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The Netherlands

Maternal morbidity and mortality in the Netherlands and their association with obstetric interventions

Kallianidis, A.F.

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Epidemiological analysis of peripartum hysterectomy across nine European countries

A.F. Kallianidis, A. Maraschini, J. Danis, L.B. Colmorn, C. Deneux-Tharaux, S. Donati, M. Gissler, M. Jakobsson, M. Knight, A. Kristufkova, P.G. Lindqvist, G. Vandenberghe, T. van den Akker

On behalf of the International Network of Obstetric Survey Systems

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ABSTRACT

Introduction: Peripartum hysterectomy is a surgical procedure performed for severe obstetric complications such as major obstetric haemorrhage. The prevalence of peripartum hysterectomy in high-resource settings is relatively low. Hence, international comparisons and studying indications and associations with mode of birth rely on the use of national obstetric survey data. Objectives were to calculate the prevalence and indications of peripartum hysterectomy and its association with national caesarean section rates and mode of birth in nine European countries.

Material and methods: We performed a descriptive, multinational, population-based study among women who underwent peripartum hysterectomy. Data were collected from national or multiregional databases from nine countries participating in the International Network of Obstetric Survey Systems. We included hysterectomies performed from 22 gestational weeks up to 48 hours postpartum for obstetric haemorrhage, as this was the most restrictive, overlapping case definition between all countries. Main outcomes were prevalence and indications of peripartum hysterectomy. Additionally, we compared prevalence of peripartum hysterectomy between women giving birth vaginally and by caesarean section, and between women giving birth with and without previous caesarean section. Finally, we calculated correlation between prevalence of peripartum hysterectomy and national caesarean section rates, as well as national rates of women giving birth after a previous caesarean section.

Results: A total of 1,302 peripartum hysterectomies were performed in 2,498,013 births, leading to a prevalence of 5.2 per 10,000 births ranging from 2.6 in Denmark to 10.7 in Italy. Main indications were uterine atony (35.3%) and abnormally invasive placenta (34.8%). Relative risk of hysterectomy after caesarean section compared with vaginal birth was 9.1 (95% CI 8.0-10.4). Relative risk for hysterectomy for birth after previous caesarean section compared with birth without previous caesarean section was 10.6 (95% CI 9.4-12.1). A strong correlation was observed between national caesarean section rate and prevalence of peripartum hysterectomy ($\rho = 0.67$, $P < 0.05$).

Conclusions: Prevalence of peripartum hysterectomy may vary considerably between high-income countries. Uterine atony and abnormally invasive placenta are the commonest indications for hysterectomy. Birth by caesarean section and birth after previous caesarean section are associated with nine-fold increased risk of peripartum hysterectomy.

INTRODUCTION

Peripartum hysterectomy refers to surgical removal of the uterus during pregnancy or postpartum.[1] It is usually performed for severe obstetric complications such as major obstetric haemorrhage, abnormally invasive placenta, uterine rupture, or sepsis. Peripartum hysterectomy is defined by the World Health Organization as a maternal near-miss criterion and used as a proxy for severe postpartum haemorrhage and therefore frequently used as an outcome of interest in obstetric surveillance.[2]

The association between peripartum hysterectomy and caesarean section has previously been described, with relative risk for women giving birth by caesarean section ranging from 8.5 to 18.3.[3-8] In addition, pregnancy in a woman who gave birth by caesarean section previously is a risk factor for abnormally invasive placentation, which may in turn lead to hysterectomy. This risk is known to increase for every additional previous caesarean section.[9] Such associations are of particular interest in light of the rising caesarean section rates worldwide because these could potentially lead to increasing rates of peripartum hysterectomies as well.

Prevalence of peripartum hysterectomy in high-resource settings is relatively low.10 Hence, indications and outcomes are often studied retrospectively, or through national obstetric survey systems. [11-15] Multinational comparisons of prevalence and outcomes to optimise management strategies may be facilitated by international collaborations combining national data.[1,16]

The main aim of this study was to compare the prevalence of peripartum hysterectomy between high-income countries, as part of the International Network of Obstetric Survey Systems (INOSS). Secondary aims were to describe the indications for hysterectomy, and perform analyses of prevalence of peripartum hysterectomy stratified by mode of birth and previous caesarean section. In addition, we examined the correlation between national rates of peripartum hysterectomy and national caesarean section rates, and the rate of women giving birth after previous caesarean section.

MATERIAL AND METHODS

This was a descriptive, multinational, population-based study. We used data from nine countries participating in INOSS that had previously conducted studies on peripartum hysterectomy. Most of these countries, except France and Slovakia, have previously published outcomes of peripartum hysterectomy surveillance.[11-15,17-20] INOSS is an international collaboration of national obstetric survey systems, aiming to increase knowledge of management of uncommon obstetric complications.[16] Participating in this study were: Slovak Obstetric Survey System (SOSS) in Slovakia, Italian Obstetric Surveillance System (ItOSS) in Italy, Belgian Obstetric Surveillance

System (B.OSS) in Belgium, Épidémiologie de la Morbidité Maternelle Sévère (EPIMOMS) in France, Nordic Obstetric Surveillance System (NOSS) with data from Denmark, Finland and Sweden, Landelijke studie naar Etnische determinanten van Maternale Morbiditeit (LEMMoN) in the Netherlands, and United Kingdom Obstetric Surveillance System (UKOSS) in the UK. All were nationwide studies except for EPIMOMS in France, which included six regions (Alsace, Auvergne, Basse-Normandie, Île-de-France, Lorraine, and Rhône-Alpes) covering 20% of national births and ItOSS, which encompassed six regions (Piedmont, Emilia-Romagna, Tuscany, Lazio, Campania, and Sicily) representing 49% of births in Italy.

Methods of data collection were described previously.[20-25] In brief, all countries performed national or multiregional survey studies in which women who underwent peripartum hysterectomy were identified. Identification of cases was performed in most countriesby monthly communication (electronic database, mailing or paper) to appointed clinicians in each maternity unit. When a case was reported, further details were requested through a data collection form. To ensure completeness of data, regular reminders were sent and a 'nothing to report' response was requested. All data were collected prospectively, except for the data from Slovakia, which were collected retrospectively. Studies were performed during different periods, from August 2004 to August 2016. Validation and identification of additional cases were performed after cross-checking health registers and hospital databases for the Nordic countries (Hospital Discharge Register, Medical Birth Register and delivery logbooks). Each country managed and cleaned their own database after which all anonymised databases were merged in Leiden, The Netherlands (see Supplementary material, Table S1).

In order to overcome differences in case selection between studies we applied a uniform case definition. Definitions used in the different survey studies were specified for inclusion criteria such as minimum gestational age, postpartum follow up, inclusion of non-obstetric indications (such as malignancy), or other specific inclusion or exclusion criteria if present (such as including only cases of obstetric haemorrhage in Italy). To arrive at a uniform definition, the most restrictive definition was chosen to account for differences. We opted not to exclude hysterectomies in case of missing information regarding indication or gestational age, as it was postulated that the very few women who would have had an indication other than obstetric haemorrhage or a peripartum hysterectomy before 22 weeks of gestation would be greatly outnumbered by those with haemorrhage or hysterectomy ≥22 weeks. The most restrictive definition was defined as hysterectomies performed from the 22nd week of gestation up to 48 hours postpartum performed for obstetric haemorrhage (see Supplementary material, Table S2).

All countries provided background data on number of births during the study period. Background data differed between countries on the lower limit of gestational age, ranging from ≥22 weeks to 25+6 weeks (see Supplementary material, Table S1). For countries registering births ≥24 weeks, calculation of births

≥22 weeks was not possible. In a previous INOSS study, correction of background data resulted in minimal non-significant differences because the proportion of births at those gestational ages was very low in all countries, so we decided not to perform such a correction.26 Additionally, all countries provided aggregate data on national caesarean section rates, and numbers of caesarean sections and vaginal births. When actual numbers of caesarean section and vaginal births were unknown, these were estimated by multiplying the total number of births by the caesarean section rate. Numbers of women giving birth with and without previous caesarean section were calculated accordingly.

There were differences between studies in coding indications of hysterectomy. Some countries reported only one indication per hysterectomy whereas others coded all indications that arose during the process leading to hysterectomy. Therefore, we included the most important indication of those registered by applying a hierarchical system. From the indications listed, the one highest in rank was used. The hierarchy of indications, which was determined after reaching consensus among researchers of participating countries, in order of importance, was as follows: abnormally invasive placenta, placenta previa, uterine rupture, placental abruption, uterine atony, infection, cervical laceration, fibroids, unspecified haemorrhage, diffuse intravascular coagulation, and other.

Main outcomes were overall prevalence and indications of peripartum hysterectomy. Secondary outcomes were prevalence of peripartum hysterectomy for women giving birth vaginally and women who underwent cesarean section, and for women giving birth with and without previous cesarean section, with calculations of relative risk. Additionally, correlations between prevalence of peripartum hysterectomy and national cesarean section rates and national proportion of women giving birth after previous caesarean section were recorded.

Statistical analyses

Prevalence was calculated per 10,000 births with 95% CI or per 10,000 caesarean sections or vaginal births where appropriate. For calculation of relative risk, individual data were used from women with hysterectomy, but only aggregate data were available for women without hysterectomy. To adjust for weighting and clustering, calculation of total proportions and relative risks was done using a fixed-effects model. Descriptive data are presented with mean (95% CI) or median (interquartile range) whenever appropriate. Proportions were calculated after subtracting the missing data from the totals, as they cannot be classified in either category of binary variables. Correlation between prevalence of peripartum hysterectomy and mode of birth and previous caesarean section rates per country were calculated using nonparametric Spearman rank order correlations (ρ). Results were considered statistically significant when $P < .05$. All analyses were performed using IBM SPSS Statistics version 18.0 (IBM Corp.), R version 6.3.6 (cran.r-project.org) and Office Excel 2019 (Microsoft Corp.).

Ethical approval

Due to the nature of this study, ethical approval was not required. Each study, from which data were used, was approved by their national or local ethics committee.

RESULTS

A total of 1393 peripartum hysterectomies were reported in the nine participating countries. During the study period, 2 498 013 births were registered. A total of 91 hysterectomies were excluded: 17 because the hysterectomy was performed at gestational age <22 weeks, 72 because of postpartum interval >48 hours, two hysterectomies because of indication other than obstetric haemorrhage (one gynecological malignancy and one necrotic uterus after uterine artery embolization). Using the uniform definition for all data sets, 1302 hysterectomies were included leading to a prevalence of 5.2 (95% CI 4.9-5.5) per 10,000 births. Prevalence was highest in Italy with 10.7 (95% CI 9.8-11.6) hysterectomies per 10,000 births and lowest in Denmark with 2.6 (CI 2.0-3.5) hysterectomies per 10,000 births (Table 1, Figure 1). As the result of differences in the time period in which studies where performed, we compared countries that included cases before 2012 (The Netherlands, Denmark, the UK, Finland, Sweden) with countries that included cases starting in 2012 (Italy, France, Belgium, Slovakia). The prevalence was 3.7 (3.4-4.0) versus 7.3 (6.8-7.9) per 10,000 births, respectively.

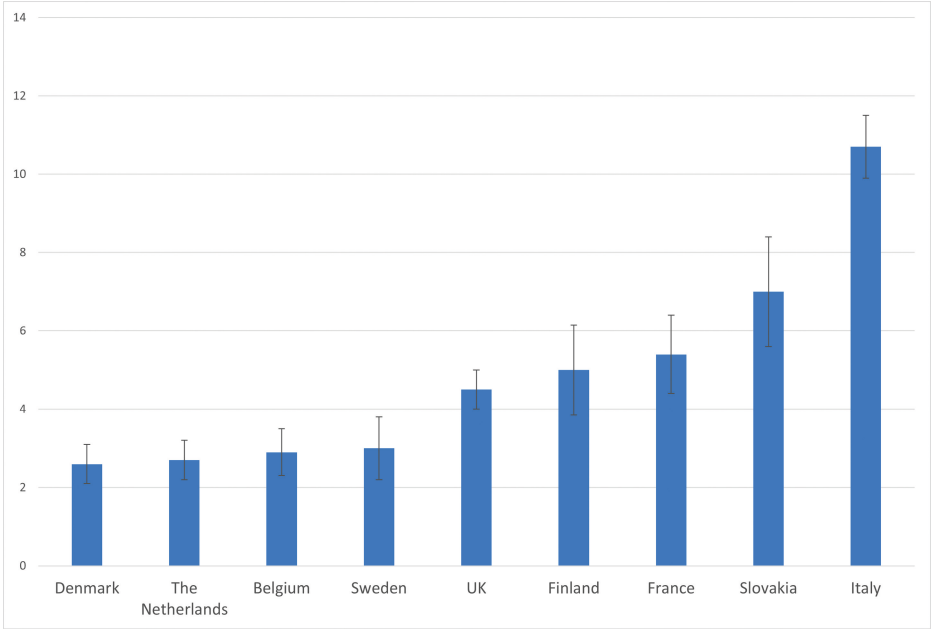

Figure 1. Prevalence of peripartum hysterectomy

Overall, background characteristics such as maternal age, parity, and body mass index were comparable between countries (Table 2). A total of 996/1292 (77.1%) women gave birth by caesarean section and 452/770 (58.7%) were planned. Moreover, 586/1177 (49.8%) women had given birth by caesarean section in a previous pregnancy.

In 670 women multiple indications were coded before use of the hierarchical system. Commonest indication was uterine atony for 459 women (35.3%) followed by abnormally invasive placenta for 453 women (34.8%), and uterine rupture in 98 women (7.5%). Observed frequencies for abnormally invasive placenta indication varied from 14/73 (19.2%) in Belgium up to 26/52 (50%) in Sweden. Hysterectomy in case of placenta previa only was not performed at all in Belgium and Denmark whereas this was the indication in 41/276 (14.9%) of women in the UK. Haemorrhage due to cervical lacerations was notably higher in Denmark (6/44) compared with other countries (Table 3).

Prevalence of peripartum hysterectomy after caesarean section was highest in Italy with 23.2 per 10,000 caesarean sections (95% CI 21.1-25.6) and lowest in Belgium with 9.0 per 10,000 caesarean sections (95% CI 6.8-11.9). Following vaginal birth, prevalence was highest in Slovakia with 4.6 per 10,000 births (95% CI 3.5-6.1) and lowest in Sweden with 0.4 per 10,000 births (95% CI 0.2-0.9). Overall relative risk for hysterectomy after caesarean section compared with vaginal birth was 9.1 (95% CI 8.0-10.4) (Table 4). Relative risk ranged from 2.5 (95% CI 1.7-3.7) in Slovakia to 38.2 (95% 16.3- 89.5) in Sweden, in the latter country this being due to a very low incidence after vaginal birth. Because of the unknown number of planned caesarean hysterectomies in case of suspected abnormally invasive placenta, calculations were repeated after excluding women with hysterectomy for abnormally invasive placenta. Relative risk of peripartum hysterectomy in women who gave birth by caesarean section versus those who gave birth vaginally was 6.8 (95% CI 5.9-8.0) per 10,000 births (see Supplementary material, Table S3). There was a strong, positive correlation between national caesarean section rate and prevalence of peripartum hysterectomy ($\rho = 0.67$, $n = 9$, $P < 0.05$) (Figure 2).

Prevalence of peripartum hysterectomy in women with previous caesarean section varied from 10.7 per 10,000 births (95% CI 7.9-14.6) in the Netherlands to 36.7 (95% CI 31.3-43.1) in the UK. In women without previous caesarean section, prevalence varied considerably less, ranging from 1.3 per 10,000 births (95% CI 0.8-2.0) in Denmark to 3.7 per 10,000 births in Finland and France. Overall relative risk for peripartum hysterectomy in women who had given birth by caesarean section in a previous pregnancy compared with women without a previous caesarean section this was 10.6 (95% CI 9.4-12.1) (Table 5). After excluding women with hysterectomy for abnormally invasive placenta this relative risk was still 6.4 (95% CI 5.5-7.6) per 10,000 births (see Supplementary material, Table S4). A statistically non-significant weak correlation was observed between national proportions of women giving birth with a previous caesarean section and national prevalence of pregnancy-related hysterectomy ($\rho = 0.26$, $n = 8$, $P = 0.5$) (Figure 3).

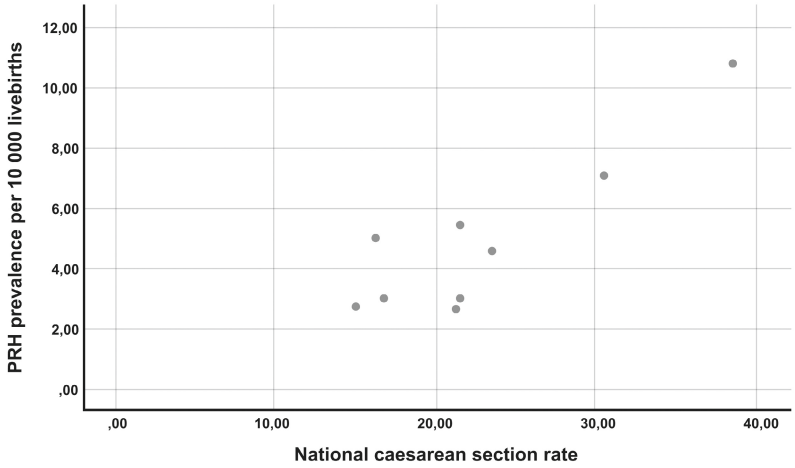

Figure 2. Correlation of peripartum hysterectomy with national caesarean section rates.

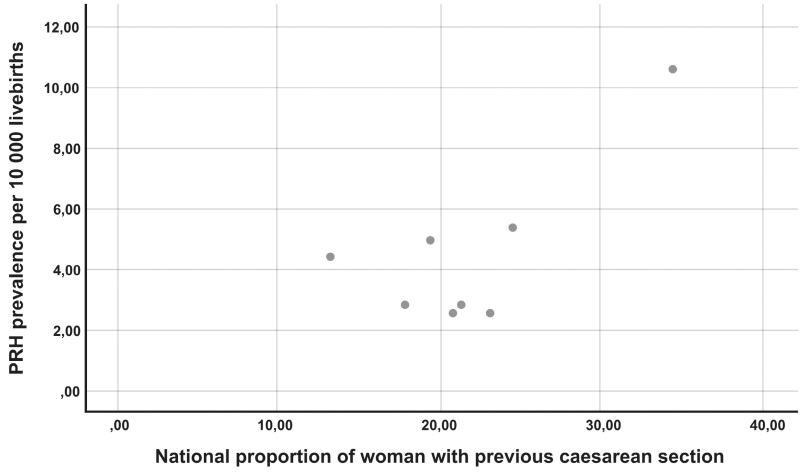

Figure 3. Correlation of prevalence of peripartum hysterectomy with national rates of women with previous caesarean section. *PRH, peripartum hysterectomy

Table 1. Prevalence of peripartum hysterectomy using national definitions and after use of uniform definition

Countries (study)	PRH [a] (n)	Births (n)	Prevalence per 10 000 births (95% CI)	PRH [a] uniform definition (n)	Prevalence -uniform definition per 10 000 births (95% CI[b])
Denmark (NOSS) Apr 2009-Dec 2011	50	168 170	3.0 (2.3 – 3.9)	44	2.6 (2.0 – 3.5)
Netherlands (LEMMoN) Aug 2004-Aug 2006	110	358 874	3.1 (2.5 – 3.7)	95	2.7 (2.2 – 3.2)
Belgium (B.OSS) Jan 2012- Dec 2013	84	252 272	3.3 (2.7 – 4.1)	73	2.9 (2.3 – 3.6)
Sweden (NOSS) Sep 2009-Aug 2011	52	175 575	3.0 (2.3 – 3.9)	52	3.0 (2.3 – 3.9)
UK (UKOSS) Feb 2005-Feb 2006	315	609 300	5.2 (4.6 – 5.8)	276	4.5 (4.0 – 5.0)
Finland (NOSS) Apr 2009-Aug 2011	74	145 546	5.1 (4.1 – 6.4)	72	5.0 (3.9 – 6.2)
France (EPIMOMS) May 2012-Nov 2013	104	182 309	5.7 (4.7 – 6.9)	98	5.4 (4.4 - 6.6)
Slovakia (SOSS) Jan 2012-Dec 2014	104	146 972	7.1 (5.8 - 8.6)	103	7.0 (5.8 - 8.5)
Italy (ITOSS) Sep 2014-Aug 016	500	458 995	10.9 (10.0 - 11.9)	489	10.7 (9.8 - 11.6)
Total	1 393	2 498 013		1 302	5.2 (4.9 - 5.5)

[a]PRH, peripartum hysterectomy; [b]CI, confidence interval

Table 2. Maternal and pregnancy characteristics at time of peripartum hysterectomy

Women's characteristics	Belgium (n=73)	Denmark (n=44)	Finland (n=72)	France (n=98)	UK (n=276)	Italy (n=489)	Netherlands (n=95)	Slovakia (n=103)	Sweden (n=52)	TOTAL (n=1032)
Maternal age, years	34.6 ± 4.4	33.7 ±5.2	34.2 ±5.1	34.4±6.0	34.0±5.4	35.6±5.7	34.3±4.3	31.7±5.5	34.2±4.9	**34.5±5.5**
Missing	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	5(1.0)	0 (0.0)	3(2.9)	0 (0.0)	**8 (0.6)**
BMI kg/m²	24.6±4.5	26.1±5.5	24.9±5.5	24.9±5.4	26.7±5.7	24.9±4.5	24.9±6.1	27.1±3.8	28.0±5.9	**25.6±5.2**
Missing n(%)	14 (19.2)	2 (4.5)	2 (2.8)	8 (8.2)	36 (13.0)	71 (14.7)	31 (32.6)	8 (7.8)	7 (13.5)	**180 (13.8)**
Parity n(%)										
Primiparous	10 (13.7)	12 (27.3)	19 (26.4)	25 (26.0)	33 (12.0)	145 (31.5)	16 (16.8)	18 (18.0)	10 (19.2)	**288/1269 (22.7)**
Multiparous	63 (86.3)	32 (72.7)	53 (73.6)	71 (74.0)	243 (88.0)	316 (68.5)	79 (83.2)	82 (82.0)	42 (80.8)	**981/1269 (77.3)**
Missing n(%)	0 (0.0)	0 (0.0)	0 (0.0)	2 (2.0)	0 (0.0)	28 (5.7)	0 (0.0)	3 (2.9)	0 (0.0)	**33 (2.5)**
Mode of birth n(%)										
Caesarean section	49 (68.1)	36 (81.8)	52 (72.2)	67 (68.4)	226 (81.9)	410 (84.5)	59 (62.1)	51 (52.0)	46 (88.5)	**996/1202 (77.1)**
Vaginal birth	23 (31.9)	8 (18.2)	20 (27.8)	31 (31.6)	50 (18.1)	75 (15.5)	36 (37.9)	47 (48)	6 (11.5)	**296/1202 (22.9)**
Missing n(%)	1 (1.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	4 (0.8)	0 (0.0)	5 (4.9)	0 (0.0)	**10 (0.8)**
Planned caesarean section n(%)[a]	13 (26.5)	15 (34.1)	28 (38.9)	43 (43.9)	N/A	285 (69.5)	11 (11.6)	26 (25.2)	31 (59.6)	**452/907 (58.7)**
Missing n(%)	1 (1.4)	0 (0.0)	0 (0.0)	0 (0.0)	N/A	88 (18.0)	0 (0.0)	0 (0.0)	0 (0.0)	**89 (6.8)**
Gestational Age										
$22^{+0} – 23^{+6}$	1 (1.4)	0 (0.0)	0 (0)	1 (1.0)	0 (0.0)	2 (0.4)	1 (1.1)	0 (0.0)	0 (0.0)	**5/992(0.4)**
24^{+0} - 31^{+6}	9 (12.3)	2 (4.5)	4 (5.6)	6 (6.1)	24 (8.9)	31 (6.8)	5 (5.3)	11 (11.1)	3 (5.8)	**95/992 (7.5)**
$32^{+0} – 36^{+6}$	23 (31.5)	13 (29.5)	20 (27.8)	22 (22.4)	80 (29.5)	166 (36.2)	16 (16.8)	26 (25.7)	21 (40.4)	**387/992 (30.7)**
$\geq 37^{+0}$	40 (54.8)	29 (65.9)	48 (66.7)	69 (70.4)	167 (61.6)	259 (56.6)	73 (76.8)	62 (61.4)	28 (53.8)	**775/992 (61.4)**
Missing	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	5 (1.8)	31 (6.3)	0 (0.0)	4 (3.9)	0 (0.0)	**40 (3.1)**
Previous caesarean section	36 (50.0)	25 (56.8)	24 (33.3)	36 (37.9)	149 (54.0)	228 (51.0)	40 (42.1)	20 (83.3)	28 (53.8)	**586/1177 (49.8)**
Missing n(%)	1 (1.4)	0 (0.0)	0 (0.0)	3 (3.1)	0 (0.0)	42 (8.6)	0 (0.0)	79 (76.7)	0 (0.0)	**125 (9.6)**

All data are presented as n (%) or mean ± standard deviation unless otherwise specified. Percentages are calculated after subtracting missing data.
[a]Presented as percentage of number of caesarean sections.

Table 3. Most important indication for peripartum hysterectomy presented as n (%).

Indications of hysterectomy	Belgium (n=73)	Denmark (n=44)	Finland (n=72)	France (n=98)	UK (n=276)	Italy (n=489)	Netherlands (n=95)	Slovakia (n=103)	Sweden (n=52)	Total (n=1302)
Uterine atony	29 (39.7)	12 (27.3)	17 (23.6)	42 (42.9)	98 (35.5)	199 (40.7)	34 (35.8)	18 (17.5)	10 (19.2)	459 (35.3)
Abnormally invasive placenta	14 (19.2)	17 (38.6)	16 (22.2)	23 (23.5)	103 (37.3)	188 (38.4)	36 (37.9)	30 (29.1)	26 (50)	453 (34.8)
Uterine rupture	10 (13.7)	2 (4.5)	17 (23.6)	9 (9.2)	17 (6.2)	14 (2.9)	10 (10.5)	16 (15.5)	3 (5.8)	98 (7.5)
Unspecified Haemorrhage	5 (6.8)	0	11 (15.3)	2 (2)	0	44 (9)	8 (8.4)	16 (15.5)	7 (13.5)	93 (7.1)
Placenta previa	0	0	9 (12.5)	2 (2)	41 (14.9)	15 (3.1)	4 (4.2)	11 (10.7)	2 (3.8)	84 (6.5)
Placental abruption	0	2 (4.5)	0	6 (6.1)	2 (0.7)	20 (4.1)	0	2 (1.9)	2 (3.8)	34 (2.6)
Cervical laceration	0	6 (13.6)	2 (2.8)	0	2 (0.7)	4 (0.8)	1 (1.1)	0	0	15 (1.2)
Fibroids	0	2 (4.5)	0	0	1 (0.4)	2 (0.4)	1 (1.1)	0	2 (3.8)	8 (0.6)
DIC[a]	0	0	0	6 (6.1)	1 (0.4)	1 (0.2)	0	0	0	8 (0.6)
Infection	0	0	0	1 (1)	0	0	1 (1.1)	0	0	2 (0.2)
Other	2 (2.7)	3 (6.8)	0	7 (7.1)	8 (2.9)	2 (0.4)	0	3 (2.9)	0	25 (1.9)
Missing	13 (17.8)	0	0	0	3 (1.1)	0	0	7 (6.8)	0	23 (1.8)

DIC, disseminated intravascular coagulopathy

Table 4. Relative risk of peripartum hysterectomy for caesarean section compared to vaginal birth

Country	Caesarean section rate (%)	Caesarean section			Vaginal birth			Relative risk
		Number of PRH [a]	Number of CS [b]	Prevalence* (95% CI [c])	Number of PRH	Number of vaginal births	Prevalence* (95% CI)	
Belgium	21.5	49	54 369	9.0 (6.8 - 11.9)	23	197 903	1.2 (0.7 - 1.7)	7.8 (4.7 - 12.7)
Denmark	21.3	36	35 821	10.1 (7.3 - 13.9)	8	132 349	0.6 (0.3 - 1.2)	16.6 (7.7 - 35.8)
Finland	16.2	52	23 542	22.1 (16.9 - 29.0)	20	122 004	1.6 (1.1 - 2.6)	13.5 (8.0 - 22.6)
France	21.5	67	39 194	17.1 (13.5 - 21.7)	31	143 115	2.2 (1.5 - 3.1)	7.9 (5.2 - 12.1)
Italy	38.5	410	176 713	23.2 (21.1 - 25.6)	75	282 282	2.6 (2.1 - 3.3)	8.8 (6.8 - 11.2)
The Netherlands	15.0	59	53 762	11.0 (8.5 - 14.2)	36	305 112	1.2 (0.9 - 1.6)	9.3 (6.1 - 14.1)
Slovakia	30.5	51	44 826	11.4 (8.7 - 15.0)	47	102 146	4.6 (3.5 - 6.1)	2.5 (1.7 - 3.7)
Sweden	16.7	46	29 327	15.7 (11.8 - 20.9)	6	146 248	0.4 (0.2 - 0.9)	38.2 (16.3 - 89.5)
United Kingdom	23.5	226	143 185	15.8 (13.9 - 18.0)	50	466 115	1.1 (0.8 - 1.4)	14.7 (10.8 - 20.0)
Total	24.0	996	600 739		296	1 897 274		9.1 (8.0-10.4)

[a] PRH: peripartum hysterectomy, [b] CS: Caesarean sections, [c] CI: Confidence Interval, *Prevalence per 10 000 births or caesarean sections.

Table 5. Relative Risk of peripartum hysterectomy for women with versus without previous caesarean section.

Country	% of women with previous CS	With previous caesarean section			Without previous caesarean section			Relative risk
		PRH [a] (n)	Births (n)	Prevalence (95% CI) *	PRH [a] (n)	Births (n)	Prevalence (95% CI [b]) *	
Belgium	10.7	36	27 007	13.3 (9.6 - 18.5)	36	225 265	1.6 (1.2 - 2.2)	8.3 (5.3 - 13.2)
Denmark	11.6	25	19 626	12.7 (8.6 - 18.8)	19	148 544	1.3 (0.8 - 2.0)	10.0 (5.5 - 18.1)
Finland	9.7	24	14 167	16.9 (11.4 - 25.2)	48	131 379	3.7 (2.8 - 4.8)	4.6 (2.8 - 7.6)
France	12.3	36	22 424	16.1 (11.6 - 22.2)	59	159 885	3.7 (2.9 - 4.8)	4.4 (2.9 - 6.6)
Italy	16.8	228	77 111	29.6 (25.9 - 33.7)	74	381 884	1.9 (1.5 - 2.4)	13.9 (10.7 - 18.1)
Netherlands	10.4	40	37 343	10.7 (7.9 - 14.6)	55	321 531	1.7 (1.3 - 2.2)	6.3 (4.2 - 9.4)
Slovakia	Data not available							
Sweden	8.9	28	15 698	17.8 (12.3 - 25.8)	24	159 877	1.5 (1.0 - 2.2)	11.9 (6.9 - 20.5)
United Kingdom	6.6	149	40 600	36.7 (31.3 - 43.1)	127	568 700	2.2 (1.9 - 2.7)	16.4 (13.0 - 20.8)
Total	10.9	566	253 976		442	2 097 065		10.6 (9.3 - 12.0)

[a] PRH: peripartum hysterectomy, [b] CI: Confidence Interval, *Prevalence per 10 000 births or caesarean sections.

DISCUSSION

The prevalence of peripartum hysterectomy varied significantly in nine European countries. Prevalence was considerably higher in women giving birth by caesarean section and in women who had given birth by caesarean section in a previous pregnancy. Additionally, indications for hysterectomy also varied notably between countries and considerable variance was observed for all reported indications. Such differences may result from differences in women's characteristics, national caesarean section rates, and national rates of pregnant women with scarred uteri. Such differences may also reflect differences in clinical management of major obstetric haemorrhage between participating countries.

Compared with a systematic review and meta-analysis where weighted prevalence for upper- and high-income countries was calculated at 7 per 10,000 births, our study demonstrated lower prevalence for all countries except Italy.[10] Another study on emergency peripartum hysterectomy in high-income countries, reported prevalence for most European countries <10 per 10,000 births, in line with our results.[8]

We found a nine-fold higher risk of hysterectomy after caesarean section. However, 77% of women undergoing hysterectomy were delivered by caesarean section and more than half of these were planned. Reason for this may be antenatal diagnosis of placenta previa with or without abnormally invasive placenta, in which case vaginal birth is not an option and risk of hysterectomy is very high.[27] The number of planned caesarean hysterectomies was not known. Therefore, we repeated calculations after excluding women who had hysterectomy for abnormally invasive placenta, which was the second most frequent indication among all hysterectomies. In these women, it is the indication for the caesarean section that places them at increased risk of hysterectomy rather than the indication itself. Some of these hysterectomies might in fact have been planned before birth. However, even following exclusion of women with abnormally invasive placenta, the prevalence of hysterectomy after caesarean section and in birth following a previous caesarean section both remained significantly higher. Our results are in line with literature, where caesarean section is a strong risk factor for emergency peripartum hysterectomy.[8] Increased risk of hysterectomy after previous caesarean section has been shown before and was demonstrated to be independent of the intended mode of birth.[8,28] As such, the variance of prevalence between countries might, to a considerable extent, be explained by the difference in national caesarean section rates.

The strength of this study is its unique multinational character including data from nine nationwide or multiregional studies. Collaboration between national and multiregional obstetric survey systems previously led to insights into prevalence and management of uterine rupture.[26] The INOSS collaboration enables the collection of considerably robust data regarding rare obstetric diseases.

Main limitations arise from the fact that included studies were performed in different time intervals, over 2 or 3 consecutive years with little or no overlap. Obstetric practice and risk factors such as caesarean section rates might have changed over time.[8,13,29] Data stratified by year would reflect differences between studies rather than being indicative of changes in practice over time. However, pooling data from recent and older studies showed a marked difference in prevalence of hysterectomy which, in light of other evidence, may be the result of rising caesarean section rates. Furthermore, there were 40 registered hysterectomies with missing information on gestational age. Given the fact that only 1% of all hysterectomies in the database were excluded because of a gestational age <22 weeks, we opted that excluding these cases would lead to exclusion of actually valid cases, which would lead to underestimation of prevalence. Also, a previous caesarean section is strongly associated with birth by caesarean in the index pregnancy. In the calculation of the correlation between prevalence of hysterectomy and mode of birth, previous caesarean section should be taken into consideration. As such, calculation of adjusted relative risks for each exposure would have led to better estimation of the independent role of each of them. However, for the background data we only had aggregate numbers for mode of birth and for previous caesarean section and could not perform such analysis. Accordingly, in the correlation of prevalence of peripartum hysterectomy with previous caesarean section, taking parity into account would lead to more valid results. Also, the number of previous caesarean sections adds up to the risk of hysterectomy and other serious morbidity with every additional operation, as previously described.[9] Unfortunately, in our database we only had access to binary information on presence of a previous caesarean section. Therefore, the effect of number of previous caesareans was not measured. Another limitation is the fact that case identification and study objectives differed between countries. Seven of nine studies were designed specifically to report peripartum hysterectomy whereas the studies from the Netherlands and France included women with severe maternal morbidity. In Slovakia, data were collected retrospectively, which may have led to some underreporting. Nonetheless, their numbers still gave them the second highest prevalence; actual prevalence may have been even higher.

For enhanced comparability of national survey studies, collectively designed surveillance studies using uniform criteria are required and INOSS may provide an important platform to perform such studies. In addition, use of a uniform definition for upcoming studies is important. Therefore, INOSS proposed a definition of 'pregnancy-related hysterectomy' using a Delphi process:[1] "Surgical removal of the uterus during pregnancy or up to 42 days postpartum". This definition is wide enough to include all indications and pregnancy intervals. As our specific study includes only a subset of women who had a hysterectomy around the time of birth, we decided to apply the common terminology "peripartum hysterectomy" in this

paper. Streamlining multiple national surveys is necessary to overcome problems related to different study intervals.

CONCLUSION

Prevalence of peripartum hysterectomy varied widely between countries and was higher in countries with higher caesarean section rates. Commonest indications were uterine atony and abnormally invasive placenta. Rate of peripartum hysterectomy was considerably higher in women who gave birth by caesarean section as well as in women with a previous caesarean section. Further investigation is necessary to fully understand the underlying factors that contribute to these differences. Further work is needed to determine optimal management strategies and comparison of those strategies between countries.

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SUPPORTING INFORMATION

Table S1. Methodology of case collection for each participating country and summary of background data of total number of births.

Country	Methodology	Background data
Denmark (NOSS) Apr '09-Dec '11	Clinicians in each maternity unit reported peripartum hysterectomies spontaneously through electronic or paper data collection forms.	Births ≥22 weeks of gestational age
Finland (NOSS) Apr '09-Aug '11	Clinicians in each maternity unit reported peripartum hysterectomies spontaneously through electronic or paper data collection forms.	Births ≥22 weeks of gestational age
Sweden (NOSS) Sep '09-Aug '11	Monthly mailing to appointed clinician in each maternity unit. When a case was reported, further details were requested through a data collection form. 'Nothing to report' response requested.	Births ≥22 weeks of gestational age
Italy (ITOSS) Sep '14-Aug '16	Maternity units reported cases through electronic collection forms followed by a monthly reminder by e-mail to promote complete reporting.	Births from 25+6 weeks of gestational age
France (EPIMOMS) May '12-Nov '13	Maternity units reported cases through electronic collection forms followed by a monthly reminder by e-mail to promote complete reporting.	Births ≥22 weeks of gestational age
Belgium (B.OSS) Jan '12- Dec '13	Monthly mailing to appointed clinician in each maternity unit. When a case was reported, further details were requested through a data collection form. 'Nothing to report' response requested.	Births ≥22 weeks of gestational age
The Netherlands (LEMMoN) Aug '04-Aug '06	Monthly mailing to maternity units to report women with severe maternal morbidity. All women with hysterectomy because of obstetric haemorrhage during pregnancy, delivery, and puerperium (limited to 6 weeks after delivery) were included. 'Nothing to report' response requested.	Births ≥24 weeks of gestational age
UK (UKOSS) Feb '05-Feb '06	Monthly mailing to appointed clinician in each maternity unit. When a case was reported, further details were requested through a data collection form. 'Nothing to report' response requested.	Births of any gestational age, including stillbirths ≥24 weeks
Slovakia (SOSS) Jan '12-Dec '14	Women who underwent peripartum hysterectomy in the year before were identified after correspondence with all maternity units. Questionnaire with additional information was filled for every case.	Births ≥24 weeks of gestational age

Table S2. National definitions of peripartum hysterectomy.

Country	Definition	Minimum gestational age	Postpartum period (days)
Denmark (NOSS) Apr '09-Dec '11	Delivery at or after 22 +0 gestational weeks and subsequent hysterectomy performed within 1 week of delivery	22+0	7
Finland (NOSS) Apr '09-Aug '11	Delivery at or after 22 +0 gestational weeks and subsequent hysterectomy performed within 1 week of delivery	22+0	7
Sweden (NOSS) Sep '09-Aug '11	Delivery at or after 22 +0 gestational weeks and subsequent hysterectomy performed within 1 week of delivery	22+0	7
Italy (ITOSS) Sep '14-Aug '16	Delivery at or after 22 +0 gestational weeks and subsequent hysterectomy performed within 1 week of delivery due to obstetric haemorrhage	22+0	7
France (EPIMOMS) May '12-Nov '13	Hysterectomy performed during pregnancy or in the 42 days postpartum, in a woman having Severe Acute Maternal Morbidity according to a multicriteria definition	22+0	42
Belgium (B.OSS) Jan '12- Dec '13	Any woman giving birth to a fetus or infant and undergoing a hysterectomy in the same clinical episode	none	42
The Netherlands (LEMMoN) Aug '04-Aug '06	Hysterectomy performed during pregnancy or in the 42 days postpartum, in a woman with Severe Acute Maternal Morbidity	none	42
UK (UKOSS) Feb '05-Feb '06	Any woman giving birth to a fetus or infant and undergoing a hysterectomy in the same clinical episode	none	42
Slovakia (SOSS) Jan '12-Dec '14	Acute hysterectomy within 48 hours from labor	none	2

Table S3. Relative risk of peripartum hysterectomy for caesarean section compared to vaginal birth after excluding hysterectomies due to abnormally invasive placenta.

Country	Caesarean section			Vaginal birth			Relative risk
	Number of PRH[a]	Number of CS[b]	Prevalence* (95% CI[c])	Number of PRH	Number of vaginal births	Prevalence* (95% CI)	
Belgium	38	54 369	7.0 (5.1 - 9.6)	20	197 903	1.0 (0.6 - 1.6)	6.9 (4.0 - 11.9)
Denmark	20	35 821	5.6 (3.6 - 8.6)	7	132 349	0.5 (0.3 - 1.1)	10.6 (4.5 - 25.0)
Finland	37	23 542	15.7 (11.4 - 21.7)	19	122 004	1.6 (1.0 - 2.4)	13.1 (7.7 - 22.3)
France	48	39 194	12.2 (9.2 - 16.2)	27	143 115	1.9 (1.3 - 2.7)	6.5 (4.1 - 11.4)
Italy	234	176 713	13.2 (11.7 - 15.0)	63	282 282	2.2 (1.7 - 2.9)	5.9 (4.5 - 7.8)
The Netherlands	35	53 762	6.5 (4.7 - 9.1)	24	305 112	0.8 (0.5 - 1.2)	8.3 (4.9 - 13.9)
Slovakia	33	44 826	7.4 (5.2 - 10.3)	35	102 146	3.4 (2.5 - 4.8)	2.1 (1.3 - 3.5)
Sweden	21	29 327	7.2 (4.6 - 10.9)	5	146 248	0.3 (0.1 - 0.8)	21.0 (7.9 – 55.6)
United Kingdom	135	143 185	9.4 (8.0 - 11.2)	38	466 115	0.8 (0.6 - 1.1)	11.6 (8.1 - 16.6)
Total	601	600 739		211	1 897 274		9.0 (7.7 - 10.5)

[a] PRH: peripartum hysterectomy, [b] CI: Confidence Interval, *Prevalence per 10 000 births or caesarean sections.

Table S4. Relative risk of peripartum hysterectomy for women with a history of previous caesarean section compared women without previous caesarean section after excluding hysterectomies due to abnormally invasive placenta.

Country	% of women with previous CS	With previous caesarean section			Without previous caesarean section			Relative risk
		PRH [a] (n)	Births (n)	Prevalence (95% CI [b]) *	PRH (n)	Births (n)	Prevalence (95% CI) *	
Belgium	10.7	27	27 007	10.0 (6.9 - 14.5)	31	225 265	1.4 (1.0 - 2.0)	7.3 (4.3 - 12.2)
Denmark	11.6	12	19 626	6.1 (3.5 - 10.7)	15	148 544	1.0 (0.6 - 1.7)	6.1 (2.8 - 12.9)
Finland	9.7	14	14 167	9.8 (5.9 – 16.6)	42	131 379	3.2 (2.4 - 4.3)	3.1 (1.7 – 5.7)
France	12.3	20	22 424	8.9 (5.8 – 13.8)	52	159 885	3.3 (2.5 - 4.3)	2.7 (1.6 – 4.6)
Italy	16.8	82	77 111	10.6 (8.6 - 13.2)	39	381 884	1.0 (0.7 - 1.4)	10.4 (7.1 – 15.3)
Netherlands	10.4	17	37 343	4.6 (2.8 – 7.3)	42	321 531	1.3 (0.9 - 1.8)	3.5 (2.0 - 6.1)
Slovakia				Data not available				
Sweden	8.9	11	15 698	7.0 (3.9 - 12.5)	15	159 877	0.9 (0.6 - 1.5)	7.5 (3.4 – 16.3)
United Kingdom	6.6	69	40 600	17.0 (13.4 – 21.5)	102	568 700	1.7 (1.5 - 2.2)	9.5 (7.0 - 12.9)
Total	10.9	254	253 976		338	2 097 065		6.2 (5.3 – 7.3)

[a] PRH: peripartum hysterectomy, [b] CI: Confidence Interval , * Prevalence per 10 000 births.