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ORIGINAL RESEARCH ARTICLE

Vaginal preparation with chlorhexidine at cesarean section to reduce endometritis and prevent sepsis: A randomized pilot trial (PREPS)

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Abstract

Introduction: Cesarean sections are the most common major operation worldwide. One in 10 women develops a surgical-site infection after cesarean section. The PREPS pilot trial was developed to assess the feasibility of a randomized controlled trial of vaginal cleansing with chlorhexidine before cesarean section, to reduce infectious morbidity.

Material and methods: A multi-center, open-label, parallel-group pilot randomized controlled trial across 4 UK maternity units. Women aged ≥16 years, undergoing elective or emergency cesarean section, ≥34 weeks of gestation, and able to give informed consent were eligible. Women were randomized 1:1 to chlorhexidine 0.05% or no cleansing and were followed up until 6 weeks after cesarean section. The feasibility of a larger randomized controlled trial was assessed by the pilot trial's recruitment, ability to use verbal consent in an emergency, adherence, follow-up and withdrawal rates. The main clinical outcome collected was Center for Disease Control and Prevention (CDC) classification of endometritis at 30 days. Trial registration number is ISRCTN33435996.

Results: A total of 320 women (128% of target) were randomized. Of these, 93% (95% CI 89%-95%) received their allocated intervention. Of the 88 women who had an emergency cesarean section, verbal consent was initially given by 32 (36%) women, with the remainder having sufficient time to give written consent. Endometritis (CDC definition) was collected from medical notes of 96% of women, 68% (95% CI 63%-73%) were followed up at both 14 and 30 days by telephone, and we were able to collect patient-reported outcomes. In the vaginal cleansing arm 2/152 (1.3%) women had endometritis compared with 1/155 (0.7%) in the no cleansing arm (RR 2.08, 95% CI 0.19-22.31).

Conclusions: It is possible to perform a randomized controlled trial in women undergoing an elective or emergency cesarean section, using a verbal-followed-by-written consent process, while maintaining high adherence and retaining women in the trial.

Abbreviations: CDC, Center for Disease Control and Prevention; CI, confidence interval; CS, cesarean section; RCT, randomized controlled trial; RR, relative risk; SSI, surgical-site infection; VC, vaginal cleansing.

KEYWORDS
cesarean section, chlorhexidine, endometritis, pilot projects, sepsis, surgical wound infection, vaginal cleansing, vaginal douching

1 | INTRODUCTION

Cesarean section (CS) is the commonest major operation worldwide; approximately 26% of pregnant women undergo a CS in the UK, equating to 177 793 per year in England.[1] One in 10 women experience a surgical-site infection (SSI) post-CS, with 90% of infections being in the abdominal wound, 5% deep incisional, and 5% endometritis.[2] The post-CS endometritis rate varies from 0.94% to 15.8%,[3] because of changes in practice related to the routine introduction of antibiotic prophylaxis (reducing endometritis from 15.7% to 5.7%) and the definition of endometritis used (eg clinically determined or Center for Disease Control and Prevention [CDC] criteria[4]).

Complications range from community-managed mild infections to sepsis requiring high-dependency care. Although maternal mortality rates from sepsis have reduced, this is a result of early identification and treatment, and reducing influenza in pregnancy through vaccination.[5] Of the women developing an SSI post-CS, 6 in 1000 require re-admission, equating to 1066 women per year in England.[2] Postoperative morbidity further impacts mothers and babies in the important immediate postnatal period, especially if they are separated.

Vaginal cleansing (VC) pre-CS may help to prevent endometritis and SSI, through inhibiting ascending infection and reducing cross-contamination of the surgical site. A systematic review and meta-analysis included 15 trials of VC pre-CS with an antiseptic (mainly povidone iodine) vs placebo or no cleansing and concluded that this reduced the endometritis incidence (4.5% vs 8.8%; relative risk [RR] 0.52, 95% confidence interval [CI] 0.37-0.72).[6] Sub-group analyses demonstrated a greater reduction in women in labor at CS and/or with ruptured membranes. VC at CS with povidone iodine has not been adopted within the UK, and does not feature within the National Institute for Health and Care Excellence guidelines,[7] because of concerns about exposure of the fetal skin to iodine causing transient hypothyroidism and potentially affecting newborn congenital hypothyroid screening.[8]

One randomized controlled trial (RCT) (n = 93) found no significant difference between povidone iodine and chlorhexidine in terms of endometritis or wound infection after elective CS (RR 2.04, 95% CI 0.39-10.62).[9] The principle of VC as an antiseptic is sound; it is the use of povidone iodine that prevents translation into practice, and therefore it is reasonable to consider an alternative antiseptic such as chlorhexidine, whose bacteriostatic and bactericidal properties make it a suitable alternative antiseptic. An RCT assessing VC with chlorhexidine at CS to reduce SSI is therefore required. There are a number of feasibility questions that need answering before a definitive RCT can be conducted. The aim of this study was to determine if verbal consent was acceptable in time-critical situations; if randomization were possible; if it were possible to perform VC; and if we could successfully follow up women post-CS who are rapidly discharged?

Key Message
A randomized controlled trial of vaginal cleansing with an antiseptic solution before elective and emergency cesarean section is feasible.

2 | MATERIAL AND METHODS

PREPS was an unblinded, parallel-group pilot RCT comparing VC using chlorhexidine 0.05% vs no cleansing (standard practice) at CS. Two qualitative focus groups (n = 15) and telephone interviews (n = 6) were conducted before the pilot RCT to identify key areas that matter to women to inform women-focused outcomes, and to obtain input regarding the proposed trial processes including verbal consent.[10]

As this was a pilot study, no formal sample-size calculations were undertaken because the study was not designed or powered to detect a statistically significant difference in efficacy between the treatment arms. A recruitment target of 250 participants was chosen as we expected this would be sufficient to estimate the feasibility outcomes. This sample size is in accordance with the literature, which suggests that the size of the pilot trial should be at least 10% of the anticipated size of the substantive study,[11] the calculations for this are detailed in the published protocol. The initial plan was to open 3 sites with individual site targets: site A, 100 women, and sites B and C, 75 women each, recruiting over a period of 12-16 weeks. During setup it became clear that sites B and C did not have 24-hour availability of trained research staff on the labor ward and were struggling to deliver intrapartum research, therefore an additional site (Site D) was added, recruiting for a shorter period (6 weeks).

Women were eligible if at ≥34 weeks of gestation, having a CS, able to give informed consent, able to receive a telephone interview, and aged ≥16 years. Women were ineligible if they had a known allergy to chlorhexidine gluconate/acetate, were receiving prophylactic intravenous antibiotics for group B streptococcus colonization or for suspected infection (standard CS intravenous prophylaxis was not an exclusion criterion), or enrolled in an RCT intending to reduce SSI. All women booking at participating sites during the study period who were ≥34 weeks of gestation received a patient information leaflet in the post. Women undergoing

elective CS were approached before surgery by a clinician who introduced the study and obtained written consent. Women presenting in labor were approached by either a clinician or a research midwife using the same patient information leaflet as posted, and were asked whether they would consider participation if a CS became necessary. When the decision to perform an emergency CS was made, if time allowed, written consent was obtained. When time was limited, women provided verbal consent for the intervention with written consent obtained before discharge. If written consent was not obtained before discharge, then confirmation of consent was sought by sending a patient information leaflet and consent form to women in the post. If written consent was still not acquired, any data collected on the participant were not included in the analysis. After the woman's eligibility was confirmed and informed consent was obtained, randomization was performed by members of the research team at the recruiting hospital, using a 24/7 telephone randomization system provided by the University of Aberdeen. Women were randomized at a 1:1 ratio to either chlorhexidine 0.05% VC or no cleansing. A minimization algorithm was used to ensure balance in the treatment allocation for randomizing center, and whether the woman was in labor. A random element was included to ensure allocation concealment.

Chlorhexidine gluconate 0.05% (Unisept®) or chlorhexidine acetate 0.05% was used to perform VC. This is indicated within the British National Formulary for obstetric swabbing[12] and the Medicines & Healthcare products Regulatory Agency deemed that this was not a Clinical Trial of an Investigational Medicinal Product. Before CS, at the time of urinary catheter insertion (after completion of the regional anesthesia or before commencement of general anesthetic), 50 mL of antiseptic was emptied into a sterile pot and a single swab/sponge mounted on a sponge-holder was soaked and used to clean the vagina and cervix for 30 seconds. The chlorhexidine was obtained through the National Health Service supply chain. No relabeling or modification of the available preparation was needed because the surgeon was not blinded to the intervention. Attempts were made to blind the women because the intervention was applied at the time of the catheter insertion and they should not be aware of the application because of anesthesia. During the 14-day interview, women were asked whether they felt that they had received the intervention, to assess whether blinding was achievable. The trial could not be blinded to the operator or the clinical-care team in theatre providing care to the women because of the nature of the intervention and no suitable sham procedure could be used. The research midwife conducting the telephone follow-up interviews was blinded to the treatment allocation. The follow-up schedule included a 6-week medical record review and 2 telephone interviews at 14 and 30 days post-randomization.

Pre-specified outcome measures were defined to assess the feasibility of the trial. As published in the protocol,[13] pre-specified stop/go criteria were outlined based on: the proportion of women randomized into the trial of the 250 recruitment target, the proportion of women who received their allocated intervention, the proportion of women remaining in the trial (ie not withdrawn) who successfully completed the planned follow-up process for both the 14- and 30-day telephone interviews, and the proportion of women who withdrew from the trial. The stop/go criteria were assessed as follows: Green light—recruitment rate >90% of target, adherence rate >75%, follow-up rate >90%, and withdrawal rate <15%; Amber light—recruitment rate 80%-90%, adherence rate 50%-75%, follow-up rate 75%-90%, and withdrawal rate 15%-30%; Red light—recruitment rate <80%, adherence rate <50%, follow-up rate <75%, and withdrawal rate >30%. Other feasibility outcomes (assessed without stop/go criteria) included: the proportion of women approached who were eligible, the proportion of elective/emergency CS recruited, the proportion of women who gave verbal consent out of the number of women who had an emergency CS and were approached, the proportion of women randomized who could successfully identify which treatment they received, the proportion of complete data for each of the clinical and patient-reported outcomes, and time taken to perform the telephone interviews.

The following clinical and patient-reported outcomes were used. These were developed in the absence of a core outcome set; 1 has since been published and is consistent with the outcomes selected.[14] The endometritis outcomes were collected up to 30 days post-CS to be consistent with the CDC definition. The sepsis-related outcomes were collected until 6 weeks post-CS to be consistent with the national collection of postnatal sepsis guidelines. The day of delivery was regarded as Day 0.

The proposed primary outcome was:

- Endometritis as per the definitions set out by the CDC. Patients must meet at least 1 of the following criteria: 1. Patient has organism(s) identified from endometrial fluid or tissue by a culture or non-culture based microbiologic testing method that is performed for purposes of clinical diagnosis or treatment, for example, not Active Surveillance Culture/Testing. 2. Patient has at least 2 of the following signs or symptoms: fever (>38.0°C), pain or tenderness (uterine or abdominal), or purulent drainage from uterus.[15]

Secondary outcomes:

- Clinical diagnosis of endometritis (days 0-30) where it is not feasible to establish that this meets the CDC definition or where the diagnosis does not meet the criteria.
- Maternal sepsis (day 0-42) defined according to the National Institute for Health and Care Excellence sepsis guideline [16]
- Length of hospital stay from randomization to discharge home or transfer to another hospital post-CS, or up to 6 weeks after randomization if not discharged.
- Re-admission to hospital after CS post-discharge for suspected or confirmed infection up until 6 weeks postnatally (day 0-42).
- Antibiotics prescribed as an inpatient and hospital-prescribed outpatient (day 0-42) and antibiotics prescriptions for suspected/confirmed SSI relating to the woman's CS (uterine, pelvic, abdominal wound, or perineal).

TABLE 1 Participant characteristics at randomization

	Vaginal cleansing (N = 158)	No vaginal cleansing (N = 161)
Labor status[a], n (%)		
In labor	19 (12)	19 (12)
Not in labor	139 (88)	142 (88)
Site[a], n (%)		
A	68 (43)	72 (45)
B	42 (27)	41 (26)
C	27 (17)	28 (17)
D	21 (13)	20 (12)
Age (y)		
Mean (SD)	33.1 (5.6)	32.0 (5.2)
Booking body mass index (kg/m^2)		
Mean (SD)	28.2 (6.8)	28.8 (6.6)
Ethnicity, n (%)		
White	122 (77)	117 (73)
Asian	24 (15)	25 (16)
Black	6 (4)	4 (2)
Other	6 (4)	15 (9)
Diabetes[b], n (%)	8 (5)	4 (2)
Hypertension[b], n (%)	6 (4)	7 (4)
Autoimmune disease[b], n (%)	3 (2)	2 (1)
Cardiac disease[b], n (%)	0 (-)	1 (1)
HIV infection[b], n (%)	1 (1)	0 (-)
Parity, n (%)		
0	40 (25)	48 (30)
1	68 (43)	56 (35)
2	33 (21)	34 (21)
3	11 (7)	20 (12)
4	5 (3)	3 (2)
≥5	1 (1)	0 (-)
Number of previous cesarean sections, n (%)		
0	65 (41)	69 (43)
1	67 (42)	65 (40)
2	22 (14)	20 (13)
3	4 (3)	7 (4)
Previous open abdominal surgery, n (%)	14 (9)	19 (12)
Gestation at delivery (wk)		
Median [IQR]	39.0 [38.3-39.4]	39.1 [38.4-39.4]
Missing[c]	1	0
Type of pregnancy, n (%)		
Singleton	154 (97)	156 (97)
Multiple	4 (3)	5 (3)
Gestational diabetes[d,e], n (%)	14 (9)	15 (9)
Pregnancy-induced hypertension[e], n (%)	5 (3)	6 (4)
Preeclampsia[e], n (%)	3 (2)	7 (4)
HELLP syndrome[e,f], n (%)	0 (-)	0 (-)
Obstetric cholestasis[e], n (%)	3 (2)	4 (2)
Ongoing smoker at booking, n (%)	23 (15)	21 (13)
Used nonprescribed recreational drugs in this pregnancy[g], n (%)	0 (–)	3 (2)
Alcohol consumption during this pregnancy, n (%)	1 (1)	1 (1)
Missing	1	0

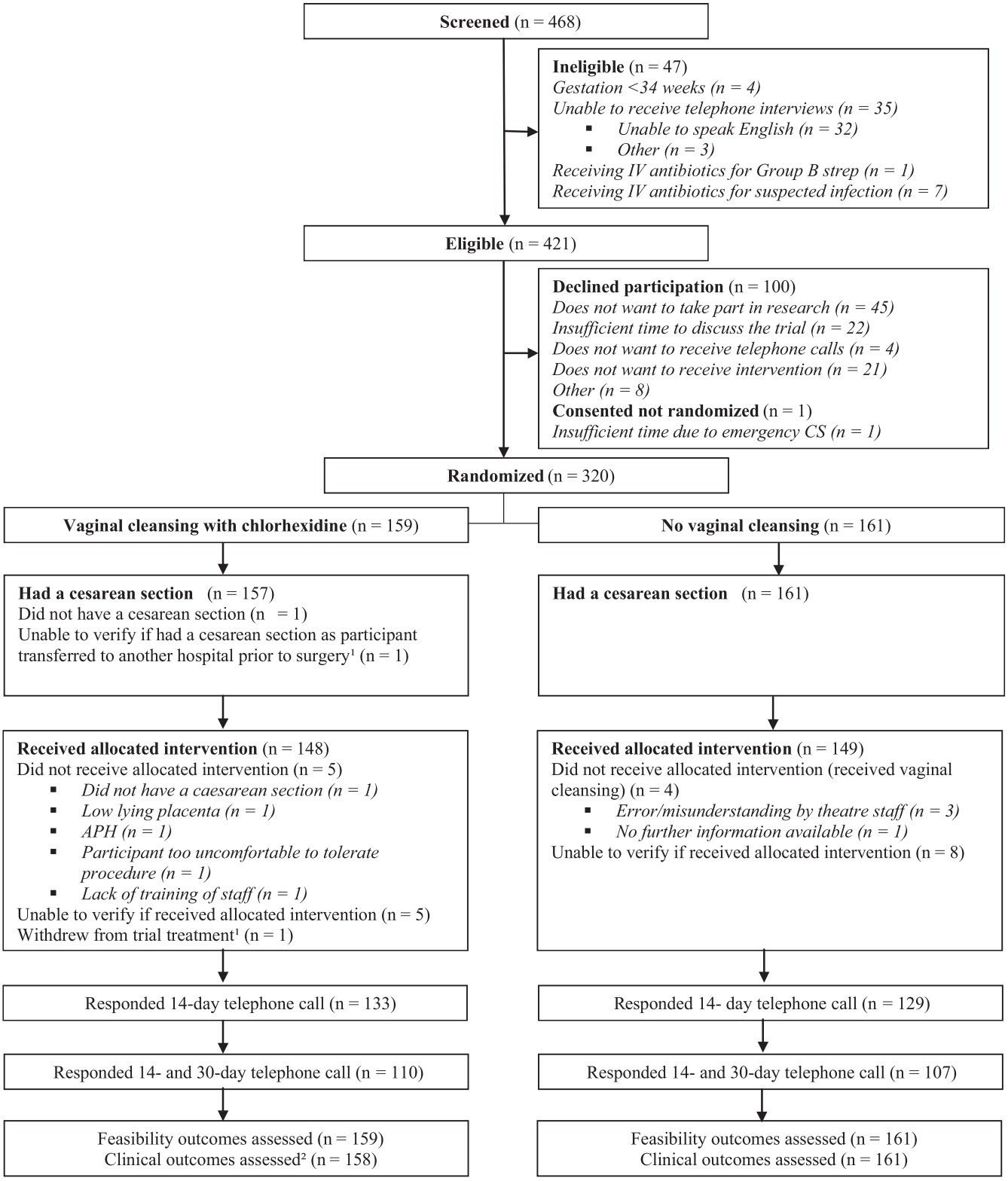
[a]Minimization variable.
[b]Prepregnancy medical condition.
[c]One participant with missing gestation data was transferred to another hospital so date baby delivered was not collected.
[d]Gestational diabetes defined as diet-, tablet-, or insulin-controlled diabetes developed during pregnancy.
[e]Medical conditions developed during pregnancy.
[f]HELLP, hemolysis, elevated liver enzymes, and low platelet count.
[g]Nonprescribed recreational drugs include cannabis and ventolin inhaler.

- Level 2 or 3 critical care (or obstetric high-dependency unit type care) as a result of an infection until 6 weeks postnatally (day 0-42).

The patient-reported outcomes were determined by the qualitative component of this project and were reported as an outcome of this pilot trial.[10]

1. Endometritis (treated)—Antibiotics (excluding nonreproductive infections such as respiratory infections and mastitis) and abnormal period pain or abnormal vaginal bleeding/discharge.
2. Endometritis (untreated)—At least 2 symptoms/signs from: abnormal period pain, abnormal vaginal bleeding/discharge, or patient-reported fever.
3. Incisional infection—Discharge from wound (pus) and antibiotics OR at least 2 signs (pain, redness, heat in skin incision) and dehiscence OR at least 2 signs and antibiotics.

Baseline characteristics are summarized with numbers and percentages for categorical variables, means and standard deviations for normally distributed continuous variables, or medians and interquartile ranges for non-normal continuous variables. Descriptive statistics are used to report feasibility outcomes between treatment arms and by center. Feasibility outcomes were analyzed by pooling both treatment arms and presenting overall estimates with 95% CI. Women who did not undergo a CS were excluded from all analyses of clinical and patient-reported outcomes. For binary clinical and patient-reported outcome measures, a log-binomial model was used to generate relative risks (and 95% CI) adjusting for the minimization variables.



[1]One participant withdrew from trial treatment and telephone interviews but was followed-up via medical notes.
[2]One participant did not have a caesarean section and therefore was not followed-up via medical notes.

FIGURE 1 CONSORT — participant flow through PREPS

Continuous clinical and patient-reported outcomes deemed to be normally distributed were summarized using means and standard deviations and a linear model was fitted to generate mean differences (and 95% CI) adjusting for the minimization parameters. Continuous outcomes not deemed to be normally distributed were summarized using medians and interquartile ranges and unadjusted differences

TABLE 2 Feasibility outcomes by center and for all participants

	Site A	Site B	Site C	Site D	All participants
Number of eligible participants					
Number screened, n	200	149	70	49	468
Eligible, n (%)	173 (87)	133 (89)	67 (96)	48 (98)	421 (90) [87-93][a]
Recruitment					
Target sample size, n	100	75	75	-	250
Participants randomized, n (%)	141	83	55	41	320 (128) [–][a]
Elective and emergency CS with verbal consent					
CS performed, n	140	82	55	41	318
Elective CS[b], n (%)	74 (53)	78 (95)	50 (91)	28 (68)	230 (72) [67-77][a]
Emergency CS[c], n (%)	66 (47)	4 (5)	5 (9)	13 (32)	88 (28) [23-33][a]
Category 1, n	9	0	0	0	9
Category 2, n	25	2	1	10	38
Category 3, n	32	2	4	3	41
Verbal consent, n (%)	24 (36)	2 (50)	1 (20)	5 (38)	32 (36) [26-47][a]
Written consent, n (%)	42 (64)	2 (50)	4 (80)	8 (62)	56 (64) [53-74][a]
Adherence					
Received allocated intervention, n (%)	137 (97)	67 (81)	53 (96)	40 (98)	297 (93) [89-95][a]
Did not receive allocated intervention, n (%)	4 (3)	2 (2)	2 (4)	1 (2)	9 (3)
Unable to confirm if received allocated intervention, n (%)	0 (–)	13 (16)	0 (–)	0 (–)	13 (4)
Withdrew from trial intervention, n (%)	0 (–)	1 (1%)	0 (–)	0 (–)	1 (<1)
Woman's recall of treatment allocation					
Treatment data available, n	141	69	55	41	306
Correctly identified treatment, n (%)	5 (4)	2 (3)	1 (2)	2 (6)	10 (4) [2-7][a]
Incorrectly identified treatment, n (%)	5 (4)	5 (9)	3 (6)	2 (6)	15 (6)
Unable to identify treatment, n (%)	103 (92)	52 (88)	43 (92)	29 (88)	227 (90)
Missing, n	28	10	8	8	54
Retention-telephone interviews					
Non-withdrawn participant's able to receive calls[d], n	141	82	55	41	319
Participants who had 14-d telephone interview, n (%)	113 (80)	69 (84)	47 (85)	33 (80)	262 (82) [77-86][a]
Participants who had 14- and 30-d telephone interview, n (%)	90 (64)	63 (77)	38 (69)	26 (63)	217 (68) [63-73][a]
Time taken to perform the telephone interviews (min)					
14-d telephone interview conducted, n	113	69	47	33	262
Time taken to perform interview, median (IQR)	5 (5-6)	5 (5-6)	5 (5-6)	4 (4-5)	5 (5-6) [5, 5][e]
Missing, n	1	1	—	—	2
30-d telephone interview conducted, n	90	63	38	26	217
Time taken to perform interview, median (IQR)	2 (2-3)	2 (2-3)	2 (2-3)	2 (2-2)	2 (2-3) [2, 2][e]
Missing, n	1	—	—	—	1
Withdrawal					
Number of participants withdrawn, n (%)	0 (-)	1 (1)	0 (-)	0 (-)	1 (<1) [0-2][a]
Type of withdrawal					
Trial treatment, n	-	1	-	-	1

(Continues)

TABLE 2 (Continues)

	Site A	Site B	Site C	Site D	All participants
Telephone interviews, n	-	1	-	-	1
Data collection from medical notes, n	-	0	-	-	0
All data previously collected, no	-	0	-	-	0

[a]n (%) [95% CI].
[b]Elective CS defined as category 4 (to suit woman and the maternity services) CS.
[c]Emergency CS defined as category 3 (early birth without compromise), category 2 (maternal or fetal compromise) or category 1 (threat to the life of the mother or fetus).
[d]One participant withdrew from telephone interviews.
[e]Median (interquartile range) [95% CI].

TABLE 3 Clinical and participant-reported outcomes

	Vaginal cleansing	No vaginal cleansing	Treatment effect estimate (95% CI)
Clinical outcomes			
Endometritis by CDC definition, n (%)	2/152 (1.3)	1/155 (0.7)	2.08 (0.19, 22.31)[a]
Clinical diagnosis of endometritis, n (%)	2/152 (1.3)	3/155 (1.9)	0.65 (0.11, 3.75)[a]
Maternal sepsis, n (%)	3/153 (2.0)	3/156 (1.9)	1.06 (0.23, 4.94)[a]
Re-admission to hospital, n (%)	2/156 (1.3)	1/161 (0.6)	2.07 (0.19, 22.30)[a]
Antibiotics (all usage), n (%)	15/156 (9.6)	23/161 (14.3)	0.69 (0.38, 1.24)[a]
Antibiotics for suspected/confirmed SSI, n (%)	12/155 (7.7)	18/161 (11.2)	0.71 (0.36, 1.41)[a]
Critical care for infection, n (%)	0/153 (-)	2/157 (1.3)	—
Length of hospital stay (d), median [IQR]	2 [1-3]	2 [1-3]	0.0 (−0.11, 0.11)[b]
Participant-reported outcomes			
Endometritis (treated), n (%)	5/111 (4.5)	4/106 (3.8)	1.21 (0.34, 4.36)[a]
Endometritis (untreated), n (%)	6/111 (5.4)	4/107 (3.7)	1.43 (0.42, 4.90)[a]
Incisional infection, n (%)	10/111 (9.0)	19/107 (17.8)	0.52 (0.25, 1.06)[a]
EQ5D5L index score at 14 d post-CS[d], mean (SD, n)	0.95 (0.08, 131)	0.93 (0.11, 129)	0.02 (−0.003, 0.04)[c]
EQ5D5L health state at 14 d post CS[e], mean (SD, n)	83.02 (13.03, 133)	82.18 (14.43, 129)	0.83 (−2.48, 4.14)[c]
EQ5D5L index score at 30 d post CS[d], mean (SD, n)	0.97 (0.08, 108)	0.98 (0.06, 103)	−0.01 (−0.03, 0.01)[c]
EQ5D5L health state at 30 d post CS[e], mean (SD, n)	87.34 (13.70, 109)	85.88 (13.88, 105)	1.50 (−2.24, 5.24)[c]

Note: Denominators are data available for analysis.
Abbreviations: CDC, Centers for Disease Control and Prevention; CS, cesarean section; EQ5D5L, 5-level EQ-5D; IQR, interquartile range; SSI, surgical-site infection.
[a]Risk ratio. Values <1 favor vaginal cleansing with chlorhexidine. Adjusted for minimization variables: center and in-labor/not-in-labor status.
[b]Difference in medians. Values <0 favor vaginal cleansing with chlorhexidine.
[c]Mean difference: values >0 favor vaginal cleansing with chlorhexidine. Adjusted for minimization variables: center and in-labor/not-in-labor status.
[d]EQ5D5L index scores range from −0.59 to 1, where 1 = perfect health, 0 = death and negative scores imply a health status worse than death.
[e]EQ5D5L health state scores range 0 to 100, where 0 = worst health you can imagine and 100 = best health you can imagine.

in medians were produced (and 95% CI) using bootstrapping methods. All analyses were based on the intention-to-treat principle using complete case data and were performed using SAS version 9.4 (SAS Institute, Cary, NC, USA) and Stata version 14 (Stata Corp., College Station, TX, USA). No subgroup or sensitivity analyses were performed.

2.1 | Ethical approval

This trial was approved by the London City & East Research Ethics Committee on 24 May 2017 (17/LO/0874) and registered as ISRCTN33435996.

3 | RESULTS

Participants had a mean age of 32.6 years, 12% of women were in labor at the time of randomization, 17% had rupture of membranes, 15% had a category 1 or 2 CS, 97% had a singleton pregnancy, and 58% of women had had a previous CS. Table 1 provides further details of participant characteristics.

Between 13 November 2017 and 3 March 2018 (15 weeks), 320 women (128% of target) were randomly assigned to either VC (n = 159) or standard practice of no VC (n = 161, Figure 1). The trial over-recruited above the 250 sample size because of the introduction of a 4th site and a pre-specified minimum recruitment time of at least 12 weeks. The allocated intervention was received by 297 (93%, 95% CI 89%-95%) of the 320 women. Across 3 of the 4 trial sites this figure was at least 96% for each. However, at 1 site, only 67/83 (83%) participants were confirmed to have received their allocated intervention because of issues recording this information in the medical notes. One woman partially withdrew from the trial a result of transfer of care. At 30 days, 319 women remained in the trial and 217 (68%, 95% CI 63%-73%) of them responded to both the 14- and 30-day telephone interviews, with 82% of women being contacted at least once (Table 2). Women were contacted a median of 1 time (IQR 1-2) for each of the 14- and 30-day interviews.

Of 468 women screened, 421 (90%) were eligible. Of these, 320 women were randomized (76% of those eligible) of whom 318 delivered by CS (1 mode of delivery unconfirmed and 1 vaginal delivery). Of the 318 women, 230 (72%) had an elective CS (category 4) and 88 (28%) had an emergency CS (categories 1-3). Of the 88 women who had an emergency CS, verbal consent was initially given by 32 (36%) women, with the remainder having sufficient time to give written consent. For all who consented verbally, written consent was obtained before discharge. Further details of feasibility outcomes are provided in Table 2.

In the VC arm, 2/152 (1.3%) women had endometritis as per the CDC definition compared with 1/155 (0.7%) in the no cleansing arm (RR 2.08, 95% CI 0.19-22.31). A clinical diagnosis of endometritis was reported in 2/152 (1.3%) women in the VC arm compared with 3/155 (1.9%) in the no cleansing arm (RR 0.65, 95% CI 0.11-3.75). Fifteen (9.6%) women received antibiotics for any indication in the VC arm in contrast to 23 (14.3%) women in the no cleansing arm (RR 0.69, 95% CI 0.38-1.24). Further details of clinical and participant reported outcomes are provided in Table 3.

4 | DISCUSSION

This pilot study demonstrates that it is possible to perform an RCT of VC at CS. We have developed study processes that can facilitate verbal consent in an urgent setting allowing recruitment of this high-risk group. This process was acceptable to clinicians and women. The telephone randomization system successfully allocated treatment for recruited women in less than 3 minutes.

The primary objective of this pilot was to assess the feasibility of performing a trial of VC, including an assessment of clinical and patient-reported outcomes and ability to collect them. We have reported these outcomes in this paper; however, the pilot trial was not powered, nor was it designed to detect differences in the clinical effectiveness of the intervention. The research question remains important and a full effectiveness evaluation should be performed.

A strength of this study is the development of a verbal-followed-by-written consent process that facilitated consent of women in urgent situations. This worked well at 2 sites and allowed recruitment of emergency cases at rates comparable to the national split of emergency and elective CS. Recruitment of emergency and 'in labor' women was limited by the availability of research-trained staff 24 hours per day at 2 sites and a larger RCT would require careful site selection, identifying those sites that have established intrapartum research infrastructure such as sites A and D. This explains the relatively low overall percentage of women in labor (12%), yet sites A and D have demonstrated that women having an emergency CS can be recruited. As those undergoing not in labor CS were recruited quickly and efficiently, sites in the full RCT would need fixed not-in-labor and in-labor targets.

It is important to collect SSI rates during the full postnatal period, because of the number of infections identified and treated in the community.[17] The telephone process for collecting these data was labor intensive; this process would be unsustainable within a larger trial, as to achieve these follow-up rates 4 attempts at 14 and 30 days were required before a woman was deemed lost to follow up. Follow-up rates were similar between emergency and elective CS. Having established the importance of collecting data from women who develop infection within the community, it is clear that the patient-reported follow-up methods need modification but should form an important part of any future research.

5 | CONCLUSION

This was a pilot trial to establish if a larger trial was feasible, through the development of processes for consent, randomization, and follow up. We have demonstrated that a larger trial of VC with chlorhexidine to prevent SSI is possible and acceptable to women/clinicians. Women can be recruited within an intrapartum emergency scenario, with the developed recruitment and consent processes. Women can also be followed up in the community. Cleansing the vagina with an antiseptic is potentially an important additional strategy to reduce SSI, especially in women undergoing a CS in labor. This trial was not designed to access the effectiveness of the intervention, but it supports the need for further evaluation of VC with an alternative antiseptic to an iodine-based solution, where there are concerns regarding fetal absorption. This trial is acceptable to women and clinicians and can be performed with the developed recruitment and follow-up processes.

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CONFLICT OF INTEREST

None.

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