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# Feasibility and acceptability of an anti-fouling silicone urinary catheter for long-term catheterisation: a single-centre, single-blind randomised pilot and feasibility study

**Yin-Chien Ou**[1]
National Cheng Kung University Hospital
**Zih-Jie Sun**
National Cheng Kung University Hospital
**Yuan-Yow Chiou**
yuanyow@mail.ncku.edu.tw

National Cheng Kung University Hospital

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# Abstract

Background: Long-term indwelling urinary catheters carry a substantial risk of catheter-associated urinary tract infection (CAUTI), biofilm encrustation and removal-related discomfort, and existing antimicrobial coatings have shown only modest clinical benefit. We evaluated the feasibility, safety and patient acceptability of an anti-fouling silicone urinary catheter, in which a zwitterionic polymer is blended into the silicone matrix rather than applied as a surface coating, to inform the design of a future confirmatory trial.

Methods: In a prospective, single-centre, two-arm, single-blind randomised pilot and feasibility study, adults (≥18 years) requiring long-term catheterisation were allocated by simple computer-generated randomisation to the anti-fouling catheter (experimental) or a conventional commercial silicone catheter (control); the two catheters were identical in appearance and dispensed by research staff so that participants were masked, while caregivers within the same institution were aware of allocation, with monthly changes for up to eight cycles (median 5). The pre-specified primary focus was feasibility and acceptability (recruitment, retention, specimen completeness, safety and patient/family acceptability), assessed against progression criteria for a future trial. Clinical and microbiological measures (CAUTI, catheter-removal pain [visual analogue scale 0–10], semi-quantitative urinalysis, urine-culture species) were exploratory and summarised with descriptive statistics and 95% confidence intervals; mixed-effect models (adjusted for age and sex) and generalised estimating equations provided exploratory effect-size estimates.

Results: Forty participants (experimental n=24, control n=16; 305 longitudinal samples) were enrolled and the monthly-change protocol was completed across the cohort, establishing feasibility in this frail, elderly population. Retention through at least one catheter change was 100% (40/40; 95% CI 91.2–100), and 80.0% (32/40; 95% CI 65.2–89.5) were retained through ≥5 cycles; longitudinal specimen completeness was high (urinalysis 100%, 95% CI 98.8–100; urine culture 97.7%, 95% CI 95.3–98.9). Acceptability of the overall intervention was high across both arms. No device-related adverse events occurred. Consistent with the feasibility design and CONSORT pilot-extension guidance, exploratory clinical endpoints are summarised descriptively with 95% confidence intervals rather than hypothesis tests: CAUTI 8.3% vs 12.5% (risk difference −4.2 percentage points, 95% CI −23.8 to 15.5); removal-associated pain 2.3 vs 2.1; culture positivity 100% vs 98.4%. Exploratory mixed-model estimates, including lower urinary ketone positivity in the experimental arm (adjusted odds ratio 0.11, 95% CI 0.02–0.63) and a divergent semi-quantitative bacterial trajectory (group-by-time interaction), are reported with confidence intervals as hypothesis-generating signals to inform effect-size assumptions for a future trial.

Conclusions: The anti-fouling catheter programme was feasible, safe and highly acceptable, supporting the design of a larger multi-centre randomised controlled trial. This exploratory, modestly powered study was not designed to test efficacy; the lower ketone positivity and the divergent bacterial trajectory are hypothesis-generating findings that require dedicated confirmation.

Trial registration This randomised pilot and feasibility study was not prospectively registered. The authors acknowledge that, under the WHO definition, a prospective randomised comparison of a health-related intervention constitutes a clinical trial that should be registered; this is addressed as a limitation, and the trial has been retrospectively registered (ClinicalTrials.gov, NCT07759986).

## Key messages regarding feasibility

**What uncertainties existed regarding the feasibility?** It was unclear whether frail, elderly, long-term catheterised patients could be recruited and retained through repeated monthly catheter changes; whether the experimental anti-fouling catheter could be deployed and tolerated in routine and home-care settings; and whether longitudinal urinalysis, urine culture and pain data could be collected reliably to estimate effect sizes for a future trial.

**What are the key feasibility findings?** Recruitment, randomisation and the monthly-change protocol were completed across 40 participants and 305 longitudinal samples, with no device-related adverse events and high acceptability of the monthly-change programme among participants and families in both arms. Exploratory clinical endpoints were estimable but, as expected for the sample size, not statistically powered.

**What are the implications of the feasibility findings for the design of the main study?** A larger multi-centre randomised controlled trial is feasible and warranted. The main study should be powered on patient-centred acceptability and microbial-dynamics endpoints rather than crude CAUTI incidence (which was limited by few events and near-universal bacteriuria), standardise specimen-collection timing, and use the effect-size estimates reported here for sample-size calculation.

## Background

Indwelling urethral catheters are among the most frequently used medical devices, yet catheter-associated urinary tract infection (CAUTI) remains one of the most frequent healthcare-associated infections, with a daily acquisition risk of bacteriuria of approximately 3–7% per catheter-day [1, 2]. CAUTI contributes to substantial morbidity, increased antimicrobial consumption, prolonged hospitalisation, and increased healthcare costs, and consensus guidelines emphasise catheter avoidance, early removal, and device innovation as core prevention strategies [2, 3, 4].

A principal driver of CAUTI and of catheter encrustation and blockage is microbial biofilm, which forms rapidly on both the intraluminal and extraluminal catheter surfaces and on the retention balloon, and which protects uropathogens such as Escherichia coli, Klebsiella pneumoniae, Pseudomonas aeruginosa, and Proteus mirabilis from host defences and antimicrobials [5, 6, 7]. Because biofilm formation begins early and is difficult to eradicate once established, material- and surface-based approaches that prevent initial microbial and protein adhesion are attractive [5].

Antimicrobial catheters, particularly silver-alloy and nitrofurazone-impregnated devices, have been evaluated extensively. The large UK CATHETER randomised trial found no clinically important reduction in symptomatic CAUTI with silver-alloy catheters and only a marginal effect with nitrofurazone catheters, the latter at the cost of greater insertion and removal discomfort [8]. Systematic reviews and meta-analyses similarly report that such coatings reduce asymptomatic bacteriuria but provide limited or inconsistent protection against symptomatic infection, underscoring the need for next-generation materials [9, 10, 11].

Anti-fouling surface chemistries offer a mechanistically distinct alternative: rather than releasing a biocide, zwitterionic polymers carrying balanced positive and negative charges bind water molecules through strong electrostatic hydration, forming a tightly bound hydration layer that resists the adhesion of bacteria and host proteins and thereby impedes biofilm initiation, swarming and encrustation [12, 22, 23, 24]. Sulfobetaine, carboxybetaine and phosphorylcholine zwitterions reduce non-specific protein adsorption and bacterial attachment by more than 90% relative to unmodified surfaces, and this passive, non-cytotoxic mechanism contrasts with biocide-releasing antimicrobial catheters [22, 23, 24, 25]. Such zwitterionic chemistries can be applied either as surface coatings or, increasingly, by incorporating the zwitterionic polymer into the bulk device material during manufacture, thereby avoiding a discrete coating layer that can wear or delaminate [25]. Recent laboratory and first-in-human studies indicate that biofilm-resistant polymer surfaces can significantly reduce biofilm biomass and biomineralisation on catheters recovered from patients [12, 13]. In parallel, catheter-related bladder discomfort and removal-associated pain are common, distressing, and under-addressed, and reducing surface fouling and encrustation may plausibly mitigate them [14, 15].

Before a definitive efficacy trial of such a device can be justified, it is essential to establish that the intervention and outcome assessment are feasible and acceptable in the intended population. We therefore conducted a randomised pilot and feasibility study, reported in accordance with the CONSORT 2010 extension to randomised pilot and feasibility trials [16, 17]. The objectives were to determine whether recruitment, randomisation, the monthly-change protocol and longitudinal data collection were feasible; whether the anti-fouling catheter was safe and acceptable to patients and families; and to obtain exploratory effect-size estimates (CAUTI, removal-associated pain, urinalysis, and culture) to inform the design and sample size of a future confirmatory trial. Consistent with feasibility-stage reporting, the study was designed to address "can it be done?" rather than to test efficacy hypotheses.

## Methods

# Study design and participants

This was a prospective, single-centre, two-arm randomised pilot and feasibility study conducted at a medical centre in Tainan, Taiwan, comparing an anti-fouling zwitterionic silicone urinary catheter with a conventional commercial silicone catheter in adults requiring long-term indwelling urethral catheterisation. Eligible participants were adults aged ≥ 18 years who required long-term catheterisation

and were at risk of CAUTI. Catheters were replaced monthly, and participants were followed for up to eight monthly cycles (median 5 cycles); a subset continued urine collection through seven or eight cycles according to clinical need (ongoing catheter requirement). The study was conducted as an efficacy, safety and feasibility clinical investigation of a medical device under the applicable national (Taiwan Food and Drug Administration) medical-device regulations and was approved by the institutional review board; written informed consent was obtained from all participants or their legal representatives.

## Investigational device and pre-clinical evaluation

The experimental device was an anti-fouling zwitterionic silicone Foley catheter (14 and 16 French; Fortune Medical Instrument Corp., Taiwan). The anti-fouling function was conferred by a biomimetic zwitterionic copolymer, which forms a surface hydration layer that passively resists protein, cellular, and bacterial adhesion. This does not require the addition of any biocidal agent [22, 23, 24, 25]. Critically, and in contrast to coated catheters, the zwitterionic polymer was not applied as a surface coating: it was physically milled to micro-sized particles (d50 < 5 μm) and bulk-blended into the medical-grade silicone compound (1.0 phr), which was then extruded and platinum-cured to form the catheter, thereby ensuring that the anti-fouling polymer is distributed throughout the device wall rather than confined to a removable surface layer. The control device was a conventional commercial silicone Foley catheter of identical French size. Both catheters were ethylene-oxide sterilised and supplied in identical packaging.

Before the clinical investigation, the device and its zwitterionic raw material underwent a pre-clinical safety and performance programme to support the application to the Taiwan Food and Drug Administration. Biological safety was evaluated under the ISO 10993 series by accredited laboratories: cytotoxicity was assessed at both the finished-device and raw-material level (ISO 10993-5; L929/L-929 fibroblasts, XTT and MTT assays; non-cytotoxic, mean viability > 90%); skin sensitisation by the guinea-pig maximisation test (ISO 10993-10; 0% positive responses, indicating no sensitisation); vaginal-mucosa irritation (ISO 10993-23; irritation index 0.0, non-irritant); and genotoxicity by both the bacterial reverse-mutation (Ames; OECD 471; five Salmonella strains with and without metabolic activation, non-mutagenic) and the mammalian L5178Y thymidine-kinase mouse-lymphoma assays (OECD 490; no significant increase in mutation frequency). Mechanical and functional performance was verified against BS EN ISO 20696:2018 for sterile urethral catheters (all parameters met specification), and the ethylene-oxide sterilization process was validated to ISO 11135. In-vitro antibacterial testing showed an approximately 86% reduction in Escherichia coli recovery from the experimental catheter relative to a reference catheter at 24 hours, and a 14-day porcine indwelling study showed lower urinary E. coli, reduced intraluminal and extraluminal biofilm and preserved urothelial histology compared with a commercial catheter. Detailed reports are held on file with the manufacturer and the regulatory submission.

## Randomisation and blinding

Participants were allocated to the experimental or control catheter using a computer-generated randomisation sequence produced in advance by a team member not involved in recruitment. Simple (unrestricted) randomisation was used; no blocking or stratification variables were applied, consistent with the exploratory feasibility design. Allocation was intended to be 1:1, but because simple randomisation does not force balance in a small sample and a small number of allocated participants did not proceed to catheter placement, the achieved allocation was experimental n = 24 and control n = 16 (approximately 3:2). This imbalance is a recognised consequence of unrestricted randomisation in small samples and is reported transparently; the future confirmatory trial will use block randomisation to ensure balance. The study was single-blind: the experimental and control catheters were identical in external appearance and packaging, and were dispensed by research staff so that participants were masked to allocation, whereas caregivers within the same institution were aware of allocation to facilitate appropriate clinical management and documentation. Outcome assessment was masked: laboratory urinalysis and urine-culture specimens were processed by the clinical laboratory without knowledge of group allocation, and group allocation was revealed to the investigators only after data lock.

## Outcomes and measurements

Consistent with the feasibility aim, the pre-specified primary outcomes were feasibility and acceptability, operationalised as: (i) recruitment feasibility (ability to enrol the target sample within the study period); (ii) retention through the monthly catheter-change protocol (proportion of participants completing at least one, and ≥ 5, monthly changes); (iii) completeness of longitudinal specimen collection (urinalysis and urine culture); (iv) safety (device-related adverse events); and (v) patient/family acceptability of the intervention and follow-up model. Pre-defined progression criteria for advancing to a definitive trial, following a traffic-light framework, were: proceed (green) if retention through ≥ 1 change and specimen completeness were both ≥ 80% with no device-related serious adverse events; proceed with amendment (amber) if either fell between 60% and 80%; and do not proceed without major revision (red) if either was < 60% or if device-related serious adverse events occurred. Exploratory clinical and microbiological measures were: CAUTI, defined per protocol as a catheter-associated event within the infection window meeting symptomatic criteria and accompanied by a urine culture ≥ $10^5$ CFU/mL; catheter-removal pain on a visual analogue scale (VAS 0–10); semi-quantitative urinalysis at each visit (leukocytes, occult blood, nitrite, dipstick bacteria, protein, pH, red blood cells, epithelial cells, and ketone bodies); urine-culture species; and safety/adverse events. Urinalysis ordinal results were coded on standardised scales. These exploratory measures were used to estimate effect sizes and their precision (confidence intervals) to inform a future trial, not to test efficacy hypotheses; no formal power calculation was performed, consistent with the feasibility design.

# Statistical analysis

Analyses followed the CONSORT 2010 extension to randomised pilot and feasibility trials, emphasising descriptive estimation with confidence intervals rather than hypothesis testing. The sample size was not based on a power calculation for a treatment effect; instead, a target of approximately 40 participants was chosen on feasibility grounds, as this size estimates a feasibility proportion (for example, retention or specimen completeness) to within a 95% confidence-interval half-width of roughly ± 15 percentage points around an anticipated value near 80%, which was judged adequate to decide whether to progress to a definitive trial. Feasibility outcomes are reported as proportions with 95% Wilson confidence intervals. Continuous descriptors are presented as mean ± SD (or median [IQR]) and categorical descriptors as n (%); between-arm differences in exploratory clinical endpoints are summarised as effect estimates (risk differences, mean differences, or odds ratios) with 95% confidence intervals, without significance testing, in keeping with the exploratory feasibility design. Baseline characteristics are described without statistical comparison, because randomisation makes any observed baseline difference a chance finding and significance testing of baseline balance is uninformative. For the longitudinal markers, generalised linear mixed models with a subject-level random intercept (adjusted for age per 10 years and male sex, control arm as reference) provided exploratory effect-size estimates: continuous/ordinal markers used linear mixed models (regression coefficient β ± SE) and binarised markers used logistic mixed models (odds ratio [OR] with 95% CI). As a secondary, exploratory analysis of temporal dynamics, the same indicators were modelled with generalised estimating equations (GEE; identity-link Gaussian, exchangeable working correlation, subject clustering, robust sandwich variance), in which a group-by-time interaction described whether the arms followed different trajectories; group-specific simple slopes (β per cycle with 95% CI) characterised the direction of divergence. Robustness of any trajectory signal was assessed by (i) adjusting for baseline level, (ii) an autoregressive AR(1) structure and (iii) a binarised (grade ≥ 2) logistic GEE, and differential dropout was examined by comparing follow-up length between groups. Given the exploratory, feasibility-stage design and small sample (N = 40), all model results are reported as hypothesis-generating effect sizes with confidence intervals, without multiplicity correction. A pre-planned sensitivity analysis restricted to the protocol window (≤ 6 cycles; 279 of 305 records) was performed. Analyses used Python (pandas, SciPy, statsmodels); mixed-model results were independently reproduced and are portable to SAS/R.

## Results

# Feasibility, recruitment and baseline characteristics

Forty participants (experimental n = 24, control n = 16) were enrolled and contributed 305 longitudinal urine samples (experimental 175, control 130). Recruitment, randomisation and the monthly catheter-change protocol were completed across the cohort. All 40 participants (100%; 95% CI 91.2–100) were retained through at least one monthly catheter change, and 32/40 (80.0%; 95% CI 65.2–89.5) were retained through ≥ 5 cycles. Longitudinal data collection was highly complete: urinalysis was recorded for 305/305 specimens (100%; 95% CI 98.8–100) and urine culture for 298/305 (97.7%; 95% CI 95.3–98.9). All pre-defined progression criteria were met in the ‘green’ range (retention and completeness ≥

80% with no device-related serious adverse events), supporting progression to a definitive trial. The two arms were similar at baseline in age, frailty, comorbidity count and sex (Table 1); consistent with the CONSORT pilot-trial extension, baseline characteristics are described without significance testing.

Table 1
Baseline characteristics by group

| Characteristic | Experimental (n = 24) | Control (n = 16) |
|---|---|---|
| Age, years | 79.3 ± 8.6 | 79.4 ± 13.4 |
| Male, n (%) | 14 (58.3) | 6 (37.5) |
| Frailty scale | 6.7 ± 0.6 | 6.9 ± 0.5 |
| Comorbidities, n | 3.6 ± 1.5 | 3.6 ± 1.8 |

Data are mean ± SD or n (%). In accordance with the CONSORT extension for pilot and feasibility trials, baseline characteristics are presented descriptively without statistical hypothesis testing.

## CAUTI incidence

CAUTI occurred in 2/24 experimental participants (8.3%; 95% CI 2.3–25.8) and 2/16 control participants (12.5%; 95% CI 3.5–36.0). At the per-sample level, events were 3/175 (1.7%) experimental versus 2/130 (1.5%) control. The between-arm absolute risk difference was − 4.2 percentage points (95% CI − 23.8 to 15.5), numerically lower in the experimental arm but with a wide confidence interval spanning zero, as anticipated for a pilot study with few events (Fig. 1). Because the estimate is imprecise and the study was not powered for this endpoint, no inferential test or number needed to treat is reported.

# Catheter-removal pain

Catheter-removal VAS pain was similar between groups, both per removal (2.3 ± 2.1 experimental vs 2.1 ± 2.4 control; mean difference 0.2, 95% CI − 0.4 to 0.8) and at participant-mean level (2.4 ± 1.4 vs 2.6 ± 2.0). Qualitative feedback nonetheless indicated marked individual improvements (Fig. 2; see Safety and qualitative findings).

# Urine culture

As expected in long-term catheterised patients, bacteriuria was near-universal: culture positivity was 100% (170/170) experimental and 98.4% (126/128) control (between-arm difference 1.6 percentage points, 95% CI − 1.5 to 4.6); culture positivity therefore did not meaningfully discriminate between arms. The species distribution differed in pattern, the experimental arm being Pseudomonas aeruginosa-predominant and the control arm Klebsiella pneumoniae-predominant (Table 2, Fig. 3).

Table 2
Top-5 urine-culture isolates by group (isolate counts)

| Rank | Experimental | Control |
|---|---|---|
| 1 | P. aeruginosa (50) | K. pneumoniae (43) |
| 2 | E. coli (41) | E. coli (24) |
| 3 | K. pneumoniae (31) | P. aeruginosa (13) |
| 4 | S. aureus (10) | E. cloacae (11) |
| 5 | C. koseri (7) | P. mirabilis (10) |

Counts are numbers of isolates. Species rank order differed between arms despite near-universal culture positivity.

# Longitudinal indicators: mixed-effect models (primary analysis)

Mixed-effect models (adjusted for age and sex; control as reference) showed no clear between-group difference for the exploratory endpoint CAUTI (OR 0.84, 95% CI 0.08–9.21; numerically lower in the experimental arm) or for removal pain (linear mixed β − 0.29, 95% CI − 1.21 to 0.63; binary ≥ 3 OR 0.52, 95% CI 0.17–1.54). Group estimates for most urinalysis markers had confidence intervals crossing the null (Table 3). Urinary ketone bodies (binary ≥ 0.5) were lower in the experimental arm (OR 0.11, 95% CI 0.02–0.63); this was the only indicator with a confidence interval excluding 1.0. Ketone positivity was not materially associated with diabetes, and diabetes was balanced between groups; after additionally adjusting for diabetes, the lower experimental-arm ketone estimate persisted (OR 0.23, 95% CI 0.09–0.61), indicating that the ketone difference is unlikely to be confounded by diabetes. As an exploratory pilot analysis, these estimates are hypothesis-generating and are not interpreted as confirmatory efficacy findings.

Table 3
Mixed-effect model results for longitudinal indicators

| Indicator (model) | Adjusted effect (95% CI) |
|---|---|
| CAUTI (binary) | OR 0.84 (0.08–9.21) |
| Removal pain (linear) | β -0.29 (-1.21 to 0.63) |
| Ketone bodies (binary ≥ 0.5) | OR 0.11 (0.02–0.63) |
| Dipstick bacteria (linear) | β 0.03 (-0.24 to 0.30) |
| Leukocytes/WBC (linear) | β 0.53 (-0.35 to 1.41) |
| Removal pain (binary ≥ 3) | OR 0.52 (0.17–1.54) |
| Nitrite (binary) | OR 1.16 (0.49–2.72) |
| Occult blood (linear) | β 0.11 (-0.46 to 0.68) |
| Protein (linear) | β 0.14 (-0.64 to 0.92) |
| pH (linear) | β -0.03 (-0.52 to 0.46) |
| Red blood cells (linear) | β 0.07 (-0.62 to 0.76) |
| Epithelial cells (linear) | β 0.03 (-0.11 to 0.17) |

Adjusted for age (per 10 years) and male sex; control arm as reference. Continuous/ordinal indicators are reported as the regression coefficient β ± SE from linear mixed models (original scale, additive); binarised indicators are reported as odds ratios (OR) with 95% confidence intervals (multiplicative) from logistic mixed models. Estimates are exploratory and hypothesis-generating; a confidence interval excluding the null (0 for β, 1.0 for OR) is indicated in the table and should not be interpreted as a confirmatory efficacy finding in this underpowered pilot.

# Urinary ketones: exploratory interpretation (secondary)

Urinary ketone-positive events were few (20 of 305 records positive; 16 control, 4 experimental) and were not explained by diabetes (diabetes-adjusted OR 0.23, 95% CI 0.09–0.61), so the difference is unlikely to be diabetes-driven. With diabetes excluded, plausible physiological and methodological mechanisms include: (i) starvation/catabolic ketonuria, since this frail, bedbound population frequently has inadequate intake, infection-related consumption and catabolism, such that if the anti-fouling catheter reduced local irritation and discomfort it might indirectly lessen metabolic stress and lower ketones [18, 19]; (ii) differences in local infection/inflammatory burden, since ketone-positive records had a higher proportion of nitrite positivity (8/20), and ketone bodies have recognised anti-inflammatory signalling roles, so an anti-fouling surface reducing biofilm and subclinical inflammation might reduce the accompanying metabolic response, although clinical CAUTI did not differ between arms [18, 20]; and (iii) specimen-level factors, since ketone-positive specimens had lower pH (6.1 vs 6.89 overall), suggesting some were concentrated or acidic urine, although specific gravity was identical between arms (1.012),

weakening this explanation [21]. Lower ketone positivity should be regarded as an exploratory, low-event secondary signal with a wide confidence interval, hypothesis-generating and requiring confirmation rather than supporting an efficacy conclusion.

# Bacteria trajectory: GEE exploratory analysis (secondary)

GEE models showed similar average levels over the whole follow-up for urine leukocytes, occult blood, nitrite and dipstick bacteria, with group main-effect confidence intervals crossing the null. However, the semi-quantitative urinary bacteria trajectory diverged between arms (group-by-time interaction): the experimental arm rose over cycles (slope + 0.073/cycle, 95% CI 0.010–0.136) while the control arm declined (slope − 0.059/cycle, 95% CI − 0.118 to 0.000), the two trajectories crossing (Table 4, Figs. 4 and 5). The divergence was consistent across sensitivity analyses (after adjustment for baseline bacterial level, under an AR(1) working-correlation structure, and in a binarised [grade ≥ 2] logistic GEE); follow-up length did not differ between groups and baseline bacteria was unrelated to dropout, arguing against a baseline-imbalance or differential-dropout artefact. Importantly, this microscopic, semi-quantitative difference was not reflected in clinical CAUTI or culture positivity; its mechanism and clinical meaning are unclear, and it should be regarded as a hypothesis-generating signal requiring confirmation rather than evidence that the device increases infection risk.

Table 4
GEE exploratory analysis of longitudinal urinalysis indicators

| Indicator | Group main effect β (95% CI) | Group-by-time (experimental vs control slope per cycle, 95% CI) |
|---|---|---|
| Leukocytes/WBC | β 0.55 (− 0.29 to 1.38) | Similar trajectories |
| Occult blood | β 0.20 (− 0.37 to 0.78) | Similar trajectories |
| Nitrite | Similar (few positive events; estimate imprecise) | Similar trajectories |
| Dipstick bacteria | β 0.03 (− 0.22 to 0.28) | Experimental + 0.073 (0.010 to 0.136) vs control − 0.059 (− 0.118 to 0.000); trajectories diverge |

Identity-link Gaussian GEE with exchangeable working correlation and robust variance. Estimates are exploratory. The semi-quantitative dipstick-bacteria group-by-time interaction indicated divergent trajectories (experimental slope + 0.073/cycle, 95% CI 0.010–0.136; control slope − 0.059/cycle, 95% CI − 0.118 to 0.000) and was consistent after baseline adjustment and under an AR(1) working-correlation structure.

# Safety and qualitative findings

Three catheter-slippage events with balloon rupture were recorded (experimental: participant 21 on day 13, participant 29 on day 4; control: participant 15 on day 5); these were distributed across both arms and were judged unrelated to the device. No device-related adverse events occurred. The overall

monthly-change programme was well accepted in both arms: participants and families in the experimental and control groups alike were willing to continue beyond the protocol period (in some cases by self-payment), reflecting acceptability of the intervention and follow-up model rather than a preference for a specific catheter, which the single-blind design precluded. Among individual experimental-arm cases (group allocation revealed to investigators only after data lock), notable observations included one long-term participant on anticoagulants (participant 14, 81 years) whose catheter-removal pain decreased from approximately 9 to 0–2 with reduced odour, and nurse-recorded reductions in crystal encrustation at the catheter tip (participants 19 and 23) (Fig. 6). One experimental participant reported occasional minor leakage.

# Discussion

In this randomised pilot and feasibility study, an anti-fouling zwitterionic silicone urinary catheter proved feasible to deploy and safe in frail, elderly adults requiring long-term catheterisation, and was highly acceptable to patients and families. Recruitment, randomisation and the monthly-change protocol were completed across the cohort with high data completeness and no device-related adverse events, satisfying the pre-specified feasibility objectives and supporting progression to a larger confirmatory trial.

Exploratory clinical measures did not differ materially between arms, with confidence intervals that were wide and crossed the null. This is unsurprising and consistent with the feasibility design: the study was not powered for efficacy, CAUTI events were few, and bacteriuria was near-universal, so culture positivity had little discriminatory value. These observations mirror the broader literature, in which even large randomised trials and meta-analyses of antimicrobial and silver-alloy catheters have shown limited or inconsistent reductions in symptomatic infection [8, 9, 10, 11]. The mechanistically distinct anti-fouling approach, which resists initial bacterial and protein adhesion through a hydration layer rather than releasing a biocide, has a strong biological rationale and emerging clinical support for reducing biofilm and encrustation [12, 13, 22, 23, 24, 25]; the bulk-blended construction, which distributes the zwitterionic polymer throughout the silicone wall rather than as a coating that could wear or delaminate, was associated with a complete pre-clinical biocompatibility profile and no device-related adverse events in this study [25]. Our clinical data neither confirm nor refute a clinical-efficacy benefit and were not intended to.

The most consistent signal favouring the experimental catheter was lower urinary ketone positivity, which persisted after adjustment for diabetes. Because ketonuria in this population most plausibly reflects starvation/catabolic states and, potentially, inflammatory burden, and because ketone bodies themselves have anti-inflammatory signalling activity, this finding is biologically interpretable but remains exploratory given the small number of ketone-positive records [18, 19, 20, 21]. The divergent semi-quantitative bacterial trajectory detected by GEE is intriguing but discordant with the clinical endpoints and should likewise be treated as hypothesis-generating; it should not be read as evidence

that the device increases infection risk, particularly given near-universal bacteriuria and the microscopic, dipstick-level nature of the measure [5, 6].

Patient-centred and acceptability outcomes were arguably the most informative at this stage. High acceptability of the monthly-change programme in both arms (including willingness to continue by self-payment), together with individual experimental-arm observations of reduced removal pain and odour and nurse-recorded reductions in tip encrustation, align with the recognised burden of catheter-related discomfort and the plausibility that reduced fouling mitigates it [14, 15]. Because the trial was single-blind to participants and outcome assessors, these acceptability findings reflect the intervention and follow-up model rather than conscious preference for a particular catheter; patient-centred discomfort and microbial-dynamics endpoints, rather than crude CAUTI incidence, may be the most appropriate primary endpoints for a definitive trial.

# Limitations

A limitation of reporting is that the study was not prospectively registered; although it was conducted under national medical-device clinical-investigation regulations with institutional ethics approval, prospective registration is expected for randomised trials under the WHO definition, and the trial has therefore been retrospectively registered (ClinicalTrials.gov, NCT07759986). The enrolled sample size (n = 40) and the small number of CAUTI events limit power for clinical-efficacy endpoints; the single-centre design and unequal allocation may introduce bias; and near-universal bacteriuria limits the discriminating value of culture positivity. Although the trial was single-blind to participants and outcome assessors, and caregivers were aware of group allocation, outcome assessment was masked, the modest sample and single-centre setting remain the principal limitations. Follow-up length varied by clinical need (median 5 cycles, maximum 8), but a pre-planned ≤ 6-cycle sensitivity analysis left all primary and secondary conclusions unchanged, indicating that unequal follow-up did not materially affect the results. A further methodological consideration is specimen freshness: urine was collected from the drainage bag and may have dwelt before testing. Pre-analytical dwell primarily affects pH (alkalinisation), nitrite (false positives), bacteria (overgrowth) and occult blood, whereas ketones tend to volatilise or degrade on standing (biasing toward under-detection). Because dwell-sensitive indicators were similarly distributed between arms (pH 6.84 vs 6.95; specific gravity 1.012 vs 1.012; comparable nitrite and bacteria), dwell time is unlikely to have differed systematically between groups; this constitutes non-differential misclassification, which biases effects toward the null rather than creating spurious between-group differences, and for ketones the under-detection bias renders the observed difference conservative. Future studies should standardise specimen-collection timing (for example, a fresh catheter draw or shortened transit time). As a pilot study, these findings are exploratory and require confirmation in a larger multi-centre randomised trial.

# Conclusions

In frail older adults requiring long-term indwelling catheterisation, an anti-fouling zwitterionic silicone catheter was feasible, safe and highly acceptable to patients and families. The pre-specified feasibility objectives and progression criteria were met, and the study is feasible to scale: a larger, multi-centre randomised controlled trial is warranted and should be powered on patient-centred acceptability and microbial-dynamics endpoints, with standardised specimen timing and prospective trial registration. This exploratory, modestly powered study was not designed to test efficacy; the lower urinary ketone positivity (adjusted OR 0.11, 95% CI 0.02–0.63) and the divergent semi-quantitative bacterial trajectory were not reflected in clinical infection endpoints and are hypothesis-generating findings that warrant dedicated future investigation. This pilot provides the feasibility, acceptability, preliminary safety and effect-size estimates needed to design and power a confirmatory trial.

# Abbreviations

AR(1)
first-order autoregressive
CAUTI
catheter-associated urinary tract infection
CFU
colony-forming units
CI
confidence interval
CONSORT
Consolidated Standards of Reporting Trials
GEE
generalised estimating equations
IQR
interquartile range
OR
odds ratio
SD
standard deviation
SE
standard error
VAS
visual analogue scale
WBC
white blood cell.

# Declarations

**Ethics approval and consent to participate**

The study was approved by the Institutional Review Board of National Cheng Kung University Hospital (No. A-BR-113-031). It was conducted in accordance with the Declaration of Helsinki and the applicable Taiwan Food and Drug Administration medical-device clinical-investigation regulations. Written informed consent to participate was obtained from all participants or their legal representatives.

**Consent for publication**

Not applicable. The manuscript contains no individual person's identifiable data, images or videos.

# Competing interests

The investigational anti-fouling catheter was jointly developed and supplied by Fortune Medical Instrument Corp. in collaboration with the Medical Device Innovation Center at National Cheng Kung University. This study was conducted as an industry-academia collaborative research project funded by Formosa Plastics Corporation. None of the authors hold any equity, shares, or other financial interests in Formosa Plastics Corporation or Fortune Medical Instrument Corp. The principal investigator (PI) received a project honorarium of NT$100,000 (approximately US$3,100). All authors declare no other financial or non-financial competing interests.

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# Author Contribution

All three authors contributed to the study design and planning discussions. Y-YC led the overall project coordination, was primarily responsible for study design, and authored the study protocol and closeout report. Y-CO and Z-JS were responsible for participant recruitment and clinical care, and contributed to the interpretation of closeout-report findings. All authors reviewed and approved the final manuscript.

# Acknowledgement

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# Data Availability

The de-identified datasets analysed during the current study (subject-level and longitudinal records) are available from the corresponding author on reasonable request, subject to institutional and regulatory approvals.

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# Figures

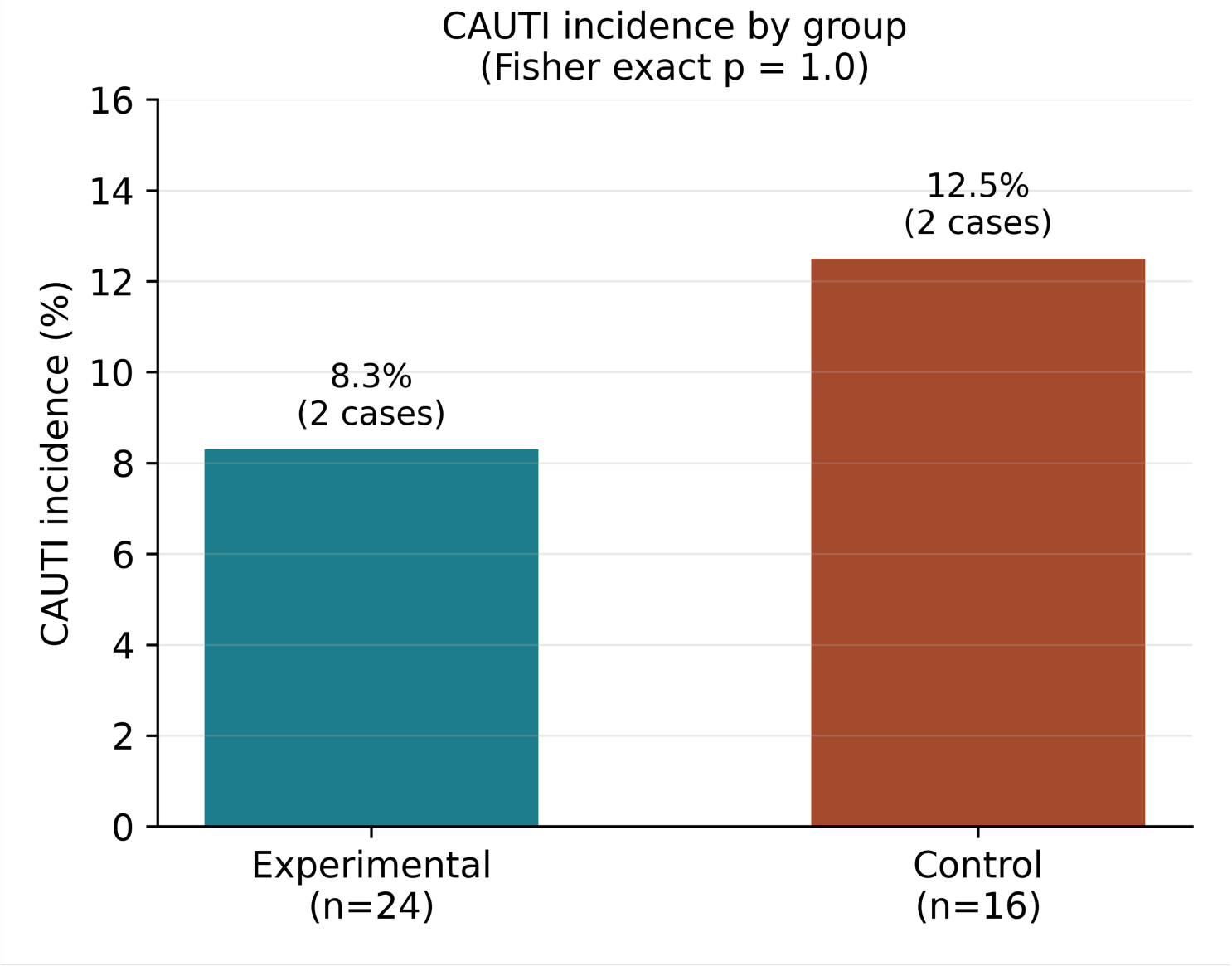



**Figure 1**

CAUTI incidence by group. Catheter-associated urinary tract infection at participant and per-sample levels in the experimental and control arms.

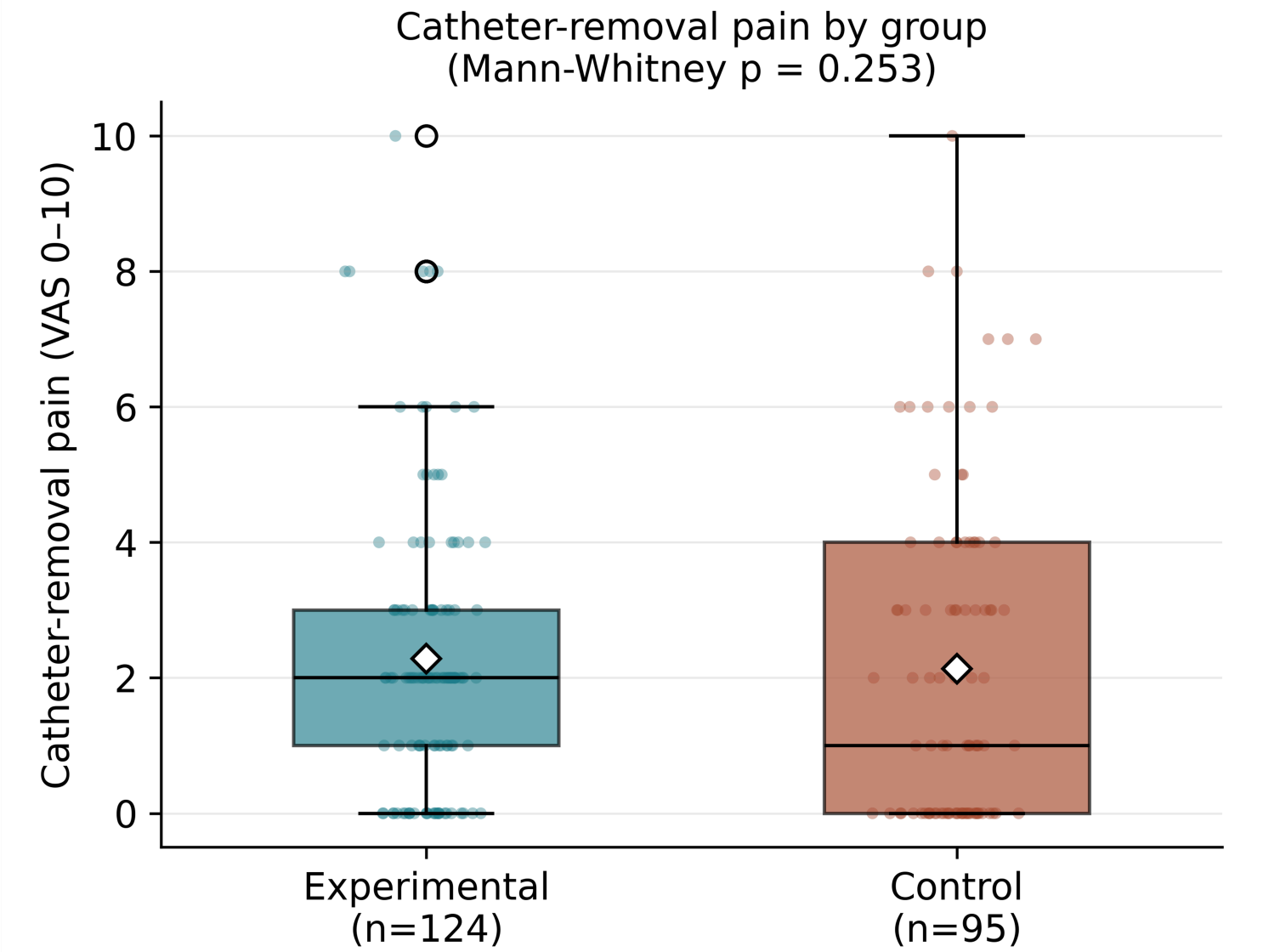



**Figure 2**

Catheter-removal pain by group. Distribution of visual analogue scale (0–10) removal-pain scores in the experimental and control arms.

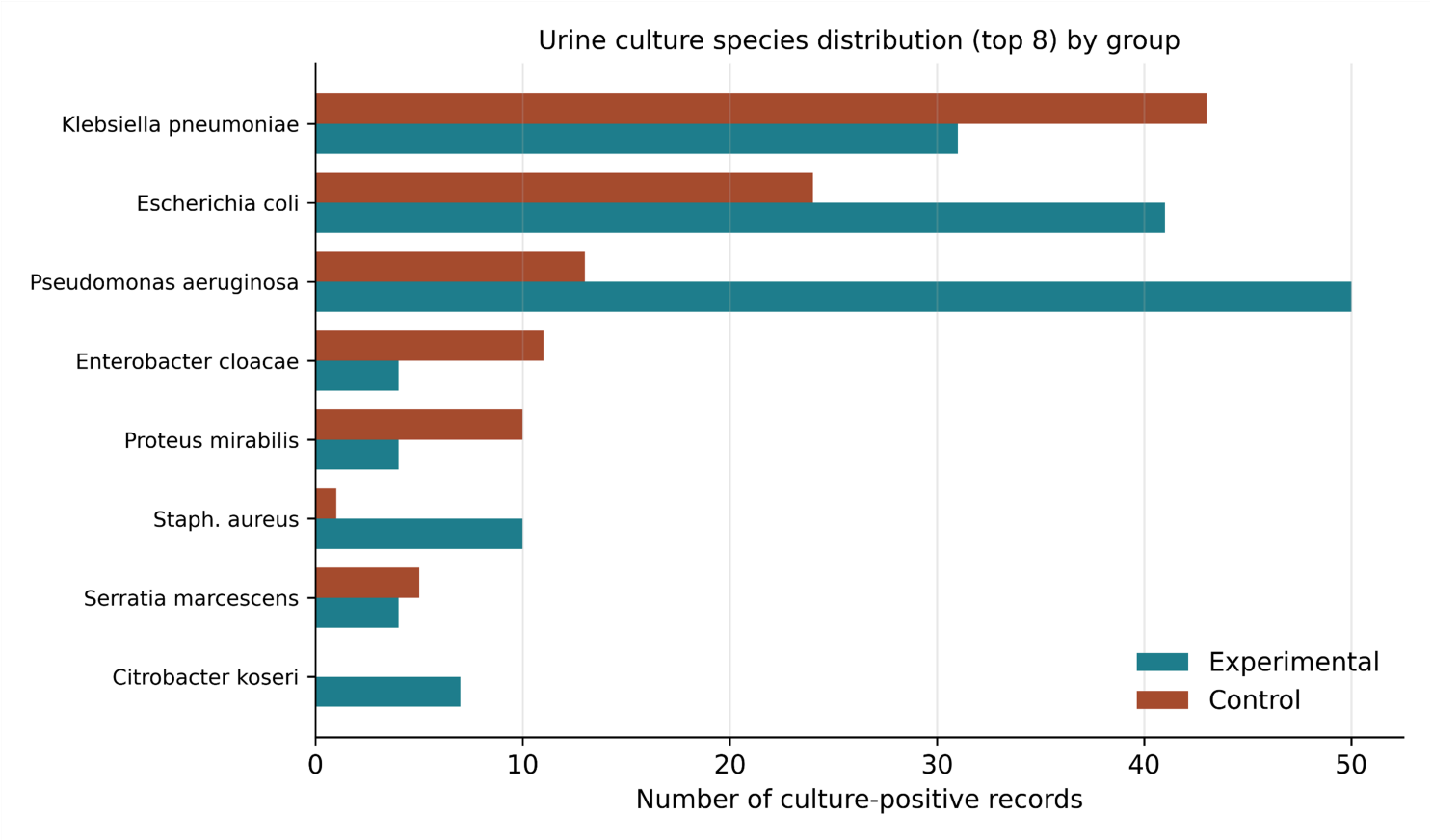



**Figure 3**

Urine-culture species distribution by group. Distribution of cultured uropathogen species in the experimental and control arms.

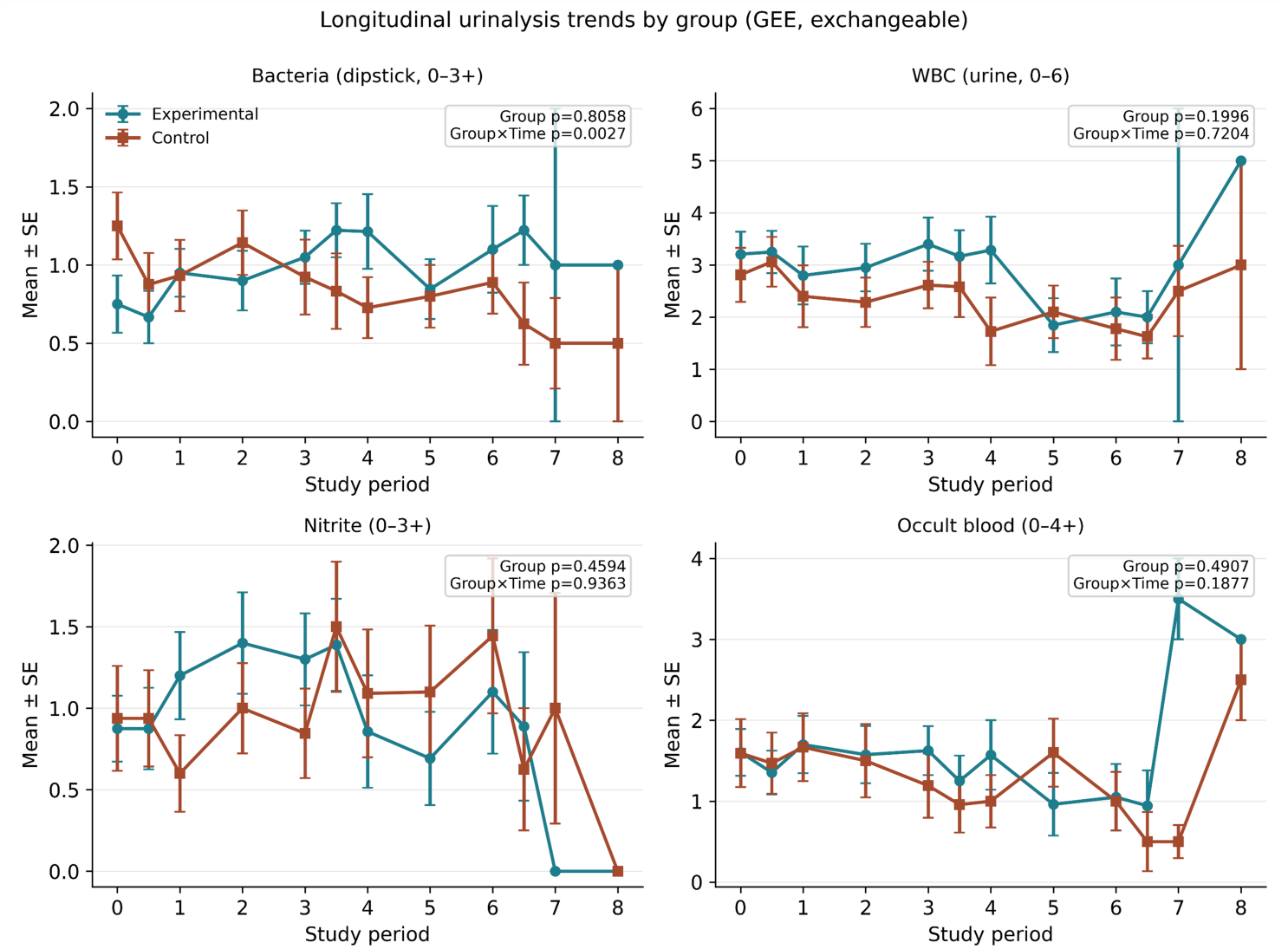



**Figure 4**

Longitudinal trends of urinalysis indicators by group. Semi-quantitative urinalysis indicators across monthly catheter cycles in the two arms.

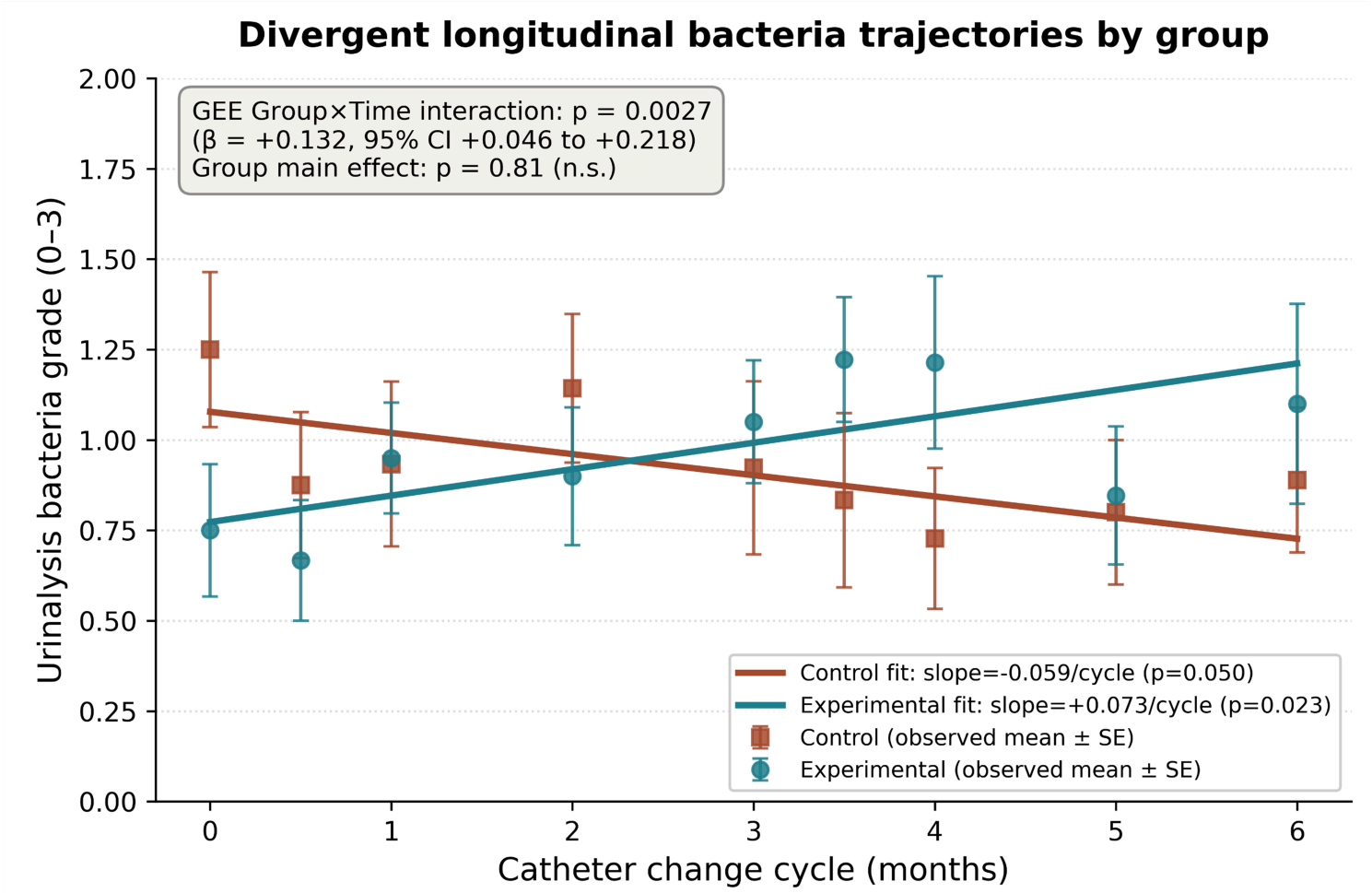
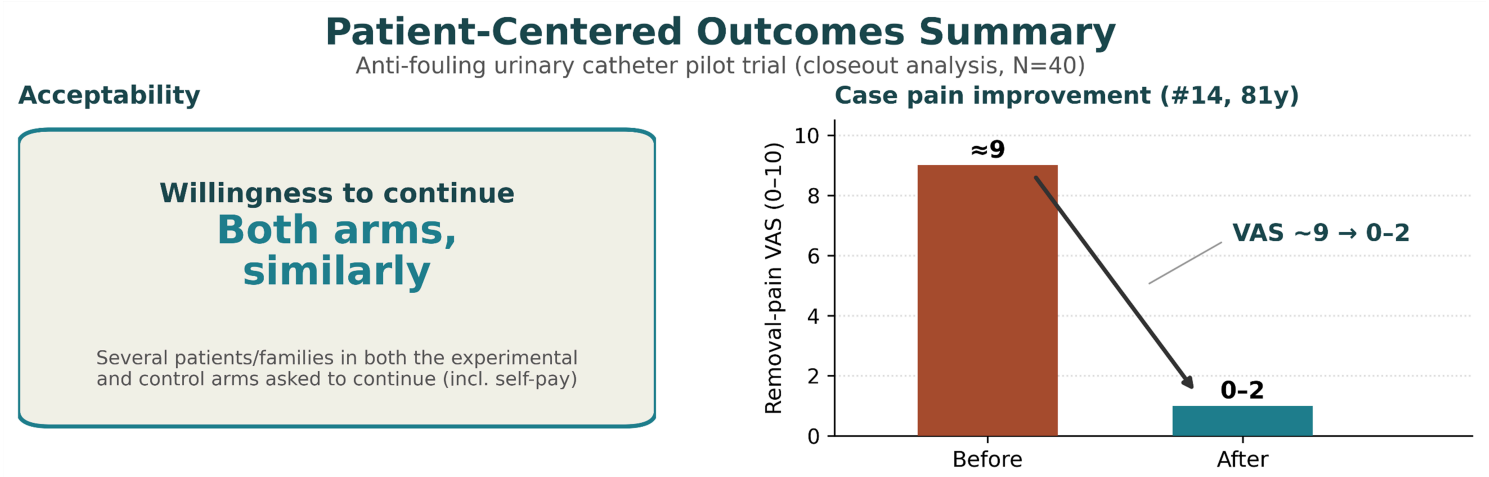



**Figure 5**

Divergent trajectories of semi-quantitative urinary bacteria by group. Group-specific simple slopes per cycle with 95% confidence intervals; group-by-time interaction.




**Qualitative & safety findings**

| Domain | Finding | Assessment |
|---|---|---|
| **Removal pain** | Case #14: VAS ~9 → 0–2 with reduced urine odor | **Positive** ✓ |
| **Encrustation** | Reduced catheter-tip crystal encrustation (#19, #23) | **Positive** ✓ |
| **Willingness to continue** | Similar in both arms: several patients/families requested continued use (incl. self-pay) | **Neutral** ○ |
| **Safety** | No device-related AE; 3 slippage/balloon events in both arms | **Neutral** ○ |
| **Minor issue** | Occasional leakage in one experimental-arm subject | **To monitor** △ |

Source: closeout qualitative feedback & safety records (N=40).

### Figure 6

Patient-centred outcomes summary. Acceptability, case-level pain improvement and qualitative and safety findings. Cases #14, #19 and #23 refer to individual experimental-arm subjects; these qualitative observations are illustrative single-case reports and do not constitute a between-arm efficacy comparison.

## Supplementary Files

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- CONSORTpilotfeasibilitychecklistRevised0812.docx