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TITLE

CATHETER II, a randomised controlled trial comparing the clinical and cost effectiveness of various washout policies versus no washout policy in preventing catheter associated complications in adults living with long term catheters

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ABSTRACT

Objectives

Do weekly prophylactic saline or acidic catheter washouts in addition to standard long-term catheter (LTC) care improve the outcomes of adults with LTC compared to standard LTC care only.

Design

Three-arm superiority open-label randomised controlled trial.

Setting

UK community-based study.

Participants

80 adults with LTC (any type/route) ≥28 days in situ with no plans to discontinue and able to self-manage the washouts/study documentation with/without a carer.

Interventions

Randomly allocated (26:27:27) to receive standard LTC care with weekly saline or weekly acidic or no prophylactic washouts for up to 24 months.

Primary and secondary outcome measures

The primary outcome was catheter blockage requiring intervention (/1000 catheter days). Secondary outcomes were symptomatic catheter-associated urinary tract infection (S-CAUTI) requiring antibiotics, adverse events, participants' quality of life and day-to-day activities, acceptability, and adherence.

Results

Outcomes reported for 25 saline, 27 acidic and 26 control participants. LTC blockages (/1000 catheter days) requiring treatment were 9.96, 10.53, and 20.92 in the saline, acidic, and control groups respectively. The incident rate ratio (IRR) favours the washout groups [saline 0.65(0.24 to 1.77); p-value=0.33 and acidic 0.59(0.22 to 1.63); p-value=0.25], albeit not statistically significant.

The S-CAUTI rate (/1000 catheter days) was 3.71, 6.72, and 8.05 in the saline, acidic, and control groups respectively. The IRR favours the saline group [saline 0.40(0.20 to 0.80); p-value=0.003 and acidic 0.98(0.54 to 1.78); p-value=0.93].

The trial closed before reaching target recruitment due to reduced research capacity during the COVID pandemic.

Conclusions

Early closure and small sample size limits our ability to provide a definite answer. However, the observed non-statistically significant differences over control are favourable for lower rates of LTC blockages without a concomitant rise in S-CAUTI. The results support a multi-national randomised controlled trial of catheter washouts in patients with LTC to ascertain their clinical and cost-effectiveness.

Trial registration

ISRCTN17116445.

STRENGTHS AND LIMITATIONS OF THIS STUDY

- CATHETER II was the largest randomised controlled trial to date investigating prophylactic catheter washouts to prevent blockage.
- A pragmatic trial design was used to evaluate the intervention in real-life practice. Participants were supported to self-manage the intervention to minimise impact on health care resources.
- A comprehensive list of outcomes was assessed and relate to patient, healthcare professional, guideline developer and other stakeholder decision making.
- Validated tools were used to assess quality of life, adherence, convenience, satisfaction, and impact on daily activities. However, outcome data was patient-reported, and it was not possible to blind participants to the intervention.
- Sample size was limited by early closure of the trial due to difficulty with recruitment during the COVID pandemic. This was primarily a result of reduced research capacity and prioritisation of COVID and cancer-related research in primary and secondary care settings.

INTRODUCTION

Long term catheter (LTC) is defined as catheter use for more than 28 days.(1) Approximately 90,000 (1 in 700) of the UK population live with LTC (urethral or suprapubic), with a higher prevalence (0.5%) in those aged over 75 and a mean duration of use of six years.(2-4) In a recently published study Gage and colleagues(5) explored catheter-related service use and costs in patients living with LTC in England. Their findings show that almost 60% of LTC users were men, 71% participants were >70 years of age, and 61% used a urethral catheter. Indications for LTC include intractable urinary incontinence or chronic retention due to spinal cord injury, multiple sclerosis, prostate enlargement, and underactive bladder.(6,7) With an ageing population(8), LTC prevalence and LTC-related use of healthcare resources is expected to rise substantially.

Standard LTC care involves a weekly valve and/or leg bag chan ge (by the patient/carer) and a 4-12 weekly catheter change (usually by the clinical team).(9)

Adverse events (AEs) associated with LTC use impact patients' quality of life (QoL) and are a significant burden on NHS resources.(10) AEs can include blockage, symptomatic catheter-associated urinary tract infection (S-CAUTI), urinary leakage, bladder spasms, pain, and accidental dislodgment.(5,6)

Blockage is the main AE with an incidence of 20-70%(11) or 8.54 per 1000 days of catheter use(6), requiring emergency treatment. A Grampian wide audit (Northeast of Scotland) in year 2017, showed 11.8 blockages requiring intervention per 1000 catheter days. Rarely, blockage may lead to serious complications of urosepsis or autonomic dysreflexia in patients with spinal cord injury at T6 or above.(11)

Various catheter washout policies are used for the prevention and treatment of catheter blockage including different types of solutions, concentrations, volumes, and frequency.(7) Washouts may work by mechanically flushing debris, dissolving mineral encrustations, and/or by antimicrobial effect.(12) Current guidelines do not recommend prophylactic washouts to prevent blockages suggesting instead more frequent change of the catheter.(1) The Cochrane review(7) concluded there is insufficient evidence to define benefits, clinical effectiveness, risks, acceptability, and impact on patient QoL. They also reported some clinical community concerns that catheter washouts may damage bladder mucosa and introduce infection and recommended a robust randomised controlled trial (RCT) to assess the clinical and cost effectiveness of prophylactic washouts in adults living with LTC.

CATHETER II hypothesised weekly prophylactic catheter washouts in addition to standard LTC care would result in a ≥25% relative reduction in catheter blockages requiring intervention. Weekly prophylactic normal saline or citric acid washouts were compared in parallel against standard LTC care only. Clinical effectiveness, patient acceptability, satisfaction, and safety were evaluated.

MATERIALS (PATIENTS) AND METHODS

CATHETER II was a pragmatic three-arm open-label multi-centre superiority RCT with internal pilot and embedded qualitative component. The trial methodology has been published.(13,14) Summary methods are included in accordance with CONSORT (Consolidated Standards of Reporting Trials) guidelines.(15)

Participants were recruited from 21 sites in Scotland, England and Wales including GP practices, community/secondary care hospitals, and using targeted social media/website advertising. Participants were aged ≥18 years with a LTC (any type/route) in use for at least 28 days with no plan to discontinue. Participants self-managed catheter washouts and completed trial documentation or had a carer to assist them. Patients unable to consent or were pregnant/contemplating pregnancy were not eligible. Also excluded were patients with a spinal cord injury at/above T6, suspected S-CAUTI, visible haematuria, known allergies to the washout solutions, current bladder cancer or bladder stones, or who the recruitment team considered unsuitable for other clinical or social reasons (Figure 1). Informed written consent was obtained from participants and, where applicable, their carers prior to randomisation.

Interventions

Participants were randomised to receive a policy of:

- weekly prophylactic normal saline (Uro-Tainer® NaCl 0.9% 100ml) catheter washouts plus standard LTC care; or
- weekly prophylactic acidic (two sequential applications of 30ml 3.23% citric acid, Uro-Tainer® Twin Suby G) catheter washouts plus standard LTC care; or
- standard LTC care only (i.e., no prophylactic catheter washouts).

Changes to washout policy during follow up, including type and frequency, were permitted when clinically necessary. Participants/carers were trained on washout technique. To minimise breakage of the closed drainage system and the risk of introducing infection, the washouts were administered during the regular change of the catheter bag or valve.

Outcomes

The primary clinical outcome was catheter blockage requiring intervention up to 24 months post-randomisation expressed as number per 1000 catheter days. The primary health economic outcome was the incremental cost per QoL year gained with each washout policy compared to standard LTC care only.

Secondary outcomes were S-CAUTI requiring antibiotics, LTC-related and other AEs, duration of LTC use, catheter change (other than for blockage), QoL (both generic (EQ-5D-5L(16)) and disease specific (ICIQ-LTCqol International Consultation on Incontinence Modular Questionnaire – LTC QoL(17))), adherence, convenience, satisfaction (adapted TSQM Treatment Satisfaction Questionnaire for medication(18)), impact on daily activities (GSE General Self-Efficacy Scale(19) and ICECAP-A / ICECAP-O ICEpop CAPability measure for Adults/Older people(20,21)), discontinuation of LTC, and changes to washout policy.

Outcome data was patient reported. Baseline data was collected prior to randomisation. Follow-up data was collected by monthly telephone call and 6-monthly postal/online questionnaires. Where participant follow-up ended early (discontinuation of LTC or early study closure), an additional EQ-5D-5L questionnaire was collected.

Sample size

A survey of experts, patients and available literature deemed a 25% reduction in LTC blockage was required for washouts to be considered worthwhile. This implied a reduction from 11.8/1000 days (control) to 8.9. We used the formula from Zhu and Lakkis(22) to derive the sample size for comparing two negative binomial rates. We needed outcome data from

200 participants per arm for 90% power, assuming two-sided significance of 2.5% (to account for two planned comparisons) and a mean 50/730 days loss to follow-up.

Randomisation

The local research team randomised participants 1:1:1 to one of three arms using a centralised computer randomisation system (created and administered by Centre for Healthcare Randomised Trials, University of Aberdeen). It was not possible to blind participants or researchers to the allocated arm. Randomisation used a minimisation algorithm with a random element and minimised on the following factors:

Region (NHS Grampian v Aneurin Bevan University Health Board v Cwm Taf University Health Board v CRN Eastern v CRN East Midlands v CRN Thames Valley South Midlands v CRN Yorkshire and Humber v CRN Wessex v CRN Greater Manchester v CRN South London v Central), gender (male v female), age (<45, 45 to 64, 65 and above), residential status (community v care home), previous blockages (zero v 1 or more), previous S-CAUTI (zero v 1 or more), urine pH (acidic (<5.1) v normal (5.1 to 6.7) v alkaline (>6.7) v not available)

Patient and Public Involvement (PPI)

PPI partners were active members of the project management group and Trial Steering Committee. They were involved in all stages of the project including development of the study protocol and study materials and oversight. PPI partners will lead the development of the dissemination to participants and the public.

Modifications due to impact of COVID-19

Recruitment commenced in December 2019 and was paused in March 2020 due to COVID-19 pandemic regulations. Following extensive efforts, the study team obtained approval

from Sponsor and the regulatory authorities and recruitment resumed in September 2020 with protocol modifications to minimise face-to-face contact (postal/ telephone consent; telephone collection of baseline data and video consultation training of washout technique). Follow up continued by post and telephone in line with the original protocol. COVID-related protocol adjustments were previously published.(13)

Recovery plans were instigated but the pandemic continued to negatively impact the set-up of research sites and recruitment to the study. In June 2022, the funder elected to terminate the study early, with recruitment ending in August 2022 and follow up ending in August 2023. The closure plan included completing the qualitative study (published alongside) and providing descriptive analysis only for the health economic measures.

Statistical methods

Analyses were based on the intention-to-treat principle. Baseline and outcome data are summarised as count and percentage for categorical data and mean and standard deviation for continuous data.

Number of blockages requiring intervention and number of S-CAUTI were summarised as a rate per 1000 catheter days and analysed using a mixed effects negative binomial regression. Fixed effects were included for the intervention (saline or acidic washout) and the minimisation variables gender, age band, previous blockage and previous S-CAUTI. A random effect (intercept) was included for region. An offset was included for the log of catheter duration (in days). Effect sizes are reported as incidence rate ratios (IRR) with 97.5% confidence intervals. QoL measures were analysed with repeated measures mixed effects linear regression. The same fixed effects were included as for the primary outcome. A dummy variable for timepoint was included as participants could report outcomes at 6-,

12-, 18- and 24-months. Random effects were included for region and participant to adjust for repeated observation on the same participant. The effect sizes are the adjusted mean differences with 97.5% confidence intervals used as an approximation to 95% confidence intervals, as the analysis model estimates the effect size of both saline and acidic washout.

A sensitivity analysis is included making additional adjustments for potential baseline imbalance. This analysis adjusted for: gender (male v female), age (<45, 45-65, >65), previous blockage (0,1-3, 4 or more), previous infection (0,1-3, 4 or more), catheter duration at baseline (<1 year, 1 to 3 years, >3 years), on washout at baseline (yes v no), neuropathic bladder (yes v no), catheter change frequency. Due to the lower recruitment and consequently smaller sample size the planned subgroup analyses were not conducted. In-addition, it was not possible to analyse and report primary (incremental cost per quality adjusted life year) or secondary (time and travel costs) economic outcomes. The health care resource use are presented as descriptive analyses.

RESULTS

Baseline

The mean age of participants in the study was 65 years with those in the control group slightly older and similar numbers of males and females in all three groups (Table 1). The urine pH and the number of participants who had blockages requiring treatment or S-CAUTI requiring antibiotics were similar in all three groups at baseline. Catheter change frequencies ranged between every week to every 12 weeks, with the highest number of participants in all three groups changing their LTC every 12 weeks. There was good balance in the patient reported QoL scores at baseline, though there are small differences between

the ICECAP-O scores. The baseline table disaggregated by gender is included as a supplemental table (S4).

Table 1 Baseline data

	Saline washouts (n=26)	Acidic washouts (n=27)	Control (n=27)
Age	64.8(17.9);[N=26]	62.4(16.7);[N=27]	67.1(15.3);[N=27]
Female	14/26(54%)	12/27(44%)	14/27(52%)
Length of time catheterised			
<1 year	7/26(27%)	5/27(19%)	5/27(19%)
1 to 3 years	9/26(35%)	6/27(22%)	9/27(33%)
>3 years	10/26(38%)	16/27(59%)	13/27(48%)
Neuropathic bladder	8/26(31%)	9/27(33%)	11/27(41%)
Urine pH	6.5(0.8);[N=24]	6.7(1.0);[N=25]	6.8(0.8);[N=25]
Current on washout	3/26(12%)	6/27(22%)	6/27(22%)
Catheter change frequency			
Every week			1/27(3.7%)
Every 2 weeks			2/27(7.4%)
Every 3 weeks			1/27(3.7%)
Every 4 weeks	4/26(15%)	4/27(15%)	5/27(19%)
Every 5 weeks		1/27(3.7%)	
Every 6 weeks	4/26(15%)	3/27(11%)	2/27(7.4%)
Every 7 weeks		1/27(3.7%)	1/27(3.7%)
Every 8 weeks	3/26(12%)	2/27(7.4%)	2/27(7.4%)
Every 10 weeks	2/26(7.7%)	5/27(19%)	3/27(11%)
Every 12 weeks	13/26(50%)	11/27(41%)	10/27(37%)
Blockages requiring treatment (prior 6 months)			
0	13/26(50%)	13/27(48%)	12/27(44%)
1 to 3	8/26(31%)	9/27(33%)	7/27(26%)
4 or more	5/26(19%)	5/27(19%)	8/27(30%)
Median [Lower, Upper quartile]	0.5;[0,3]	1;[0,3]	1;[0,5]
S-CAUTI requiring antibiotics (prior 6 months)			
0	14/26(54%)	13/27(48%)	14/27(52%)
1 to 3	9/26(35%)	9/27(33%)	10/27(37%)
4 or more	3/26(12%)	5/27(19%)	3/27(11%)
Median [Lower, Upper quartile]	0;[0,2]	1;[0,2]	0;[0,2]
General self efficacy scale[1]	29.1(9.1);[N=25]	29.4(5.7);[N=27]	27.8(7.6);[N=27]
ICIQ-LTCqol function and concern[2]	18.3(9.1);[N=26]	17.3(9.7);[N=26]	19.1(9.0);[N=27]
ICIQ-LTCqol lifestyle[2]	6.7(3.4);[N=24]	8.1(3.3);[N=27]	7.6(2.9);[N=27]
EQ-5D-5L[3]	0.368(0.405);[N=25]	0.365(0.359);[N=26]	0.348(0.373);[N=27]
ICECAP-A[4]	0.551(0.216);[N=10]	0.487(0.223);[N=11]	0.496(0.218);[N=9]

ICECAP-O[4]	0.488(0.320);[N=15]	0.601(0.206);[N=14]	0.669(0.204);[N=15]

[1]The general self-efficacy (GSE) scale assesses ability to cope with daily life. It has 10 questions and scores are between 10 and 40 with higher scores better.
[2]ICIQ long-term catheterisation quality of life questionnaire is a specific quality of life measure. It produces the function and concern score and the lifestyle score. The function & concern score has 10 questions and is on the scale 0 to 42. The lifestyle score has 3 questions and is on the scale 3 to 15. For both higher scores are worse.
[3]The EQ-5D-5L is a generic quality of life measure. It has 5 questions and is on the scale -0.594 to 1 where higher scores indicate better quality of life.
[4]The ICECAP-A and ICEPOP-O measure capability in adults and older people respectively. Both have 5 question and are on the scale 0 to 1 with higher scores better. The treatment satisfaction questionnaire assesses satisfaction with medication. It produces the effectiveness, convenience, and overall satisfaction scores. Each score has 3 questions to give 9 in total, with each score on the scale 0 to 100 with higher scores better.
Apart from where indicated, the summary statistics for the continuous outcomes are mean, standard deviation, and count while the categorical variables are summarised with count and percentage.

Outcomes

The follow-up of participants varied from 12 to 24 months due to early closure of the study. A CONSORT diagram is provided (Figure 1) and this shows adherence to washouts. In the saline group one participant changed to acidic washout and seven stopped washouts while in the acidic group two changed to saline and three stopped washouts. The three changes were all recommendations by the clinical team, while three participants stopped because they were unable to perform the washout and six stopped for various medical reasons. In the control group, participants experienced a mean of one catheter blockage per month; in the acidic and saline washout groups this was lower, 0.73 and 0.34 respectively. In the washout groups the rate of LTC blockages requiring treatment was approximately 10 blockages per 1000 catheter days while in the control group the rate was approximately 21 per 1000 catheter days (Table 2). The IRR favour the washout groups (0.65 (0.24 to 1.77);p-value=0.33 and 0.59 (0.22 to 1.63);p-value=0.25 for saline and acidic respectively), albeit not statistically significant. When the two washout groups are combined in a post-hoc analyses (Table 2), the IRR was 0.62 (0.26 to 1.49;p-value=0.22). A disaggregation of blockages

requiring treatment and S-CAUTI by randomised intervention and gender is included as a supplemental table (S5).

Table 2 Blockage requiring treatment (primary outcome) and S-CAUTI

	Saline washouts (n=26)	Acidic washouts (n=27)	Either washout (n=53)	Control (n=27)
Participants providing follow-up data	25	27	52	26
Total months of follow-up	387	409	796	420
Catheterisation duration (days) [mean,(SD)]	468(182)	459(191)	463(185)	492(167)
Total number of blockages requiring treatment	105	115	220	Total=236
Blockages requiring treatment (rate per 1000 catheter days) [mean,(SD)]	9.96(14.48)	10.53(15.77)	10.25(15.02)	20.92(27.77)
IRR (97.5% CI) compared to control	0.65(0.24 to 1.77);0.33	0.59(0.22 to 1.63);0.25	0.62(0.26 to 1.49);0.22	
Total instances of S-CAUTI	37	81	118	98
S-CAUTI (rate per 1000 catheter days) [mean,(SD)]	3.71(8.45)	6.72(7.10)	5.27(7.85)	8.05(11.29)
IRR compared to control (97.5% CI)	0.40(0.20 to 0.80);0.003	0.98(0.54 to 1.78);0.93	0.69(0.39 to 1.23);0.14	

IRR is the incidence rate ratio, 97.5% CI and p-value.

In the control group the S-CAUTI rate was 8 episodes per 1000 catheter days. In the acidic washout group the rate was slightly lower at 6.72 per 1000 catheter days, resulting in an IRR of 0.98 (0.54,1.78): p-value=0.93. In the saline washout group the S-CAUTI rate was significantly lower at 3.71 per 1000 catheter days and the IRR is 0.40 (0.20,0.80);p-value=0.003.

A supplemental table (S1) shows a sensitivity analysis adjusting for additional factors which had potential imbalance between groups at baseline. This analysis was consistent with the

main analysis and showed that weekly prophylactic LTC washouts reduced LTC blockages requiring intervention and S-CAUTI.

The mean bladder spasm days per month was similar in the washout groups at 3.48 and 3.23 and slightly higher in the control group at 4.38 (Table 3).

Table 3 Secondary outcomes

	Saline washouts (n=26)	Acidic washouts (n=27)	Control (n=27)
Any catheter blockage (mean per month)	0.34(0.45)	0.73(1.84)	1.00(1.97)
Bladder spasm (mean days per month)	3.5(5.7)	3.2(5.9)	4.4(6.5)
Urine retention (mean days per month)	0.22(0.45)	0.18(0.38)	0.37(0.57)
Blood in urine (mean days per month)	0.25(0.51)	1.8(3.8)	1.2(1.8)
Pus in urine (mean days per month)	1.7(5.6)	1.3(4.0)	0.84(3.3)
Urine leakage (mean days per month)	5.9(8.7)	4.4(7.7)	2.0(6.0)
Catheter kinks (mean instances per month)	0.20(0.50)	0.051(0.11)	0.12(0.31)
Routine catheter changes (mean number per month)	0.34(0.22)	0.33(0.23)	0.36(0.23)
Regular / preventative washouts (mean number per month)	3.1(1.4)	3.9(2.3)	2.6(6.5)
Treatment of LTC related AEs			
Hospital visits (mean number per month)	0.0067(0.024)	0.034(0.076)	0.051(0.18)
Primary care visits[1] (mean number per month)	0.56(0.41)	0.77(0.47)	0.92(0.67)
GP home visits (mean number per month)	0.014(0.038)	0.031(0.066)	0.0019(0.0098)
GP surgery visits (mean number per month)	0.046(0.12)	0.067(0.11)	0.11(0.17)
Nurse home visits (mean number per month)	0.49(0.36)	0.58(0.44)	0.72(0.71)
Nurse practice visits (mean number per month)	0.0087(0.026)	0.10(0.24)	0.089(0.13)
Complication managed by self or informal carer (mean number per month)	0.45(0.78)	0.62(1.74)	0.74(1.59)

The summary statistic in the cells is the mean and standard deviation.

[1]Primary care visits are GP home or surgery visits or nurse home or practice visits.

Patient-reported blood in urine was lowest for those receiving a saline washout and highest for those on an acidic washout. Patient-reported pus in urine was higher than control for both washout groups. Instances of urine leakage were similar for all three groups but both washout groups had a higher mean number of days than the control group.

LTC-related AEs were predominantly managed by the individual/their carer or by a nurse home visit.

The number of participants experiencing other AEs are generally small. (Table 4).

Table 4 Other adverse events

	Saline washouts (n=26)	Acidic washouts (n=27)	Control (n=27)
Any adverse event	9/26(35%)	11/27(41%)	12/27(44%)
Bladder stones	0/25(0%)	2/27(7.4%)	4/26(15%)
Long-term catheterisation discontinuation	3/25(12%)	2/27(7.4%)	1/26(3.8%)
Epididymitis	0/26(0%)	1/27(3.7%)	0/27(0%)
Urosepsis	0/26(0%)	0/27(0%)	1/27(3.7%)
Pyelonephritis	0/26(0%)	1/27(3.7%)	0/27(0%)
Pain at catheter site	1/25(4.0%)	2/27(7.4%)	2/26(7.7%)
Skin irritation / penile trauma at catheter site	2/25(8.0%)	1/27(3.7%)	4/26(15%)
Bleeding or discharge at catheter site	5/25(20%)	4/27(15%)	4/26(15%)
Granulation problems	2/25(8.0%)	4/27(15%)	0/26(0%)
Sepsis/Pneumonia	0/26(0%)	1/27(3.7%)	0/27(0%)
Cause of death certified as MI secondary to CCF and cardiomyopathy	0/26(0%)	0/27(0%)	1/27(3.7%)
Death due to 1a) Urosepsis 1b) Prostate Cancer2) Type 2 Diabetes mellitus, ischaemic heart disease	1/26(3.8%)	0/27(0%)	0/27(0%)
Death due to Metastatic Breast Cancer.	0/26(0%)	0/27(0%)	1/27(3.7%)

The summary in the cells is the count and percentage.

All instances of granulation are from participants using a suprapubic catheter at the time of the event. All patients reporting skin irritation had a suprapubic catheter at the time. One participant in the control group reported penile trauma and changed from a urethral catheter to a suprapubic catheter and did not report further trauma or irritation.

A supplemental table (Table S2) shows the participant reported QoL outcomes throughout the study. Participants in both washout groups had better scores inEQ-5D-5L and ICECAP-A (Adult version) than the control group indicating better QoL, and better impact on day-to-day activities. None, however, are statistically significant. On the GSE scale, those in the acidic washout group appeared to be better but the difference again was not significant.

Participants either received the ICECAP-A for adults or ICECAP-O for the older population. This had the effect of splitting the trial population and increasing the uncertainty around the effect sizes. For the ICIQ-LTCqol scores there was little evidence of any difference between the groups.

The treatment satisfaction questionnaire, only completed by those in the washout groups, suggest participants in the saline group were more satisfied.

The time and travel questionnaire was completed at 18 months by 24 participants. A supplemental table (S3) summarises the distance travelled for appointments and admissions, the cost of journeys, and the total time taken.

DISCUSSION

The CATHETER II RCT was terminated early primarily due to the impact of the COVID-19 pandemic. The vast majority of NHS research capacity in the UK, especially in primary care, was directed to COVID-19 research with QoL research, including CATHETER II, categorised as

lower priority. Four months after starting CATHETER II, recruitment was temporarily paused and never recovered satisfactorily due to limited research capacity in primary and secondary care. The funder elected for early termination of the study. Consequently, our results are limited by the significantly smaller sample size (n=80) than originally planned (n=600).

However, the CATHETER II results indicated a favourable trend for lower rates of LTC blockages in both the prophylactic washouts groups albeit not statistically significant. The rate of LTC blockages per 1000 catheter days requiring treatment were 9.96, 10.53, and 20.92 in the saline, acidic, and control groups respectively. The IRR favours the washout groups [0.65(0.24 to 1.77); p-value=0.334 and 0.59 (0.22 to 1.63); p-value=0.25 for saline and acidic respectively], but neither reach statistical significance most likely due to the small sample size. Gage and colleagues(5) indicated that hospital resource use accounted for almost half of health services cost mainly due to unplanned hospital admission for LTC blockage or CAUTI. Reduction in LTC blockage is likely to reduce the healthcare costs as fewer emergency treatments will be required. In CATHETER II, there were fewer visits to and by health care professionals in the washout groups. However, we were unable to perform a full health economic analysis due to the early termination and consequently small sample size.

Catheter blockages impact up to 50% of individuals living with LTC leading to discomfort and emotional distress.(23) Shepherd and colleagues (7) conducted a Cochrane Systematic Review comparing washout policies in patients with LTC. They summarised results of 7 RCTs and include 349 participants, out of which 217 participants completed these trials. The authors concluded that evidence on the benefits and risks of various washout policies were limited and generally low-quality. Moore and colleagues(24) conducted a three-arm RCT

using saline or acidic solutions and compared it with standard care with no washout. They reported results from 53 participants and found insufficient evidence to determine whether prophylactic LTC washout with saline or acidic solution was more effective than standard care without washout in preventing blockages. Muncie(25)(n = 32) provided data on the mean catheter replacement rate per 100 days of catheterisation. They reported the mean was 5.5 catheters replaced for the saline washout period and 4.7 catheters replaced for no washout periods, indicating no significant impact on the incidence of the total number of catheter replacements. The British Association of Urological Surgeons (BAUS) and Nurses (BAUN) consensus document indicates that prophylactic bladder washouts or catheter maintenance solutions can be employed to minimise the risk of catheter blockages in patients with LTC.(26) In CATHETER II, the observed trends in reduced LTC blockage rates in the washout groups, despite the lack of statistical significance, suggest a potential benefit of prophylactic washouts in preventing LTC blockages. Hence, we propose further research with larger sample sizes to validate these findings. This can be best achieved by an international RCT in countries with similar healthcare systems.

S-CAUTI is the main safety issue with prophylactic LTC washouts and was the concern stated in the NICE guideline development group as potential harm and one of the main reasons for not recommending prophylactic LTC washouts.(1,27) The Cochrane review(7) included four trials comparing saline or acidic washouts with no washout. There was insufficient evidence from these trials and the Cochrane review could not draw a conclusion if there was an effect on S-CAUTI incidence or catheterisation duration. It is therefore reassuring to see in CATHETER II, despite the small sample size, the S-CAUTI rate is significantly lower at 3.71 per 1000 catheter days in the saline washout group compared to 8 per 1000 catheter days in the standard LTC care only group [IRR is 0.40(0.20 to 0.80);p-value=0.003]. There are also lower

rates of S-CAUTI in the acidic washout group at 6.72 per 1000 catheter days (IRR of 0.98(0.54 to 1.78): p-value=0.926), albeit not reaching statistical significance. Moore(24) (n=32) reported no incidence of S-CAUTI in their trial participants. Self-reported UTIs, however, were reported in each group (citric acid 5/24, saline 2/18, no washout 3/23).

In CATHETER II, the mean monthly occurrence of bladder spasms was comparable between the washout groups and slightly higher in the control group. All three groups had less than one day of urine retention per month. In the Cochrane review(7), only one trial reported results of bladder spasm; saline 0/29 participants, acetic acid 1/30 participants, neomycin-polymyxin 2/30 participants.(28)

Participants receiving a saline washout experienced fewer episodes of blood in urine compared to the control group, while those on an acidic washout had higher occurrences. Moore(24) presented findings from urine dipstick testing, revealing a consistent presence of blood in the urine for all participants, regardless of their assigned groups.

Washout groups had more days of leakage (catheter bypass) on average than the control. Muncie(25) in their cross-over trial reported 32 events of urine leakage, 11/32 in the saline washout period and 21/32 in no washout period. Catheter kinks were rare in all groups. Although some differences were observed between the washout groups and the control group in terms of self-reported blood and pus in urine and pus in urine, the incidence of other events was similar.

The incidence of adverse events among participants in all groups was low. Bleeding or discharge at the catheter site shows comparable rates across all three groups. Granulation problems, however, are exclusively noted in the washout groups, with two occurrences in

the saline group and four in the acidic group. Most complications were primarily handled by either the individual themselves, their carer, or through a nurse's home visit.

In this trial, participants performed prophylactic washouts with selfcare and minimal dependence on healthcare resources. The participants were provided with video training that was proven to be effective with only four participants stopping the intervention for inability to perform washouts. Results of the TSQM questionnaire showed relatively high scores for convenience, effectiveness, and overall satisfaction in both the LTC washout groups. There are no other studies in the literature that made similar comparisons.

Acceptability of prophylactic LTC washouts and the selfcare program was further confirmed in the embedded qualitative study (reported in a separate publication).

The Cochrane review(7) noted that none of the RCTs assessed patients' acceptability and/or impact on QoL and recommended these outcomes should be assessed in future RCTs. In CATHETER II, participants in both washout groups showed higher EQ-5D-5L scores than the control group, indicating potential for greater improvement in QoL albeit not statistically significant. There was little evidence of differences between groups in terms of ICIQ-LTC scores.

Strengths and limitations

CATHETER II is a robustly designed pragmatic RCT abiding by the principles and recommendations of the CONSORT statement. The RCT included an embedded qualitative study highlighting the views and experience of patients and healthcare professionals (reported separately). We assessed a comprehensive list of outcomes which are related for patients, healthcare professional, guideline developers and other stakeholders' decision

making. Women constituted approximately 50% of the study population and were balanced between groups confirming generalisability of our results.

Despite being the largest reported RCT on this topic, a significant limitation is the small sample size hence the study was underpowered to detect the 25% reduction in catheter blockage it set out to demonstrate.

Conclusions

The early closure and small sample size of the CATHETER II RCT limits our ability to determine the comparative effectiveness between saline or acidic catheter washout solutions in addition to standard LTC care compared to standard LTC care only. However the results are favourable, albeit not statically significant, for lower rates of LTC blockages without a rise in S-CAUTI when employing prophylactic LTC washouts. We therefore recommend an international RCT to ascertain the clinical and cost-effectiveness of LTC washouts.

ABBREVIATIONS

AE: Adverse event

CONSORT: Consolidated Standards of Reporting Trials

EQ-5D-5L: EuroQol questionnaire – 5 dimensions – 5 levels

GSE: The General Self-Efficacy Scale

ICECAP-A: ICEpop CAPability measure for Adults

ICECAP-O: ICEpop CAPability measure for Older people

ICIQ-LTCqol: International Consultation on Incontinence Modular Questionnaire – Long Term Catheter quality of life

IRR: Incidence rate ratio

LTC: Long term catheter

QoL: Quality of Life

RCT: Randomised controlled trial

S-CAUTI: Symptomatic catheter-associated urinary tract infection

DECLARATIONS

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Authors' contributions

The corresponding author attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted. MAF is the Chief Investigator and guarantor; he conceived the study, led the proposal and protocol development, contributed to writing the manuscript and approved the final version for publication. MIO contributed to the development of the study protocol and contributed to writing the manuscript. DJ and LC contributed to writing the manuscript, contributed to study design, development and implementation of the protocol and managed the coordination of the study. DC led on statistical aspects of the study and contributed to writing the manuscript. SC contributed to study design, development of the protocol and contributed to writing the manuscript. ST contributed to qualitative aspects of the study. SE and KP contributed to developing the proposal, protocol and study materials. SM led on qualitative aspects of protocol development. KD, HH, JL, PL, PM, PKM, JND, CP and NK contributed to clinical aspects of protocol development. MK and GS led on health economics aspects of protocol development. JN and GM contributed to proposal and protocol development. All authors

contributed to oversight of the study via the Project Management Group, read and commented on the manuscript and approved the final manuscript.

Competing interests

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Ethics approval

This study was ethically approved by Wales Research Ethics Committee 6 (19/WA/0015). All participants and their carers gave informed consent before taking part.

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Transparency statement

The lead author affirms that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that discrepancies from the study as originally planned and registered have been explained.

Data availability statement

Data are available for bona fide researchers who request it from the authors.

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FIGURE LEGENDS

Figure 1 CONSORT diagram

Randomised	(n=80)

Saline	(n = 26)
Baseline completed	(n = 26)
Changed to acidic washout	(n = 1)
Changed to saline washout	n/a
Stopped washout	(n = 7)
Declined all monthly phone calls	(n = 1)
Provided monthly CRF data	(n = 25)
Six month follow-up	
completed	(n = 20)
missing	(n = 4)
declined follow-up	(n = 2)
deceased	
Twelve month follow-up	
completed	(n = 18)
missing	(n = 4)
declined follow-up	(n = 4)
deceased	
Eighteen month follow-up	
completed	(n = 10)
missing	
declined follow-up	(n = 2)
deceased	(n = 1)
did not receive questionnaire	(n = 13)
Twenty four month follow-up	
completed	(n = 4)
missing	
declined follow-up	
deceased	(n = 1)
did not receive questionnaire	(n = 21)
Completed exit questionnaire	(n = 6)

Acidic	(n = 27)
Baseline completed	(n = 27)
Changed to acidic washout	n/a
Changed to saline washout	(n = 2)
Stopped washout	(n = 3)
Declined all monthly phone calls	
Provided monthly CRF data	(n = 27)
Six month follow-up	
completed	(n = 21)
missing	(n = 5)
declined follow-up	(n = 1)
deceased	
Twelve month follow-up	
completed	(n = 18)
missing	(n = 6)
declined follow-up	(n = 3)
deceased	
Eighteen month follow-up	
completed	(n = 8)
missing	(n = 4)
declined follow-up	(n = 1)
deceased	
did not receive questionnaire	(n = 14)
Twenty four month follow-up	
completed	(n = 4)
missing	(n = 1)
declined follow-up	(n = 1)
deceased	
did not receive questionnaire	(n = 21)
Completed exit questionnaire	(n = 4)

Control	(n = 27)
Baseline completed	(n = 27)
Changed to acidic washout	(n = 0)
Changed to saline washout	(n = 0)
Stopped washout	n/a
Declined all monthly phone calls	(n = 1)
Provided monthly CRF data	(n = 26)
Six month follow-up	
completed	(n = 23)
missing	(n = 3)
declined follow-up	
deceased	(n = 1)
Twelve month follow-up	
completed	(n = 21)
missing	(n = 3)
declined follow-up	(n = 1)
deceased	(n = 2)
Eighteen month follow-up	
completed	(n = 8)
missing	(n = 4)
declined follow-up	
deceased	(n = 2)
did not receive questionnaire	(n = 13)
Twenty four month follow-up	
completed	(n = 4)
missing	(n = 1)
declined follow-up	
deceased	(n = 2)
did not receive questionnaire	(n = 20)
Completed exit questionnaire	(n = 4)

SUPPLEMENTARY MATERIALS

Table S1 Sensitivity analyses

	Saline washouts (n=26)	Acidic washouts (n=27)	Either washout (n=53)	Control (n=27)
Participants providing follow-up data	25	27	52	26
Total months of follow-up	387	409	796	420
Mean catheterisation duration (days)	468(182)	459(191)	463(185)	492(167)
Blockages requiring treatment (rate per 1000 catheter days)	9.96(14.48)	10.53(15.77)	10.25(15.02)	20.92(27.77)
IRR compared to control	0.65(0.24 to 1.77);0.33	0.59(0.22 to 1.63);0.25	0.62(0.26 to 1.49);0.22	
Sensitivity analysis	0.85(0.29 to 2.49);0.74	0.68(0.24 to 1.94);0.41	0.76(0.30 to 1.95);0.52	
S-CAUTI (rate per 1000 catheter days)	3.71(8.45)	6.72(7.10)	5.27(7.85)	8.05(11.29)
IRR compared to control	0.40(0.20 to 0.80);0.003	0.98(0.54 to 1.78);0.93	0.69(0.39 to 1.23);0.14	
Sensitivity analysis	0.30(0.16 to 0.56);<0.001	0.66(0.38 to 1.15);0.09	0.47(0.28 to 0.80);0.001	

Due to the early closure of the trial and small sample size there was potential imbalance at baseline that would have been eliminated if 200 participants had been randomised to each group. Therefore, an additional analysis was conducted of blockage requiring intervention and S-CAUTI.

The results of the sensitivity analysis show the IRR for the primary outcome are closer to 1. This indicates either washout reduces the number of blockages requiring treatment, but the effects are not as strong. The sensitivity analysis of infections requiring antibiotics show lower IRR from both saline and acidic washout. There is a strong suggestion that both washouts reduce S-CAUTI. Compared to the trial analysis the effect from acidic washout on S-CAUTI is stronger.

Table S2 Quality of life outcomes

	Saline washouts (n=26)	Acidic washouts (n=27)	Control (n=27)
EQ-5D-5L[1]			
Baseline	0.368(0.405);[N=25]	0.365(0.359);[N=26]	0.348(0.373);[N=27]
6-month	0.356(0.513);[N=18]	0.335(0.313);[N=20]	0.270(0.348);[N=22]
12-month	0.386(0.430);[N=18]	0.412(0.321);[N=17]	0.339(0.414);[N=21]
18-month	0.493(0.403);[N=10]	0.302(0.453);[N=7]	0.139(0.264);[N=8]
24-month	0.349(0.414);[N=4]	0.621(0.339);[N=3]	-0.077(0.082);[N=4]
exit	0.445(0.541);[N=6]	0.327(0.491);[N=4]	0.229(0.211);[N=4]
Effect size compared to control	0.056(-0.022 to 0.134);0.11	0.053(-0.024 to 0.131);0.12	
General self-efficacy scale[2]			
Baseline	29.1(9.1);[N=25]	29.4(5.7);[N=27]	27.8(7.6);[N=27]
6-month	27.7(9.3);[N=19]	27.6(6.0);[N=20]	26.8(8.5);[N=23]
12-month	27.4(9.7);[N=18]	29.2(5.5);[N=18]	25.1(7.5);[N=21]
18-month	28.3(7.7);[N=9]	29.3(6.0);[N=8]	28.3(3.6);[N=9]
24-month	28.3(3.3);[N=4]	30.4(4.9);[N=4]	27.3(7.4);[N=4]
Effect size compared to control	0.9(-1.5 to 3.2);0.40	2.2(-0.1 to 4.5);0.030	
ICECAP-A[3]			
Baseline	0.551(0.216);[N=10]	0.487(0.223);[N=11]	0.496(0.218);[N=9]
6-month	0.671(0.176);[N=8]	0.592(0.256);[N=10]	0.620(0.200);[N=8]
12-month	0.606(0.233);[N=7]	0.450(0.282);[N=7]	0.611(0.146);[N=7]
18-month	0.849(0.000);[N=2]	0.246(0.349);[N=2]	0.669(0.203);[N=4]
24-month	0.766(0.117);[N=2]	0.304(0.281);[N=3]	0.486(0.137);[N=2]
Effect size compared to control	-0.076(-0.221 to 0.068);0.24	-0.086(-0.214 to 0.042);0.13	
ICECAP-O[3]			
Baseline	0.488(0.320);[N=15]	0.601(0.206);[N=14]	0.669(0.204);[N=15]
6-month	0.554(0.268);[N=12]	0.657(0.227);[N=11]	0.673(0.241);[N=15]
12-month	0.569(0.329);[N=11]	0.611(0.239);[N=9]	0.707(0.161);[N=13]
18-month	0.511(0.239);[N=7]	0.614(0.331);[N=6]	0.666(0.230);[N=5]
24-month	0.637(0.078);[N=2]	0.940(.);[N=1]	0.641(0.219);[N=2]
Effect size compared to control	0.036(-0.069 to 0.142);0.44	-0.038(-0.145 to 0.070);0.43	
ICIQ-LTC function and concern[4]			
Baseline	18.3(9.1);[N=26]	17.3(9.7);[N=26]	19.1(9.0);[N=27]
6-month	15.6(10.1);[N=19]	16.4(10.2);[N=19]	19.8(9.6);[N=23]
12-month	12.5(6.9);[N=15]	18.1(11.6);[N=15]	17.9(10.7);[N=20]
18-month	11.9(5.5);[N=7]	12.3(7.5);[N=7]	14.2(12.5);[N=6]
24-month	9.3(3.3);[N=4]	19.5(4.4);[N=4]	18.5(10.0);[N=4]
Effect size compared to control	-1.2(-4.1 to 1.7);0.34	0.7(-2.2 to 3.5);0.60	
ICIQ-LTC lifestyle[4]			
Baseline	6.7(3.4);[N=24]	8.1(3.3);[N=27]	7.6(2.9);[N=27]
6-month	7.4(3.8);[N=19]	7.6(4.0);[N=17]	8.4(3.2);[N=21]
12-month	7.8(4.3);[N=16]	8.1(3.7);[N=14]	8.4(3.6);[N=20]
18-month	7.0(2.6);[N=8]	10.0(3.5);[N=7]	7.3(3.4);[N=6]
24-month	7.5(2.1);[N=2]	8.8(4.2);[N=4]	5.3(2.9);[N=4]
Effect size compared to control	-0.1(-1.6 to 1.4);0.90	-0.4(-1.9 to 1.2);0.60	

	Saline washouts (n=26)	Acidic washouts (n=27)	Control (n=27)
Treatment satisfaction questionnaire			
Effectiveness[5]			
6-month	67.0(27.9);[N=17]	67.6(31.3);[N=18]	
12-month	74.2(30.5);[N=14]	71.8(18.9);[N=14]	
18-month	83.3(22.9);[N=5]	77.8(21.2);[N=5]	
24-month	83.3(23.6);[N=2]	77.8(25.5);[N=3]	
Convenience[5]			
6-month	82.0(15.3);[N=17]	73.8(23.3);[N=18]	
12-month	89.7(11.3);[N=14]	77.0(18.9);[N=14]	
18-month	90.7(13.5);[N=6]	80.0(18.7);[N=5]	
24-month	91.7(3.9);[N=2]	74.1(8.5);[N=3]	
Overall satisfaction[5]			
6-month	76.1(22.7);[N=17]	78.2(27.7);[N=17]	
12-month	86.7(20.2);[N=14]	73.0(29.5);[N=14]	
18-month	88.1(22.9);[N=6]	84.3(27.4);[N=5]	
24-month	75.0(15.2);[N=2]	69.0(28.9);[N=3]	

The EQ-5D-5L exit questionnaire was for participants who exited the study early or were not at a notional follow-up point when the study ended.

All effect sizes come from a mixed effects linear regression including fixed effects for the two treatment groups, gender, age band, previous blockage, previous S-CAUTI and baseline measure of the outcome. Dummy variables are also included for the timepoint when the follow-up is completed. Random effects (intercepts) are included for region and participant to allow for repeated measures across time. The summary statistics are the mean, standard deviation, and count and the effects sizes are the adjusted mean difference, 97.5% confidence interval and p-value.

[1]The EQ-5D-5L is a generic QoL measure. It has 5 questions and is on the scale -0.594 to 1 with higher scores indicating better QoL.

[2]The general self-efficacy (GSE) scale assesses ability to cope with daily life. It has 10 questions and scores are between 10 and 40 with higher scores better.

[3]The ICECAP-A and ICEPOP-O measure capability in adults and older people respectively. Both have 5 question and are on the scale 0 to 1 with higher scores better.

[4]ICIQ long-term catheterisation quality of life questionnaire is a specific quality of life measure. It produces the function and concern score and the lifestyle score. The function & concern score has 10 questions and is on the scale 0 to 42. The lifestyle score has 3 questions and is on the scale 3 to 15. For both higher scores are worse.

[5]The treatment satisfaction questionnaire assesses satisfaction with medication. It produces the effectiveness, convenience, and overall satisfaction scores. Each score has 3 questions to give 9 in total, with each score on the scale 0 to 100 with higher scores better.

Table S3 Time and travel data

	Saline washouts (n=26)	Acidic washouts (n=27)	Control (n=27)
Participants completed questionnaire	8	7	9
Travel to outpatient consultation			
distance (miles)	15.0(n/a);[N=1]	16.0(12.5);[N=3]	13.6(6.5);[N=7]
cost (£)	0.00(0.00);[N=2]	0.00(0.00);[N=3]	1.11(1.97);[N=7]
Total outpatient time (hours)	5.33(n/a);[N=1]	3.33(1.53);[N=3]	3.09(1.80);[N=7]
Travel to GP appointment			
distance (miles)		1.0(n/a);[N=1]	3.3(1.9);[N=6]
cost (£)		0.00(n/a);[N=1]	0.00(0.00);[N=6]
Total time for GP appointment (hours)		1.00(n/a);[N=1]	1.56(1.12);[N=6]
Travel to hospital admission			
distance (miles)		8.0(0.0);[N=2]	13.8(1.5);[N=4]
cost (£)		0.00(n/a);[N=1]	1.00(1.73);[N=3]
Total time for hospital admission(days)		6.00(n/a);[N=1]	6.76(2.06);[N=4]

The summary statistic in the cells is the mean, standard deviation, and count.

Table S4 Baseline data (disaggregated by gender)

	Saline - female N=14	Saline - male N=12	Acidic - female N=12	Acidic - male N=15	Control - female N=14	Control - male N=13
Age	53.6(16.1);[N=14]	78.0(8.2);[N=12]	54.8(17.9);[N=12]	68.4(13.4);[N=15]	62.1(16.4);[N=14]	72.6(12.3);[N=13]
Length of time catheterised						
<1 year	2/14(14%)	5/12(42%)	2/12(17%)	3/15(20%)	3/14(21%)	2/13(15%)
1 to 3 years	4/14(29%)	5/12(42%)	3/12(25%)	3/15(20%)	3/14(21%)	6/13(46%)
>3 years	8/14(57%)	2/12(17%)	7/12(58%)	9/15(60%)	8/14(57%)	5/13(39%)
Neuropathic bladder	7/14(50%)	1/12(8.3%)	5/12(42%)	4/15(27%)	9/14(64%)	2/13(15%)
Urine pH	6.9(0.8);[N=13]	6.1(0.5);[N=11]	6.7(1.0);[N=12]	6.8(1.0);[N	6.8(0.7);[N=13]	7.0(0.9);[N=12]
Current on washout	3/14(21%)	0/12(0%)	3/12(25%)	3/15(20%	4/14(29%)	2/13(15%)
Catheter change frequency						
Every week					1/14(7.1%)	
Every 2 weeks					2/14(14%)	
Every 3 weeks						1/13(7.7%)
Every 4 weeks	4/14(29%)		2/12(17%)	2/15(13%)	4/14(29%)	1/13(7.7%)
Every 5 weeks			1/12(8.3%)			
Every 6 weeks	3/14(21%)	1/12(8.3%)	1/12(8.3%)	2/15(13%)	1/14(7.1%)	1/13(7.7%)
Every 7 weeks				1/15(67%)		1/13(7.7%)
Every 8 weeks	2/14(14%)	1/12(8.3%)	1/12(8.3%)	1/15(67%)		2/13(15%)
Every 10 weeks	1/14(7.1%)	1/12(8.3%)	4/12(33%)	1/15(67%)	1/14(7.1%)	2/13(15%)
Every 12 weeks	4/14(29%)	9/12(75%)	3/12(25%)	8/15(53%)	5/14(36%)	5/13(38%)
Blockages requiring treatment (prior 6 months)						
0	5/14(36%)	8/12(67%)	6/12(50%)	7/15(47%)	4/14(29%)	8/13(62%)
1 to 3	4/14(29%)	4/12(33%)	4/12(33%)	5/15(33%)	4/14(29%)	3/13(23%)
4 or more	5/14(36%)	0/12(0%)	2/12(17%)	3/15(20%)	6/14(43%)	2/13(15%)
Median [Lower, Upper quartile]	2.5;[0.0,6.0]	0.0;[0.0,2.0]	0.5;[0.0,2.5]	2.0;[0.0	2.0;[0.0,6.0]	0.0;[0.0,2.0]
S-CAUTI requiring antibiotics (prior 6 months)						
0	5/14(36%)	9/12(75%)	6/12(50%)	7/15(47%)	3/14(21%)	11/13(85%)
1 to 3	8/14(57%)	1/12(8.3%)	1/12(8.3%)	8/15(53%)	8/14(57%)	2/13(15%)
4 or more	1/14(7.1%)	2/12(17%)	5/12(42%)	0/15(0%)	3/14(21%)	0/13(0%)
Median [Lower, Upper quartile]	1.0;[0.0,2.0]	0.0;[0.0,1.5]	0.5;[0.0,5.0]	1.0;[0.0,2.0	1.5;[1.0,3.0]	0.0;[0.0,0.0]
General self efficacy scale[1]	24.4(10.0);[N=13]	34.2(4.1);[N=12]	30.3(5.6);[N=12]	28.7(5.8);[N=15	27.5(8.8);[N=14]	28.2(6.2);[N=13]
ICIQ-LTCqol function and concern[2]	21.3(10.1);[N=14]	14.9(6.8);[N=12]	18.8(11.4);[N=12]	16.0(8.1);[N=14	22.8(5.8);[N=14]	15.2(10.4);[N=13]
ICIQ-LTCqol lifestyle[2]	6.3(3.9);[N=13]	7.1(2.7);[N=11]	8.4(3.4);[N=12]	7.8(3.4);[N=15	8.0(3.3);[N=14]	7.1(2.4);[N=13]

EQ-5D-5L[3]	0.110(0.353);[N=14]	0.695(0.143);[N=11]	0.230(0.362);[N=12]	0.480(0.325);[N=14]	0.217(0.359);[N=14]	0.488(0.348);[N=13]
ICECAP-A[4]	0.551(0.216);[N=10]	n/a(n/a);[N=0]	0.461(0.250);[N=7]	0.531(0.192);[N=4]	0.485(0.251);[N=6]	0.518(0.178);[N=3]
ICECAP-O[4]	0.799(0.182);[N=3]	0.410(0.302);[N=12]	0.698(0.163);[N=4]	0.562(0.216);[N=10]	0.788(0.060);[N=7]	0.566(0.232);[N=8]

[1]The general self-efficacy (GSE) scale assesses ability to cope with daily life. It has 10 questions and scores are between 10 and 40 with higher scores better.

[2]ICIQ long-term catheterisation quality of life questionnaire is a specific quality of life measure. It produces the function and concern score and the lifestyle score. The function & concern score has 10 questions and is on the scale 0 to 42. The lifestyle score has 3 questions and is on the scale 3 to 15. For both higher scores are worse.

[3]The EQ-5D-5L is a generic quality of life measure. It has 5 questions and is on the scale -0.594 to 1 where higher scores indicate better quality of life.

[4]The ICECAP-A and ICEPOP-O measure capability in adults and older people respectively. Both have 5 question and are on the scale 0 to 1 with higher scores better. The treatment satisfaction questionnaire assesses satisfaction with medication. It produces the effectiveness, convenience, and overall satisfaction scores. Each score has 3 questions to give a total, with each score on the scale 0 to 100 with higher scores better.

Apart from where indicated, the summary statistics for the continuous outcomes are mean, standard deviation, and count while the categorical variables are summarised with count and percentage.

Table S5 Blockage requiring treatment (primary outcome) and S-CAUTI (disaggregated by gender)

	Saline – female (n=14)	Saline – male (n=12)	Acidic – female (n=12)	Acidic – male (n=15)	Control – female (n=14)	Control – male (n=13)
Participants providing follow-up data	13	12	12	15	14	12
Total months of follow-up	217	170	181	228	220	200
Mean catheterisation duration (days)	503(185)	430(179)	458(195)	460(194)	481(193)	505(137)
Total number of blockages requiring treatment	76	29	51	64	175	61
Blockages requiring treatment (rate per 1000 catheter days)	13.71(17.02)	5.90(10.36)	10.31(17.62)	10.70(14.77)	29.39(31.77)	11.04(19.03)
Total instances of S-CAUTI	29	8	48	33	78	20
S-CAUTI (rate per 1000 catheter days)	5.85(11.27)	1.38(2.40)	9.80(8.35)	4.26(4.91)	11.65(13.49	3.86(6.25)

The summary statistics in the cells are mean(standard deviation)

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CATHETER II, a randomised controlled trial comparing the clinical effectiveness of various washout policies versus no washout policy in preventing catheter associated complications in adults living with long term catheters

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TITLE

CATHETER II, a randomised controlled trial comparing the clinical effectiveness of various washout policies versus no washout policy in preventing catheter associated complications in adults living with long term catheters

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ABSTRACT

Objectives

Do weekly prophylactic saline or acidic catheter washouts in addition to standard long-term catheter (LTC) care improve the outcomes of adults with LTC compared to standard LTC care only.

Design

Three-arm superiority open-label randomised controlled trial.

Setting

UK community-based study.

Participants

80 adults with LTC (any type/route) ≥28 days in situ with no plans to discontinue and able to self-manage the washouts/study documentation with/without a carer.

Interventions

Randomly allocated (26:27:27) to receive standard LTC care with weekly saline or weekly acidic or no prophylactic washouts for up to 24 months.

Primary and secondary outcome measures

The primary outcome was catheter blockage requiring intervention (/1000 catheter days). Secondary outcomes were symptomatic catheter-associated urinary tract infection (S-CAUTI) requiring antibiotics, adverse events, participants' quality of life and day-to-day activities, acceptability, and adherence.

Results

Outcomes reported for 25 saline, 27 acidic and 26 control participants. LTC blockages (/1000 catheter days) requiring treatment were 9.96, 10.53, and 20.92 in the saline, acidic, and control groups respectively. The incident rate ratio (IRR) favours the washout groups [saline 0.65(0.24 to 1.77); p-value=0.33 and acidic 0.59(0.22 to 1.63); p-value=0.25], albeit not statistically significant.

The S-CAUTI rate (/1000 catheter days) was 3.71, 6.72, and 8.05 in the saline, acidic, and control groups respectively. The IRR favours the saline group [saline 0.40(0.20 to 0.80); p-value=0.003 and acidic 0.98(0.54 to 1.78); p-value=0.93].

The trial closed before reaching target recruitment due to reduced research capacity during the COVID pandemic.

Conclusions

Early closure and small sample size limits our ability to provide a definite answer. However, the observed non-statistically significant differences over control are favourable for lower rates of LTC blockages without a concomitant rise in S-CAUTI. The results support a multi-national randomised controlled trial of catheter washouts in patients with LTC to ascertain their clinical and cost-effectiveness.

Trial registration

ISRCTN17116445.

STRENGTHS AND LIMITATIONS OF THIS STUDY

- CATHETER II was the largest randomised controlled trial to date investigating prophylactic catheter washouts to prevent blockage.
- A pragmatic trial design was used to evaluate the intervention in real-life practice. Participants were supported to self-manage the intervention to minimise impact on health care resources.
- A comprehensive list of outcomes was assessed and relate to patient, healthcare professional, guideline developer and other stakeholder decision making.
- Validated tools were used to assess quality of life, adherence, convenience, satisfaction, and impact on daily activities. However, outcome data was patient-reported, and it was not possible to blind participants to the intervention.
- Sample size was limited by early closure of the trial due to difficulty with recruitment during the COVID pandemic. This was primarily a result of reduced research capacity and prioritisation of COVID and cancer-related research in primary and secondary care settings.

INTRODUCTION

Long term catheter (LTC) is defined as catheter use for more than 28 days.[1] Approximately 90,000 (1 in 700) of the UK population live with LTC (urethral or suprapubic), with a higher prevalence (0.5%) in those aged over 75 and a mean duration of use of six years.[2-4] In a recently published study Gage and colleagues[5] explored catheter-related service use and costs in patients living with LTC in England. Their findings show that almost 60% of LTC users were men, 71% participants were >70 years of age, and 61% used a urethral catheter. Indications for LTC include intractable urinary incontinence or chronic retention due to spinal cord injury, multiple sclerosis, prostate enlargement, and underactive bladder.[6,7] With an ageing population[8], LTC prevalence and LTC-related use of healthcare resources is expected to rise substantially.

Standard LTC care involves a weekly valve and/or leg bag change (by the patient/carer) and a 4-12 weekly catheter change (usually by the clinical team).[9]

Adverse events (AEs) associated with LTC use impact patients' quality of life (QoL) and are a significant burden on NHS resources.[10] AEs can include blockage, symptomatic catheter-associated urinary tract infection (S-CAUTI), urinary leakage, bladder spasms, pain, and accidental dislodgment.[5,6]

Blockage is the main AE with an incidence of 20-70%[11] or 8.54 per 1000 days of catheter use[6], requiring emergency treatment. A Grampian wide audit (Northeast of Scotland) in year 2017, showed 11.8 blockages requiring intervention per 1000 catheter days. Rarely, blockage may lead to serious complications of urosepsis or autonomic dysreflexia in patients with spinal cord injury at T6 or above.[11]

Various catheter washout policies are used for the prevention and treatment of catheter blockage including different types of solutions, concentrations, volumes, and frequency.[7] Washouts may work by mechanically flushing debris, dissolving mineral encrustations, and/or by antimicrobial effect.[12] Current guidelines do not recommend prophylactic washouts to prevent blockages suggesting instead more frequent change of the catheter.[1] The Cochrane review[7] concluded there is insufficient evidence to define benefits, clinical effectiveness, risks, acceptability, and impact on patient QoL. They also reported some clinical community concerns that catheter washouts may damage bladder mucosa and introduce infection and recommended a robust randomised controlled trial (RCT) to assess the clinical and cost effectiveness of prophylactic washouts in adults living with LTC.

CATHETER II hypothesised weekly prophylactic catheter washouts in addition to standard LTC care would result in a ≥25% relative reduction in catheter blockages requiring intervention. Weekly prophylactic normal saline or citric acid washouts were compared in parallel against standard LTC care only. Clinical effectiveness, patient acceptability, satisfaction, and safety were evaluated.

MATERIALS (PATIENTS) AND METHODS

CATHETER II was a pragmatic three-arm open-label multi-centre superiority RCT with internal pilot and embedded qualitative component. The trial methodology has been published.[13,14] Summary methods are included in accordance with CONSORT (Consolidated Standards of Reporting Trials) guidelines.[15]

Participants were recruited from 21 sites in Scotland, England and Wales including GP practices, community/secondary care hospitals, and using targeted social media/website advertising. Participants were aged ≥18 years with a LTC (any type/route) in use for at least 28 days with no plan to discontinue. Participants self-managed catheter washouts and completed trial documentation or had a carer to assist them. Patients unable to consent or were pregnant/contemplating pregnancy were not eligible. Also excluded were patients with a spinal cord injury at/above T6, suspected S-CAUTI, visible haematuria, known allergies to the washout solutions, current bladder cancer or bladder stones, or who the recruitment team considered unsuitable for other clinical or social reasons (Figure 1). Informed written consent was obtained from participants and, where applicable, their carers prior to randomisation.

Interventions

Participants were randomised to receive a policy of:

- weekly prophylactic normal saline (Uro-Tainer® NaCl 0.9% 100ml) catheter washouts plus standard LTC care; or
- weekly prophylactic acidic (two sequential applications of 30ml 3.23% citric acid, Uro-Tainer® Twin Suby G) catheter washouts plus standard LTC care; or
- standard LTC care only (i.e., no prophylactic catheter washouts).

A survey of opinion from relevant stakeholders identified these washouts as the most commonly used washouts in the UK.[13] They were also the most frequently used interventions identified in the Cochrane systematic review.[7] A secondary consideration for choice of intervention was product availability within the required timeframe. Due to the choice of comparators and the inclusion of a no prophylactic washout standard care only

arm, it was not possible to blind participants to the intervention. Changes to washout policy during follow up, including type and frequency, were permitted when clinically necessary. Participants/carers were trained on best practice washout technique by trained delegated members of staff. To standardise washout delivery, all participants were provided with the same training resources.[13] Additional training was provided when identified by staff or participant/carer. To minimise breakage of the closed drainage system and the risk of introducing infection, the washouts were administered during the regular change of the catheter bag or valve.

Outcomes

The primary clinical outcome was catheter blockage requiring intervention up to 24 months post-randomisation expressed as number per 1000 catheter days. An intervention was defined as an unplanned catheter removal or change, or washout performed by the participant or carer, or requiring unplanned visits to/from any healthcare provider, or hospital admission. The primary health economic outcome was the incremental cost per quality adjusted life year gained with each washout policy compared to standard LTC care only.

Secondary outcomes were S-CAUTI requiring antibiotics, LTC-related and other AEs, duration of LTC use, catheter change (other than for blockage), QoL (both generic (EQ-5D-5L[16]) and disease specific (ICIQ-LTCqol International Consultation on Incontinence Modular Questionnaire – LTC QoL[17])), adherence, convenience, satisfaction (adapted TSQM Treatment Satisfaction Questionnaire for medication[18]), impact on daily activities (GSE General Self-Efficacy Scale[19] and ICECAP-A / ICECAP-O ICEpop CAPability measure for Adults/Older people[20,21]), discontinuation of LTC, and changes to washout policy.

Outcome data was patient reported. Baseline data was collected prior to randomisation. Follow-up data was collected by monthly telephone call and 6-monthly postal/online questionnaires. Where participant follow-up ended early (discontinuation of LTC or early study closure), an additional EQ-5D-5L questionnaire was collected.

Sample size

A survey of experts, patients and available literature deemed a 25% reduction in LTC blockage was required for washouts to be considered worthwhile. This implied a reduction from 11.8/1000 days (control) to 8.9. We used the formula from Zhu and Lakkis[22] to derive the sample size for comparing two negative binomial rates. We needed outcome data from 200 participants per arm for 90% power, assuming two-sided significance of 2.5% (to account for two planned comparisons) and a mean 50/730 days loss to follow-up.

Randomisation

The local research team randomised participants 1:1:1 to one of three arms using a centralised computer randomisation system (created and administered by Centre for Healthcare Randomised Trials, University of Aberdeen). It was not possible to blind participants or researchers to the allocated arm. Randomisation used a minimisation algorithm with a random element and minimised on the following factors:

Region (NHS Grampian v Aneurin Bevan University Health Board v Cwm Taf University Health Board v CRN Eastern v CRN East Midlands v CRN Thames Valley South Midlands v CRN Yorkshire and Humber v CRN Wessex v CRN Greater Manchester v CRN South London v Central), gender (male v female), age (<45, 45 to 64, 65 and above), residential status

(community v care home), previous blockages (zero v 1 or more), previous S-CAUTI (zero v 1 or more), urine pH (acidic (<5.1) v normal (5.1 to 6.7) v alkaline (>6.7) v not available)

Patient and Public Involvement (PPI)

PPI partners were active members of the project management group and Trial Steering Committee. They were involved in all stages of the project including development of the study protocol and study materials and oversight. PPI partners will lead the development of the dissemination to participants and the public.

Modifications due to impact of COVID-19

Recruitment commenced in December 2019 and was paused in March 2020 due to COVID-19 pandemic regulations. Following extensive efforts, the study team obtained approval from Sponsor and the regulatory authorities and recruitment resumed in September 2020 with protocol modifications to minimise face-to-face contact (postal/ telephone consent; telephone collection of baseline data and video consultation training of washout technique). Follow up continued by post and telephone in line with the original protocol. COVID-related protocol adjustments were previously published.[13]

Recovery plans were instigated but the pandemic continued to negatively impact the set-up of research sites and recruitment to the study. In June 2022, the funder elected to terminate the study early, with recruitment ending in August 2022 and follow up ending in August 2023. The closure plan included completing the qualitative study (published alongside) and providing descriptive analysis only for the health economic measures.

Statistical methods

Analyses were based on the intention-to-treat principle. Baseline and outcome data are summarised as count and percentage for categorical data and mean and standard deviation for continuous data.

Number of blockages requiring intervention and number of S-CAUTI were summarised as a rate per 1000 catheter days and analysed using a mixed effects negative binomial regression. Fixed effects were included for the intervention (saline or acidic washout) and the minimisation variables gender, age band, previous blockage and previous S-CAUTI. A random effect (intercept) was included for region. An offset was included for the log of catheter duration (in days). Effect sizes are reported as incidence rate ratios (IRR) with 97.5% confidence intervals. QoL measures were analysed with repeated measures mixed effects linear regression. The same fixed effects were included as for the primary outcome. A dummy variable for timepoint was included as participants could report outcomes at 6-, 12-, 18- and 24-months. Random effects were included for region and participant to adjust for repeated observation on the same participant. The effect sizes are the adjusted mean differences with 97.5% confidence intervals used as an approximation to 95% confidence intervals, as the analysis model estimates the effect size of both saline and acidic washout.

A sensitivity analysis is included making additional adjustments for potential baseline imbalance. This analysis adjusted for: gender (male v female), age (<45, 45-65, >65), previous blockage (0,1-3, 4 or more), previous infection (0,1-3, 4 or more), catheter duration at baseline (<1 year, 1 to 3 years, >3 years), on washout at baseline (yes v no), neuropathic bladder (yes v no), catheter change frequency. Due to the lower recruitment and consequently smaller sample size the planned subgroup analyses were not conducted. In-addition, it was not possible to analyse and report primary (incremental cost per quality

adjusted life year) or secondary (time and travel costs) economic outcomes. The health care resource use are presented as descriptive analyses.

RESULTS

Baseline

The mean age of participants in the study was 65 years with those in the control group slightly older and similar numbers of males and females in all three groups (Table 1). The urine pH and the number of participants who had blockages requiring treatment or S-CAUTI requiring antibiotics were similar in all three groups at baseline. Catheter change frequencies ranged between every week to every 12 weeks, with the highest number of participants in all three groups changing their LTC every 12 weeks. There was good balance in the patient reported QoL scores at baseline, though there are small differences between the ICECAP-O scores.

Table 1 Baseline data

	Saline washouts (n=26)	Acidic washouts (n=27)	Control (n=27)
Age	64.8(17.9);[N=26]	62.4(16.7);[N=27]	67.1(15.3);[N=27]
Female	14/26(54%)	12/27(44%)	14/27(52%)
Length of time catheterised			
<1 year	7/26(27%)	5/27(19%)	5/27(19%)
1 to 3 years	9/26(35%)	6/27(22%)	9/27(33%)
>3 years	10/26(38%)	16/27(59%)	13/27(48%)
Neuropathic bladder	8/26(31%)	9/27(33%)	11/27(41%)
Urine pH	6.5(0.8);[N=24]	6.7(1.0);[N=25]	6.8(0.8);[N=25]
Current on washout	3/26(12%)	6/27(22%)	6/27(22%)
Catheter change frequency			
Every week			1/27(3.7%)
Every 2 weeks			2/27(7.4%)
Every 3 weeks			1/27(3.7%)

Every 4 weeks	4/26(15%)	4/27(15%)	5/27(19%)
Every 5 weeks		1/27(3.7%)	
Every 6 weeks	4/26(15%)	3/27(11%)	2/27(7.4%)
Every 7 weeks		1/27(3.7%)	1/27(3.7%)
Every 8 weeks	3/26(12%)	2/27(7.4%)	2/27(7.4%)
Every 10 weeks	2/26(7.7%)	5/27(19%)	3/27(11%)
Every 12 weeks	13/26(50%)	11/27(41%)	10/27(37%)
Blockages requiring treatment (prior 6 months)			
0	13/26(50%)	13/27(48%)	12/27(44%)
1 to 3	8/26(31%)	9/27(33%)	7/27(26%)
4 or more	5/26(19%)	5/27(19%)	8/27(30%)
Median [Lower, Upper quartile]	0.5;[0,3]	1;[0,3]	1;[0,5]
S-CAUTI requiring antibiotics (prior 6 months)			
0	14/26(54%)	13/27(48%)	14/27(52%)
1 to 3	9/26(35%)	9/27(33%)	10/27(37%)
4 or more	3/26(12%)	5/27(19%)	3/27(11%)
Median [Lower, Upper quartile]	0;[0,2]	1;[0,2]	0;[0,2]
General self efficacy scale[1]	29.1(9.1);[N=25]	29.4(5.7);[N=27]	27.8(7.6);[N=27]
ICIQ-LTCqol function and concern[2]	18.3(9.1);[N=26]	17.3(9.7);[N=26]	19.1(9.0);[N=27]
ICIQ-LTCqol lifestyle[2]	6.7(3.4);[N=24]	8.1(3.3);[N=27]	7.6(2.9);[N=27]
EQ-5D-5L[3]	0.368(0.405);[N=25]	0.365(0.359);[N=26]	0.348(0.373);[N=27]
ICECAP-A[4]	0.551(0.216);[N=10]	0.487(0.223);[N=11]	0.496(0.218);[N=9]
ICECAP-O[4]	0.488(0.320);[N=15]	0.601(0.206);[N=14]	0.669(0.204);[N=15]

[1]The general self-efficacy (GSE) scale assesses ability to cope with daily life. It has 10 questions and scores are between 10 and 40 with higher scores better.
[2]ICIQ long-term catheterisation quality of life questionnaire is a specific quality of life measure. It produces the function and concern score and the lifestyle score. The function & concern score has 10 questions and is on the scale 0 to 42. The lifestyle score has 3 questions and is on the scale 3 to 15. For both higher scores are worse.
[3]The EQ-5D-5L is a generic quality of life measure. It has 5 questions and is on the scale -0.594 to 1 where higher scores indicate better quality of life.
[4]The ICECAP-A and ICEPOP-O measure capability in adults and older people respectively. Both have 5 question and are on the scale 0 to 1 with higher scores better. The treatment satisfaction questionnaire assesses satisfaction with medication. It produces the effectiveness, convenience, and overall satisfaction scores. Each score has 3 questions to give 9 in total, with each score on the scale 0 to 100 with higher scores better.
Apart from where indicated, the summary statistics for the continuous outcomes are mean, standard deviation, and count while the categorical variables are summarised with count and percentage.

Outcomes

The follow-up of participants varied from 12 to 24 months due to early closure of the study. A CONSORT diagram is provided (Figure 1) and this shows adherence to washouts. In the saline group one participant changed to acidic washout and seven stopped washouts while in the acidic group two changed to saline and three stopped washouts. The three changes

were all recommendations by the clinical team, while three participants stopped because they were unable to perform the washout and six stopped for various medical reasons. In the control group, participants experienced a mean of one catheter blockage per month; in the acidic and saline washout groups this was lower, 0.73 and 0.34 respectively. In the washout groups the rate of LTC blockages requiring treatment was approximately 10 blockages per 1000 catheter days while in the control group the rate was approximately 21 per 1000 catheter days (Table 2). The IRR favour the washout groups (0.65 (0.24 to 1.77);p-value=0.33 and 0.59 (0.22 to 1.63);p-value=0.25 for saline and acidic respectively), albeit not statistically significant. When the two washout groups are combined in a post-hoc analyses (Table 2), the IRR was 0.62 (0.26 to 1.49;p-value=0.22).

Table 2 Blockage requiring treatment (primary outcome) and S-CAUTI

	Saline washouts (n=26)	Acidic washouts (n=27)	Either washout (n=53)	Control (n=27)
Participants providing follow-up data	25	27	52	26
Total months of follow-up	387	409	796	420
Catheterisation duration (days) [mean,(SD)]	468(182)	459(191)	463(185)	492(167)
Total number of blockages requiring treatment	105	115	220	Total=236
Blockages requiring treatment (rate per 1000 catheter days) [mean,(SD)]	9.96(14.48)	10.53(15.77)	10.25(15.02)	20.92(27.77)
IRR (97.5% CI) compared to control	0.65(0.24 to 1.77);0.33	0.59(0.22 to 1.63);0.25	0.62(0.26 to 1.49);0.22	
Total instances of S-CAUTI	37	81	118	98
S-CAUTI (rate per 1000 catheter days) [mean,(SD)]	3.71(8.45)	6.72(7.10)	5.27(7.85)	8.05(11.29)
IRR compared to control (97.5% CI)	0.40(0.20 to 0.80);0.003	0.98(0.54 to 1.78);0.93	0.69(0.39 to 1.23);0.14	

IRR is the incidence rate ratio, 97.5% CI and p-value.

In the control group the S-CAUTI rate was 8 episodes per 1000 catheter days. In the acidic washout group the rate was slightly lower at 6.72 per 1000 catheter days, resulting in an IRR of 0.98 (0.54,1.78): p-value=0.93. In the saline washout group the S-CAUTI rate was significantly lower at 3.71 per 1000 catheter days and the IRR is 0.40 (0.20,0.80);p-value=0.003.

Table S1 in the supplementary material shows a sensitivity analysis adjusting for additional factors which had potential imbalance between groups at baseline. This analysis was consistent with the main analysis and showed that weekly prophylactic LTC washouts reduced LTC blockages requiring intervention and S-CAUTI.

The mean bladder spasm days per month was similar in the washout groups at 3.48 and 3.23 and slightly higher in the control group at 4.38 (Table 3).

Table 3 Secondary outcomes

	Saline washouts (n=26)	Acidic washouts (n=27)	Control (n=27)
Any catheter blockage (mean per month)	0.34(0.45)	0.73(1.84)	1.00(1.97)
Bladder spasm (mean days per month)	3.5(5.7)	3.2(5.9)	4.4(6.5)
Urine retention (mean days per month)	0.22(0.45)	0.18(0.38)	0.37(0.57)
Blood in urine (mean days per month)	0.25(0.51)	1.8(3.8)	1.2(1.8)
Pus in urine (mean days per month)	1.7(5.6)	1.3(4.0)	0.84(3.3)
Urine leakage (mean days per month)	5.9(8.7)	4.4(7.7)	2.0(6.0)
Catheter kinks (mean instances per month)	0.20(0.50)	0.051(0.11)	0.12(0.31)
Routine catheter changes (mean number per month)	0.34(0.22)	0.33(0.23)	0.36(0.23)
Regular / preventative washouts (mean number per month)	3.1(1.4)	3.9(2.3)	2.6(6.5)
Treatment of LTC related AEs			

Hospital visits (mean number per month)	0.0067(0.024)	0.034(0.076)	0.051(0.18)
Primary care visits[1] (mean number per month)	0.56(0.41)	0.77(0.47)	0.92(0.67)
GP home visits (mean number per month)	0.014(0.038)	0.031(0.066)	0.0019(0.0098)
GP surgery visits (mean number per month)	0.046(0.12)	0.067(0.11)	0.11(0.17)
Nurse home visits (mean number per month)	0.49(0.36)	0.58(0.44)	0.72(0.71)
Nurse practice visits (mean number per month)	0.0087(0.026)	0.10(0.24)	0.089(0.13)
Complication managed by self or informal carer (mean number per month)	0.45(0.78)	0.62(1.74)	0.74(1.59)

The summary statistic in the cells is the mean and standard deviation.
[1]Primary care visits are GP home or surgery visits or nurse home or practice visits.

Patient-reported blood in urine was lowest for those receiving a saline washout and highest for those on an acidic washout. Patient-reported pus in urine was higher than control for both washout groups. Instances of urine leakage were similar for all three groups but both washout groups had a higher mean number of days than the control group.

LTC-related AEs were predominantly managed by the individual/their carer or by a nurse home visit.

The number of participants experiencing other AEs are generally small. (Table 4).

Table 4 Other adverse events

	Saline washouts (n=26)	Acidic washouts (n=27)	Control (n=27)
Any adverse event	9/26(35%)	11/27(41%)	12/27(44%)
Bladder stones	0/25(0%)	2/27(7.4%)	4/26(15%)
Long-term catheterisation discontinuation	3/25(12%)	2/27(7.4%)	1/26(3.8%)
Epididymitis	0/26(0%)	1/27(3.7%)	0/27(0%)
Urosepsis	0/26(0%)	0/27(0%)	1/27(3.7%)
Pyelonephritis	0/26(0%)	1/27(3.7%)	0/27(0%)
Pain at catheter site	1/25(4.0%)	2/27(7.4%)	2/26(7.7%)

Skin irritation / penile trauma at catheter site	2/25(8.0%)	1/27(3.7%)	4/26(15%)
Bleeding or discharge at catheter site	5/25(20%)	4/27(15%)	4/26(15%)
Granulation problems	2/25(8.0%)	4/27(15%)	0/26(0%)
Sepsis/Pneumonia	0/26(0%)	1/27(3.7%)	0/27(0%)
Cause of death certified as MI secondary to CCF and cardiomyopathy	0/26(0%)	0/27(0%)	1/27(3.7%)
Death due to 1a) Urosepsis 1b) Prostate Cancer2) Type 2 Diabetes mellitus, ischaemic heart disease	1/26(3.8%)	0/27(0%)	0/27(0%)
Death due to Metastatic Breast Cancer.	0/26(0%)	0/27(0%)	1/27(3.7%)

The summary in the cells is the count and percentage.

All instances of granulation are from participants using a suprapubic catheter at the time of the event. All patients reporting skin irritation had a suprapubic catheter at the time. One participant in the control group reported penile trauma and changed from a urethral catheter to a suprapubic catheter and did not report further trauma or irritation.

Table 5 show the participant reported QoL outcomes throughout the study. Participants in both washout groups had better scores inEQ-5D-5L and ICECAP-A (Adult version) than the control group indicating better QoL, and better impact on day-to-day activities. None, however, are statistically significant. On the GSE scale, those in the acidic washout group appeared to be better but the difference again was not significant.

Table 5 Quality of life outcomes

	Saline washouts (n=26)	Acidic washouts (n=27)	Control (n=27)
EQ-5D-5L[1]			
Baseline	0.368(0.405);[N=25]	0.365(0.359);[N=26]	0.348(0.373);[N=27]
6-month	0.356(0.513);[N=18]	0.335(0.313);[N=20]	0.270(0.348);[N=22]
12-month	0.386(0.430);[N=18]	0.412(0.321);[N=17]	0.339(0.414);[N=21]
18-month	0.493(0.403);[N=10]	0.302(0.453);[N=7]	0.139(0.264);[N=8]
24-month	0.349(0.414);[N=4]	0.621(0.339);[N=3]	-0.077(0.082);[N=4]
exit	0.445(0.541);[N=6]	0.327(0.491);[N=4]	0.229(0.211);[N=4]

	Saline washouts (n=26)	Acidic washouts (n=27)	Control (n=27)
Effect size compared to control	0.056(-0.022 to 0.134);0.11	0.053(-0.024 to 0.131);0.12	
General self-efficacy scale[2]			
Baseline	29.1(9.1);[N=25]	29.4(5.7);[N=27]	27.8(7.6);[N=27]
6-month	27.7(9.3);[N=19]	27.6(6.0);[N=20]	26.8(8.5);[N=23]
12-month	27.4(9.7);[N=18]	29.2(5.5);[N=18]	25.1(7.5);[N=21]
18-month	28.3(7.7);[N=9]	29.3(6.0);[N=8]	28.3(3.6);[N=9]
24-month	28.3(3.3);[N=4]	30.4(4.9);[N=4]	27.3(7.4);[N=4]
Effect size compared to control	0.9(-1.5 to 3.2);0.40	2.2(-0.1 to 4.5);0.030	
ICECAP-A[3]			
Baseline	0.551(0.216);[N=10]	0.487(0.223);[N=11]	0.496(0.218);[N=9]
6-month	0.671(0.176);[N=8]	0.592(0.256);[N=10]	0.620(0.200);[N=8]
12-month	0.606(0.233);[N=7]	0.450(0.282);[N=7]	0.611(0.146);[N=7]
18-month	0.849(0.000);[N=2]	0.246(0.349);[N=2]	0.669(0.203);[N=4]
24-month	0.766(0.117);[N=2]	0.304(0.281);[N=3]	0.486(0.137);[N=2]
Effect size compared to control	-0.076(-0.221 to 0.068);0.24	-0.086(-0.214 to 0.042);0.13	
ICECAP-O[3]			
Baseline	0.488(0.320);[N=15]	0.601(0.206);[N=14]	0.669(0.204);[N=15]
6-month	0.554(0.268);[N=12]	0.657(0.227);[N=11]	0.673(0.241);[N=15]
12-month	0.569(0.329);[N=11]	0.611(0.239);[N=9]	0.707(0.161);[N=13]
18-month	0.511(0.239);[N=7]	0.614(0.331);[N=6]	0.666(0.230);[N=5]
24-month	0.637(0.078);[N=2]	0.940(.);[N=1]	0.641(0.219);[N=2]
Effect size compared to control	0.036(-0.069 to 0.142);0.44	-0.038(-0.145 to 0.070);0.43	
ICIQ-LTC function and concern[4]			
Baseline	18.3(9.1);[N=26]	17.3(9.7);[N=26]	19.1(9.0);[N=27]
6-month	15.6(10.1);[N=19]	16.4(10.2);[N=19]	19.8(9.6);[N=23]
12-month	12.5(6.9);[N=15]	18.1(11.6);[N=15]	17.9(10.7);[N=20]
18-month	11.9(5.5);[N=7]	12.3(7.5);[N=7]	14.2(12.5);[N=6]
24-month	9.3(3.3);[N=4]	19.5(4.4);[N=4]	18.5(10.0);[N=4]
Effect size compared to control	-1.2(-4.1 to 1.7);0.34	0.7(-2.2 to 3.5);0.60	
ICIQ-LTC lifestyle[4]			
Baseline	6.7(3.4);[N=24]	8.1(3.3);[N=27]	7.6(2.9);[N=27]
6-month	7.4(3.8);[N=19]	7.6(4.0);[N=17]	8.4(3.2);[N=21]
12-month	7.8(4.3);[N=16]	8.1(3.7);[N=14]	8.4(3.6);[N=20]
18-month	7.0(2.6);[N=8]	10.0(3.5);[N=7]	7.3(3.4);[N=6]
24-month	7.5(2.1);[N=2]	8.8(4.2);[N=4]	5.3(2.9);[N=4]
Effect size compared to control	-0.1(-1.6 to 1.4);0.90	-0.4(-1.9 to 1.2);0.60	
Treatment satisfaction questionnaire			

	Saline washouts (n=26)	Acidic washouts (n=27)	Control (n=27)
Effectiveness[5]			
6-month	67.0(27.9);[N=17]	67.6(31.3);[N=18]	
12-month	74.2(30.5);[N=14]	71.8(18.9);[N=14]	
18-month	83.3(22.9);[N=5]	77.8(21.2);[N=5]	
24-month	83.3(23.6);[N=2]	77.8(25.5);[N=3]	
Convenience[5]			
6-month	82.0(15.3);[N=17]	73.8(23.3);[N=18]	
12-month	89.7(11.3);[N=14]	77.0(18.9);[N=14]	
18-month	90.7(13.5);[N=6]	80.0(18.7);[N=5]	
24-month	91.7(3.9);[N=2]	74.1(8.5);[N=3]	
Overall satisfaction[5]			
6-month	76.1(22.7);[N=17]	78.2(27.7);[N=17]	
12-month	86.7(20.2);[N=14]	73.0(29.5);[N=14]	
18-month	88.1(22.9);[N=6]	84.3(27.4);[N=5]	
24-month	75.0(15.2);[N=2]	69.0(28.9);[N=3]	

The EQ-5D-5L exit questionnaire was for participants who exited the study early or were not at a notional follow-up point when the study ended.

All effect sizes come from a mixed effects linear regression including fixed effects for the two treatment groups, gender, age band, previous blockage, previous S-CAUTI and baseline measure of the outcome. Dummy variables are also included for the timepoint when the follow-up is completed. Random effects (intercepts) are included for region and participant to allow for repeated measures across time. The summary statistics are the mean, standard deviation, and count and the effects sizes are the adjusted mean difference, 97.5% confidence interval and p-value.

[1]The EQ-5D-5L is a generic QoL measure. It has 5 questions and is on the scale -0.594 to 1 with higher scores indicating better QoL.

[2]The general self-efficacy (GSE) scale assesses ability to cope with daily life. It has 10 questions and scores are between 10 and 40 with higher scores better.

[3]The ICECAP-A and ICEPOP-O measure capability in adults and older people respectively. Both have 5 question and are on the scale 0 to 1 with higher scores better.

[4]ICIQ long-term catheterisation quality of life questionnaire is a specific quality of life measure. It produces the function and concern score and the lifestyle score. The function & concern score has 10 questions and is on the scale 0 to 42. The lifestyle score has 3 questions and is on the scale 3 to 15. For both higher scores are worse.

[5]The treatment satisfaction questionnaire assesses satisfaction with medication. It produces the effectiveness, convenience, and overall satisfaction scores. Each score has 3 questions to give 9 in total, with each score on the scale 0 to 100 with higher scores better.

Participants either received the ICECAP-A for adults or ICECAP-O for the older population.

This had the effect of splitting the trial population and increasing the uncertainty around the

effect sizes. For the ICIQ-LTCqol scores there was little evidence of any difference between the groups.

The treatment satisfaction questionnaire, only completed by those in the washout groups, suggest participants in the saline group were more satisfied.

The time and travel questionnaire was completed at 18 months by 24 participants. Table S2 (supplementary materials) summarises the distance travelled for appointments and admissions, the cost of journeys, and the total time taken.

DISCUSSION

The CATHETER II RCT was terminated early primarily due to the impact of the COVID-19 pandemic. The vast majority of NHS research capacity in the UK, especially in primary care, was directed to COVID-19 research with QoL research, including CATHETER II, categorised as lower priority. Four months after starting CATHETER II, recruitment was temporarily paused and never recovered satisfactorily due to limited research capacity in primary and secondary care. The funder elected for early termination of the study. Consequently, our results are limited by the significantly smaller sample size (n=80) than originally planned (n=600).

However, the CATHETER II results indicated a favourable trend for lower rates of LTC blockages in both the prophylactic washouts groups albeit not statistically significant. The rate of LTC blockages per 1000 catheter days requiring treatment were 9.96, 10.53, and 20.92 in the saline, acidic, and control groups respectively. The IRR favours the washout groups [0.65(0.24 to 1.77); p-value=0.334 and 0.59 (0.22 to 1.63); p-value=0.25 for saline and acidic respectively], but neither reach statistical significance most likely due to the small

sample size. Gage and colleagues[5] indicated that hospital resource use accounted for almost half of health services cost mainly due to unplanned hospital admission for LTC blockage or CAUTI. Reduction in LTC blockage is likely to reduce the healthcare costs as fewer emergency treatments will be required. In CATHETER II, there were fewer visits to and by health care professionals in the washout groups. However, we were unable to perform a full health economic analysis due to the early termination and consequently small sample size.

Catheter blockages impact up to 50% of individuals living with LTC leading to discomfort and emotional distress.[23] Shepherd and colleagues [7] conducted a Cochrane Systematic Review comparing washout policies in patients with LTC. They summarised results of 7 RCTs and include 349 participants, out of which 217 participants completed these trials. The authors concluded that evidence on the benefits and risks of various washout policies were limited and generally low-quality. Moore and colleagues[24] conducted a three-arm RCT using saline or acidic solutions and compared it with standard care with no washout. They reported results from 53 participants and found insufficient evidence to determine whether prophylactic LTC washout with saline or acidic solution was more effective than standard care without washout in preventing blockages. Muncie[25](n = 32) provided data on the mean catheter replacement rate per 100 days of catheterisation. They reported the mean was 5.5 catheters replaced for the saline washout period and 4.7 catheters replaced for no washout periods, indicating no significant impact on the incidence of the total number of catheter replacements. The British Association of Urological Surgeons (BAUS) and Nurses (BAUN) consensus document indicates that prophylactic bladder washouts or catheter maintenance solutions can be employed to minimise the risk of catheter blockages in patients with LTC.[26] In CATHETER II, the observed trends in reduced LTC blockage rates in

the washout groups, despite the lack of statistical significance, suggest a potential benefit of prophylactic washouts in preventing LTC blockages. Hence, we propose further research with larger sample sizes to validate these findings. This can be best achieved by an international RCT in countries with similar healthcare systems.

S-CAUTI is the main safety issue with prophylactic LTC washouts and was the concern stated in the NICE guideline development group as potential harm and one of the main reasons for not recommending prophylactic LTC washouts.[1,27] The Cochrane review[7] included four trials comparing saline or acidic washouts with no washout. There was insufficient evidence from these trials and the Cochrane review could not draw a conclusion if there was an effect on S-CAUTI incidence or catheterisation duration. It is therefore reassuring to see in CATHETER II, despite the small sample size, the S-CAUTI rate is significantly lower at 3.71 per 1000 catheter days in the saline washout group compared to 8 per 1000 catheter days in the standard LTC care only group [IRR is 0.40(0.20 to 0.80);p-value=0.003]. There are also lower rates of S-CAUTI in the acidic washout group at 6.72 per 1000 catheter days (IRR of 0.98(0.54 to 1.78): p-value=0.926), albeit not reaching statistical significance. Moore[24] (n=32) reported no incidence of S-CAUTI in their trial participants. Self-reported UTIs, however, were reported in each group (citric acid 5/24, saline 2/18, no washout 3/23).

In CATHETER II, the mean monthly occurrence of bladder spasms was comparable between the washout groups and slightly higher in the control group. All three groups had less than one day of urine retention per month. In the Cochrane review[7], only one trial reported results of bladder spasm; saline 0/29 participants, acetic acid 1/30 participants, neomycin-polymyxin 2/30 participants.[28]

Participants receiving a saline washout experienced fewer episodes of blood in urine compared to the control group, while those on an acidic washout had higher occurrences. Moore[24] presented findings from urine dipstick testing, revealing a consistent presence of blood in the urine for all participants, regardless of their assigned groups.

Washout groups had more days of leakage (catheter bypass) on average than the control. Muncie[25] in their cross-over trial reported 32 events of urine leakage, 11/32 in the saline washout period and 21/32 in no washout period. Catheter kinks were rare in all groups. Although some differences were observed between the washout groups and the control group in terms of self-reported blood and pus in urine and pus in urine, the incidence of other events was similar.

The incidence of adverse events among participants in all groups was low. Bleeding or discharge at the catheter site shows comparable rates across all three groups. Granulation problems, however, are exclusively noted in the washout groups, with two occurrences in the saline group and four in the acidic group. Most complications were primarily handled by either the individual themselves, their carer, or through a nurse's home visit.

In this trial, participants performed prophylactic washouts with selfcare and minimal dependence on healthcare resources. The participants were provided with video training that was proven to be effective with only four participants stopping the intervention for inability to perform washouts. Results of the TSQM questionnaire showed relatively high scores for convenience, effectiveness, and overall satisfaction in both the LTC washout groups. There are no other studies in the literature that made similar comparisons.

Acceptability of prophylactic LTC washouts and the selfcare program was further confirmed in the embedded qualitative study (reported in a separate publication).

The Cochrane review[7] noted that none of the RCTs assessed patients' acceptability and/or impact on QoL and recommended these outcomes should be assessed in future RCTs. In CATHETER II, participants in both washout groups showed higher EQ-5D-5L scores than the control group, indicating potential for greater improvement in QoL albeit not statistically significant. There was little evidence of differences between groups in terms of ICIQ-LTC scores.

Strengths and limitations

CATHETER II is a robustly designed pragmatic RCT abiding by the principles and recommendations of the CONSORT statement. The RCT included an embedded qualitative study highlighting the views and experience of patients and healthcare professionals (reported separately). We assessed a comprehensive list of outcomes which are related for patients, healthcare professional, guideline developers and other stakeholders' decision making. Women constituted approximately 50% of the study population and were balanced between groups confirming generalisability of our results.

Despite being the largest reported RCT on this topic, a significant limitation is the small sample size hence the trial was underpowered to detect the 25% reduction in catheter blockage it set out to demonstrate. Hence the results cannot be used on their own to implement change in current clinical practice. However, they can be part of a wider meta-analyses in this field. A large adequately powered RCT may be required in the future, however its feasibility may be doubtful.

Conclusions

The early closure and small sample size of the CATHETER II RCT limits our ability to determine the comparative effectiveness between saline or acidic catheter washout solutions in addition to standard LTC care compared to standard LTC care only. However the results are favourable, albeit not statically significant, for lower rates of LTC blockages without a rise in S-CAUTI when employing prophylactic LTC washouts. We therefore recommend an international RCT to ascertain the clinical and cost-effectiveness of LTC washouts.

ABBREVIATIONS

AE: Adverse event

CONSORT: Consolidated Standards of Reporting Trials

EQ-5D-5L: EuroQol questionnaire – 5 dimensions – 5 levels

GSE: The General Self-Efficacy Scale

ICECAP-A: ICEpop CAPability measure for Adults

ICECAP-O: ICEpop CAPability measure for Older people

ICIQ-LTCqol: International Consultation on Incontinence Modular Questionnaire – Long Term Catheter quality of life

IRR: Incidence rate ratio

LTC: Long term catheter

QoL: Quality of Life

RCT: Randomised controlled trial

S-CAUTI: Symptomatic catheter-associated urinary tract infection

DECLARATIONS

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Authors' contributions

The corresponding author attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted. MAF is the Chief Investigator and guarantor; he conceived the study, led the proposal and protocol development, contributed to writing the manuscript and approved the final version for publication. MIO contributed to the development of the study protocol and contributed to writing the manuscript. DJ and LC contributed to writing the manuscript, contributed to study design, development and implementation of the protocol and managed the coordination of the study. DC led on statistical aspects of the study and contributed to writing the manuscript. SC contributed to study design, development of the protocol and contributed to writing the manuscript. ST contributed to qualitative aspects of the study. SE and KP contributed to developing the proposal, protocol and study materials. SM led on qualitative aspects of protocol development. KD, HH, JL, PL, PM, PKM, JND, CP and NK contributed to clinical aspects of protocol development. MK and GS led on health economics aspects of protocol development. JN and GM contributed to proposal and protocol development. All authors

contributed to oversight of the study via the Project Management Group, read and commented on the manuscript and approved the final manuscript.

Competing interests

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might have an interest in the submitted work in the previous three years are declared by the authors.

Ethics approval

This study was ethically approved by Wales Research Ethics Committee 6 (19/WA/0015). All participants and their carers gave informed consent before taking part.

Funding, support, and role of the sponsor

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Transparency statement

The lead author affirms that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that discrepancies from the study as originally planned and registered have been explained.

Data availability statement

A request to access the datasets generated during the trial should be directed in the first instance to the corresponding author (Professor Mohamed Abdel-fattah, m.abdelfattah@abdn.ac.uk). The datasets collected in questionnaires at all timepoints and the baseline, monthly and serious adverse event case report forms for all 80 participants recruited to the trial are available. The dataset is available in fully anonymised electronic form, at an individual level, and in accordance with participant consent. The data dictionaries, study protocol, statistical analysis plan, patient information leaflets and template case report forms are also available on request to facilitate interpretation of data. Questionnaire templates, or parts thereof, may be available pending review of the relevant licensing agreements. Data for the study is currently available within a local repository at the University of Aberdeen and will be retained for a period of at least 10 years after close of trial in accordance with funder, Sponsor and local archiving procedures. Applicants will require to complete a data request form, which will be reviewed by a Data Sharing Committee which includes the Chief Investigator. Applications will be considered on a case-by-case basis from bonafide researchers. We are obligated to ensure that optimal use is made of the data that is collected for research and we recognise the value of sharing individual level data. The interests of research participants, researchers and other stakeholders will be considered when considering each application. A fully authorised data sharing agreement will be required prior to the release of data.

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FIGURE LEGENDS

Figure 1 CONSORT diagram

Randomised	(n=80)

Saline	(n = 26)
Baseline completed	(n = 26)
Changed to acidic washout	(n = 1)
Changed to saline washout	n/a
Stopped washout	(n = 7)
Declined all monthly phone calls	(n = 1)
Provided monthly CRF data	(n = 25)
Six month follow-up	
completed	(n = 20)
missing	(n = 4)
declined follow-up	(n = 2)
deceased	
Twelve month follow-up	
completed	(n = 18)
missing	(n = 4)
declined follow-up	(n = 4)
deceased	
Eighteen month follow-up	
completed	(n = 10)
missing	
declined follow-up	(n = 2)
deceased	(n = 1)
did not receive questionnaire	(n = 13)
Twenty four month follow-up	
completed	(n = 4)
missing	
declined follow-up	
deceased	(n = 1)
did not receive questionnaire	(n = 21)
Completed exit questionnaire	(n = 6)

Acidic	(n = 27)
Baseline completed	(n = 27)
Changed to acidic washout	n/a
Changed to saline washout	(n = 2)
Stopped washout	(n = 3)
Declined all monthly phone calls	
Provided monthly CRF data	(n = 27)
Six month follow-up	
completed	(n = 21)
missing	(n = 5)
declined follow-up	(n = 1)
deceased	
Twelve month follow-up	
completed	(n = 18)
missing	(n = 6)
declined follow-up	(n = 3)
deceased	
Eighteen month follow-up	
completed	(n = 8)
missing	(n = 4)
declined follow-up	(n = 1)
deceased	
did not receive questionnaire	(n = 14)
Twenty four month follow-up	
completed	(n = 4)
missing	(n = 1)
declined follow-up	(n = 1)
deceased	
did not receive questionnaire	(n = 21)
Completed exit questionnaire	(n = 4)

Control	(n = 27)
Baseline completed	(n = 27)
Changed to acidic washout	(n = 0)
Changed to saline washout	(n = 0)
Stopped washout	n/a
Declined all monthly phone calls	(n = 1)
Provided monthly CRF data	(n = 26)
Six month follow-up	
completed	(n = 23)
missing	(n = 3)
declined follow-up	
deceased	(n = 1)
Twelve month follow-up	
completed	(n = 21)
missing	(n = 3)
declined follow-up	(n = 1)
deceased	(n = 2)
Eighteen month follow-up	
completed	(n = 8)
missing	(n = 4)
declined follow-up	
deceased	(n = 2)
did not receive questionnaire	(n = 13)
Twenty four month follow-up	
completed	(n = 4)
missing	(n = 1)
declined follow-up	
deceased	(n = 2)
did not receive questionnaire	(n = 20)
Completed exit questionnaire	(n = 4)

SUPPLEMENTARY MATERIALS

Table S1 Sensitivity analyses

	Saline washouts (n=26)	Acidic washouts (n=27)	Either washout (n=53)	Control (n=27)
Participants providing follow-up data	25	27	52	26
Total months of follow-up	387	409	796	420
Mean catheterisation duration (days)	468(182)	459(191)	463(185)	492(167)
Blockages requiring treatment (rate per 1000 catheter days)	9.96(14.48)	10.53(15.77)	10.25(15.02)	20.92(27.77)
IRR compared to control	0.65(0.24 to 1.77);0.33	0.59(0.22 to 1.63);0.25	0.62(0.26 to 1.49);0.22	
Sensitivity analysis	0.85(0.29 to 2.49);0.74	0.68(0.24 to 1.94);0.41	0.76(0.30 to 1.95);0.52	
S-CAUTI (rate per 1000 catheter days)	3.71(8.45)	6.72(7.10)	5.27(7.85)	8.05(11.29)
IRR compared to control	0.40(0.20 to 0.80);0.003	0.98(0.54 to 1.78);0.93	0.69(0.39 to 1.23);0.14	
Sensitivity analysis	0.30(0.16 to 0.56);<0.001	0.66(0.38 to 1.15);0.09	0.47(0.28 to 0.80);0.001	

Due to the early closure of the trial and small sample size there was potential imbalance at baseline that would have been eliminated if 200 participants had been randomised to each group. Therefore, an additional analysis was conducted of blockage requiring intervention and S-CAUTI.

The results of the sensitivity analysis show the IRR for the primary outcome are closer to 1. This indicates either washout reduces the number of blockages requiring treatment, but the effects are not as strong. The sensitivity analysis of infections requiring antibiotics show lower IRR from both saline and acidic washout. There is a strong suggestion that both washouts reduce S-CAUTI. Compared to the trial analysis the effect from acidic washout on S-CAUTI is stronger.

Table S2 Time and travel data

	Saline washouts (n=26)	Acidic washouts (n=27)	Control (n=27)
Participants completed questionnaire	8	7	9
Travel to outpatient consultation			
distance (miles)	15.0(n/a);[N=1]	16.0(12.5);[N=3]	13.6(6.5);[N=7]
cost (£)	0.00(0.00);[N=2]	0.00(0.00);[N=3]	1.11(1.97);[N=7]
Total outpatient time (hours)	5.33(n/a);[N=1]	3.33(1.53);[N=3]	3.09(1.80);[N=7]
Travel to GP appointment			
distance (miles)		1.0(n/a);[N=1]	3.3(1.9);[N=6]
cost (£)		0.00(n/a);[N=1]	0.00(0.00);[N=6]
Total time for GP appointment (hours)		1.00(n/a);[N=1]	1.56(1.12);[N=6]
Travel to hospital admission			
distance (miles)		8.0(0.0);[N=2]	13.8(1.5);[N=4]
cost (£)		0.00(n/a);[N=1]	1.00(1.73);[N=3]
Total time for hospital admission(days)		6.00(n/a);[N=1]	6.76(2.06);[N=4]

The summary statistic in the cells is the mean, standard deviation, and count.