=catheter-associated urinary tract infection. PTFE=polytetrafluoroethylene. *Participants whose catheterisation status could not be ascertained.

Table 4: **Timing of report of CAUTI relative to catheterisation status**

	Silver alloy catheter (n=2097)		Nitrofural catheter (n=2153)		PTFE catheter control (n=2144)	
	Available data (n)	Score	Available data (n)	Score	Available data (n)	Score
Baseline (before randomisation)	2076	0·72 (0·29)	2127	0·72 (0·29)	2123	0·72 (0·30)
3 days after catheter removal	1801	0·58 (0·28)	1860	0·59 (0·27)	1871	0·59 (0·27)
1 week after catheter removal	1308	0·60 (0·29)	1363	0·62 (0·27)	1366	0·61 (0·27)
2 weeks after catheter removal	1328	0·69 (0·27)	1405	0·70 (0·26)	1398	0·70 (0·25)
6 weeks after randomisation	1665	0·78 (0·24)	1705	0·78 (0·24)	1721	0·80 (0·23)

Data are n or mean (SD). Higher scores show better health statuses. PTFE=polytetrafluoroethylene.

Table 5: **Participant health state measured by responses to the EQ-5D questionnaire**

ineffective. The early change in practice made by some hospitals was based on incomplete evidence of effectiveness that mainly came from underpowered studies; the contrast between the finding of no difference from a robustly designed, large, multicentre pragmatic trial, and initial promising findings from smaller explanatory trials has been reported previously.[23]

The best estimate of effectiveness for the nitrofural catheter was that they would prevent one symptomatic CAUTI in every 48 people catheterised, but that the true effect could lie between one in 24 people and no protective effect at all. This estimate was less than the effect size we required and the 95% CI of the absolute risk difference included zero so we regarded routine use of nitrofural catheters for short-term catheterisation as not clinically beneficial. Moreover, the potential for increased discomfort, which was reported by about one in nine participants, adds to the distress of an already intimate invasive intervention. The estimate of effectiveness in our trial was smaller than that from meta-analyses of previous trials[8,11] and in particular contrasts with a report[24] of a relative risk for antibiotic-treated CAUTI recorded as a secondary outcome of 0·27 (95% CI 0·10–0·69) in favour of nitrofural catheters. However, use of bacteriuria as a primary outcome and missing data for the secondary outcomes in that report[24] restricted useful comparison with our results. The contrasting lack of effectiveness noted in our trial might be because of our wider eligibility

criteria, shorter catheter duration, and pragmatic design. Our results for microbiological CAUTI and bacteriuria were suggestive of a relevant antimicrobial effect, but this might be offset by public health concerns about widespread use of antimicrobial drugs. Nitrofuran-based antimicrobial drugs are less prone to development of bacterial resistance,[25] although we did not monitor this factor in our trial. The silicone material of manufacture might have contributed to greater antimicrobial effect compared with the latex control catheter, but we did not explore this because we aimed to test the effectiveness of the device as an available technology and thus rejected the option of inclusion of a standard silicone catheter as a second control group.

We pragmatically designed our trial to assess clinical effectiveness of two widely available antimicrobial catheters. We aimed to resolve uncertainty about the benefit of antimicrobial catheters for short-term use, focusing on the clinically relevant outcome of symptomatic urinary tract infection treated with antibiotics rather than microbiologically defined bacteriuria.[8] We believed that our chosen primary outcome would be measurable and represent a clinically important event that shows patients' experience. This definition and our successful attribution of the outcome across the trial population allowed strong and practically useful conclusions to be made about the clinical effectiveness of antimicrobial catheters. We also adopted a pragmatic approach to recruitment, which ensured that participants were representative of patients needing short-term catheterisation in hospital, with particular emphasis on those individuals who were admitted for elective surgery (the population most often requiring this intervention) meaning that the results can be readily generalised. The wide spectrum of hospital types, specialties, and surgical procedures that we included was protective against selection bias but we did not recruit patients admitted directly to intensive care units and the number of eligible patients identified and recruited from acute medical wards was small.

The trial had 90% power to detect a clinically meaningful benefit from routine use of the antimicrobial catheters. For both comparisons, the central estimate was less than the effect size required and the 95% CI of the absolute risk difference included zero. The results therefore allow the firm conclusion that the silver alloy catheter and the nitrofural catheter did not differ in terms of effectiveness from control. Assuming that our hypothesised effect size of 3·3% and CAUTI incidence with a standard catheter of 11% were correct, we had about 10% chance of a type II error (ie, to wrongly conclude that the catheters are ineffective). Other investigations might have regarded a lesser absolute difference in CAUTI risk to be worth exploring and powered the study accordingly. However, we are confident that the 3·3% difference we set out to identify is a plausible estimate of the minimum benefit needed to change routine practice.

***Panel:* Research in context**

Systematic review

This trial was commissioned because a Cochrane Review[11] (published in 2004 and updated in 2008) reported that although the summarised evidence from published randomised trials suggested that antimicrobial catheters reduced the rate of microbiological bacteriuria, no evidence existed for an associated reduction in morbidity related to symptomatic catheter-associated urinary tract infection (CAUTI). This suggestion was confirmed by a further systematic review and reappraisal of the Cochrane meta-analysis published by the US Centers for Disease Control and Prevention in 2009,[1] which emphasised the need for large pragmatic trials using symptomatic CAUTI as the primary outcome.

Interpretation

The pragmatic design of our trial, large sample size, and use of primary outcomes combining perspectives from patients, clinicians, and health-care providers, provide clear information about the relative benefit of two widely available antimicrobial catheters. Our finding that silver-alloy catheters and nitrofural-impregnated catheters do not provide the prestated minimum level of clinical effectiveness will allow better decisions to be made about use of these devices in health care.

To minimise misclassification of participants' self-report of urinary tract infection, we successfully resolved any missing data and confirmed CAUTI through verification of clinician prescription of antibiotics. Because of the size of the trial and available resources, we could not independently verify that participants reporting no CAUTI after discharge from hospital had not received a prescription of antibiotic for urinary tract infection. We believe that misclassification of absence of CAUTI was unlikely to differ between trial groups because decisions by participants not to report symptoms and treatment decisions by primary care clinicians would not be influenced by the type of catheter used. Some episodes of community-acquired urinary tract infections were probably captured, especially for participants with short catheter duration. However recent catheterisation would remain a risk factor and there was no interaction between duration and effectiveness. Telephone and internet-based trial entry with computer-generated simple randomisation reduced risk of allocation bias. Withdrawals after randomisation were mainly attributable to patients not receiving a catheter because of changes to treatment decisions or refusal to participate after unplanned catheterisation, which were factors unrelated to allocated catheter type. We could not mask the allocated catheter, but clinical staff who inserted the catheter were unlikely to be involved in decisions about timing of removal or prescription of antibiotics for CAUTI.

We used 10 000 cfu per mL or more as the threshold for a positive urine culture because this value is consistently reported by participating hospital laboratories. However, this cutoff might have resulted in higher absolute rates for microbiologically driven outcomes than is noted in studies that use the more common cutoff of 100 000 cfu

per mL. We did not monitor use of other CAUTI prevention actions in participating hospitals, but noted no evidence for interaction between hospital and comparative effectiveness. This finding provides some reassurance that any possible differences between institutions or individual clinicians in terms of diagnosis of clinical CAUTI or criteria used to initiate antibiotic treatment did not affect our primary outcome. Duration of catheter use by most participants may have been too short to allow the antimicrobial effect of the tested catheters to become apparent. The study was designed to align with routine hospital practice, and patients in this setting are unlikely to be able to be stratified as requiring different short periods of catheterisation and receive different catheters. We noted no significant interaction between catheter duration and differences in incidence of CAUTI. The median duration seen in our trial was representative of current practice.[26]

Our results provide no support for the routine use of silver alloy-coated catheters. The nitrofural catheter was not effective according to our prestated criteria and we would therefore regard our trial as showing no evidence to justify its use. However some individuals, particularly patients requiring short-term catheterisation, or providers seeking to reduce rates of health-care-acquired infections, might regard the low degree of benefit sufficient and be encouraged by our finding of significance for secondary microbiological outcomes. However, we caution against such alternative conclusions because they are not supported by the primary trial result. Hospitals will need to carefully consider the lack of effectiveness of the tested catheters, taking into account differences between the UK NHS and their own health-care system. Organisations that have already implemented use of silver-alloy catheters might be able to reallocate resources without loss of benefit, whereas organisations planning their implementation might wish to reconsider. Overall, patients, clinicians, and health-care providers probably ought to persist with straightforward strategies to prevent CAUTI and await any adjustment of guidance on CAUTI prevention in the light of our results before making a decision.[1,7,22,27]

Contributors

JN'D was the chief investigator of the study, had complete involvement and oversight of the study design, execution, and data collection, and was responsible for the final report. RP contributed clinical expertise to the design of the study, supported conduct of the trial, interpreted the trial findings and contributed to the report as first author. TL contributed clinical expertise to the design of the study, helped with clinical support of the trial, and contributed to the report as joint first author. GM led the statistical analysis of the study and writing up and display of the results. KS was responsible for the day-to-day management of the trial and also contributed to the report. MK did the health-related quality of life analysis. GMc designed the programming of the study database, data analysis, and contributed to writing the report. KG was responsible for the establishment of the trial and its initial day-to-day management. AM contributed to the design of the study and provided design support to the trial staff. KW led the microbiological aspects of trial design and planning, advised on conduct of the trial, and provided the microbiologist perspective for data interpretation and preparation of the report. BB contributed to the consumer aspect of the study and writing of the report. CG contributed to the design of the study and the writing of the report. CB did much of the statistical analysis required for the trial results. JB contributed to the delivery of the trial and to the writing of the report. JN was instrumental for the design of the study. LV contributed extensively to report writing. AG contributed to the overall study design and gave expert guidance on the final report.

Conflicts of interest

AG receives salary support from the UK National Institute for Health Research for his role as Director of their Programme Grants for Applied Research Programme. TL and KG authored the Cochrane Review on antimicrobial catheters. RP, GM, KS, MK, GMc, AM, KW, BB, CG, CB, JB, JN, LV, and JN'D declare that they have no conflicts of interest.

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