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Induction of Labor and Nulliparity: A Nation-wide Clinical Practice Pilot Evaluation

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Abstract

Introduction

Induction of labor has become an increasingly common obstetric procedure. However, in nulliparous women or women with a previous cesarean section, induction of labor can pose a clinical challenge. Despite an overall expansion of medical indications for labor induction, there is little international consensus regarding the criteria for induction of labor, or for the recommended methods among nulliparous women. In this light, we assessed variations in the practice of induction of labor among 21 birth units in a nation-wide cohort of women with no prior vaginal birth.

Material and methods

We carried out a prospective observational pilot study of women with induced labor, and no prior vaginal birth, across 21 Norwegian birth units. We registered induction indications, methods and outcomes from Sept 1st – Dec 31st 2018 using a web-based case record form. Women were grouped into 'Nulliparous term cephalic', 'Previous CS' and 'Other Robson' (Robson groups 6, 7, 8 or 10).

Results

More than 98% of eligible women (n=1818) were included. There was a wide variety of methods used for induction of labor. In nulliparous term cephalic pregnancies, cesarean section rates ranged from 11.1 - 40.6% between birth units, whereas in the previous CS group, rates ranged from 22.7 - 67.5%. The indications 'large fetus' and 'other fetal' indications were associated with the highest cesarean rates. Failed inductions and failure to progress in labor contributed most to the cesarean rates. Uterine rupture occurred in two women (0.11%), both in the previous CS group. In neonates, 1.6% had Apgar <7 at 5 minutes, and 0.4% had an umbilical artery pH <7.00.

Conclusions

Cesarean rates and applied methods for induction of labor varied widely in this nation-wide cohort of women without a prior vaginal birth. Neonatal outcomes were similar to that of normal birth populations. Results could indicate the need to move towards more standardized induction protocols associated with optimal outcomes for mother and baby.

Keywords
Labor, Induced; Cesarean Section; Delivery, Obstetric; Nulliparous term cephalic; Robson, Clinical Audit.

Abbreviations

CS	cesarean section
BMI	body mass index
GDM	gestational diabetes mellitus
IQR	interquartile range

Key Message

In induction of labor among women without a prior vaginal birth, large variations in methods used and cesarean rates were observed in this nation-wide clinical practice evaluation.

INTRODUCTION

The worldwide rate of induction of labor has been rising steadily over the last 15 years. Currently approximately 25 % of births in high-income countries are induced. (1, 2) When faced with unfavorable factors for the mother or the baby if pregnancy continues, induction of labor can be indicated. (3) In pregnancies complicated by maternal diabetes or preeclampsia, post-term pregnancies and prolonged prelabor rupture of membranes (PROM), induction of labor compared to expectant management reduces the risk of perinatal death and maternal complications. (3-7) Over the last decades an expansion of medical indications for labor induction has occurred, including such conditions as hypertensive disorders, (5) advanced maternal age, (8) gestational diabetes (GDM) (9) and suspected large fetus for gestation. (10) Newer studies have demonstrated the safety of induction of labor without a medical indication, with fetal outcomes and cesarean section (CS) rates comparable to rates among women awaiting spontaneous labor. (11)

However, there are some concerns as to the generalizations of these findings into routine practice. First, results produced in setting with relatively high overall CS rates cannot necessarily be extrapolated to settings with average low CS rates. A clinical challenge is also posed by the considerable number of nulliparous women and women with a previous uterine scar, (12) giving birth today. Furthermore, induction of labor is not risk-free as more interventions are performed in induced compared to spontaneous labors. (13, 14) Finally, in recent studies of induction of labor, few have used standardized and consistent protocols in terms of the methods used. There is currently no international agreement as to what is the best induction method in women without a prior vaginal birth, (1, 15) and there is large diversity in clinical practice. (1, 2)

The authors of this study considered that assessing variation in induction practices in a national sample from a setting with free universal public delivery care and low average CS rates, (16) such as Norway, might be a good start to evaluate current practices and results. The aim of this pilot study was to examine variation in indications for induction of labor, methods and associated CS prevalence among women with no previous vaginal birth across 21 birth units nationwide. We used the Robson classification framework to distinguish women with nulliparous term cephalic pregnancies versus those with a previous uterine scar attempting a vaginal birth after cesarean section. (17) Ultimately, we aimed to identify practices associated with the best outcomes in terms of maternal and neonatal safety to inform obstetric providers.

MATERIAL AND METHODS

We carried out a prospective pilot registration of women undergoing induction of labor with a live fetus beyond 23 completed gestational weeks and with no prior vaginal birth between September 1st - December 31st 2018. We invited Norwegian obstetric departments with >1000 annual births to participate in the study. Out of 22 eligible units, 21 units were included (Supplementary Figure A). Participating units selected women whose labor was to be induced and decided upon the method(s) according to local practices, guidelines and definitions. Out-patient induction of labor was not practiced. Anonymous individual patient data were prospectively registered by clinicians in each department into a web-based electronic case record form. Only women with induction of labor were included. The number of nulliparous women without a previous birth and the induction rate during the period was also reported. The paper is reported using the STROBE guidelines for cohort studies.(18) Data were stored in Services for Sensitive Data, University of Oslo, Norway. The project is registered in ClinicalTrials.gov, no. NCT03730220.(19)

The primary outcome was the occurrence of cesarean section (CS) according to indication for induction and method of induction, stratified by obstetric group. Indications for CS were defined according to national/regional guidelines. We also assessed CS rates according to level of birth unit (university hospital or not). Secondary outcomes included uterine rupture, estimated maternal blood loss, adverse neonatal outcomes and the time interval from drug administration to birth. Estimated postpartum blood loss in ml was reported in categories. Adverse neonatal outcomes were defined as a composite outcome of Apgar score <7 at 5 minutes and/or transfer to neonatal intensive care unit and/or pH in umbilical artery <7.10 within one hour of birth.

We categorized cases into three groups. These were: “Nulliparous term cephalic” (Robson 2), "Previous CS" (classified as Robson 5: multiparous women with a previous uterine scar, with a single cephalic term pregnancy; however with no previous vaginal birth), and “Other Robson” (including Robson groups 6 and 7: women with a single breech pregnancy; Robson group 8: women with multiple pregnancies, and Robson group 10: women with a single cephalic pregnancy < 37 weeks’ gestation).
The indication for induction was categorized into 12 groups: Postdates (as defined locally; latest 42+0), PROM, preeclampsia/hypertension, intrauterine growth restriction (IUGR)/oligohydramnios, insulin-treated diabetes in pregnancy including insulin-treated GDM, non-insulin treated GDM, suspected large fetus, reduced fetal movements, intrahepatic cholestasis of pregnancy, maternal request, ‘other maternal’ and ‘other fetal’. The starting method for induction was categorized as Foley balloon catheter, misoprostol (oral, vaginal insert or vaginal tablet), or dinoprostone. As according to the protocol, we performed three comparisons: induction regime with Foley balloon catheter versus no catheter; induction regime including

misoprostol vaginal insert versus other misoprostol administration forms, and induction regime including dinoprostone versus misoprostol.

Other covariates included maternal age in categories, pre-pregnancy body mass index (BMI) (< 30 or ≥30), gestational age at induction, Bishop score at induction (≤5, >5 or missing), epidural, infant birthweight and tachysystole (>5 contractions per 10" with abnormal fetal tracing).

Statistical analysis

A statistical analysis plan included a power analysis. Assuming two groups of birth units with different induction methods resulting in a difference in CS rate between 20 to 25%, a significance level (α) of 0.05, and 80% power (β), the study would need 2182 participants. Applying the inclusion criteria, we estimated 2250 births during the period. (20) Baseline characteristics and outcomes were summarized according to the obstetric group. Small cell numbers (n<10) were censored when calculating CS rates. For categorical outcomes we compared proportions with 95% CI with the Chi-Square test and/or Fisher's exact test. We estimated the risk of CS by logistic regression analysis in generalized linear models adjusting for confounders as identified in the literature and according to biological plausibility, estimating crude and adjusted effect estimates as odds ratios (OR) with 95% CI with corresponding p-values We restricted analyses to nulliparous term cephalic and previous CS only due to small cell numbers. In sub analyses of CS deliveries only, we determined indications for the procedure and the subtype (type 1- immediate delivery; type 2- within 20-30 minutes or type 3 - within a given timeframe >30 min < 8 hours). Calculated *P*-values were two-sided and compared to a 5% significance level. Statistical analyses were performed in SPSS version 25 (IBM Corp. Released 2017. IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp.)

Ethical approval

All women received oral and written information about the study. As routine data were gathered anonymously, informed consent was waivered; however, women were able to opt out of the study upon request. The project was approved by the Norwegian Ethics Board, Region Health South East C, reference 2018/1087 and each hospital's Data Protection Officer.

RESULTS

During the study period, a total of 7160 women without a prior vaginal birth gave birth in the 21 participating departments. Among these, labor was induced in 1874 women (26.2%; range 11.7-34.3% between hospitals). Of all 1874 eligible women for inclusion in the study,1818 (98.5%) were included (Figure 1). Most birth units had a written induction protocol; however, most were not differentiated according to their Robson group.

Nulliparous term cephalic pregnancies constituted 80.4% of births, followed by previous CS pregnancies (12.2%) (Table 1). The "Other Robson' group included 52 twin pregnancies (2.9%), 59 preterm births (3.2%) and 25 planned breech births (1.4%). Overall, 20.3% were aged 35 years or more and 18.4% had a pre-pregnancy BMI of 30 or more. Of all women, 16.6% had a registered comorbidity where preeclampsia/hypertension was most prevalent. PROM, postdate pregnancy and preeclampsia/hypertension were the most common indications for induction. Maternal request was an indication for induction in only 3.5% of women.

In the nulliparous term cephalic group, one in five women gave birth by CS, whereas rates were doubled in the previous CS group and in the Other Robson group (Table 2). Hospital CS rates varied between 9.4% and 45.5% in the nulliparous term cephalic group and between 31.3% and 54.5% in the previous CS group (Figure 2). In the whole cohort, university hospital CS rates did not differ significantly from non-university hospitals (24.2% vs 26.8%, *P*=0.22). In the nulliparous term cephalic group CS rates by indication for the induction of labor ranged from 11.1 to 40.6%, whereas in the previous CS group rates were overall higher and ranged from 22.7 to 67.5% (Figure 3; Table S1.). In the nulliparous term cephalic group 'non-insulin GDM', 'other fetal' and 'large fetus' were the indications associated with the highest CS rates (40.6-33.3%). In the previous CS group 'large fetus', 'insulin-treated diabetes' and 'other fetal' were associated with the highest CS rates (62.5-60.0%).

The most common CS indication was suspected fetal hypoxia in the nulliparous term cephalic group, and failed induction in the previous CS group (Table 3). Of all cesarean procedures, 9.2% were reported as grade 1 (immediate) (Table 3). Overall 2.1% of women in the nulliparous term cephalic group and 3.6% of the previous CS group experienced an immediate CS. Suspected uterine rupture or abruptio placentae were indications for seven (0.4%) cesarean procedures.

The most common methods for induction are presented in Table 4. In the nulliparous term cephalic group, a combination of Foley + misoprostol was the most common initiation method (37.3%), followed by Foley + amniotomy/oxytocin (11.9%) (Table 4). In the previous CS group, most women received Foley + dinoprostone (34.4%), followed by Foley + amniotomy/oxytocin. However, altogether, more than 40 different method combinations and sequences were registered.

Use of Foley catheter was associated with birth by CS in the nulliparous term cephalic group (aOR 1.71, 95% CI 1.14-2.55, *P*=0.009), but not in the previous CS group (aOR 0.62, 95% CI 0.19-2.06, *P*=0.44) (Table 5). Use of dinoprostone showed a borderline significant association with birth by CS compared to misoprostol. There was no association between route of administration of misoprostol and risk of CS (data not shown).

Uterine rupture occurred in two women (0.11%), both in the previous CS group (Table 6). Maternal blood loss differed between groups (p=0.049, Chi-Square); however, tachysystole did not. The composite adverse infant outcome occurred in 9.5% and 10.0% in the nulliparous term cephalic and the previous CS group respectively. A higher proportion (30.9%) was found in the Other Robson groups due to more transfers to the neonatal ward due to prematurity. Overall 29 infants (1.6%) had an Apgar score of less than 7 at 5'. Seven infants (0.4%) had an umbilical artery pH<7.00, of whom one infant was transferred to the neonatal ward. The method of induction was not associated with adverse maternal or neonatal outcome.

Among nulliparous term cephalic births, 26.5% were still undelivered 48 hours after induction start, as were 31.6% in the previous CS group and 26.5% in the Other Robson group (data not shown). In the three groups median duration from start of induction to birth were 32.6 hours (IQR 31.8), 34.1 hours (IQR 35.1) and 30.6 hours (IQR 32.6), respectively.

DISCUSSION

Our study showed large variations in the practice and results of induction of labor in this nation-wide sample. The frequency of CS after induction of labor was highest in the previous CS group, where about two out of five women gave birth by CS and lowest in the nulliparous term cephalic group, where about one out of five women gave birth by CS. CS rates after induction differed widely between units. CS performed due to failed induction of labor and prolonged first stage of labor accounted for nearly half of all CS. Our study found a wide variation of induction methods, with few units using standard induction protocols. Maternal and fetal safety outcomes were comparable to existing literature.

The strengths of this pilot study include the nation-wide prospective design with more than 98% of eligible women included. We had access to detailed information regarding indications, the methods used, including the order and route of administration, as well as important safety and efficiency outcomes.

One of the limitations of the study is that we lacked control data from induced multiparous women as well as on spontaneous labors. For this reason, we cannot comment on whether induction increases the rate of CS or adverse outcomes compared to spontaneous birth. Furthermore, we lacked detailed data on the local birth units, such as the number of referrals, socioeconomic spread etc. that might influence outcomes in terms of mode of birth. In the previous CS group we lacked information regarding the previous birth. However, CS rates were slightly lower in tertiary referral university hospitals compared to non-university hospitals, where an accumulation of risks would be expected. Finally, our observational design does not warrant causal inference.

Induction by "large fetus" indication revealed high rates of CS in our study. However, the CS rate at 33.3% is similar to other studies of induction in woman with 'large babies. In the comprehensive study by Boulvain et al, (10) there was a CS rate of 28%, even though 53% were parous. These rates might be the result of a high gestational age in combination with maternal diabetic comorbidity. GDM non-insulin comorbidity had the highest CS rate whereas insulin-treated pregestational or gestational diabetes comorbidity had a relatively low CS rate in nulliparous term cephalic pregnancies. In Norway, insulin users are induced between week 38 and 40, but non-insulin GDM are induced primarily on additional indications. (21)

"Other fetal indication" for induction of labor had one of the highest CS rates in both nulliparous term cephalic and previous CS pregnancies. This is a mixed group including fetal malformations, polyhydramnios, non-reassuring antenatal fetal tracing and unknown gestational length. Polyhydramnios may give insufficient contractions due to an over distended uterus (22) and non-reassuring fetal tracing have to be handled with care; delivery, rather than expectant management is preferred, if it continues. The group "maternal request" was surprisingly low with 3.5 % of all inductions and we found a low CS rate both in the nulliparous term cephalic and the previous CS group. This is lower than previously reported. (23) The distinction between 'maternal request' or 'medical problem' can be a fine one, especially when considering mental health and pregnancy complaints. However, this finding indicates a restrictive attitude among providers, in contrast to upcoming trends elsewhere. (24)

The overall proportion of failed induction and prolonged first stage was unexpectedly high in our sample. However, as 27-32% of women were undelivered 48 hours after the start of induction, this is not likely to reflect a use of rigid time limits. The 22-35% rate of failed induction/poor progress in the first stage that we found in our sample might imply a practice emphasizing safety rather than effectiveness. This is also reflected in a relatively low uterine rupture rate, a low tachysystole rate of 5% and few immediate CS procedures.

At present, there are conflicting reports of how and when induction of labor should be offered to women. Trials have been conducted among women at term with no medical indication. (11, 25) These randomized trials indicate no major safety concerns in terms of the CS risk or adverse infant or maternal outcomes. In addition, although the ARRIVE trial has been criticized as including many overweight and obese women, (26) the 18.6% CS rate in the trial's induced group (who were all low risk nulliparous women) is similar to the 16.7% rate seen in 'maternal request' in the nulliparous term cephalic group in our study. A Cochrane review looking at induction at 40 weeks versus expectant management found improved outcomes in the induction group, except for a higher operative vaginal delivery rate. (3) However, a prerequisite in generalizing findings is that the induction process and labor is well managed with the necessary staff at hand. Like most high-resource countries, Norway has a rapidly increasing induction rate that reached 23%

of all births in 2018, (20) but at the same time, overall CS rates - 16.0% in 2017 – are the second lowest rate across the OECD area. (16) However, CS rates vary considerably between regions beyond what can be expected due to case-mix. (27) A national induction guideline lists medical indications and methods, but leaves the choice among these methods to individual departments and staff. (21) In this clinical practice evaluation, we found that multiple induction protocols are used even within nulliparous term cephalic and previous CS groups. What this means is that women across the country do not have similar treatment when undergoing induction of labor.

Translating RCT evidence into practical clinical protocols can be challenging in obstetric units facing logistical restraints such as delays in timely administration of uterotonics and performing rupture of membranes. (28) Results from practice evaluations are therefore important to inform decisions in induction regimes tailored to specific groups. Women should be offered joint decision making based on these facts. Careful selection of women for induction who have previously had a cesarean section, as well as taking women's preferences into account, are important factors in a pragmatic induction of labor protocol.

CONCLUSION

A wide variation of induction methods and CS rates after induction, as well as a high rate of failed inductions in women without a prior vaginal birth, points to a potential for improvement by moving towards more standardized protocols. The Robson groups provide a framework for the counselling of women about particular risks and benefits regarding induction of labor while working towards shared decision-making.

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Tweetable abstract:

There is considerable variation in outcomes after induction of labor, depending on where a primiparous woman chooses to have her birth.

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Legends of supporting information

Supporting Information Figure 1 Map of participating birth units in Norway.

Legends of Tables and Figures

Table 1 Maternal characteristics in 1818 women with no prior vaginal birth undergoing induction of labor.

Table 2 Delivery mode after induction of labor in 1818 women with no prior vaginal birth according to obstetric group.

Table 3 Main indication and subtype of 459 cesarean sections[1] after induction of labor according to obstetric group.

Table 4 Induction methods in 1818 women with no prior vaginal birth according to obstetric group.

Table 5 Method and risk of cesarean section in nulliparous term cephalic and previous CS pregnancies after induction of labor.

Table 6 Maternal and fetal secondary outcomes after induction of labor according to obstetric groups.

Supporting information Table S1. Indication for induction according to indication for CS in three obstetric groups.

Figure 1 Flowchart of study participants

Figure 2 Proportions of cesarean section after induction of labor by delivery unit in nulliparous term cephalic (a) and previous CS pregnancies (b).

Figure 3 Cesarean section rates according to indication for induction of labor in nulliparous term cephalic and previous CS pregnancies.

Tables

Table 1 Maternal characteristics in 1818 women with no prior vaginal birth undergoing induction of labor.

	All		Nulliparous term cephalic		Previous CS		Other Robson	
	n	%	n=1461	%	n=221	%	n=136	%
Maternal age (years)								
16-24	246	13.5	222	15.2	15	6.8	9	6.6
25-34	1203	66.2	956	65.4	149	67.4	98	72.1
35-54	369	20.3	283	19.4	57	25.8	29	21.3
BMI prepregnancy[1]								
<30	1458	81.6	1185	82.3	160	74.8	113	85.0
>= 30	328	18.4	254	17.7	54	25.2	20	15.0
Bishops score[2]								
0-5	1366	82.8	1077	81.8	185	88.9	104	83.2
6-10	284	17.2	240	18.2	23	11.1	21	16.8
Birth at University hospital								
Yes	1173	64.5	957	65.5	124	56.1	93	68.4
Gest. age median (IQR)	40+1 (21)		40+3 (18)		40+0 (18)		36+5 (16)	
Maternal comorbidity[3]								
IDDM/GDM insulin	137	7.5	105	7.2	22	10.0	10	7.4
GDM, non-insulin	91	5.0	74	6.4	7	3.2	10	7.4
Preeclampsia/ hypertension	238	13.1	189	12.9	13	5.9	37	27.2
Intrahepatic cholestasis	34	1.9	25	1.7	6	2.7	3	2.2
Another comorbidity	272	15.0	210	14.4	39	17.6	23	5.9
Decision induction								
Consultant	1181	65.0	897	61.4	162	72.4	123	90.4
Resident	534	29.4	472	32.3	49	22.2	13	9.6
Midwife	103	5.7	93	6.4	10	4.5	0	0
Main indication for induction								
PROM	357	19.3	286	19.6	47	21.3	24	17.6
Postdates	336	18.5	299	20.5	33	14.9	4	2.9
Preeclampsia/hypertension	279	15.3	228	15.6	17	7.7	34	25.0
IUGR/oligohydramnios	280	15.4	231	15.8	24	10.9	25	18.4
IDDM/GDM - insulin	97	5.3	81	5.5	13	5.9	3	2.2
Large fetus	67	3.7	45	3.1	16	7.2	6	4.4
Maternal request	61	3.5	36	2.5	22	10.0	3	2.2
GDM, non-insulin	35	1.9	32	2.2	3	1.4	0	0
Intrahepatic cholestasis	43	2.4	35	2.4	5	2.3	3	2.2
Reduced fetal movements	40	2.2	36	2.5	3	1.4	1	0.7
Other maternal[4]	164	9.0	101	6.9	33	14.9	30	22.1
Other fetal[5]	59	3.2	51	3.5	5	2.3	3	2.2

Other Robson includes Robson groups 6, 7, 8 and 10. BMI= Body Mass Index. IQR=interquartile range. IDDM=insulin-dependent diabetes mellitus. GDM=gestational diabetes mellitus. PROM=prelabor rupture of membranes. IUGR=intrauterine growth restriction.[1]Missing 1.8%. [2]Not assessed in 9.2%. [3]More than one condition might be registered. [4]Incl. twin pregnancy, previous obstetric history, chronic disease, prolonged latency phase, vaginal bleeding. [5]incl. polyhydramnios, non-reassuring fetal tracing, known malformations, unknown gestational length.

Table 2 Delivery mode after induction of labor in 1818 women with no prior vaginal birth according to obstetric group.

		Cesarean section[1]			Operative vaginal			Spontaneous vaginal		
	N	n	%	95% CI	n	%	95% CI	n	%	95% CI
Nulliparous term cephalic	1461	320	21.9	19.8-24.1	314	21.5	19.4-23.7	827	56.6	54.0-59.2
Previous CS	221	89	40.3	33.7-47.1	40	18.1	13.3-23.8	92	41.6	35.1-48.4
Other Robson	136	50	36.8	28.9-45.8	28	20.6	14.2-28.6	60	44.1	35.9-53.2
All	1818	459	25.2	23.3-27.3	382	21.0	19.2-23.0	979	53.9	51.5-56.2

Other Robson includes Robson groups 6, 7, 8 and 10. [1]Including cesarean section second twin.

Table 3 Main indication and subtype of 459 cesarean sections[1] after induction of labor according to obstetric group.

	All		Nulliparous term cephalic		Previous CS		Other Robson	
	n=459	%	n=320	%	n=89	%	n=50	%
Main cesarean indication								
Prolonged 1.stage	117	25.5	85	26.6	23	25.8	9	18.8
Prolonged 2. stage	26	5.7	19	5.9	4	4.5	3	6.5
Susp. fetal hypoxia	143	31.2	112	35.0	19	21.3	12	25.0
Failed induction	109	23.7	69	21.6	31	34.8	9	18.8
Uterine rupture	2	0.4	0	0	2	2.2	0	0
Abruptio placentae	5	1.1	3	0.9	1	1.1	1	2.1
Other	55	12.0	31	9.7	10	11.2	14	29.2
Subtype								
Type 1 (immediate)	42	9.2	30	9.4	8	9.0	6	12.0
Type 2 (<20 minutes)	234	51.0	172	53.8	36	40.4	26	52.0
Type 3 (>20 minutes)	181	39.4	118	36.9	45	50.6	18	36.0

[1]Including cesarean section of second twin only (n=2). Other Robson includes Robson groups 6, 7, 8 and 10.

Table 4 Induction methods in 1818 women with no prior vaginal birth according to obstetric group.

	All		Nulliparous term cephalic		Previous CS		Other	
Induction method	N=1818	%	N=1461	%	N=221	%	N=136	%
Foley start combinations								
Foley alone	135	7.4	102	7.0	19	8.6	14	10.3
Foley + oral misoprostol ± AT/oxytocin	191	10.5	178	12.2	4	1.8	9	6.6
Foley + insert misoprostol ± AT/oxytocin	198	10.9	190	13.0	1	0.5	7	5.1
Foley + vaginal misoprostol ± AT/oxytocin	213	11.7	177	12.1	11	5.0	25	18.4
Foley + dinoprostone ± AT/oxytocin	108	5.9	28	1.9	76	34.4	4	2.9
Foley ± AT/oxytocin	241	13.3	174	11.9	49	22.2	18	13.2
Misoprostol start combinations								
Oral misoprostol alone	118	6.5	107	7.3	1	0.5	10	7.4
Oral misoprostol ± AT/oxytocin	45	2.5	41	2.8	0	0	4	2.9
Insert misoprostol alone	67	3.7	66	4.5	0	0	1	0.7
Insert misoprostol ± AT/oxytocin	29	1.6	28	1.9	0	0	1	0.7
Vaginal misoprostol alone	165	9.0	148	10.1	3	1.4	14	10.3
Vaginal misoprostol ± AT/oxytocin	88	4.8	79	5.4	1	0.5	8	5.9
Other combinations								
Dinoprostone alone	39	2.1	9	0.6	26	11.8	4	2.9
Dinoprostone ± AT/oxytocin	11	0.6	2	0.1	8	3.6	1	0.7
Amniotomy ±oxytocin	130	7.2	103	7.0	19	8.6	8	5.9
Any misoprostol/dinoprostone + successive Foley ± AT/oxytocin	24	1.3	17	1.2	3	1.4	4	2.9
Other	16	0.9	12	0.8	0	0	4	2.9

Other Robson includes Robson groups 6, 7, 8 and 10. AT=amniotomy.

Table 5 Method and risk of cesarean section in nulliparous term cephalic and previous CS pregnancies after induction of labor.

	Proportion CS		Risk of Caesarean section					
	CS	%	OR	95% CI	p	aOR[2]	a95% CI[2]	P[2]
1. Foley[1] (n=1356)								
Nulliparous term cephalic								
Foley catheter	212	25.2	1.55	1.13-2.13	0.007	1.71	1.14-2.55	0.009
No Foley catheter	61	17.9	1			1		
Previous CS								
Foley catheter	60	40.3	1.08	0.46-2.54	0.86	0.62	0.19-2.06	0.44
No Foley catheter	10	38.5	1			1		
2. Dinoprostone vs misoprostol (n=1195)								
Nulliparous term cephalic								
Dinoprostone	14	34.1	1.80	0.93-3.49	0.082	1.90	0.90-4.03	0.09
Misoprostol	230	22.4	1			1		
Previous CS								
Dinoprostone	49	47.1	1.29	0.51-3.27	0.60	1.02	0.32-3.23	0.97
Misoprostol	9	40.9	1			1		

[1]Excluding women with prelabor rupture of membranes. [2]Adjusted for maternal age groups 16-24, 25-34, and ≥35; prepregnancy BMI <25, 25-29, 30-34, ≥35; Bishop score ≤5, >5 and missing; birthweight in grams and Foley catheter yes/no.

Table 6 Maternal and fetal secondary outcomes after induction of labor according to obstetric groups.

	All		Nulliparous term cephalic		Previous CS		Other	
Maternal	n	%	N	%	n	%	n	%
Uterine rupture	2	0.1	0	0	2	0.9	0	0
Tachysystole	96	5.3	79	5.4	10	4.5	7	5.1
Epidural	1355	74.5	1090	74.6	157	71.0	108	79.4
Blood loss in ml								
<500	1051	57.8	863	59.1	120	54.3	68	50.0
500-999	552	30.4	439	30.0	69	31.2	44	32.4
1000-1999	178	9.8	135	9.2	24	10.9	19	14.0
2000-2999	33	1.8	22	1.5	6	2.7	5	3.7
3000+	4	0.2	2	0.1	2	0.9	0	0
Fetal[1]								
Mean birthweight in grams(SD)	3485	(597)	3513	(550)	3664	(522)	2887	(808)
Adverse neonatal outcome[2]	203	11.2	139	9.5	22	10.0	42	30.9
Transfer NICU	132	7.4	85	5.9	10	4.6	37	27.6
Apgar <7 at 5 minutes	29	1.6	20	1.4	7	3.2	2	1.5
pH art umb <7.10[3]	72	4.0	59	4.0	9	4.0	4	2.9
pH art umb <7.00[3]	7	0.4	6	0.4	1	0.5	0	0

Other Robson includes Robson groups 6.7.8.and 10. [1]Outcomes for first twin only. SD= standard deviation. [2]Adverse neonatal outcome incl. pH arteria umbilicalis <7.10 and/or Apgar score at 5' <7 and/or transfer neonatal intensive care unit. NICU= neonatal intensive care unit excluding planned transfers (n=18). [3]Missing 19.5%.

Figures

Figure 1 Flowchart of study participants

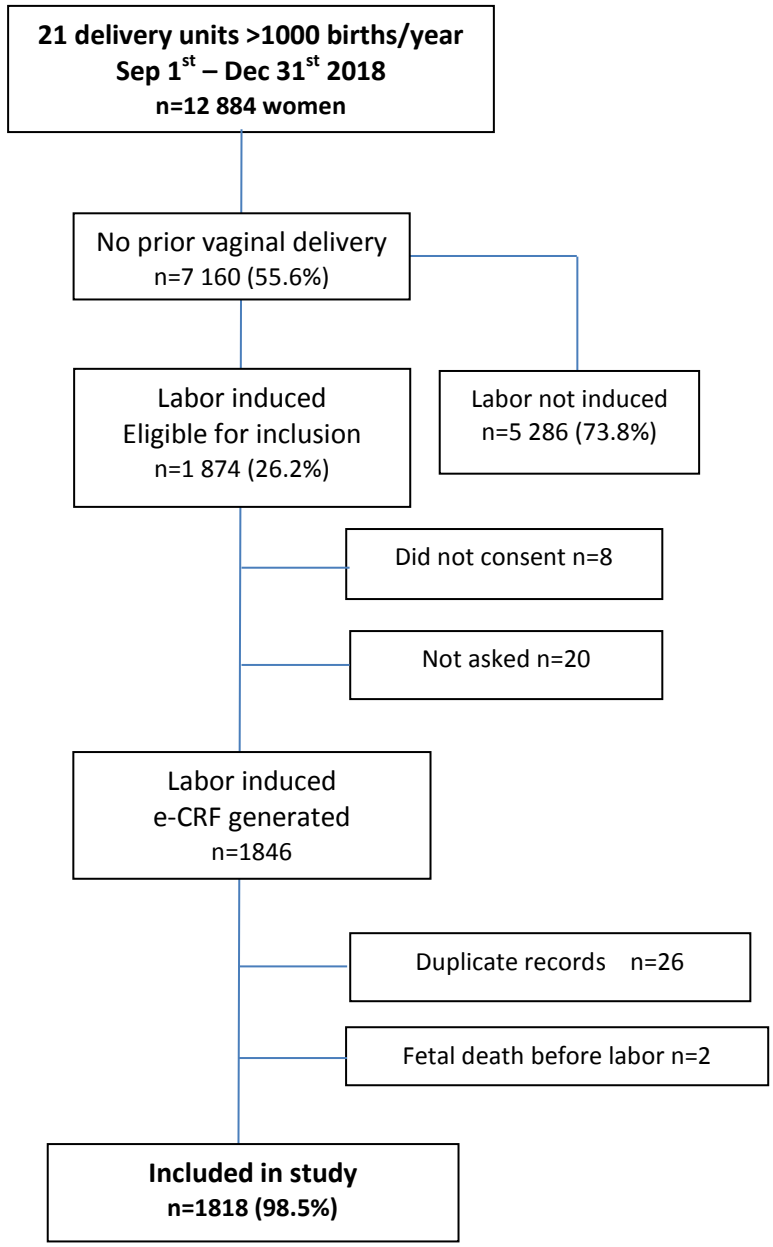
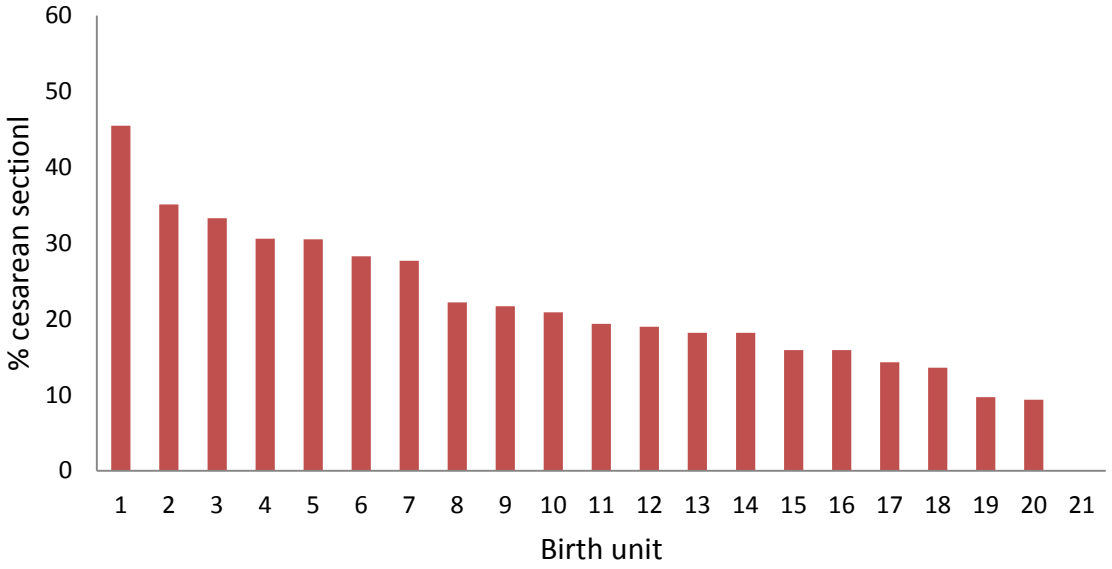
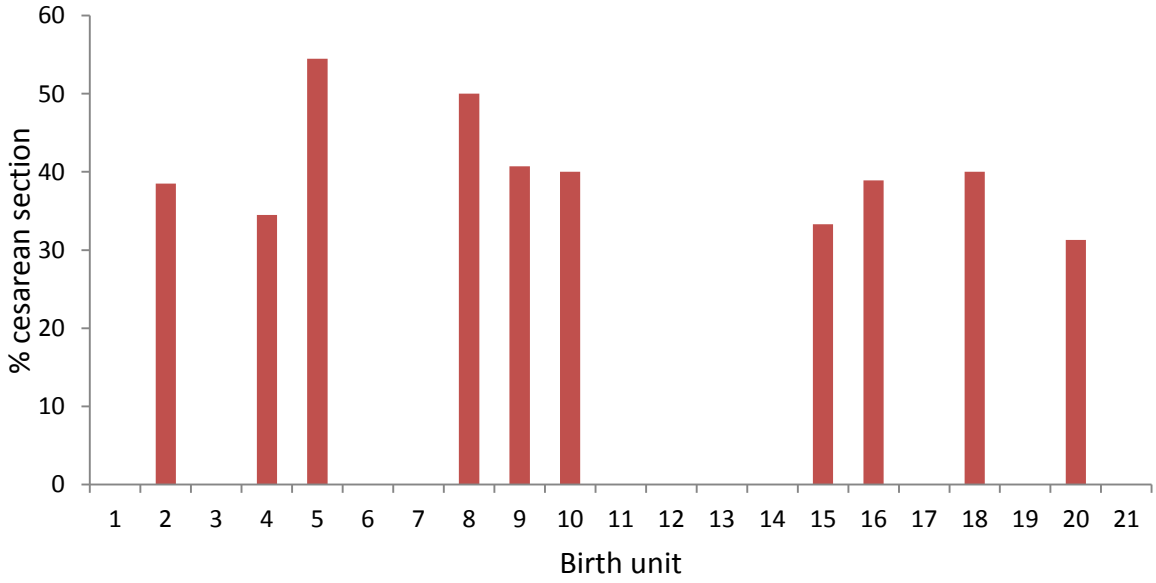


Figure 2 Proportions of cesarean section after induction of labor by delivery unit in nulliparous term cephalic (a) and previous CS pregnancies (b).

(a) Nulliparous term cephalic

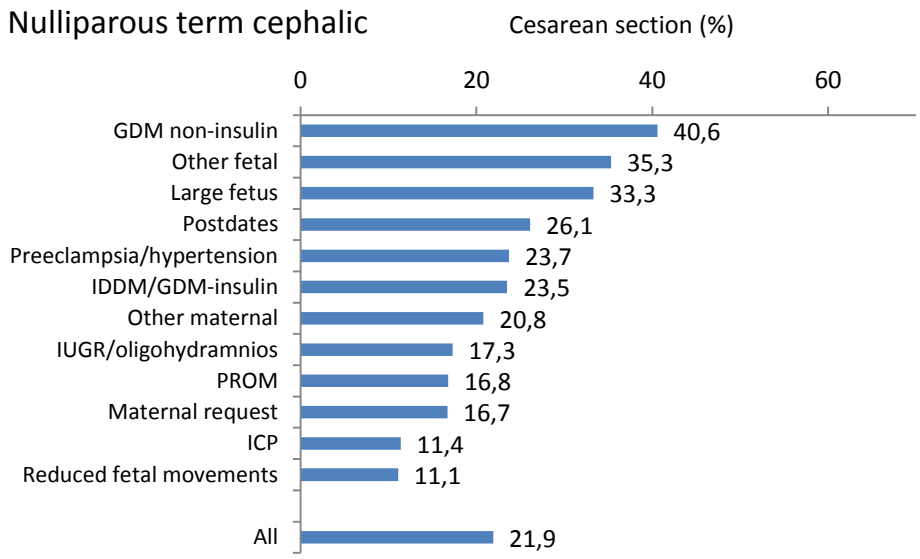


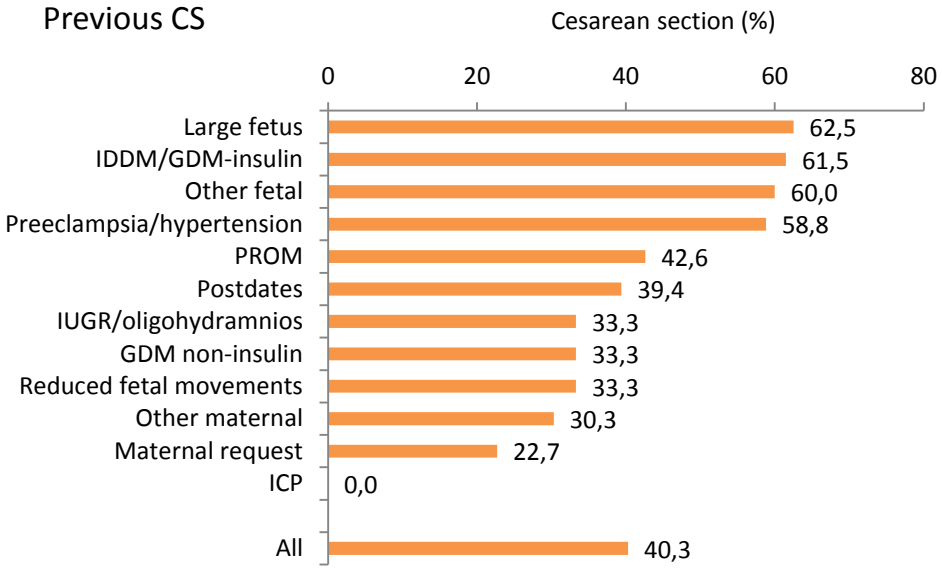
(b) Previous CS



Other Robson includes Robson groups 6, 7,8 and 10. Results from delivery units with n<10 deliveries per cell are censored.

Figure 3 Cesarean section rates according to indication for induction of labor in nulliparous term cephalic and previous CS pregnancies.





GDM= gestational diabetes mellitus; IDDM= insulin-dependent diabetes mellitus; IUGR=intrauterine growth restriction; PROM=prelabor rupture of membranes; ICP= intrahepatic cholestasis of pregnancy.

Supporting information Table S1. Indication for induction according to indication for CS in three obstetric groups.

Nulliparous term cephalic		Prolonged 1st stage	Prolonged 2nd stage	Fetal hypoxia	Failed induction	Uterine rupture	Abruptio placenta	Other	Total
Indication	Postdates	27	6	24	13	1	1	6	78
	PROM	14	5	17	6	0	0	6	48
	Preeclampsia/hypertension	10	4	17	13	0	0	10	54
	IUGR/oligohydramnios	9	0	19	9	0	2	1	40
	IDDM/GDM-insulin	1	1	6	11	0	0	0	19
	GDM, non-insulin	5	0	6	1	0	0	1	13
	Other maternal	4	1	8	6	0	0	2	21
	Reduced fetal movements	0	0	3	1	0	0	0	4
	Intrahepatic cholestasis	2	0	1	0	0	0	1	4
	Maternal request	2	1	1	0	0	0	2	6
	Suspected large fetus	6	1	3	4	0	0	1	15
	Other fetal	5	0	7	5	0	0	1	18
	Total	**85**	**19**	**112**	**69**	**1**	**3**	**31**	**320**
Previous CS		Prolonged 1st stage	Prolonged 2nd stage	Fetal hypoxia	Failed induction	Uterine rupture	Abruptio placenta	Other	Total
Indication	Postdates	4	0	3	4	0	0	2	13
	PROM	5	0	3	8	0	0	4	20
	Preeclampsia/hypertension	3	0	2	4	1	0	0	10
	IUGR/oligohydramnios	2	0	3	3	0	0	0	8
	IDDM/GDM-insulin	1	1	2	3	0	1	0	8
	GDM, non-insulin	1	0	0	0	0	0	0	1
	Other maternal	3	0	1	5	0	0	1	10
	Reduced fetal movements	1	0	0	0	0	0	0	1
	Maternal request	2	0	1	1	0	0	1	5
	Suspected large fetus	1	3	2	2	0	0	2	10
	Other fetal	0	0	2	1	0	0	0	3
Total		**23**	**4**	**19**	**31**	**1**	**1**	**10**	**89**
Other (Robson 6,7,8,10)		Prolonged 1st stage	Prolonged 2nd stage	Fetal hypoxia	Failed induction	Uterine rupture	Abruptio placenta	Other	Total
Indications	Postdates	0	0	2	1	0	0	1	4
	PROM	2	1	0	0	0	1	2	6
	Preeclampsia/hypertension	1	0	3	1	0	0	4	9
	IUGR/oligohydramnios	0	0	4	1	0	0	4	9
	IDDM/GDM-insulin	2	0	0	1	0	0	0	3
	Other maternal	2	2	2	2	0	0	3	11
	Reduced fetal movements	0	0	0	1	0	0	0	1
	Maternal request	0	0	0	1	0	0	0	1
	Suspected large fetus	2	0	1	1	0	0	0	4
Total		**9**	**3**	**12**	**9**	**0**	**1**	**14**	**48**

PROM=prelabor rupture of membranes. IUGR=intrauterine growth restriction. IDDM/GDM=insulin-dependent/gestational diabetes.

Supporting Information Figure 1 Map of participating birth units in Norway.