Outpatient balloon catheter vs inpatient prostaglandin for induction of labor: a randomized trial

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BACKGROUND: Approximately 1 in 4 pregnant women undergo induction of labor. Meta-analyses have shown that mechanical methods of induction of labor are safe and effective, as is starting induction in an outpatient setting. However, few studies have evaluated outpatient balloon catheter induction in comparison with pharmacologic methods.

OBJECTIVE: This study aimed to determine whether women who underwent outpatient induction of labor with a balloon catheter would have a lower cesarean delivery rate than women who underwent inpatient induction of labor with vaginal prostaglandin E2 without an increase in adverse maternal or neonatal events.

STUDY DESIGN: This was a superiority randomized controlled trial. The eligibility criteria were pregnant women (nullipara and multipara) with a live singleton fetus in vertex presentation with any medical comorbidity who underwent planned induction of labor at term and who had an initial modified Bishop Score of 0 to 6 at 1 of 11 public maternity hospitals in New Zealand. The intervention groups were outpatient single balloon catheter induction in comparison with inpatient vaginal prostaglandin E2 induction. The primary hypothesis was that participants who started their induction at home with a balloon catheter would have a lower risk for cesarean delivery than participants who started their induction with prostaglandins and remained in hospital throughout. The primary outcome was cesarean delivery rate. Participants were randomized using a centralized secure online randomization website in a 1:1 ratio, stratified by parity and hospital. The participants and outcome assessors were not blinded to group allocation. An intention-to-treat analysis with adjustment for stratification variables was used.

RESULTS: A total of 539 participants were randomized to outpatient balloon catheter induction, and 548 participants were randomized to inpatient prostaglandin induction; the mode of birth was reported for all participants. The cesarean delivery rate was 41.0% among participants allocated to outpatient balloon induction and 35.2% among those allocated to inpatient prostaglandin induction (adjusted odds ratio, 1.27; 95% confidence interval, 0.98−1.65). Women in the outpatient balloon catheter group were more likely to have artificial rupture of membranes and to received oxytocin and an epidural. No differences were found in the rates of adverse maternal or neonatal events.

CONCLUSION: Outpatient balloon catheter induction was not found to reduce the cesarean delivery rate when compared with inpatient vaginal prostaglandin E2 induction. However, the use of balloon catheters in an outpatient setting does not seem to increase the rate of adverse events for mothers or babies and can be offered routinely.

Key words: balloon catheter, cervical ripening, induced, labor, prostaglandins, randomized controlled trial

Introduction

Induction of labor (IOL) is a common intervention in childbirth. Globally, approximately 1 in 4 pregnant women undergo IOL with significant variation by country.[1] In New Zealand, the rate is 27%,[2] and it is 31% in the United States[3] and 34% in Canada.[4] Induction is usually started with pharmacologic methods. However, there is moderate quality evidence that show that starting IOL with a balloon catheter instead of prostaglandin (PG) E2 probably reduces the risks for uterine hyperstimulation (risk ratio, 0.35; 95% confidence interval [CI], 0.18−0.67) and serious neonatal morbidity or perinatal death (risk ratio, 0.48; 95% CI, 0.25−0.93) with little or no difference in the cesarean delivery rate (risk ratio, 1.00; 95% CI, 0.92−1.09).[5]

A meta-analysis of 6 randomized trials (571 women) that compared cervical ripening with a balloon catheter in the outpatient vs inpatient setting found that women who were treated in an outpatient setting had a lower rate of cesarean delivery (21% vs 27%) and spent 7 fewer hours in hospital from admission to birth than those who were treated in an inpatient setting.[6] The authors concluded that among low-risk patients, outpatient balloon cervical ripening should be considered to be a safe, effective, and beneficial option, but acknowledged the limitation of a small study size. A meta-analysis of 26 studies (8292 women) on balloon catheter induction found that the risk for adverse events during the period between insertion and expulsion of a balloon was very low (ranging from 0.0% to 0.26%).[7] Studies also showed women's preferences for and satisfaction with outpatient management using a balloon catheter when compared with inpatient methods.[8−11] Women preferred spending more time in the privacy and comfort of their own home.

In summary, an appropriately powered study was needed to investigate the clinical effectiveness and safety of outpatient balloon catheter induction. The Outpatient Balloon vs Inpatient Prostaglandin for Induction of Labour (OBLIGE) trial addressed the hypothesis that women who underwent outpatient IOL with a balloon catheter would have a lower cesarean delivery rate than women who underwent inpatient IOL with vaginal PG E2 without an increase in adverse maternal or neonatal events.

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AJOG MFM at a Glance

Why was this study conducted?

Induction of labor (IOL) is common and is usually started using pharmacologic methods while the women remain in hospital throughout the process. Mechanical methods of cervical ripening, such as placement of a balloon catheter, are effective and lead to fewer complications than pharmacologic methods and women are satisfied and spend less time in hospital with outpatient IOL than with inpatient IOL. Early evidence suggests that outpatient balloon catheter induction is associated with reduced rates of cesarean delivery when compared with inpatient balloon catheter induction.

Key findings

The Outpatient Balloon Catheter vs Inpatient Prostaglandin for Induction of Labour trial found that outpatient balloon catheter IOL did not reduce the risk for cesarean deliveries when compared with inpatient vaginal prostaglandin E2 IOL, and women allocated to outpatient balloon catheter placement had more medical interventions during labor. There was no difference found in the rate of adverse outcomes for both mothers and babies.

What does this add to what is known?

This large, multicenter randomized controlled trial of women who underwent IOL at term provides high quality evidence about the methods and setting of cervical ripening. Balloon catheter placement for IOL can be routinely offered in an outpatient setting.

Materials and Methods

Design

The OBLIGE trial was a multicenter, superiority, randomized controlled trial conducted across 11 public hospitals in New Zealand. The protocol has been published.[12] The participating hospitals served urban, regional, and rural areas, covering 50% of the annual births nationally.[2] All hospitals had publicly funded midwifery primary maternity care, whereas a few additionally hospitals had private obstetricians who provided primary maternity care. The hospital characteristics are provided in Supplementary Table 3.

Ethics

This trial received ethical approval from the Health and Disability Ethics Committee New Zealand on November 23, 2016 (16/CEN/121).

Participants

The inclusion criteria were pregnant women (nullipara and multipara) with a live singleton baby in a vertex presentation with planned IOL at ≥37weeks' gestation, intact membranes, a normal nonstress test, Bishop score < 7, and able to remain within 1 hour of the hospital with someone who could speak sufficient English to communicate with hospital staff.

The exclusion criteria were a previous cesarean delivery, major fetal anomaly, suspected severe intrauterine growth restriction, and a maternal or fetal condition for which the clinician felt that outpatient care was contraindicated. The demographics that were collected were age, body mass index, self-reported and prioritized ethnicity,[13] and neighborhood deprivation score.[14]

Intervention and comparison

Outpatient balloon catheter. Hospital clinicians placed a single 50 mL Foley balloon catheter (Bard, 2-way, 20F) and provided detailed information about what to expect and when to return to the hospital (18 to 24 hours or earlier if concerned). Participants were offered travel or accommodation vouchers. On return to hospital, clinicians performed artificial rupture of membranes (ARM) if possible or switched to a second method (inpatient PG). The clinical team included midwives who underwent training to place balloon catheters and who had to perform at least 5 insertions under direct supervision before being accredited to provide this intervention within the trial.

Inpatient prostaglandins. Hospital clinicians either applied dinoprostone gel (Prostin E2) or placed a controlled-release pessary (Cervidil) in the vagina. It was considered to be safer for women who received PG to remain in hospital for monitoring throughout because of the risk for uterine hyperstimulation.[5] After 6 hours (for gel) or 12 to 24 hours (for the pessary), the clinician reassessed the cervix and performed ARM if possible or repeated PGE2 administration until ARM was possible (maximum 6 gels or 2 pessaries) or spontaneous rupture of membranes or labor occurred or if the patient or clinician wanted to change to second method (inpatient balloon).

Relevant concomitant care and interventions. Following ruptured membranes, labor was managed by clinicians according to local hospital protocols, including use of epidural and/or oxytocin. Labor management was undertaken primarily by registered midwives in 1-to-1 care with clear referral guidelines to an obstetrician if any complication arises. Women usually had cervical examinations every 4 hours during the first stage. Oxytocin for delayed labor progression was usually started 1 to 2 hours after ARM. Oxytocin was considered for nullipara with dilation of <1 cm per hour and was used with caution in multipara. Assessment by an obstetrician was required if the second stage exceeded 2 hours for nullipara or 1 hour for multipara.[15]

Outcomes

The primary outcome was the proportion of participants who gave birth by cesarean delivery. Secondary outcomes included those listed in the core outcome set listed hereafter.[16] The outcome definitions are provided in the published protocol and are listed below.[12]

Maternal outcomes. Duration of cervical ripening, duration of labor, pain score at insertion of first cervical ripening method (pictorial pain scale from 0 [no pain] to 10 [worst possible pain]), need for second method, need for ARM, pain score at ARM, use of oxytocin, use of epidural, use of fetal blood sampling, mode of birth, vaginal birth within 24 hours, reason for cesarean delivery, failed induction (cesarean delivery at <4 cm), arrested labor (determined by clinician), stillbirth, uterine hyperstimulation (tachysystole [>5 contractions in 10 minutes] or hypertonus [contractions lasting >2 minutes] in the presence of fetal heart rate abnormalities), clinically significant antepartum hemorrhage, chorioamnionitis (fever during labor with maternal or fetal tachycardia for which broad-spectrum intravenous antibiotics were administered), postpartum hemorrhage, endometritis (fever, fundal tenderness or purulent lochia for which intravenous antibiotics were administered), uterine rupture (full thickness requiring surgical repair), malpresentation, cord prolapse, intensive care admission, and length of hospital stay were recorded.

Neonatal outcomes. Sex, birthweight, 5-minute Apgar score, birth injury (severe bruising, nerve trauma, or fracture), arterial umbilical cord gas, intensive care admission, respiratory support, time in intensive care unit, infection (either culture proven or clinically suspected with supporting laboratory evidence, eg, raised white blood cell count or C-reactive protein), seizures, neonatal encephalopathy (moderate or severe), early neonatal death, and length of hospital stay data were collected.

Sample size calculation

At the Auckland Hospital in 2015, the cesarean delivery rate among women who underwent IOL (excluding women with previous cesarean deliveries) was 24.8% and almost all of these women were induced using PGs.[17] In the small trial of outpatient vs inpatient balloon catheter IOL, the cesarean delivery rate decreased from 43% to 29% (a relative reduction of 32%).[18] To detect a clinically meaningful reduction in the cesarean delivery rate from 24.8% to 18.8% (a relative risk reduction of 24%) with 80% power to detect a difference and a 2-sided type 1 error of 0.05, a sample size of 743 women for each study group was required. Adding a continuity correction, the total sample size required was 1552 women.

Recruitment, randomization, allocation, blinding

Potential participants were identified at the time an IOL was planned and were approached to participate by a clinician or a member of the research team. Participants were encouraged to watch a 4-minute informational video.[19] On the day of IOL, after confirming eligibility, the clinician obtained written consent and randomized the participant using a centralized secure online randomization website. The 1:1 ratio randomization schedule, stratified by hospital and parity, was prepared by the OBLIGE trial statistician. The clinician allocated the intervention to the participant. Because of the nature of the interventions, clinicians and participants were unable to be blinded to treatment allocation.

Data collection, management, analysis, monitoring, storage

Hospital clinicians collected data on preprinted reporting forms in real time after which the local research team entered the data into the centralized REDCap online study database (https://www.project-redcap.org/) (Vanderbilt University, Nashville, TN). The trial manager regularly checked and cleaned the data.

The data were deidentified before analysis; analysis was performed using SAS v9.4 (SAS Institute, Cary, NC). The baseline characteristics were described. The primary analysis followed the principle of intention-to-treat with the participants analyzed according to the assigned intervention group at randomization. Binary endpoints were analyzed using a logistic regression to estimate the odds ratios (ORs) for the intervention with stratification variables (parity and hospital) included as strata variables.[20] Normally distributed continuous outcomes were modeled using a mixed model to estimate any changes in outcomes between the 2 interventions with random effects included for the stratification variables. Nonnormally distributed continuous variables are presented as median and interquartile range and compared using the Hodges-Lehmann method to estimate differences between the groups. Per protocol analyses were conducted as sensitivity analyses.

Analyses were additionally performed according to the predefined stratification variables, namely (1) nulliparous vs multiparous; (2) Auckland-based hospital (largest contribution to recruited participants) vs 10 other hospitals; and (3) 7 hospitals with level 2 (secondary) neonatal unit vs 4 with level 3 (tertiary) units. Exploratory analyses were also undertaken to investigate the length of stay in hospital before and after birth.

A *P* value of.05 was considered statistically significant. Missing data were not imputed.

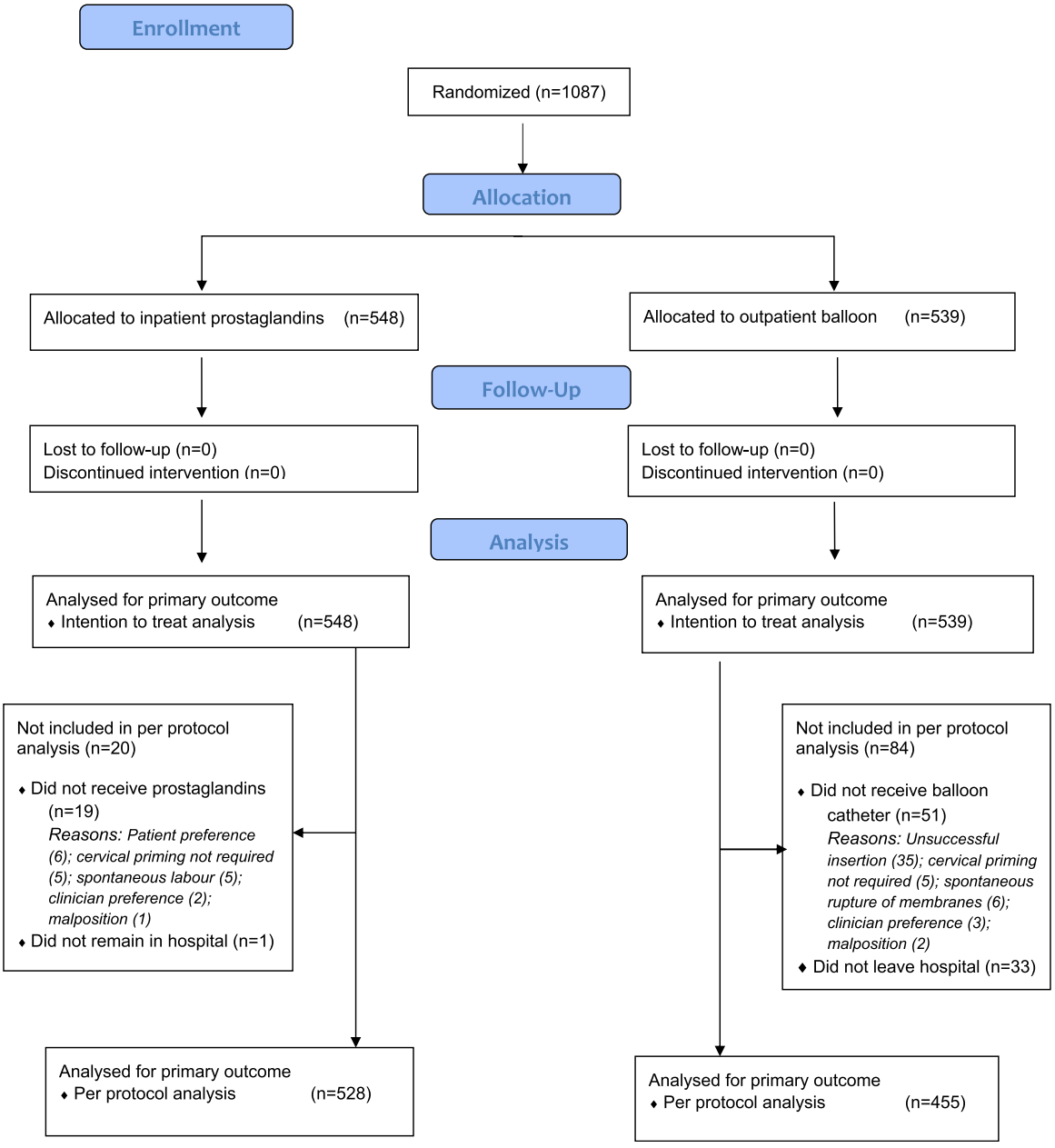
The Data Safety and Monitoring Committee (DSMC) a priori defined the serious adverse events (SAE) to be reported. Notice of SAEs reported to the principal investigator were provided to the DSMC for review. The Trial Steering Committee provided regular written reports to the DSMC throughout the study. An interim analysis was not planned.

Results

Women were recruited from October 2017 to November 2021. In Auckland, the largest recruiting site, full screening data were provided—of 4428 women who underwent IOL during the study period, 1834 (41%) were eligible and, of those, 1293 (70%) were approached and 477 (26%) were randomized.

In total, 1087 participants were randomly allocated, with 539 to the outpatient balloon catheter group and 548 to the inpatient PG group (Figure 1). The baseline characteristics are reported in Table 1. The most common indications for IOL were postterm pregnancy and diabetes in pregnancy. Mode of birth was known for all participants, including those who withdrew from the study after being allocated but consented for

FIGURE 1
CONSORT 2010 flow diagram for the OBLIGE trial



CONSORT, Consolidated Standards of Reporting Trials; *OBLIGE*, Outpatient Balloon vs Inpatient Prostaglandin for Induction of Labour.

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their data to be collected (4 outpatient balloon catheter participants and 6 inpatient PG participants).

The Trial Steering Committee, while still blinded to the results and in consultation with the DSMC, determined that the trial should be stopped early because recruitment was slower than anticipated. Reasons included the COVID-19 pandemic, women or clinician preference, midwifery resource constraints, and the new recommendation to use misoprostol for cervical ripening in the national guideline.[21]

Primary outcome

The cesarean delivery rate was 221 of 539 (41.0%) in the outpatient balloon catheter group and 193 of 548 (35.2%) in the inpatient PG group (adjusted OR [aOR], 1.27; 95% CI, 0.98−1.65) (Table 2).

When stratified by parity, there was no difference in the cesarean delivery rate between the allocated study groups for nullipara or multipara (nullipara: 49.5% balloon catheter vs 43.9% PGs;

TABLE 1
Participant characteristics

Characteristics	Inpatient prostaglandins (n=548)		Outpatient balloon (n=539)	
	Number or mean	% or standard deviation	Number or mean	% or standard deviation
Age (y)	32.3	5.0	32.3	5.5
Age (y) categories				
<35	385	70.3%	370	68.6%
≥35	163	29.7%	169	31.4%
BMI (kg/m^2)	27.6	6.7	27.4	6.6
BMI categories				
Normal (<25 kg/m^2)	249	45.4%	239	44.3%
Overweight (25–29 kg/m^2)	133	24.3%	136	25.2%
Obese (≥30 kg/m^2)	166	30.3%	164	30.4%
Ethnicity				
Maori	58	10.6%	71	13.2%
Pacific	34	6.2%	29	5.4%
Indian	45	8.2%	45	8.3%
Asian	47	8.6%	64	11.9%
European	350	63.9%	314	58.3%
Other	14	2.6%	16	3.0%
New Zealand Index of Multiple Deprivation				
1–2 (least deprived)	105	19.2%	89	16.5%
3–4	116	21.2%	118	21.9%
5–6	130	23.7%	137	25.4%
7–8	115	21.0%	121	22.5%
9–10 (most deprived)	81	14.8%	74	13.7%
Missing	1	0.2%	0	0%
Nulliparous	417	76.1%	420	77.9%
Gestational age at start of IOL (wk)	40	1.3	39.9	1.3
Gestational age at start of IOL, categories:				
37+0 to 38+6 wk	129	23.5%	137	25.4%

(continued)

TABLE 1
Participant characteristics *(continued)*

Characteristics	Inpatient prostaglandins (n=548)		Outpatient balloon (n=539)	
	Number or mean	% or standard deviation	Number or mean	% or standard deviation
39+0 to 40+6 wk	245	44.7%	235	43.6%
≥41+0 wk	174	31.8%	167	31.0%
Indication for IOL				
Post date	177	32.3%	171	31.7%
Diabetes mellitus	136	24.8%	146	27.1%
Small for date or intrauterine growth restriction	54	9.9%	51	9.5%
Hypertension	36	6.6%	41	7.6%
Late maternal age	28	5.1%	34	6.3%
Large for date o macrosomia	29	5.3%	22	4.1%
Reduced fetal movements	27	4.9%	20	3.7%
In vitro fertilization pregnancy	22	4.0%	11	2.0%
Other[a]	39	7.1%	43	8.0%
Bishop score at start of IOL				
0–2	173	31.6%	172	31.9%
3–4	256	46.7%	252	46.8%
5–6	115	21.0%	112	20.8%
Missing	4	0.7%	3	0.6%
Lead maternity carer type				
Independent midwife	418	76.3%	406	75.3%
Hospital midwife	77	14.1%	90	16.7%
Private obstetrician	53	9.7%	43	8.0%
Hospital site				
Auckland	231	42.2%	246	45.6%
Dunedin	8	1.5%	9	1.7%
Hawke's Bay	38	6.9%	44	8.2%
Hutt	22	4.0%	18	3.3%
North Shore	44	8.0%	35	6.5%
Taranaki	9	1.6%	9	1.7%

(continued)

TABLE 1
Participant characteristics *(continued)*

Characteristics	Inpatient prostaglandins (n=548)		Outpatient balloon (n=539)	
	Number or mean	% or standard deviation	Number or mean	% or standard deviation
Tauranga	64	11.7%	60	11.1%
Waikato	84	15.4%	74	13.7%
Waitakere	2	0.4%	6	1.1%
Wellington	40	7.3%	33	6.1%
Whakatane	6	1.1%	5	0.9%

BMI, body mass index; *IOL*, induction of labor.

[a] Other indications for IOL by group (prostaglandin, balloon): antepartum hemorrhage (1,1), oligohydramnios (5,3), obesity (0,1), obstetrical cholestasis (11,12), maternal medical condition (4,14), maternal request (11,6), fetal condition (3,1), other (4,5).

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OR, 1.25; 95% CI, 0.96−1.65; multipara: 10.9% balloon catheter vs 7.6% PGs; OR, 1.48; 0.63−3.50) (Supplementary Table 1). When stratified by hospital, participants at the non-Auckland hospitals had a higher cesarean delivery rate in the outpatient balloon catheter group than in the inpatient PG group (aOR, 1.53; 95% CI, 1.08−2.18); this was not observed for participants at the Auckland hospital (aOR, 1.02; 95% CI, 0.70−1.49). A test for interaction did not reach statistical significance (P=.12). There was no difference in the analysis that was stratified by level of the neonatal unit (aOR, 1.58; 95% CI, 1.00−2.52 for level 2 neonatal units and aOR, 1.15; 95% CI, 0.84−1.58 for level 3 units).

A per protocol analysis was also performed. For 528 participants who received PGs and remained in hospital, the cesarean delivery rate was 34.7% compared with 40.7% for 455 participants who received a balloon catheter and left the hospital for any amount of time (aOR, 1.27; 95% CI, 0.96−1.67) (Table 2).

Figure 1 shows how 51 of 539 participants allocated to the outpatient balloon catheter group did not receive their allocation with the most common reason being unsuccessful balloon insertion; 33 of 488 who received the balloon catheter did not go home, mostly for clinical reasons. Figure 2 illustrates the outcomes for the 455 women who received a balloon catheter and left the hospital.

Secondary maternal outcomes

The median pain score for 452 women at the time of attempted balloon catheter insertion was higher than for 435 women who initially received PG (3 vs 2; P<.001) (Table 2).

Of 539 women allocated to the outpatient balloon catheter group, 26.2% progressed to a second method of cervical ripening when compared with 7.7% of the 548 women allocated to the inpatient PGs group (aOR, 4.27; 95% CI, 2.95−6.17). The most common reason for a second method in both groups was the inability to perform ARM.

Women allocated to the outpatient balloon catheter group were more likely to undergo ARM (82.2% vs 67.2%; aOR,

TABLE 2
Maternal outcomes

Outcome	Inpatient prostaglandins (n=548) N	Number or median	% or IQR	Outpatient balloon (n=539) N	Number or median	% or IQR	Odds ratio or Hodges-Lehmann estimator (95% CI)	*P* value
Primary outcome								
Cesarean delivery	548	193	35.2%	539	221	41.0%	1.27 (0.98–1.65)[a]	.07
Cesarean delivery (per protocol analysis)	528	183	34.7%	455	185	40.7%	1.27 (0.96–1.67)[a]	.09
Secondary outcomes								
Primary reason for cesarean delivery								
Failed IOL (<4 cm)	548	21	3.8%	539	35	6.5%	χ^2 (4, n=1087)=6.8	.15
Failed to progress in established or active labor		92	16.8%		107	19.9%		
Fetal distress		69	12.6%		70	13.0%		
Other reason		11	2.0%		9	1.7%		
Not applicable—vaginal birth		355	64.8%		318	59.0%		
Mode of birth								
Yes—spontaneous vaginal birth	548	264	48.2%	539	210	39.0%	0.70 (0.53–0.91)	.009
Yes—instrumental vaginal birth		91	16.6%		108	20.0%	1.04 (0.74–1.46)	
No—cesarean delivery		193	35.2%		221	41.0%	Reference	
Cervix dilation at time of cesarean (median, IQR)	189	5	3–9	218	5	4–6	0.00 (-1.00–0.00)[b]	.26
Failed IOL (dilation <4 cm at cesarean delivery)	189	51	27.0%	218	54	24.8%	0.88 (0.57–1.38)[a]	.59
Vaginal birth within 24 h of starting IOL	548	171	31.2%	539	72	13.4%	0.32 (0.24–0.45)[a]	<.0001
Pain score at placement of prostaglandin or balloon (median, IQR)	435	2	1–4	452	3	2–5	1.00, (1.00–2.00)[b]	<.0001
Need for second method of IOL	548	42	7.7%	539	141	26.2%	4.27 (2.95–6.17)[a]	<.0001
Artificial rupture of membranes	548	368	67.2%	539	443	82.2%	2.34 (1.74–3.15)[a]	<.0001
If yes, pain score at time of ARM (median, IQR)	242	3	1–5	310	4	2–5	0.00 (0.00–1.00)[b]	0.29
Oxytocin	548	335	61.1%	539	394	73.1%	1.72 (1.33–2.23)[a]	<.0001
If yes, cervix dilation at time of starting oxytocin (median, IQR)	326	3	2.0–4.0	385	3	2.0–4.0	0.00 (0.0–0.00)[b]	0.06
Epidural	548	331	60.4%	539	380	70.5%	1.58 (1.20–2.07)[a]	.001
If yes, cervix dilation at time of starting epidural (median, IQR)	314	3.0	2.0–4.0	369	4.0	3.0–5.0	0.00 (0.00–0.00)[b]	.11
Total time in hospital for mother (median, IQR)	548	74.5	47.1–100.9	539	73.0	42.8–102.4	−0.33 (−4.82 to 3.27)[b]	.43
Total time in hospital for mother (mean, SD)		77.4	44.3		76.2	44.0		

ARM, artificial rupture of membranes; *CI*, confidence intervals; *IOL*, induction of labor; *IQR*, interquartile range; *SD*, standard deviation.

[a] Stratified by parity (nulliparous yes or no) and site (Auckland yes or no); [b] Hodges-Lehmann estimator (95% confidence limits), unstratified. *P* value was determined using a stratified Wilcoxon (Van Elteren) test.

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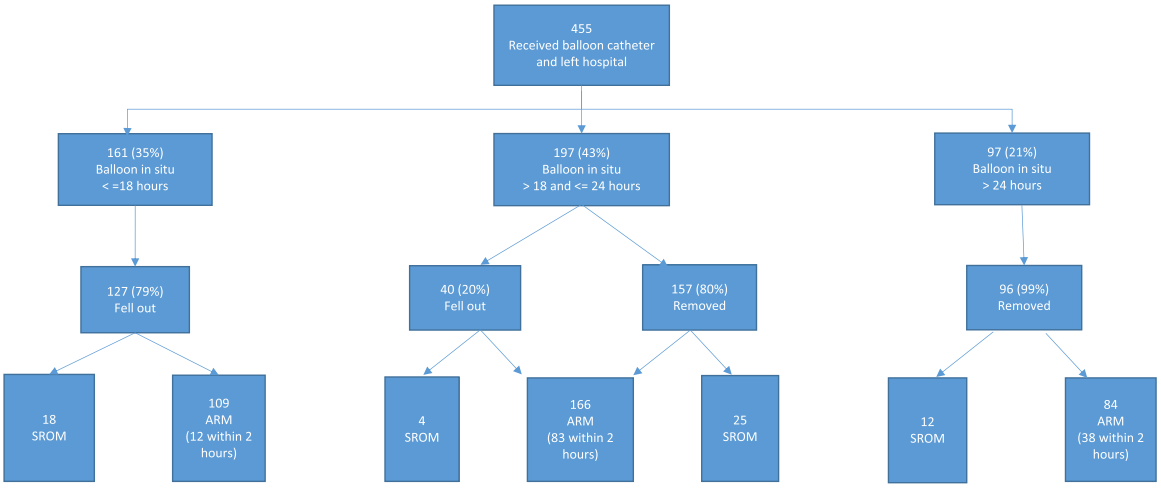
FIGURE 2
Outcomes of participants who received balloon catheter and left hospital



ARM, artificial rupture of membrane; *SROM*, Spontaneous rupture of membranes.

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2.34; 95% CI, 1.74−3.15) and receive oxytocin (73.1% vs 61.1%; aOR, 1.72; 95% CI, 1.33−2.23) and epidural (70.5% v 60.4%; aOR, 1.58; 95% CI, 1.20−2.07) than women allocated to the inpatient PG group. Women allocated to the outpatient balloon catheter group were not more likely to have an instrumental vaginal birth but were less likely to have a spontaneous vaginal birth (aOR, 0.70; 95% CI, 0.53−0.91). Women allocated to the outpatient balloon catheter group were less likely to have a vaginal birth within 24 hours of balloon catheter placement or receiving the initial PG treatment (13.4% vs 31.2%; aOR, 0.32; 95% CI, 0.24−0.45). We found no difference in the pain score at the time of ARM (3 vs 4; *P*=.29), nor in the primary reason for cesarean delivery.

There was no difference in the overall maternal length of stay (time from admission to discharge) (median, 73.0 vs 74.5 hours; *P*=.43). Women allocated to the outpatient balloon catheter group had a shorter time in hospital before the birth by 12 hours (median, 21.5 vs 32.7 hours; *P*<.001) and a longer time in hospital after the birth by 5 hours (median, 43.0 vs 37.5 hours; *P*=.001) (Supplementary Table 2).

Adverse maternal outcomes

This study found no difference in any adverse maternal outcomes between the groups (Table 3).

SAEs were uncommon and included 1 uterine rupture in the outpatient balloon catheter group, 1 umbilical cord prolapse in the inpatient PG group, and 1 maternal admission to the intensive care unit in each group. These all occurred during labor in hospital and were reviewed by the DSMC who concluded that they were unrelated to the study intervention. There were no stillbirths.

Neonatal outcomes

Umbilical cord lactate or gas levels were measured in 61% of those allocated to the inpatient PG group and in 64% of the outpatient balloon catheter participants. There were some differences in the individual umbilical cord blood parameters. This study found no difference in any other neonatal adverse outcome or in the composite neonatal outcome (Table 4).

There was 1 case of moderate-severe neonatal encephalopathy in the inpatient PG group, which was reviewed by the DSMC and determined to be unrelated to the study intervention. There were 3 cases of suspected sepsis in the outpatient balloon catheter group and 2 in the inpatient PG group; all cases were culture negative. There were no early neonatal deaths.

Comment

Principal findings

The OBLIGE trial found that there was no reduction in the cesarean delivery rate among women who started IOL with a balloon catheter out of hospital when compared with women who started IOL with vaginal PGE2 in hospital. Women in the outpatient balloon catheter group were more likely to undergo ARM and to received oxytocin and an epidural. The OBLIGE trial found that women allocated to the outpatient balloon catheter group and their babies were not at increased risk for adverse outcomes.

Results in the context of what is known

The findings from the OBLIGE trial are consistent with 2 Australian trials with the same research question that found that when compared with inpatient PG IOL, outpatient balloon catheter induction did not reduce the cesarean delivery rate, did not increase the incidence of

TABLE 3
Maternal adverse events

	Inpatient prostaglandins (n=548)			Outpatient balloon (n=539)				
Adverse events	N	n	%	N	n	%	Odds ratio (95% CI) or chi-square	*P* value
Antepartum hemorrhage after starting IOL	548	19	3.5	539	23	4.3	1.24 (0.67–2.30)[a]	.50
Timing of APH								
During IOL	548	9	1.6	539	19	3.5	χ^2 (2, N=1086)=7.41	.02
During labor or birth		10	1.8		3	0.6		
No APH		529	96.5		516	95.7		
APH caused by placental abruption	548	3	0.5	539	1	0.2	0.34 (0.04–3.26)[b]	.35
Uterine hyperstimulation	548	62	11.3	539	63[c]	11.7	1.02 (0.70–1.48)[a]	.93
Chorioamnionitis in labor	548	19	3.5	539	26	4.8	1.39 (0.76–2.54)[a]	.29
Noncephalic presentation after starting IOL	548	2	0.4	539	5	0.9	2.56 (0.50–13.26)[b]	.26
Postpartum hemorrhage	548	212	38.7	539	219	40.6	1.06 (0.82–1.35)[a]	.67
Total estimated blood loss								
<500 mL	548	336	61.3	539	320	59.4	χ^2 (3, N=1087)=4.01	.26
500–999 mL		144	26.3		160	29.7		
1000–1499 mL		52	9.5		38	7.1		
≥1500 mL		16	2.9		21	3.9		
Blood transfusion for PPH	548	4	0.7	539	10	1.9	2.58 (0.80–8.26)[b]	.11
Transfer to theater for PPH	548	10	1.8	539	4	0.7	0.41 (0.13–1.33)[a]	.14
Postpartum endometritis	548	6	1.1	539	9	1.7	1.61 (0.57–4.56)[a]	.37

APH, antepartum hemorrhage; *CI*, confidence interval; *IOL*, induction of labor; *PPH*, postpartum hemorrhage.

[a] Stratified by parity (nulliparous yes or no) and site (Auckland yes or no); [b] Unstratified analysis because of loss of noninformative observations; [c] A total of 62 of 63 women with hyperstimulation in the balloon catheter group had prostaglandins and/or oxytocin. Hyperstimulation did not occur while the balloon catheter was in situ.

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adverse events for mothers or babies, and did increase the need for maternal interventions during labor. Henry et al[22] randomized 101 women in a tertiary hospital and found that women who were randomized to outpatient balloon catheter induction were less likely to achieve vaginal birth within 12 hours of admission to the birthing unit (28% vs 53%; *P*=.01) than women randomized to inpatient PG, they had comparable rates of cesarean delivery (34% vs 29%; *P*=.62), needed oxytocin more often (88% vs 59%; *P*<.01), and spent 11 fewer hours in hospital before the birth. The Physiological-based Cord Clamping in Congenital Diaphragmatic Hernia trial was a multicenter trial that reported a per protocol analysis for the 448 women who received an intervention (64% of those randomized).[23] The trial was stopped early after the planned interim analysis because of slow recruitment and high attrition. They found no difference between the groups in their primary outcome of adverse composite neonatal outcome (18.6% outpatient balloon catheter vs 25.8% inpatient PG; *P*=.07) and no difference in the mode of delivery (*P*=.24), reporting cesarean delivery rates of 32.6% in the outpatient balloon catheter group and 25.8% in the inpatient PG group. More women in the outpatient balloon catheter group underwent ARM (89% vs 71%; *P*<.01) and received oxytocin (87% vs 66%; *P*<.01), and there was no difference in the time from IOL to birth.

The cesarean delivery rate in this study was consistent with the previously mentioned 2 trials but higher than expected based on the cesarean delivery rate used for the sample size calculation in 2016[17]—this may be because of an annual increase in the overall cesarean delivery rate,[2,17] a higher-risk population that required IOL, and that many IOLs may have been performed without an evidence-based indication in this pragmatic study.

We surmise that women who received inpatient PGs in the current study had more clinician involvement, examinations, fetal monitoring, and pain management and may have been prioritized for ARM and oxytocin within a constrained public healthcare system when compared with women who received a balloon catheter after their return to the hospital; it is possible that this more interventional management of labor and

TABLE 4
Neonatal outcomes and adverse events

Outcome	Inpatient prostaglandins (N = 548)			Outpatient balloon (N = 539)			Odds ratio or mean difference or Hodges-Lehmann estimator (95% CI)	*P* value
	N	Number or mean or median	% or IQR	N	Number or mean or median	% or IQR		
Neonatal characteristics								
Birthweight (g), mean, SD	548	3567.1	451.6	539	3553.7	498.8	−9.04 (−65.26 to 47.19)[a]	.75
Female sex	548	281	51.3%	539	288	53.4%	1.09 (0.86−1.38)[a]	.48
Duration of neonatal stay in hospital (h), median, IQR	548	37.5	14.7−62.5	539	43.3	21.4−69.4	6.02 (1.92−10.43)[b]	.0005
Neonatal adverse events								
5-min Apgar score (median, IQR)	548	10	9−10	538	10	9−10	0 (0−0)[b]	.22
5-min Apgar score <7	548	11	2.0%	539	18	3.3%	1.73 (0.81−3.71)[a]	.16
Birth injury	548	8	1.5%	539	3	0.6%	0.38 (0.10−1.43)[c]	.15
Scalp lactate or pH performed during labor	548	29	5.3%	539	30	5.6%	1.06 (0.62−1.78)[c]	.84
If yes, scalp lactate (mmol/L), median, IQR	29	2.8	1.8−4.0	30	2.9	2.0 - 3.6	0.1 (−0.6 to 0.8)[b]	.86
Cord lactate or gases measured	548	332	60.6%	539	344	63.8%	1.14 (0.88−1.46)[a]	.32
If yes, UA pH (median, IQR)	285	7.3	17.2−7.3	300	7.3	7.2−7.3	0.00 (−0.01 to 0.01)[b]	.93
UA pH <7.0	285	7	2.5%	300	4	1.3%	0.54 (0.16−1.85)[c]	.33
UA pH <7.1	285	23	8.1%	300	12	4.0%	0.48 (0.23−0.97)[c]	.04
UA base deficit ≥12 meq/L	280	20	7.1%	294	8	2.7%	0.36 (0.16−0.84)	.02
UA lactate (mmol/L), median, IQR	321	4.5	3.2−6.2	334	4.1	3.0−5.6	−0.40 (−0.70 to −0.10)[b]	.02
UA lactate ≥ 8 mmol/L	321	37	11.5%	334	18	5.4%	0.44 (0.24−0.79)[c]	.006
Admission to neonatal unit	548	37	6.8%	539	44	8.2%	1.28 (0.81−2.03)[a]	.29
If yes, length of stay (h), median, IQR	37	47.7	22.3−94.3	44	38.3	23.9−83.4	−2.48 (−26.17 to 15.93)[b]	.51
Admission to neonatal unit >4 h	548	34	6.2%	539	40	7.4%	0.56 (0.12−2.75)[a]	.48
Need for respiratory support	548	21	3.8%	539	25	4.6%	1.26 (0.70−2.29)[a]	.44
Seizures	548	2	0.4%	539	1	0.2%	0.51 (0.05−5.59)[c]	.58
Composite measure of fetal and neonatal outcome[d]	548	69	12.6%	539	71	13.2%	1.08 (0.75−1.55)[a]	.68

CI, confidence intervals; *IQR* interquartile range; *SD* standard deviation; *UA* umbilical artery.

[a] Stratified by parity (nulliparous yes or no) and site (Auckland yes or no); [b] Hodges-Lehmann estimator (95% confidence limits), unstratified. *P* value was determined using a stratified Wilcoxon (Van Elteren) test; [c] Unstratified analysis because of loss of noninformative observations; [d] Composite measure comprising one or more of the following: admission to the neonatal unit; umbilical cord arterial pH <7.10 or base deficit ≥12 or lactate ≥8; hypoxic ischemic encephalopathy; neonatal seizure; neonatal infection; Ssillbirth; early neonatal death; and neonatal 5-minute Apgar score <7.

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the faster action of PGs may have contributed to more vaginal births within 24 hours.

Clinical implications

This large trial provides high quality information to women, clinicians, and hospitals to support evidence-based decisions about IOL and help to set expectations about the journey. Outpatient balloon catheter induction did not reduce the cesarean delivery rate and there was no benefit with respect to medical interventions in labor. There was less time spent in hospital before birth, but the total time in hospital was no different. Women may experience balloon catheter induction as a lesser medical intervention for their induction and may want to spend some of the time during their induction out of hospital, especially during the COVID-19 pandemic. Outpatient balloon catheter induction, within the limitations of power to address uncommon adverse outcomes, was found to be safe. There may be a place for outpatient balloon catheter induction as a choice for women as part of a shared decision-making model of care.

Research implications

Formal analysis of the maternal and clinician satisfaction and economic cost-effectiveness in the OBLIGE trial is ongoing. The 2 Australian trials and now the OBLIGE trial have each found a similar but nonstatistically significant higher rate of cesarean delivery among women who started IOL with an outpatient balloon catheter; an individual patient data meta-analysis is planned, which could provide a more definitive answer.

Results from this trial can be used to update national IOL clinical practice guidelines.[21,24,25] Further research evaluating tools for implementing trial findings and IOL guidelines, such as a decision aid, would be useful.

We suggest that future IOL research trials should not use cesarean delivery rate as the primary outcome and instead they should focus on other clinical maternal or neonatal outcomes[16] that are better indicators of quality of care, because cesarean delivery is an intervention with multiple drivers that are not necessarily related to the IOL.

Strengths and limitations

Strengths are the large sample size, strong study design, high proportion of participants who received their allocated intervention, no loss to follow-up, diverse ethnicity of participants, and representation from urban and regional hospitals with secondary and tertiary neonatal units. Although recruitment did not reach the planned sample size, this was offset by the finding that the observed cesarean delivery rate in the control group (35.2%) was higher than expected (24.8%).

Weaknesses were the lack of blinding of participants and clinicians, incomplete eligibility screening of potential participants because of multiple providers and pathways for IOL, and lack of power to detect differences in uncommon adverse outcomes. The inability to detect adverse outcomes in an outpatient setting is a potential limitation. Low recruitment might have influenced the results because of the low consent rate among eligible women and the lack of demographic data on women who declined, which may limit the generalizability of our findings. Although only 62% of babies had umbilical cord gases measured, it is consistent with the usual practice of selective measurement of universal gases for babies with risk factors, however, this may limit the accuracy of the neonatal estimates. Although many hospitals now use misoprostol for cervical ripening, misoprostol and vaginal PGE2 are equivalent in terms of important clinical outcomes, thus our comparison is relevant.[26]

Conclusion

Outpatient balloon catheter induction was not found to reduce the cesarean delivery rate when compared with inpatient vaginal PGE2 induction and was found to increase medical interventions during labor. However, the use of balloon catheters in an outpatient setting does not seem to increase the incidence of adverse events for mothers or babies and can be offered routinely. ■

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Supplementary materials

Supplementary material associated with this article can be found in the online version at doi:10.1016/j.ajogmf.2023.100958.

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This trial was prospectively registered with the Australia New Zealand Clinical Trials Registry on June 6, 2016 (ACTRN: 12616000739415). The first participant was enrolled on October 25, 2016. (URL: https://www.anzctr.org.au/Trial/Registration/TrialReview.aspx?id=370330&isReview=true)

The relevant de-identified participant level data can be made available for use in future research, such as Individual participant data metanalysis, on reasonable request to the Trial Steering Committee (through the principal investigator). This includes participant characteristics and maternal and neonatal clinical outcomes and additional documents such as data dictionary, protocol, and statistical analysis plan. Data will be made available after publication and for up to 10 years. Data can be shared securely via a data transfer service such as Web DropOFF Box.

This trial adheres to the Consolidated Standards of Reporting Trials guidelines.

The findings of this study were presented at the annual congress of the Perinatal Society of Australia & New Zealand, Adelaide, South Australia, Australia, May 15–18, 2022 (URL: https://web.cvent.com/event/cea2cd64-043a-4004-a54b-186a5897d743/summary).

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