Efficacy and safety of oral misoprostol versus transvaginal balloon catheter for labor induction: An observational study within the SWEdish Postterm Induction Study (SWEPIS)

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Abstract
Introduction: Induction of labor is increasing. A common indication for induction of labor is late term and postterm pregnancy at 41 weeks or more. We aimed to evaluate if there are any differences regarding efficacy, safety, and women's childbirth experience between oral misoprostol and transvaginal balloon catheter for cervical ripening in women with a low-risk singleton pregnancy and induction of labor at 41+0 to 42+0 weeks of gestation.

Material and methods: In this observational study, based on data from the Swedish Postterm Induction Study (SWEPIS), a multicenter randomized controlled trial, a total of 1213 women with a low-risk singleton pregnancy at 41 to 42 weeks of gestation were induced with oral misoprostol (n = 744) or transvaginal balloon catheter (n = 469) at 15 Swedish delivery hospitals. The primary efficacy outcome was vaginal delivery within 24 h and primary safety outcomes were neonatal and maternal composite adverse outcomes. Secondary outcomes included time to vaginal delivery and mode of delivery. Women's childbirth experience was assessed with the Childbirth Experience Questionnaire (CEQ 2.0) and visual analog scale. We present crude and adjusted mean differences and relative risks (RR) with 95% CI. Adjustment was performed for a propensity score based on delivery hospital and baseline characteristics including Bishop score.

Results: Vaginal delivery within 24 h was significantly lower in the misoprostol group compared with the balloon catheter group (46.5% [346/744] versus 62.7% [294/469]; adjusted RR 0.76 [95% CI 0.640.89]). Primary neonatal and maternal safety outcomes did not differ between groups (neonatal composite 3.5% [36/744] vs 3.2% [15/469]; adjusted RR 0.77 [95% CI 0.31–1.89]; maternal composite 2.3% [17/744] versus 1.9% [8/469]).

Abbreviations: CEQ, Childbirth Experience Questionnaire; CI, confidence interval; GW, gestational week; IOL, induction of labor; OM, oral misoprostol; RCT, randomized controlled trial; RR, relative risk; SWEPIS, Swedish Postterm Induction Study; TVBC, transvaginal balloon catheter; VAS, visual analogue scale.

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INTRODUCTION

Induction of labor (IOL) is increasing and 14%–36% of deliveries in high-income countries were induced during 2013. IOL is considered when the risk of continuing the pregnancy, for the mother and/or the fetus, exceeds the risk of IOL. Indications for IOL are both maternal and fetal, including preeclampsia, diabetes, oligohydramnios, intrauterine growth restriction, premature rupture of membranes, and late term/postterm pregnancies from 41 gestational weeks (GW) and onwards. The latter constitutes one of the largest groups and is increasing because of a shift in management towards IOL at 41 GW instead of at 42 GW. This shift is based on evidence showing a reduction in perinatal mortality and morbidity without increasing maternal morbidity, including cesarean and operative vaginal delivery rates.

In Sweden, IOL in women with an unripe cervix is performed by either oral misoprostol (OM) or a transvaginal balloon catheter (TVBC). The latest Cochrane review on mechanical IOL methods reported, with moderate certainty of evidence, IOL with a TVBC compared with OM to be less effective with fewer vaginal deliveries achieved within 24 h (two trials, n = 782 women) and with a slightly higher rate of cesarean deliveries (seven trials, n = 3178 women). However, in other studies, IOL with a TVBC has been associated with fewer operative vaginal deliveries and a shorter time-to-delivery interval compared with oral/vaginal misoprostol. Concerning safety and women’s childbirth experience, it is still unclear which method is most advantageous.

In the wide range of studies on IOL methods, only a few have been carried out exclusively on pregnancies at 41–42 GW. We found only two randomized trials comparing IOL with OM and TVBC at this gestational time-point. Goonewardene et al compared two doses of 25 µg misoprostol (n = 74 women) administered 4 h apart with a 24-h treatment with a TVBC (n = 78 women). They concluded that IOL with a TVBC was more effective in pre-labor ripening of the cervix. Somirathne et al compared three doses of 50 µg misoprostol 4 h apart (n = 91 women) with a 24-h treatment with a TVBC (n = 89 women) and concluded that the misoprostol regimen was more effective.

Using data from the SWEdish Postterm Induction Study (SWEPIS), we aimed to evaluate if there were any differences regarding efficacy, safety, or women’s childbirth experience between IOL with OM and IOL with TVBC in uncomplicated singleton pregnancies with a fetus in cephalic presentation and an unripe cervix at 41+0 to 42+0 GW.

MATERIAL AND METHODS

This observational study was based on women included in SWEPIS, a register-based multicenter randomized controlled trial (RCT) at 15 hospitals in Sweden conducted from 2016 to 2018. The method and results from SWEPIS have been presented elsewhere. Briefly, the SWEPIS population consisted of 2760 women with a low-risk pregnancy randomly assigned to IOL at 41+0 to 2 GW or expectant management until 42+0 GW. Uncomplicated singleton pregnancies with a live fetus in cephalic presentation between 40+0 and 41+3 GW were the inclusion criteria. Women with a previous cesarean delivery or other major uterine surgery, hypertensive disorder of pregnancy,
insulin-dependent diabetes, ultrasonographic assessment indicating oligohydramnios, or a small-for-gestational-age fetus, diagnosed fetal malformation, or a contraindication to vaginal delivery were excluded. Assessment of the cervix was performed at admission to the delivery ward and IOL was performed according to local protocol. In general, if the Bishop score of the cervix was less than 6 for nulliparous and less than 5 for parous women, cervical ripening was initiated using oral or vaginal misoprostol, a TVBC or vaginal dinoprostone.

### 2.1 Study population

For this study, we included the women in SWEPIS who received OM or a TVBC as the primary method of IOL. Women who received dinoprostone or vaginal misoprostol were excluded, as were women who were induced with amniotomy or oxytocin as the primary method of IOL (Figure 1). Women with intrauterine fetal death before the start of IOL were also excluded.

### 2.2 Exposure

Exposure was IOL by either OM or a TVBC, including single and double balloons of various brands. The different treatment protocols for each participating center are presented in the Supporting Information Table S1. Misoprostol was mainly administered as 25 µg 2 h apart until start of labor with a maximum of eight doses per 24 h. A regimen with 50 µg 4 h apart was more rarely used. The TVBC regimen generally consisted of a single balloon with 50 mL sterile saline or water, and it remained in place until expelled or removed, at the longest until 24 h. The method that initiated IOL was considered the exposure. The need for additional ripening methods was noted. The ripening treatment usually continued 24 h a day for a maximum of 3 days without any pause and was followed by amniotomy (if membranes were still intact) when possible. Subsequently, oxytocin was administered if no contractions were present 1–2 h after amniotomy or if there was no progress in active labor, diagnosed by crossing the action line in the partograph.
2.3 | Outcome measures

Outcome measures were chosen according to the short-term core outcome set presented in Dos Santos et al. However, because a lack of information on hyperstimulation was present, this outcome could not be presented. In order to mirror only severe perinatal outcomes, we chose to define "admission to the neonatal unit" as an admission lasting 4 days or more, in accordance with advice from consultant neonatologists.

2.3.1 | Efficacy outcomes

The primary outcome regarding efficacy was vaginal delivery achieved within 24 h from the start of IOL. Secondary outcomes included vaginal delivery achieved within 36 and 48 h, time to delivery including and not including cesarean deliveries, duration of stay at the delivery hospital, non-operative vaginal delivery, cesarean delivery including indications for cesarean delivery, operative vaginal delivery, oxytocin use (both for IOL and/or labor augmentation), use of epidural anesthesia, and more than one cervical ripening agent required.

2.3.2 | Safety outcomes: maternal

The primary outcome regarding maternal safety was a composite of perinatal mortality or any serious maternal morbidity, including stillbirth after start of IOL, neonatal mortality defined as live births with death day 0–27 (not including deaths due to accidents or lethal malformation not known before randomization), Apgar score <4 at 5 min, metabolic acidosis defined as pH <7.05 and base excess <−12 mmol/L in the umbilical artery or pH <7.00 in the umbilical artery, hypoxic ischemic encephalopathy I–III, intracranial hemorrhage, neonatal convulsions, meconium aspiration syndrome, mechanical ventilation within the first 72 h, obstetrical brachial plexus injury, admission to neonatal unit for 4 or more days or severe neonatal infection (sepsis and/or pneumonia). Secondary outcomes were all components of the neonatal composite outcome presented separately, the composite outcome with Apgar <7 instead of Apgar <4 at 5 min, Apgar score <7 at 5 min, and any admission to neonatal unit.

2.3.3 | Safety outcomes: maternal

The primary outcome regarding maternal safety was a composite of mortality and serious morbidity, including maternal mortality (deaths due to accidents were excluded) up to 42 days after delivery, uterine rupture, hysterectomy for any complications resulting from birth, admission to intensive care unit, cardiorespiratory arrest, injury to internal organs, sepsis, maternal venous thromboembolism (deep vein thromboembolism or pulmonary embolism), stroke, and/or postpartum hemorrhage of more than 2000 mL. Secondary outcomes included all components of the maternal composite outcome presented separately, as well as postpartum hemorrhage of more than 1000 mL, perineal lacerations III–IV, intravenous antibiotics during labor (therapeutic), fever during labor (≥38°C), chorioamnionitis, endometritis, and hypertensive disorder of pregnancy.

2.3.4 | Women's childbirth experience

Women's childbirth experience was assessed using the Childbirth Experience Questionnaire (CEQ 2.0) and visual analog scale (VAS). The specifics of the CEQ 2.0 and VAS data collection within SWEPIS will be presented elsewhere (Nilvér et al., 2021, Women’s childbirth experience in the Swedish Postterm Induction Study [SWEPIS]: a multicenter, randomized, controlled trial, revision submitted December 2020). Briefly, the CEQ 2.0 was collected 3 months postpartum from a subpopulation consisting of 389 women with IOL delivered at Sahlgrenska University Hospital in Gothenburg, Örebro University Hospital, and Falu Hospital. The units were chosen to represent different geographical areas and various sizes of hospitals and towns. The questionnaire consists of four subscales of the childbirth experience: own capacity, perceived safety, professional support, and participation. Both the subscales and the total score are used for analysis. Each subscale score ranges from 0 to 4, the higher the score, the better the childbirth experience (0 = totally disagree, 2 = mostly disagree, 3 = mostly agree and 4 = totally agree). An effect size of 0.2–0.5 is regarded as small, 0.5–0.8 as moderate, and >0.8 as large. The remaining participating centers (824 women) evaluated women’s overall childbirth experience within 3 days postpartum on a VAS; a score from one (extremely bad experience) to 10 (extremely good experience). A score of eight or more was considered a very good childbirth experience and a score of two or less was considered a very poor experience.

2.4 | Data collection

Most data regarding efficacy were collected in an electronic case report form, for example time-point of IOL measures, Bishop score at first assessment, and IOL methods. Data regarding safety, delivery, and maternal childbirth experience (VAS) outcomes were obtained from the Swedish Pregnancy Register, the Swedish Neonatal Quality Register, and Statistics Sweden. In addition, CEQ 2.0 was distributed by e-mail and data were collected electronically.

2.5 | Statistical analyses

Data on maternal and neonatal outcomes are a subject for re-analysis in this subgroup (women in need of cervical ripening). However, the efficacy data regarding the two different cervical ripening methods have not been used or published before. For categorical outcomes we
**TABLE 1** Baseline characteristics in low-risk women undergoing induction of labor at 41 to 42 gestational weeks with oral misoprostol or a transvaginal balloon catheter

| Variable                        | Oral misoprostol (n = 744) | Transvaginal balloon catheter (n = 469) | p value |
|---------------------------------|-----------------------------|----------------------------------------|---------|
| **Age at randomization (years)** |                              |                                        |         |
| Mean (SD)                       | 31.0 (4.7)                  | 30.6 (4.7)                             | 0.17    |
| ≥35 years                       | 150/744 (20.2)              | 92/469 (19.6)                          | 0.83    |
| **Parity**                      |                              |                                        |         |
| Nulliparous                     | 495/744 (66.5)              | 313/469 (66.7)                         | 0.95    |
| Parous                          | 249/744 (33.5)              | 156/469 (33.3)                         |         |
| **Smoking at first antenatal visit** |                          |                                        |         |
| No                              | 696/715 (97.3)              | 396/410 (96.6)                         | 0.57    |
| Alcohol screening at first antenatal visit (points)\(^a\) |                          |                                        |         |
| 0–5 (low risk)                  | 613/667 (91.9)              | 353/383 (92.2)                         | 0.91    |
| ≥6 (risk behavior)              | 54/667 (8.1)                | 30/383 (7.8)                           |         |
| **Medical history**             |                              |                                        |         |
| Psychiatric disease             | 79/614 (12.9)               | 20/267 (7.5)                           | 0.02    |
| Pre-pregnancy diabetes          | 0/732 (0.0)                 | 1/465 (0.2)                            | 0.39    |
| Endocrine disease               | 49/730 (6.7)                | 34/465 (7.3)                           | 0.73    |
| Chronic hypertension            | 0/731 (0.0)                 | 1/465 (0.2)                            | 0.39    |
| **BMI at first antenatal visit (kg/m\(^2\))** |                          |                                        |         |
| Mean (SD)                       | 25.2 (5.1)                  | 25.2 (4.8)                             | 0.98    |
| ≥30                             | 91/710 (12.8)               | 64/416 (15.4)                          | 0.24    |
| **Height (cm) at first antenatal visit** |                          |                                        |         |
| Mean (SD)                       | 167.1 (6.3)                 | 167.8 (5.9)                            | 0.07    |
| **Last recorded weight during pregnancy (kg)** |                          |                                        |         |
| Mean (SD)                       | 83.7 (14.9)                 | 85.0 (14.2)                            | 0.15    |
| **Region of birth**             |                              |                                        |         |
| Sweden                          | 582/701 (83.0)              | 368/433 (85.0)                         | 0.85    |
| Other Nordic countries          | 42/701 (6.0)                | 22/433 (5.1)                           |         |
| Europe outside Nordic countries | 14/701 (2.0)                | 8/433 (1.8)                            |         |
| Outside Europe                  | 63/701 (9.0)                | 35/433 (8.1)                           |         |
| **Highest education**           |                              |                                        |         |
| 10–12 years (high school)       | 207/676 (30.6)              | 144/407 (35.4)                         | 0.49    |
| University or similar           | 440/676 (65.1)              | 251/407 (61.7)                         |         |
| **Employment status**           |                              |                                        |         |
| Employed, student, maternity leave and sick leave | 687/709 (96.9) | 422/432 (97.7) | 0.68    |
| Unemployed, other               | 22/709 (3.1)                | 10/432 (2.3)                           |         |

(Continues)

**TABLE 1** (Continued)

| Variable                        | Oral misoprostol (n = 744) | Transvaginal balloon catheter (n = 469) | p value |
|---------------------------------|-----------------------------|----------------------------------------|---------|
| **Living status**               |                              |                                        |         |
| Cohabitation with partner       | 688/737 (93.4)              | 392/462 (84.8)                         | <0.001  |
| **Mode of conception**          |                              |                                        |         |
| Assisted (IVF/ICSI)             | 41/744 (5.5)                | 24/469 (5.1)                           | 0.80    |
| **Indication for induction**    |                              |                                        |         |
| Randomization to 41 GW          | 522/744 (70.2)              | 334/469 (71.2)                         | 0.55    |
| Randomization to 42 GW          | 180/744 (24.2)              | 100/469 (21.3)                         |         |
| Maternal condition              | 12/744 (1.6)                | 12/469 (2.6)                           |         |
| Fetal condition                 | 6/744 (0.8)                 | 6/469 (1.3)                            |         |
| Maternal request\(^b\)         | 8/744 (1.1)                 | 8/469 (1.7)                            |         |
| Other                           | 16/744 (2.2)                | 9/469 (1.9)                            |         |
| **Gestational age (days) at start of IOL** |                          |                                        |         |
| n                               | 744                         | 469                                    |         |
| Mean (SD)                       | 289.5 (2.8)                 | 289.3 (2.7)                            | 0.16    |
| **Bishop score at first assessment** |                          |                                        |         |
| n                               | 713                         | 460                                    |         |
| Median (IQR)                    | 3 (2; 4)                    | 4 (3; 5)                               | <0.001  |
| 0–2                             | 286/713 (40.1)              | 83/460 (18.0)                          | <0.001  |
| 3–4                             | 273/713 (38.3)              | 241/460 (52.4)                         |         |
| ≥5                              | 154/713 (21.6)              | 136/460 (29.6)                         |         |
| Missing                         | 31 (4.2)                    | 9 (1.9)                                |         |

The data are presented as n (%), mean (standard deviation [SD]), or median (interquartile range [IQR] or minimum or maximum). Women receiving a transvaginal balloon catheter were used as reference. Abbreviations: BMI, body mass index; GW, gestational weeks; ICSI, intracytoplasmic sperm injection; IOL, induction of labor; IQR, interquartile range; IVF, in vitro fertilization; SD, standard deviation. \(^a\)Alcohol screening by AUDIT (alcohol use disorders identification test) tool according to antenatal care routines. \(^b\)Maternal request outside study protocol (for example women in the early induction group were induced on request later than 41 weeks and women in expectant management group were induced on request before 42 weeks).

calculated crude and adjusted relative risks (RR) and risk differences with 95% confidence intervals (CI). For continuous variables we calculated adjusted mean with standard error of the mean and adjusted mean differences with 95% CI between the groups. Values of p and adjusted values of p were calculated. Women receiving a TVBC were the reference group. Regression adjustment was performed for a propensity score based on center (n = 15, Supporting Information Table S1) and all baseline characteristics presented in Table 1 except for medical history of pre-gestational diabetes, medical history of chronic hypertension, height, and last recorded weight during pregnancy. In case of a missing Bishop score at the first assessment these values were imputed with stochastic regression imputation using a fully conditional specification method based on Bishop scores and their components at the four first assessments, age, parity, and body mass index. In case
of missing body mass index at the first antenatal visit these values were imputed with stochastic regression imputation using a fully conditional specification method based on maternal age, height and weight at first antenatal visit, parity, and body mass index. Fisher’s exact test was used for dichotomous variables, Pearson’s chi-squared test was used for non-ordered categorical variables, Mantel-Haenszel chi-squared test was used for ordered categorical variables, and Fisher’s non-parametric permutation test was used for continuous variables. The 95% CI for the mean difference between groups was based on Fisher’s non-parametric permutation test. The adjusted RR was calculated using generalized linear models using the link log function. For CEQ 2.0 the Cohen effect size was calculated.

Kaplan-Meier analyses and log rank tests on time to vaginal delivery, where cesarean deliveries were censored, and time to delivery (all types) for the OM and TVBC groups, were performed (p < 0.05 was regarded as significant). In addition, we also present these Kaplan-Meier analyses stratified by Bishop score (0–4 vs 5–10) and parity (nulliparous vs parous) and stratified by Bishop score (0–2, 3–4, 5–10).

An interaction analysis was performed to assess if the effect of IOL method on the primary efficacy outcome and the primary neonatal and maternal safety composite outcome differed according to pre-specified subgroups of Bishop score (0–4 and 5–10) and parity (nulliparous and parous). An interaction p < 0.05 was considered to indicate that the effect of intervention differed between subgroups. In addition, a post-hoc analysis on women using only one cervical ripening agent (OM or TVBC) was performed.

All significance tests were two-sided at the 0.05 level. Statistical analyses were performed using SAS 9.4 (SAS Institute, Cary, NC, USA).

2.6 | Ethical approval

This study was approved by the regional ethics board in Gothenburg in May 2014 (Dnr: 285–14) with amendments (T 905–15, T 291–16, T 1180–16, T 330–17, T 1066–17, T 087–18, T 347–18, T 961–18, T 1110–18). All participants gave written informed consent before taking part in the study.

3 | RESULTS

In total, 1638 women underwent IOL in the SWEPIS, of whom 1244 needed cervical ripening. In our study, we included 744 women in whom IOL was initiated with OM and 469 women in whom IOL was initiated with a TVBC (Figure 1). The groups were similar regarding most of the characteristics including maternal age, parity, body mass index, and indication for IOL (Table 1). Women with a higher Bishop score more frequently received a TVBC, whereas women with a low Bishop score were more frequently induced with OM (Table 1). Distribution by center and treatment, and total number of deliveries per center, as well as routines for IOL at the centers, are presented in the Supporting Information Table S1.

3.1 | Primary and secondary efficacy outcomes

The primary efficacy outcome “vaginal delivery within 24 h” was significantly lower in the OM group compared with the TVBC group (Table 2). Vaginal delivery within 36 h was also significantly lower in the OM group (Table 2). Time-to-delivery and time-to-vaginal delivery were both significantly longer in the OM group compared with the TVBC group (Table 3). The differences in time-to-delivery and time-to-vaginal delivery are illustrated in Figure 2A,B. The difference between the groups was significant for nulliparous and parous women with Bishop score 0–4 but not with Bishop score 5–10. The use of oxytocin (both for IOL and for labor augmentation) was significantly lower in the OM group compared with the TVBC group. There was no significant difference between the groups regarding non-operative vaginal delivery, cesarean delivery, operative vaginal delivery, or using more than one cervical ripening agent (Table 2). Indications for cesarean delivery were similar in both groups (Table 2).

3.2 | Primary and secondary safety outcomes: Neonatal

The primary neonatal safety composite outcome did not differ significantly between the groups (Table 4). The secondary outcome, metabolic acidosis, was significantly higher in the OM group. None of the other secondary neonatal outcomes differed significantly between the groups.

3.3 | Primary and secondary safety outcomes: Maternal

There was no significant difference in the primary maternal safety composite outcome between the groups (Table 4). Fever during labor and therapeutic intravenous treatment with antibiotics during labor were significantly less frequently observed in the OM group compared with the TVBC group, but rates of sepsis or endometritis did not differ between the groups (Table 4).

3.4 | Women’s experiences

The response rate was high overall for both the CEQ 2.0 (72.0%) and VAS (78.3%) (Table 5). The total score of the CEQ 2.0 did not differ between the groups, neither did the score in three out of four domains (Table 5). The subscale “own capacity” had a significantly lower score, but with a low effect size, in the OM group compared with the TVBC group. The childbirth experience measured with VAS did not differ between the groups, nor did the rate of women estimating the childbirth
experience as very good (VAS 8–10) (RR 0.98, 95% CI 0.86–1.12 and adjusted RR 0.96, 95% CI 0.96–1.14) or as very bad (VAS 1–2) (RR 1.00, 95% CI 0.33–3.03 and adjusted RR 1.14, 95% CI 0.28–4.56).

### 3.5 Subgroup analysis

The subgroup analysis for interaction is presented in the Supporting Information Figure S2A–C. The analysis on the primary efficacy outcome showed a treatment effect according to Bishop score and according to parity (p-value for interaction 0.003 and <0.001, respectively) (Figure S2A). The chance of vaginal delivery within 24 h in the OM group compared with the TVBC group was significantly lower in women with a Bishop score 0–4, but not for women with Bishop score 5–10. The chance of vaginal delivery within 24 h in the OM group was significantly lower compared with the TVBC group in both nulliparous and parous women, but with a larger effect in nulliparous women. There was no treatment effect according to Bishop
We report, in a late term and postterm low-risk population, a significantly lower rate of vaginal delivery within 24 and 36 h in the OM group compared with the TVBC group, especially in women with a low Bishop score. Further, we found a 3.8-h increase in time to vaginal delivery for IOL with OM. We chose this primary efficacy outcome because it reflects both mode of delivery and the time aspect and the results are easy to compare with results from the Cochrane review. We also show, as did Wollmann et al, that IOL with a TVBC was more effective in the group with women with Bishop score 0–2. Goonewardene et al, an RCT, showed a preference, in low-risk late term women with a singleton pregnancy, for TVBC treatment to ripen the cervix. This is in agreement with two RCTs, Prager et al (full-term pregnancies, n = 397) and Gelisen et al (low-risk late term singleton pregnancies, n = 600). We also report a shorter time-to-delivery with a TVBC regimen compared with vaginal misoprostol (4.4 and 1.4 h, respectively). In contrast, the latest Cochrane review from 2019 comparing TVBC with OM concludes that using a TVBC probably slightly decreases the chance of a vaginal delivery within 24 h. The conclusion was based on two contributing RCTs: Mundle et al from India and Somirathne et al. from Sri Lanka. The Mundle trial (n = 602) investigated IOL in women with hypertensive disorder of pregnancy and included women at 28 GW onwards. Somirathne et al. (n = 180) trial explored IOL in low-risk pregnancies at 41 GW. The PROBAAT-II trial, the largest RCT (1845 women with a term singleton pregnancy) included in the Cochrane review, showed an increase in deliveries, including cesarean deliveries, within 24 h in the OM group, but at 36 h a larger proportion were delivered in the TVBC group. Furthermore, we found a decreased use of oxytocin for IOL and augmentation in the OM group. This may be the result of caregivers’ fear of hyperstimulation when using prostaglandins as an IOL agent or more women going into active labor without the need for oxytocin when induced with misoprostol. Another explanation might be that misoprostol stimulates contractility with a long-lasting effect at tissue level and therefore entails less need to stimulate contractions. Several hospitals in our study also had a policy of waiting at least 4 h after the last misoprostol dose before administering oxytocin.

Regarding safety outcomes, we found a substantial difference in metabolic acidosis in favor of TVBC, but there was a considerable amount of missing data, which makes the result uncertain. The PROBAAT-II RCT could not show any difference between groups regarding metabolic acidosis or any other adverse neonatal outcome, nor could Mundle et al. We also report a lower frequency of fever and use of therapeutic antibiotics during labor in the OM group. This

TABLE 3 Time-to-delivery (cesarean deliveries included and excluded) and total duration of hospital stay in low-risk women undergoing induction of labor at 41 to 42 gestational weeks with oral misoprostol or a transvaginal balloon catheter

| Variable | Oral misoprostol (n = 744) | Transvaginal balloon catheter (reference) (n = 469) | Adjusted mean difference between groupsa (95% CI) |
|----------|---------------------------|-----------------------------------------------|-----------------------------------------------|
|          | Mean (SD) | Median (IQR) | Adjusted meansa (SEM [95% CI]) | Mean (SD) | Median (IQR) | Adjusted meansa (SEM [95% CI]) | p value | Adjusted p valuea | p value |
| Time to delivery (hours)b | 25.9 (15.5) | 23.7 (14.3;33) | 25.8 (0.6 [24.5–27.0]) | 21.3 (13.3) | 17.7 (12.1; 27.7) | 21.5 (0.9 [19.9–23.2]) | <0.001 | <0.001 | 4.3 (1.84; 6.7) |
| Time to vaginal delivery (hours)b | 24.3 (14.6) | 22.0 (13.7; 31.8) | 24.1 (0.7 [22.8–25.3]) | 19.9 (12.8) | 16.4 (11.6; 25.6) | 20.3 (0.9 [18.6–22.0]) | <0.001 | 0.002 | 3.8 (1.3; 6.2) |
| Total duration of hospital stay (days) | 3.18 (1.40) | 3.01 (2.04; 4.01) | 3.17 (0.06 [3.05–3.29]) | 2.95 (1.40) | 2.94 (1.92; 3.86) | 2.96 (0.08 [2.80–3.13]) | 0.008 | 0.09 | 0.21 (−0.03; 0.44) |

Values are in numbers (percentages) unless stated otherwise.
Abbreviations: CI, confidence interval; IQR, interquartile range; SD, standard deviation; SEM, standard error of the mean.

aAdjusted for propensity score based on center (n = 15, Table S1) and all baseline characteristics presented in Table 1 except for medical history of pre-gestational diabetes, medical history of chronic hypertension, height, and last recorded weight during pregnancy.

bFrom start of induction to delivery.
FIGURE 2  Kaplan-Meier plots of time to vaginal delivery and time to delivery. (A) Time to vaginal delivery. (B) Time to delivery [Color figure can be viewed at wileyonlinelibrary.com]
FIGURE 3  Kaplan-Meier plots of time to delivery stratified by Bishop score and parity. (A) Women with Bishop score 0–4. (B) Women with Bishop score 5–10 [Color figure can be viewed at wileyonlinelibrary.com]
TABLE 4  Primary and secondary neonatal and maternal outcomes in low-risk women undergoing induction of labor at 41 to 42 gestational weeks with oral misoprostol or a transvaginal balloon catheter

| Variable                                                                 | Oral misoprostol (n = 744) | Transvaginal balloon catheter (reference) (n = 469) | p value | Relative risk (95% CI) | Adjusted p value | Adjusted relative risk (95% CI) | Risk difference between groups (95% CI) |
|--------------------------------------------------------------------------|----------------------------|-----------------------------------------------------|---------|------------------------|-----------------|------------------------------|----------------------------------------|
| **Neonatal primary composite outcome**<sup>b</sup>                       | 26 (3.5)                  | 15 (3.2)                                            | 0.87    | 1.09 (0.58; 2.04)      | 0.57            | 0.77 (0.31; 1.89)              | 0.3 (-1.9; 2.5)                       |
| **Secondary neonatal outcomes**                                          |                            |                                                     |         |                        |                 |                              |                                        |
| Subcomponents of the primary outcome                                     |                            |                                                     |         |                        |                 |                              |                                        |
| Stillbirth after start of IOL                                            | 0                          | 0                                                   | 1.00    | NA                     | NA              | NA                           | NA                                     |
| Neonatal mortality<sup>c</sup>                                           | 0                          | 0                                                   | 1.00    | NA                     | NA              | NA                           | NA                                     |
| Apgar score <4 at 5 min                                                  | 1 (0.1)                   | 1 (0.2)                                             | 1.00    | 0.63 (0.04; 10.05)     | NA              | NA                           | -0.1 (-0.7; 0.6)                      |
| Metabolic acidosis<sup>d</sup>                                           | 10/334 (3.0)              | 0                                                   | 0.006   | NA                     | NA              | NA                           | 3.0 (0.8; 5.2)                        |
| HIE I–III                                                               | 1 (0.1)                   | 0                                                   | 1.00    | NA                     | NA              | NA                           | 0.1 (-0.3; 0.6)                       |
| Intracranial hemorrhage                                                 | 0                          | 0                                                   | 1.00    | NA                     | NA              | NA                           | NA                                     |
| Neonatal convulsions                                                    | 0                          | 0                                                   | 1.00    | NA                     | NA              | NA                           | NA                                     |
| Meconium aspiration syndrome                                            | 1 (0.1)                   | 0                                                   | 1.00    | NA                     | NA              | NA                           | 0.1 (-0.3; 0.6)                       |
| Mechanical ventilation within first 72 h                                 | 2 (0.3)                   | 0                                                   | 0.53    | NA                     | NA              | NA                           | 0.3 (-0.3; 0.8)                       |
| Obstetrical brachial plexus injury                                      | 1 (0.1)                   | 3 (0.6)                                             | 0.30    | 0.21 (0.02; 2.01)      | NA              | NA                           | -0.5 (-1.4; 0.4)                      |
| Admission to neonatal unit for ≥4 days                                   | 14 (1.9)                  | 13 (2.8)                                            | 0.32    | 0.68 (0.32; 1.43)      | 0.08            | 0.38 (0.13; 1.12)             | -0.9 (-2.8; 1.1)                      |
| Severe neonatal infection<sup>e</sup>                                    | 6 (0.8)                   | 9 (1.9)                                             | 0.11    | 0.42 (0.15; 1.17)      | NA              | NA                           | -1.1 (-2.7; 0.5)                      |
| Neonatal composite outcome with Apgar <7 instead of <4                  | 31 (4.2)                  | 19 (4.1)                                            | 1.00    | 1.03 (0.59; 1.80)      | 0.48            | 0.75 (0.34; 1.68)             | 0.1 (-2.3; 2.6)                       |
| Apgar score <7 at 5 min                                                  | 10 (1.3)                  | 6 (1.3)                                             | 1.00    | 1.05 (0.38; 2.87)      | 0.73            | NA                           | 0.1 (-1.4; 1.5)                       |
| Admission to neonatal unit                                              | 37 (5.0)                  | 26 (5.5)                                            | 0.69    | 0.90 (0.55; 1.46)      | 0.33            | 0.71 (0.35; 1.43)             | -0.6 (-3.3; 2.2)                      |
| Maternal primary composite outcome<sup>f</sup>                           | 17 (2.3)                  | 9 (1.9)                                             | 0.84    | 1.19 (0.54; 2.65)      | 0.33            | 1.70 (0.58; 4.97)             | 0.4 (-1.4; 2.2)                       |
| **Secondary maternal outcomes**                                         |                            |                                                     |         |                        |                 |                              |                                        |
| Subcomponents of primary outcome                                         |                            |                                                     |         |                        |                 |                              |                                        |
| Maternal mortality within 42 days after delivery                         | 0                          | 0                                                   | 1.00    | NA                     | NA              | NA                           | NA                                     |
| Uterine rupture                                                          | 0                          | 0                                                   | 1.00    | NA                     | NA              | NA                           | NA                                     |
| Non-elective hysterectomy                                                | 0                          | 0                                                   | 1.00    | NA                     | NA              | NA                           | NA                                     |
| Admission to ICU                                                         | 2 (0.3)                   | 0                                                   | 0.53    | NA                     | NA              | NA                           | 0.3 (-0.3; 0.8)                       |
| Cardiorespiratory arrest                                                 | 0                          | 0                                                   | 1.00    | NA                     | NA              | NA                           | NA                                     |

(Continues)
| Variable                                      | Oral misoprostol (n = 744) | Transvaginal balloon catheter (reference) (n = 469) | \( p \) value | Relative risk (95% CI) | Adjusted \( p \) value\(^a\) | Adjusted relative risk (95% CI) | Risk difference between groups (95% CI) |
|-----------------------------------------------|-----------------------------|-----------------------------------------------------|----------------|------------------------|-------------------------------|-------------------------------------|--------------------------------------|
| Injury to internal organs (includes bowel, bladder or ureter) | 0                           | 0                                                   | 1.00           | NA                     | NA                            | NA                                  | NA                                   |
| Sepsis                                        | 0                           | 0                                                   | 1.00           | NA                     | NA                            | NA                                  | NA                                   |
| Venous thromboembolism                        | 0                           | 0                                                   | 1.00           | NA                     | NA                            | NA                                  | NA                                   |
| Stroke                                        | 0                           | 0                                                   | 1.00           | NA                     | NA                            | NA                                  | NA                                   |
| Postpartum hemorrhage \( >2000 \) mL          | 16 (2.2)                    | 9 (1.9)                                             | 0.84           | 1.12 (0.50; 2.52)      | 0.33                          | 1.72 (0.58; 5.05)                   | 0.2 (−1.6; 2.0)                      |
| Postpartum hemorrhage \( >1000 \) mL          | 74 (9.9)                    | 43 (9.2)                                            | 0.69           | 1.08 (0.76; 1.55)      | 0.48                          | 1.19 (0.73; 1.96)                   | 0.8 (−2.8; 4.3)                      |
| Perineal lacerations III-IV                   | 24 (3.2)                    | 11 (2.3)                                            | 0.48           | 1.38 (0.68; 2.78)      | 0.59                          | 1.31 (0.49; 3.47)                   | 0.9 (−1.2; 2.9)                      |
| Antibiotics during labor, therapeutic use only\(^g\) | 50 (6.7)                    | 57 (12.2)                                           | 0.002          | 0.55 (0.39; 0.79)      | 0.41                          | 0.81 (0.49; 1.34)                   | −5.4 (−9.1; 1.8)                     |
| Fever during labor \( ≥38.0°C \)             | 71 (9.5)                    | 73 (15.6)                                           | 0.002          | 0.61 (0.45; 0.83)      | 0.27                          | 0.79 (0.51; 1.20)                   | −6.0 (−10.1; 1.9)                    |
| Chorioamnionitis                              | 2 (0.3)                     | 2 (0.4)                                             | 0.64           | 0.63 (0.09; 4.46)      | NA                            | NA                                  | −0.2 (−1.0; 0.7)                     |
| Endometritis                                  | 8 (1.1)                     | 9 (1.9)                                             | 0.32           | 0.56 (0.22; 1.44)      | 0.59                          | 0.69 (0.18; 2.63)                   | −0.8 (−2.5; 0.8)                     |
| Hypertensive disorder of pregnancy            | 21 (2.8)                    | 11 (2.3)                                            | 0.71           | 1.20 (0.59; 2.47)      | 0.97                          | 1.02 (0.37; 2.79)                   | 0.5 (−1.5; 2.5)                      |

Values are in numbers (percentages).

Abbreviations: CI, confidence interval; HIE, hypoxic ischemic encephalopathy; ICU, intensive care unit; IOL, induction of labor; NA, not applicable; NICU, neonatal intensive care unit.

\(^a\) Adjusted for propensity score based on center (\( n = 15, \) Table S1) and all baseline characteristics presented in Table 1 except for medical history of pre-gestational diabetes, medical history of chronic hypertension, height, and last recorded weight during pregnancy.

\(^b\) Includes: stillbirth after start of induction, neonatal mortality defined as live births with death day 0–27 (deaths due to accidents or lethal malformation not known before randomization will be excluded), Apgar score <4 at 5 min, metabolic acidosis defined as pH <7.05 and base excess >12 mmol/L in umbilical artery or pH <7.00 in umbilical artery, hypoxic ischemic encephalopathy I–III, intracranial hemorrhage, neonatal convulsions, meconium aspiration syndrome, mechanical ventilation within first 72 h, obstetrical brachial plexus injury, admission to neonatal care >4 days and/or neonatal sepsis and/or pneumonia.

\(^c\) Live births with death day 0–27.

\(^d\) Denominator based on validated umbilical cord blood samples at birth. Validated samples defined as arterial pH less than venous pH and arterial partial pressure of carbon dioxide (pCO\(_2\)) greater than venous pCO\(_2\).

\(^e\) Defined as sepsis and/or pneumonia.

\(^f\) Includes: maternal death (deaths due to accidents are excluded) up to 42 days after delivery, uterine rupture, hysterectomy for any complications resulting from birth, admission to intensive care unit, cardiorespiratory arrest, damage to internal organs, sepsis, venous thromboembolism (deep venous thrombosis or pulmonary embolism), stroke, and/or postpartum hemorrhage (>2000 mL).

\(^g\) Including antibiotics given only on indication suspected infection.
finding contrasts with the findings of PROBAAT-II (no difference) and a cohort study by Aghideh et al (fewer cases in the TVBC group compared with vaginal misoprostol). However, we found no difference in the prevalence of endometritis postpartum between the groups, which is in line with PROBAAT-II and Kruit et al (an RCT on women at term with premature rupture of membranes comparing IOL with TVBC with OM). The reason for increased fever and use of antibiotics is not clear. An expected finding would be more fever in the misoprostol group, as hyperthermia is a known adverse effect of misoprostol. Possibly an indwelling catheter may cause an inflammatory reaction with fever caused by infection (or interpreted as infection). For other safety outcomes, no differences were found.

Childbirth experience has been reported, in qualitative and cohort studies, to be negatively affected by IOL when compared with spontaneous onset of labor. However, Heimstad et al, the only RCT comparing IOL at 41 GW with expectant management, reported that most women in both groups would prefer to be induced at 41 GW in a future late term pregnancy. Furthermore, women’s childbirth experience in SWEPIS did not differ between the IOL and the expectant management groups and were overall good (Nilvér et al, 2021, Women’s childbirth experience in the Swedish Postterm Induction Study [SWEPIS]: a multicenter, randomized, controlled trial, revision submitted December 2020). Also, women faced with the possibility of IOL in post-term pregnancy may prefer IOL because of worries about their unborn baby’s health, want unbiased information about their options and potential outcomes, and want time to reflect on their preferences. Within RCTs, information is in general more detailed than in clinical practice. Hence, this might be one explanation for why women in RCTs report more positively about IOL, than in qualitative and cohort studies. In our study, the response rate was high and we report an overall positive childbirth experience in both treatment groups. The RCT by Mundle et al reported more women being satisfied with their IOL in the OM group, compared with the transvaginal balloon group. The comparison between our study and that of Mundle et al is, however, difficult because of the different indication for IOL, the different gestational lengths included, and a different cultural context. Furthermore, it is plausible that a TVBC could give more discomfort, but our study could not confirm this hypothesis.

Taking into account that the two IOL methods did not differ regarding cesarean delivery rate and women’s childbirth experience, and are probably comparable regarding safety, other aspects of the IOL methods are important to discuss. For example, applying a TVBC

| Variable | Oral misoprostol (n = 744) | Transvaginal balloon catheter (reference) (n = 469) | Effect size | p value | Mean (95% CI) difference between groups |
|----------|----------------------------|-----------------------------------------------|-------------|---------|----------------------------------------|
| CEQ 2.0, n (%) | 76/101 (75.2) | 212/299 (71.0) | | | |
| Total score Mean (SD) | 3.20 (0.49) | 3.27 (0.53) | 0.13 | 0.33 | −0.07 (−0.20; 0.07) |
| Median (IQR) | 3.24 (2.88; 3.59) | 3.42 (2.9; 3.68) | | | |
| Own capacity Mean (SD) | 2.60 (0.64) | 2.76 (0.58) | 0.27 | 0.047 | −0.16 (−0.32; −0.003) |
| Median (IQR) | 2.63 (2.13; 3.13) | 2.88 (2.38; 3.13) | | | |
| Perceived safety Mean (SD) | 3.15 (0.72) | 3.28 (0.69) | 0.19 | 0.16 | −0.13 (−0.31; 0.05) |
| Median (IQR) | 3.33 (2.67; 3.75) | 3.50 (2.83; 3.83) | | | |
| Professional support Mean (SD) | 3.58 (0.51) | 3.52 (0.59) | 0.11 | 0.42 | 0.06 (−0.08; 0.22) |
| Median (IQR) | 3.8 (3.4; 4) | 3.80 (3.2; 4) | | | |
| Participation Mean (SD) | 3.48 (0.60) | 3.52 (0.63) | 0.06 | 0.67 | −0.04 (−0.20; 0.13) |
| Median (IQR) | 3.67 (3; 4) | 3.67 (3.17; 4) | | | |
| VAS n (%) | 493/652 (75.6) | 152/172 (88.4) | | | |
| Mean (SD) | 7.83 (2.15) | 7.94 (1.89) | 0.06 | 0.55 | −0.12 (−0.50; 0.26) |
| Median (IQR) | 8 (7; 10) | 8 (7; 9) | | | |
| VAS ≥8, n (%) | 321 (65.1) | 101 (66.4) | 0.85 | | −1.3 (−10.4; 7.7) |
| VAS ≤2, n (%) | 13 (2.6) | 4 (2.6) | 1.00 | | 0.0 (−3.3; 3.3) |

Abbreviations: CEQ, childbirth experience questionnaire; CI, confidence interval; IQR, interquartile range; SD, standard deviation; VAS, visual analogue scale.

Denominator includes women randomized at Sahlgrenska University hospital (total n = 326; 317 delivered at Sahlgrenska University Hospital, 6 delivered at SÄS and 5 delivered at Varbergs Hospital), Falu Hospital (n = 51) and Örebro University Hospital (n = 21).
requires a greater effort by the obstetricians than prescribing OM. Moreover, depending on local routines, the duration and/or frequency of fetal surveillance with cardiotocography may be different between OM and TVBC regimens, which may affect the workload for midwives. Lastly, economical aspects of the different methods will also be an aspect to consider when deciding on which method to use.

This is one of few studies performed on IOL with OM compared with TVBC in women with postdate low-risk pregnancies. One of its strengths is that we report on women's childbirth experience. An additional advantage is that we report on all but one core outcome according to the consensus document by Dos Santos et al. We also collected information prospectively specifically in order to answer our research question.

A limitation of the study is that it is not an RCT and, as in all observational studies, there is a risk of residual confounding even though we adjusted for all available covariates. We do not report on hyperstimulation, but results on important outcomes such as cesarean delivery because of fetal distress and severe neonatal morbidity are presented. Another limitation is that the compared methods of IOL were used at different rates and in somewhat different ways in the participating centers. In SWEPIS, no standard protocol for OM or TVBC was used. However, we used a propensity score in our regression model to adjust for the center effect. Furthermore, the lack of blinding of IOL methods might affect the management of the IOL and therefore introduce a treatment bias. Furthermore, the use of two different methods of measuring women's experience could be perceived both as a strength and limitation due to data collection occurring at different time-points. The CEQ 2.0 is a multidimensional measurement of childbirth experience compared with VAS that is a non-specific and simplified measure of childbirth experience. Moreover, VAS is part of clinical practice in Sweden and is measured/evaluated within 3 days after giving birth. The CEQ 2.0 was distributed 3 months after childbirth. The VAS and CEQ 2.0 might not be comparable because childbirth experience may shift over time as the new family adjusts to its new situation. However, both methods are validated and correlate with women's overall childbirth experience.30,35,36 Lastly, our study was not powered for assessing neonatal and maternal safety outcomes. Our study could contribute to a meta-analysis of safety outcomes in observational studies in the advent of a sufficiently powered RCT.

### 5 | CONCLUSION

We found that IOL in low-risk late term and postterm women using OM was associated with a lower probability of vaginal delivery within 24 and 36 h and a slightly longer time to delivery and time to vaginal delivery. However, the rate of non-operative vaginal delivery did not differ between the groups and women's childbirth experience was overall positive and similar in both groups. The study was underpowered to exclude difference in maternal or neonatal safety. Both methods can be recommended in women with low-risk postdate pregnancies. Hence, women's and their caregivers' preference and health economical aspects should determine the method of choice.

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### CONFLICTS OF INTEREST

None.

### AUTHOR CONTRIBUTIONS

UBW, HH, HE, and VS conceived and designed the SWEPIS study and MA, UBW, and HH conceived and designed the current study. UBW, HH, AW, SS, AKW, MJ, and HF oversaw recruitment of study participants and collection of data at the local centers. MA, UBW, YC, and HH wrote the statistical analysis plan together with a statistician (Mattias Molin, the Statistical Consulting Group, Gothenburg). UBW and MA did the data cleaning together with statistician Mattias Molin. MA, UBW, HH, YC, SS, LL, VS, SBW, and HE interpreted the data. MA and UBW wrote the first draft of the manuscript, which was then critically reviewed and revised by the other co-authors.

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### REFERENCES

1. Seijmonsbergen-Schermers AE, van den Akker T, Rydahl E, et al. Variations in use of childbirth interventions in 13 high-income countries: a multinational cross-sectional study. PLoS Medicine. 2020;17:e1003103.
2. WHO. WHO Recommendations: Induction of Labour at or Beyond Term. Geneva: World Health Organisation; 2018.
3. NICE. Induction of labour: new NICE quality standard. Midwives. 2014;17:8.
4. Alkmark M, Berglin L, Dencker A, et al. Igångsättning av förlossning vid 41 eller 42 fullgångna graviditetsveckor. [Induction of labour at 41 or 42 weeks of gestation]. In Swedish. Göteborg: Västra
7. Wennerholm U-B, Saltvedt S, Wessberg A, et al. Induction of labour at 41 weeks versus expectant management until 42 weeks (SWEdish Post-term Induction Study, SWEPIS): multicentre, randomised, non-inferiority trial. BMJ. 2019;364:i344.

5. Keulen JKJ, Bruinsma A, Kortekaas JC, et al. Induction of labour at 41 weeks or expectant management until 42 weeks: a systematic review and an individual participant data meta-analysis of randomised trials. PLoS Med. 2020;17:e1003436.

10. de Vaan MDT, ten Eikelder MLG, Jozwiak M, et al. Mechanical methods for induction of labour. Cochrane Database Syst Rev. 2019;10:CD001233.

11. ten Eikelder MLG, Oude Rengerink K, Jozwiak M, et al. Induction of labour at term with oral misoprostol versus a Foley catheter (PROBAAT-II): a multicentre randomised controlled non-inferiority trial. Lancet. 2016;387:1619-1628.

12. Wollmann CL, Ahlberg M, Petersson G, Saltvedt S, Stephansson O. Time-to-delivery and delivery outcomes comparing three methods of labor induction in 7551 nulliparous women: a population-based cohort study. J Perinatal. 2017;37:1197-1203.

13. Prager M, Eneroth-Grimfors E, Edlund M, Marions L. A randomised controlled trial of intravaginal dinoprostone, intravaginal misoprostol and transcervical balloon catheter for labour induction. BJOG. 2008;115:1443-1450.

14. Goonewardene M, Kumara D, Ziard M, Bhabu B. Intra Cervical Foley Catheter vs oral misoprostol for pre induction cervical ripening of postdated pregnancies. Sri Lanka J Obstetr Gynaecol. 2014;36.

15. Somirathne D, Goonewardene M, Dasanayake L. Randomised controlled trial of intravaginal dinoprostone, intravaginal misoprostol and transcervical balloon catheter for labour induction. BJOG. 2008;115:1443-1450.

16. Elden H, Hagberg H, Wessberg A, et al. Study protocol of SWEPIS a Swedish multicentre register based randomised controlled trial to compare induction of labour at 41 completed gestational weeks versus expectant management and induction at 42 completed gestational weeks. BMC Pregnancy Childbirth. 2016;16:49.

17. Dos Santos F, Drymotou S, Antequera Martin A, et al. Development of a core outcome set for trials on induction of labour: an international multistakeholder Delphi study. BJOG. 2018;125:1673-1680.

18. The Swedish Pregnancy Register yearly report 2018 2019. https://www.medscinet.com/GR/english.aspx.

22. Stephansson O, Petersson K, Björk C, Conner P, Wikström AK. The Swedish Pregnancy Register – for quality of care improvement and research. Acta Obstet Gynecol Scand. 2018;97:466-476.

23. Norman M, Källén K, Wahlström E, et al. The Swedish Neonatal Quality Register – contents, completeness and validity. Acta Paediat. 2019;108:1411-1418.

24. Statistics Sweden. https://www.scb.se/en/

25. Rubin DB. Multiple Imputation for Nonresponse in Survey. New York: John Wiley & Sons; 1987;166-167.

26. Gelisen O, Caliskan E, Dilbaz S, et al. Induction of labor with three different techniques at 41 weeks of gestation or spontaneous follow-up until 42 weeks in women with definitely unfavorable cervical scores. Eur J Obstet Gynecol Reprod Biol. 2005;120:164-169.

27. Mundle S, Bracken H, Khedikar V, et al. Foley catheterisation versus oral misoprostol for induction of labour in hypertensive women in India (INFORM): a multicentre, open-label, randomised controlled trial. Lancet. 2017;390:669-680.

28. Aghideh FK, Mullin PM, Ingles S, et al. A comparison of obstetrical outcomes with labor induction agents used at term. J Matern Fetal Neonatal Med. 2014;27:592-596.

29. Kruit H, Tihtonen K, Raudaskoski T, et al. Foley catheter or oral misoprostol for induction of labor in women with term premature rupture of membranes: a randomized multicenter trial. Am J Perinatol. 2016;33:866-872.

30. Falk M, Nelson M, Blomberg M. The impact of obstetric interventions and complications on women's satisfaction with childbirth a population based cohort study including 16,000 women. BMC Pregnancy Childbirth. 2019;19:494.

31. Hildingson I, Karlström A, Nystedt A. Women's experiences of induction of labour–findings from a Swedish regional study. Aust N Z J Obstet Gynaecol. 2011;51:151-157.

32. Lou S, Hvidman L, Uldbjerg N, et al. Women's experiences of post-term induction of labor: a systematic review of qualitative studies. Birth. 2019;46:400-410.

33. Heimstad R, Romundstad PR, Hyett J, Mattsson LA, Salvesen KA. Women's experiences and attitudes towards expectant management and induction of labor for post-term pregnancy. Acta Obstet Gynecol Scand. 2007;86:950-956.

34. Wessberg A, Lundgren I, Elden H. Being in limbo: Women's lived experiences of pregnancy at 41 weeks of gestation and beyond - a phenomenological study. BMC Pregnancy Childbirth. 2017;17:162.

35. Turkmén S, Tjernström M, Dahmoun M, Bolin M. Post-partum duration of satisfaction with childbirth. J Obstet Gynaecol Res. 2018;44:2166-2173.

36. Larsson C, Saltvedt S, Edman G, Wiklund I, Andolf E. Factors independently related to a negative birth experience in first-time mothers. Sex Reprod Healthc. 2011;2:83-89.

37. Göransson M, Magnusson A, Heilig M. Identifying hazardous alcohol consumption during pregnancy: implementing a research-based model in real life. Acta Obstet Gynecol Scand. 2006;85:657-662.

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Additional supporting information may be found online in the Supporting Information section.