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Trends in postpartum hemorrhage and manual removal of the placenta and the association with childbirth interventions: A Dutch nationwide cohort study

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Abstract

Background: Because the cause of increasing rates of postpartum hemorrhage (PPH) and manual placental removal (MROP) is still unknown, we described trends in PPH, MROP, and childbirth interventions and examined factors associated with changes in rates of PPH and MROP.

Methods: This nationwide cohort study used national perinatal registry data from 2000 to 2014 ($n = 2{,}332{,}005$). We included births of women who gave birth to a term singleton child in obstetrician-led care or midwife-led care. Multivariable logistic regression analyses were used to examine associations between characteristics and interventions, and PPH ≥ 1000 mL and MROP.

Results: PPH rates increased from 4.3% to 6.6% in obstetrician-led care and from 2.5% to 4.8% in midwife-led care. MROP rates increased from 2.4% to 3.4% and from 1.0% to 1.4%, respectively. A rising trend was found for rates of induction and augmentation of labor, pain medication, and cesarean section, while rates of episiotomy and assisted vaginal birth declined. Adjustments for characteristics and childbirth interventions did not result in large changes in the trends of

PPH and MROP. After adjustments for childbirth interventions, in obstetrician-led care, the odds ratio (OR) of PPH in 2014 compared with the reference year 2000 changed from 1.66 (95% CI 1.57–1.76) to 1.64 (1.55–1.73) among nulliparous women and from 1.56 (1.47–1.66) to 1.52 (1.44–1.62) among multiparous women. For MROP, the ORs changed from 1.51 (1.38–1.64) to 1.36 (1.25–1.49) and from 1.56 (1.42–1.71) to 1.45 (1.33–1.59), respectively.

Conclusions: Rising PPH trends were not associated with changes in population characteristics and rising childbirth intervention rates. The rising MROP was to some extent associated with rising intervention rates.

KEYWORDS

interventions, manual removal of the placenta, postpartum hemorrhage, trends

1 | INTRODUCTION

Over the last years, rising rates of postpartum hemorrhage (PPH) of more than 1000 mL in high-income countries have been reported.[1,2] Although maternal mortality is very rare in these countries, PPH is one of its major causes as well as a cause of severe maternal morbidity.[3] Therefore, the fact that PPH rates are rising is a subject of concern. Only a few studies provide insight into possible contributing factors to these rising rates.[4–7] One study showed that the rising rate was primarily due to an increase in uterine atony, which was not associated with rising childbirth intervention rates.[8] In contrast, another study showed that this trend was associated with rising rates of previous cesarean section (CS) and augmentation of labor.[7] However, both studies neglect the association between PPH and manual removal of the placenta (MROP). A retained placenta is associated with approximately 18% of cases of PPH.[9] Conversely, a retained placenta is accompanied by PPH in 61% of cases.[10] Because PPH and MROP are strongly correlated, these outcomes cannot be seen as independent of each other. However, simply adjusting the outcomes for one another neglects the potential causal pathway between MROP and PPH. Besides, other childbirth interventions may be associated with PPH.[2,11] A rise in incidence of some childbirth interventions, such as the global CS rate which has increased from 12% in 2000 to 21% in 2015,[12] raises questions about the contributing factor of childbirth interventions to the rising PPH rate in high-income countries.

In the Netherlands, low-risk women give birth under the responsibility of community midwives, i.e., midwife-led care, and can choose to give birth at home or in the hospital. If risks increase, complications occur, or childbirth interventions such as induction or augmentation of labor, request for pain relief, assisted vaginal birth, or cesarean section are needed, women are referred to obstetrician-led care.[13] Also in the Netherlands, rates of some childbirth interventions have risen over the last years.[2] Describing the incidence of PPH and MROP over earlier years in both obstetrician-led care and midwife-led care will provide more insight into contributing factors to the increase in these adverse maternal outcomes among both medium- or high-risk and low-risk women (i.e., obstetrician-led care or midwife-led care). In this study, trends in incidences of PPH, MROP, and childbirth interventions from 2000 to 2014 were described, and factors were examined which may be associated with the trends in MROP and PPH among subgroups of women in obstetrician-led care or midwife-led care.

2 | METHODS

2.1 | Data collection

For this nationwide study, data were used from the Dutch national perinatal registry 'Perined', which covers 98% of all births in the Netherlands.[14] Births in midwife-led care are registered in the national perinatal database 1, births in obstetrician-led care in the national perinatal database 2, and data from pediatric care in the national neonatal register. These databases are combined by means of a validated linkage method into a complete Perined register.[15]

We included all births of single-term children between 2000 and 2014 registered in the perinatal database. We excluded cases with missing information on gestational age, on whether there was a multiple pregnancy, or on parity. Women who were referred from midwife-led care to obstetrician-led care during or after labor were also excluded if information from database 1 was missing.

2.2 | Selection of variables

For most variables, Perined has created combined variables based on the different national perinatal databases. However, not all combined variables were appropriate for the analyses of the current study. Therefore, we redefined the following variables: PPH, MROP, ethnic background, socioeconomic status, disorders in the current pregnancy, previous PPH/MROP/CS, augmentation of labor, and pain medication.

2.2.1 | Definition of outcomes

Primary outcomes were PPH of ≥1000 mL in the first 24 h after birth and MROP, both defined as yes or no. Blood loss was estimated and measured by the attending care provider in either obstetrician-led care or midwife-led care. For MROP, women with a CS were excluded, because the placenta is always manually removed during the operation.

2.2.2 | Definition of characteristics

Maternal characteristics were as follows: parity (nulliparous, multiparous para 1–2, multiparous ≥3); maternal age (<20, 20–24, 25–29, 30–34, 35–9, ≥40 years); ethnic background (Dutch, non-Dutch); socioeconomic status (low, middle, high); hypertensive disorders (yes, no); coagulation disorders (yes, no); previous CS among multiparous women (yes, no); previous PPH among multiparous women (yes, no); and previous MROP among multiparous women (yes, no). Socioeconomic status was based on the level of education, employment, and income of the total population in the Netherlands for each postal code, as calculated by the Netherlands Institute for Social Research (SCP). Hypertensive disorders comprised hypertension, preeclampsia, HELLP-syndrome, eclampsia, and non-infectious proteinuria in the current pregnancy. Coagulation disorders included all codes for HELLP and coagulation disorders in the current pregnancy.

Neonatal characteristic was birthweight (<3000, 3000–3999, ≥4000 g). Birth characteristics were as follows: gestational age at birth (37 + 0–37 + 6, 38 + 0–40 + 6, 41 + 0–41 + 6, ≥42 weeks) and obstetric anal sphincter injury (yes, no). Care provider characteristic was as follows: responsible care provider at the time of birth (obstetrician, midwife).

2.2.3 | Childbirth interventions

Induction of labor included all pharmacological and mechanical methods to stimulate uterine contractions before spontaneous rupture of membranes and uterine contractions. Women with an induced labor were excluded from the variable augmentation of labor. Prelabor CS was defined as a CS before rupture of membranes and uterine contractions. A CS which occurred after the membranes ruptured or the start of uterine contractions was defined as intrapartum CS. Women with a prelabor CS were excluded from the variable pain medication during labor. Other methods for pharmacological pain relief were specified in the Perined register as sedatives, non-opioid analgesia, and opioid analgesia. Mostly, this would have been pethidine injections or patient-controlled remifentanil.[16] Women with a prelabor or intrapartum CS were excluded from the analyses for episiotomy.

2.3 | Data analyses

2.3.1 | Characteristics and trend graphs

Characteristics were described in numbers and percentages of the total study population, and in percentages in the years 2000 and 2014. Trend graphs were shown for the incidences of primary outcomes and childbirth interventions and the significance ($p < 0.05$) was estimated with a chi-squared test.

2.3.2 | Trend analyses

Incidences of PPH and MROP were described in both obstetrician-led care and midwife-led care in the years 2000 and 2014, stratified for parity. The ratio of CS to assisted vaginal births was calculated by dividing the CS rate by the assisted vaginal birth rate.[17] Univariable logistic regression analyses were conducted to estimate the odds ratio (OR) with accompanying 95% confidence intervals (CI) of the primary outcomes for each year compared with the year 2000 as the reference. In addition, multivariable logistic regressions were conducted to examine which factors were associated with the trend in the primary outcomes. In model 1, adjustments were made for population characteristics and in model 2, adjustments were added for induction or augmentation of labor, cesarean section, and pain medication, because the rate of these interventions has increased over the study period. For women in midwife-led care, only model 1 was performed, because interventions in model 2 are not performed in midwife-led care.

We did not apply adjustments for MROP when analyzing the trend in PPH, and vice versa. PPH and MROP can be causally related to each other. However, the direction of the causal path is not similar in all cases. By adjusting

for the other outcome variable, we would assume that in all cases in the analyses, the causal direction is similar and that the other outcome variable may be associated with the trend. In this cohort study, it is not possible to examine the direction of the causal pathway with respect to these outcome variables.

2.3.3 | Childbirth interventions

All analyses concerning childbirth interventions and primary outcomes were stratified for parity. Descriptive analyses and univariable logistic regression analyses were performed to show the numbers, incidences, and OR (95% CI) of primary outcomes for each childbirth intervention. Multivariable logistic regression analyses were conducted to adjust for possible confounding. In model 1, adjustments were made for maternal age, ethnic background, socioeconomic status, hypertensive disorders, coagulation disorders, birth weight, and year of birth. For multiparous women, adjustments for previous CS, previous PPH, and previous MROP were added. In model 2, adjustments for induction of labor, augmentation after spontaneous onset of labor, mode of birth, pain medication during labor, and episiotomy were added. We decided not to adjust for differences in gestational age, because of collinearity with induction of labor. Equally, induction and augmentation of labor were combined in one variable for the adjustments because of collinearity. For CS, no adjustments were made for episiotomy, because an episiotomy in combination with cesarean section rarely occurs.

In all logistic regression analyses, a CI of 95% was used. The percentage of missing data was lower than 5% for all variables and therefore, multiple imputation was not performed. Statistical analyses were performed using STATA version 14 (StataCorp).

3 | RESULTS

3.1 | Characteristics

The total number of women in this study was 2,332,005 (Figure 1). Population characteristics are shown in Table 1. Women in 2014 were older and more frequently of non-Dutch ethnic background compared with women in 2000. In addition, the incidence of hypertensive disorders decreased from 6.4% to 6.2% and the previous CS rate increased from 11.1% to 14.4%. The incidence of a birthweight ≥4000 g decreased from 16.4% in 2000 to 14.5% in 2014 and a gestational age of ≥42 weeks decreased from 6.1% to 1.4%. While 40.1% of women in 2000 received midwife-led care at the time of birth, this percentage decreased to 29.1% in 2014.

The overall incidences in the total study population for the years 2000–2014 were 4.9% for PPH and 2.5% for MROP (data not shown).

3.2 | Trends of PPH and MROP

Trends of incidences in primary outcomes between 2000 and 2014 are shown in Figures 2A,B. Figure 3 shows the trend in incidences of childbirth interventions. All trends were significant with a p-value <0.001. For women in obstetrician-led care at the time of birth, incidences of primary outcomes increased from 4.3% to 6.6% for PPH over the years, and from 2.4% to 3.4% for MROP. In midwife-led care, incidences of primary

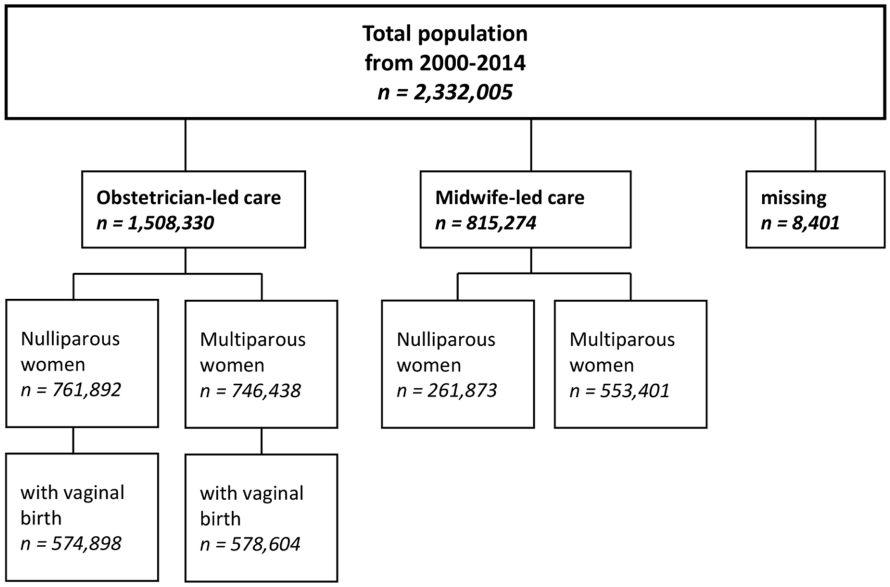

FIGURE 1 Flowchart of the included study population.

TABLE 1 Maternal, neonatal, birth, and care provider characteristics of births for the years 2000 and 2014 separately ($n = 2{,}332{,}005$).

	Total, *n*	% in 2000	% in 2014
Maternal characteristics			
Parity			
Nulliparous	1,028,656	44.8	43.9
Multiparous para 1–2	1,171,717	49.4	50.2
Multiparous para ≥3	131,632	5.8	5.9
Maternal age			
<20 years	33,961	1.7	1.0
20–24 years	232,422	9.5	9.5
25–29 years	681,839	30.5	30.9
30–34 years	902,168	40.5	38.2
35–39 years	413,027	15.7	17.2
≥40 years	65,831	2.1	3.3
Ethnic background			
Dutch	1,856,938	82.4	77.3
Non-Dutch	456,789	17.6	22.8
Socioeconomic status			
Low	615,726	26.0	27.4
Middle	1,075,151	47.5	47.1
High	598,861	26.5	25.5
Hypertensive disorders			
Yes	144,686	6.4	6.2
No	2,187,319	93.6	93.8
Coagulation disorders			
Yes	14,669	0.7	0.6
No	2,317,336	99.3	99.4
Previous CS among multiparous women			
Yes	165,852	11.1	14.4
No	1,137,497	88.9	85.6
Previous PPH among multiparous women			
Yes	33,850	3.2	2.8
No	1,269,499	96.8	97.2
Previous MROP among multiparous women			
Yes	12,587	1.1	1.0
No	1,290,762	98.9	99.0
Neonatal characteristics			
Birthweight			
<3000 g	323,359	14.5	14.4
3000–3999 g	1,627,872	69.1	71.1
≥4000 g	379,270	16.4	14.5
Birth characteristics			
Gestational age at birth			
37 + 0 – 37 + 6 weeks	153,035	6.5	7.6
38 + 0 – 40 + 6 weeks	1,643,191	69.1	73.1
41 + 0 – 41 + 6 weeks	437,691	18.3	17.9
≥42 weeks	98,088	6.1	1.4
Obstetric anal sphincter injury			
Yes	52,599	2.4	2.5
No	1,930,589	97.6	97.5
Care provider			
Responsible care provider at the time of birth			
Obstetrician	1,508,330	59.9	70.9
Midwife	815,274	40.1	29.1

Note: Percentages of missing data: 0% for parity, 0.1% for maternal age, 0.8% for ethnic background, 1.9% for socioeconomic status, 0% for hypertensive disorders, 0% for coagulation disorders, 0% for previous CS, 0% for previous PPH, 0% for previous MROP, 0.1% for birthweight, 0% for gestational age at birth, 1.1% for obstetric anal sphincter injury, and 0.4% for responsible care provider.

outcomes increased from 2.5% to 4.1% for PPH over the years, and from 1.0% to 1.5% for MROP.

Rates of the following childbirth interventions increased: pain medication, augmentation of labor, induction of labor, and CS, whereas rates of assisted vaginal birth and episiotomy decreased. The ratio of CS to assisted vaginal births increased from 1 CS to 1 assisted vaginal birth in 2000 to 2 CSs to 1 assisted birth in 2014.

The increase in primary outcomes was statistically significant for both primary outcomes and remained significant after adjustments for available characteristics (Tables 2 and 3 and Supplementary Tables S1-S4). Adjustments for characteristics and childbirth interventions did not alter the ORs of the PPH trend. The increased trend of MROP was larger after adjustments for characteristics and decreased after adjustments for induction or augmentation of laborand pain medication during labor among women in obstetrician-led care.

3.3 | Childbirth interventions

All birth interventions provided for either nulliparous or multiparous women, except for other pharmacological pain relief, showed significant positive or negative associations with PPH and MROP. After adjustments, these associations slightly decreased but the estimator of interest remained significant (Table 4 and 5), except for the

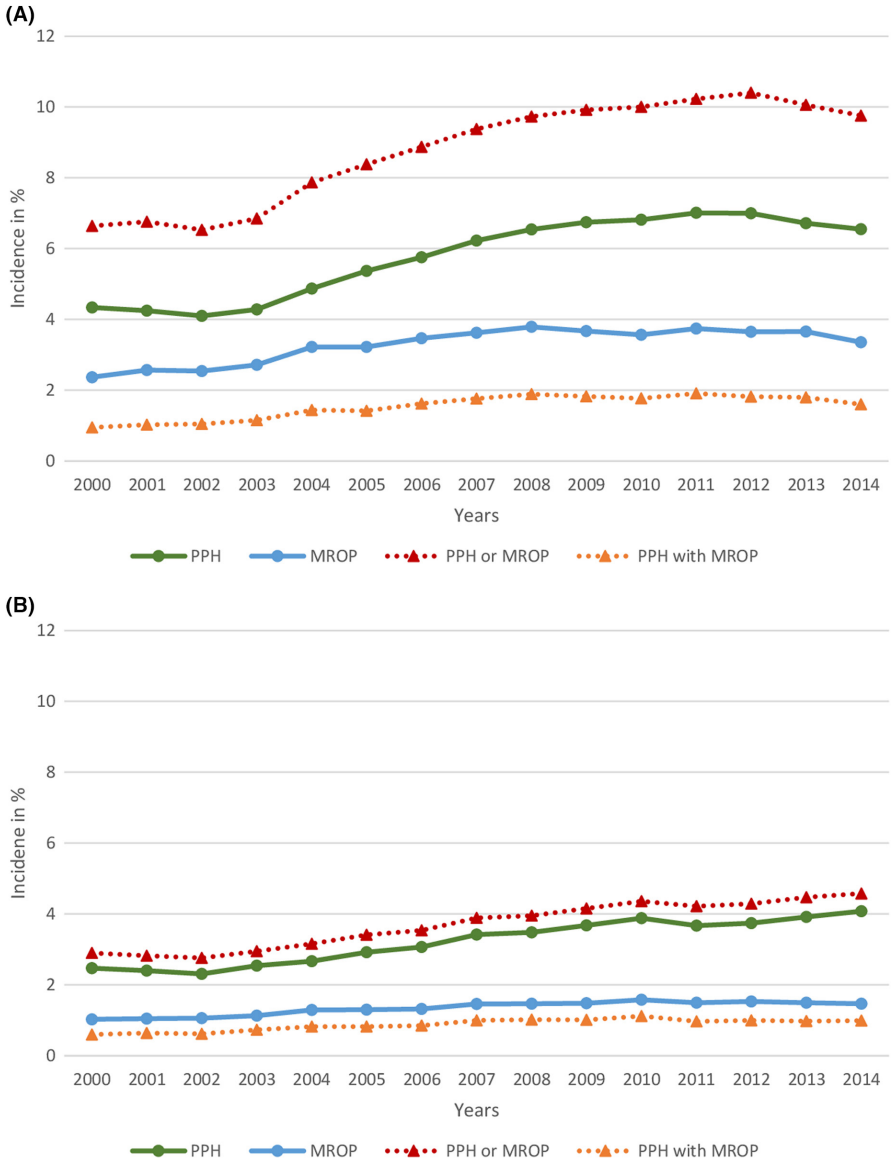

FIGURE 2 (A) Trend in incidences of postpartum hemorrhage (PPH) and manual removal of the placenta (MROP) between 2000 and 2014 for women in obstetrician-led care at the time of birth ($n = 1{,}508{,}330$). (B) Trend in incidences of PPH and MROP between 2000 and 2014 for women in midwife-led care at the time of birth ($n = 815{,}274$). [Color figure can be viewed at wileyonlinelibrary.com]

association between induction of labour without oxytocin and MROP and other pharmacological pain relief and MROP among nulliparous women (Table 4).

A higher incidence of induction of labor with oxytocin use was found, compared with induction without oxytocin use. The aOR (model 2) of the association between induction and PPH was 1.29 (95% CI 1.26–1.32) among nulliparous and 1.34 (95% CI 1.31–1.37) among multiparous women. The association between induction with oxytocin and MROP among nulliparous women was comparable to PPH and slightly stronger among multiparous women (1.60; 95% CI 1.54–1.66). A similar pattern was found for augmentation of labor, with stronger associations between augmentation and MROP than PPH.

Although the incidence of PPH was lower for women who gave birth by CS compared with vaginal birth if they were nulliparous, this incidence was higher in multiparous women. A higher incidence of MROP was found among both nulliparous and multiparous women with an assisted vaginal birth compared with spontaneous birth. After adjustments, the aOR was 1.11 (95% CI 1.08–1.15) and 1.17 (95% CI 1.10–1.24), respectively.

Among nulliparous women, the lowest aOR in the association between mode of birth and PPH was reported for intrapartum CS, with an aOR of 0.53 (95% 0.52–0.55), followed by an aOR of 0.71 (95% 0.68–0.75) for prelabor CS compared with spontaneous birth.

Among both nulliparous and multiparous women, we found higher incidences of PPH and MROP among both nulliparous and multiparous women with epidural analgesia and other pharmacological pain relief compared with no pain medication. The significant association between other pharmacological pain relief and PPH became negative among nulliparous women after adjustments (aOR 0.96; 95% CI 0.94–0.98) and was not significant for MROP.

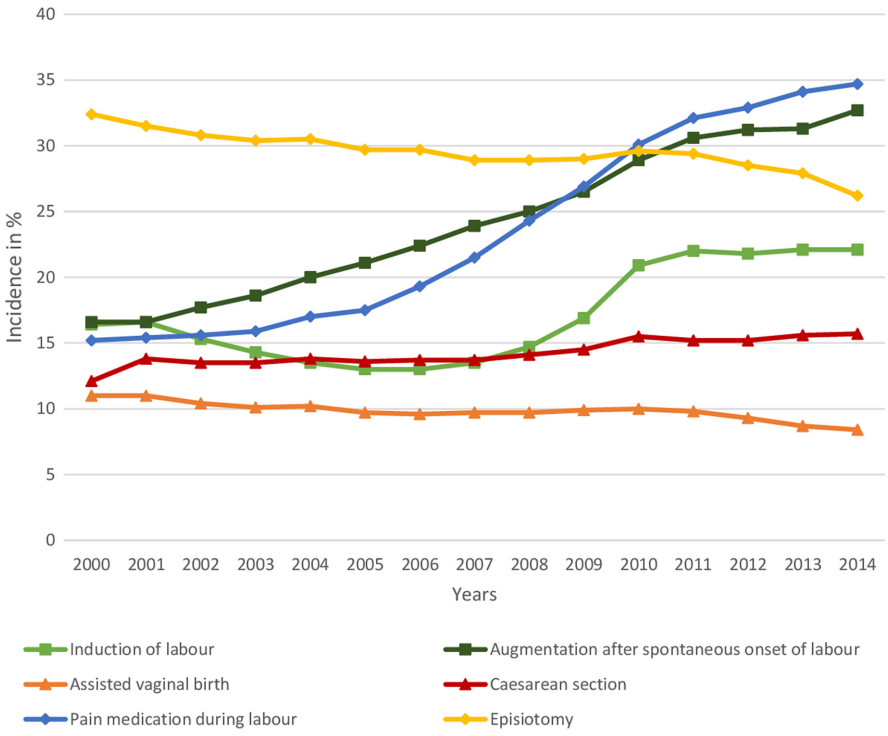

FIGURE 3 Trend in incidences of childbirth interventions during labor between 2000 and 2014 ($n = 2{,}332{,}005$). [Color figure can be viewed at wileyonlinelibrary.com]

Incidences and ORs of both PPH and MROP were increased for women with an episiotomy compared with women with no episiotomy.

4 | DISCUSSION

This nationwide cohort study carried out in the Netherlands showed a rising trend in PPH and MROP among term singleton pregnancies in both obstetrician-led care and midwife-led care at the time of birth. Rates of induction and augmentation of labor, pain medication, and CS were shown to be higher in 2014 compared with 2000, but rates of assisted vaginal birth and episiotomy (only vaginal births) in 2014 were lower when compared with those in 2000. The rising trend in PPH was not associated with a change in population characteristics or rate of childbirth interventions over the years. The rising trend in MROP was to some extent associated with rising incidences of induction or augmentation of labor and pain medication during labor.

4.1 | Limitations and strengths

Some important variables with known associations with the primary outcomes were not available in the data set, such as the maternal body mass index, underlying diseases, detailed ethnic backgrounds, and smoking. Besides, a previous study reported that the occurrence of previous CS was underreported for approximately 25% of women with a previous CS in the Dutch perinatal registry.[18] Despite this underreporting, adjusting for previous CS still influenced the ORs in our current study. Another issue in routinely collected data is reporting bias of subjective outcomes. This is particularly true for PPH, the primary outcome of this study, as the amount of blood loss is established by the responsible care provider, and is known to be underestimated when it is not weighed.[19]

A major strength of this study was the use of a nationwide registration database enabling the use of a large number of birth data, including almost all births in the Netherlands in the included years. Furthermore, most studies focus on PPH solely, without investigating MROP, or only including MROP as a confounding factor, because MROP is also a risk factor for PPH.[2,20] In our study, we were able to show that the trends for both outcomes are rising and that the number of women with both PPH and MROP followed a similar trend. Moreover, we were able to distinguish women giving birth in obstetrician-led care from women giving birth in midwife-led care at the time of birth, which clarified which subgroups' rising trends were more prevalent. Last, we were able to distinguish nulliparous from multiparous women, which is absent in most previous studies.[2,21–23]

4.2 | Interpretation and further research

Rising trends in PPH and MROP have been described previously.[1,2,23] Van Stralen et al. (2016) showed an increasing trend in the rate of PPH in the Netherlands and a decreasing trend in the rate of blood transfusion,

TABLE 2 Unadjusted and adjusted ORs of trend in PPH between 2000 and 2014 in obstetrician-led care ($n = 2{,}332{,}005$) and midwife-led care ($n = 815{,}274$) at the time of birth.

		PPH in obstetrician-led care at the time of birth					PPH in midwife-led care at the time of birth			
Year	**Total *n***	**Total *n***	**%**	**OR (95% CI)**	**aOR[a] (95% CI)**	**aOR[b] (95% CI)**	**Total *n***	**%**	**OR (95% CI)**	**aOR[c] (95% CI)**
Nulliparous women										
2000	69,395	47,442	4.6	1.00	1.00	1.00	21,953	3.3	1.00	1.00
2014	66,539	53,621	7.0	1.56 (1.48–1.65)	1.66 (1.57–1.76)	1.64 (1.55–1.73)	12,918	5.4	1.68 (1.51–1.87)	1.70 (1.53–1.90)
Multiparous women										
2000	86,069	45,255	4.1	1.00	1.00	1.00	40,814	2.0	1.00	1.00
2014	84,850	53,770	6.1	1.53 (1.44–1.62)	1.56 (1.47–1.66)	1.52 (1.44–1.62)	31,080	3.5	1.76 (1.61–1.93)	1.79 (1.63–1.96)

[a]Obstetrician-led care: adjusted for maternal age, ethnic background, socioeconomic status, hypertensive disorders, coagulation disorders, birthweight, gestational age, and obstetric anal sphincter injury.

[b]Adjusted for the factors mentioned above, and for the following childbirth interventions: induction or augmentation of labor, cesarean section, and pain medication for pain relief during labor.

[c]Midwife-led care: adjusted for maternal age, ethnic background, socioeconomic status, birthweight, gestational age, and obstetric anal sphincter injury.

TABLE 3 Unadjusted and adjusted ORs of trend in MROP among vaginal births between 2000 and 2014 in obstetrician-led care ($n = 2{,}332{,}005$) and in midwife-led care at the time of birth ($n = 815{,}274$).

		MROP in obstetrician-led care at the time of birth					MROP in midwife-led care at the time of birth			
Year	**Total *n***	**Total *n***	**%**	**OR (95% CI)**	**aOR[a] (95% CI)**	**aOR[b] (95% CI)**	**Total *n***	**%**	**OR (95% CI)**	**aOR[c] (95% CI)**
Nulliparous women										
2000	58,386	36,344	2.5	1.00	1.00	1.00	22,042	1.3	1.00	1.00
2014	53,674	40,711	3.5	1.39 (1.27–1.51)	1.51 (1.38–1.64)	1.36 (1.25–1.49)	12,963	2.2	1.67 (1.42–1.98)	1.72 (1.45–2.03)
Multiparous women										
2000	77,140	36,383	2.2	1.00	1.00	1.00	40,757	0.9	1.00	1.00
2014	71,710	40,443	3.2	1.49 (1.36–1.63)	1.56 (1.42–1.71)	1.45 (1.33–1.59)	31,267	1.2	1.36 (1.17–1.57)	1.39 (1.20–1.62)

[a]Obstetrician-led care: adjusted for maternal age, ethnic background, socioeconomic status, hypertensive disorders, coagulation disorders, birthweight, gestational age, and obstetric anal sphincter injury.

[b]Adjusted for the adjustments mentioned above, and for the following childbirth interventions: induction or augmentation of labor and pain medication for pain relief during labor.

[c]Midwife-led care: adjusted for maternal age, ethnic background, socioeconomic status, birthweight, gestational age, and obstetric anal sphincter injury.

TABLE 4 Unadjusted and adjusted associations between childbirth interventions and PPH and MROP for nulliparous women.

	PPH ($n = 1{,}003{,}782$)				MROP[c] ($n = 813{,}943$)			
Birth interventions	**Total, *n* (%)**	**OR (95% CI)**	**aOR[a] (95% CI)**	**aOR[b] (95% CI)**	**Total, *n* (%)**	**OR (95% CI)**	**aOR[a] (95% CI)**	**aOR[b] (95% CI)**
Induction of labor								
No	42,516 (5.2)	1.0	1.0	1.0	18,553 (2.7)	1.0	1.0	1.0
Yes	13,069 (7.4)	1.47 (1.44–1.50)	1.30 (1.27–1.32)	1.29 (1.26–1.32)	5716 (4.3)	1.60 (1.55–1.65)	1.42 (1.38–1.47)	1.29 (1.24–1.33)
Induction with oxytocin	10,539 (8.0)	1.59 (1.55–1.63)	1.36 (1.33–1.39)	1.35 (1.31–1.38)	4656 (4.6)	1.72 (1.67–1.78)	1.53 (1.47–1.58)	1.36 (1.32–1.41)
Induction without oxytocin	2530 (5.8)	1.13 (1.08–1.18)	1.08 (1.04–1.13)	1.12 (1.08–1.17)	1060 (3.3)	1.22 (1.14–1.30)	1.09 (1.03–1.17)	1.04 (0.98–1.11)
Missing	*14,969 (1.5)*							
Augmentation after spontaneous onset of labor								
No	22,192 (4.6)	1.0	1.0	1.0	9401 (2.1)	1.0	1.0	1.0
Yes	18,435 (6.5)	1.46 (1.43–1.49)	1.27 (1.25–1.30)	1.28 (1.24–1.31)	9238 (4.1)	2.00 (1.95–2.06)	1.86 (1.80–1.91)	1.71 (1.65–1.78)
Missing	*9470 (1.2)*							
Mode of birth								
Spontaneous	35,621 (5.5)	1.0	1.0	1.0	17,349 (2.7)	1.0	1.0	1.0
Assisted vaginal birth	13,152 (7.3)	1.33 (1.31–1.36)	1.20 (1.18–1.23)	1.10 (1.08–1.13)	7053 (4.0)	1.47 (1.43–1.51)	1.33 (1.29–1.37)	1.11 (1.08–1.15)
Intrapartum CS	5025 (4.1)	0.73 (0.71–0.75)	0.60 (0.58–0.62)	0.53 (0.52–0.55)	—	—	—	—
Prelabor CS	1743 (3.6)	0.63 (0.60–0.66)	0.61 (0.58–0.64)	0.71 (0.68–0.75)	—	—	—	—
Missing	*17,054 (1.7)*							
Pain medication during labor[d]								
No	32,797 (5.0)	1.0	1.0	1.0	13,920 (2.6)	1.0	1.0	1.0
Epidural analgesia	12,340 (7.2)	1.41 (1.38–1.44)	1.21 (1.18–1.24)	1.10 (1.08–1.13)	5412 (4.2)	1.55 (1.50–1.60)	1.45 (1.41–1.50)	1.12 (1.08–1.16)
Other pharmacological pain relief	11,835 (6.2)	1.15 (1.13–1.18)	1.11 (1.08–1.13)	0.96 (0.94–0.98)	5646 (3.5)	1.21 (1.18–1.25)	1.22 (1.19–1.26)	1.01 (0.98–1.04)
Missing	*18,753 (1.8)*							
Episiotomy								
No	20,579 (4.8)	1.0	1.0	1.0	10,898 (2.6)	1.0	1.0	1.0
Yes	28,578 (7.1)	1.61 (1.58–1.63)	1.41 (1.39–1.44)	1.35 (1.32–1.38)	13,480 (3.5)	1.34 (1.30–1.37)	1.25 (1.22–1.28)	1.08 (1.05–1.11)
Missing	*3652 (0.4)*							

[a]Adjusted for characteristics (maternal age, ethnic background, socioeconomic status, hypertension, coagulation disorders, and birth weight) and year of birth.

[b]Adjusted for characteristics, year of birth, and interventions in the table (induction of labor, augmentation after spontaneous onset of labor, mode of birth, pain medication during labor, and episiotomy). Induction and augmentation are combined due to collinearity; adjustment for episiotomy was not conducted for the outcome of cesarean section.

[c]Data for MROP are shown for women with a vaginal birth only.

[d]Pain medication during labor: total numbers exceed the total number of women in the study because more than one method can be used.

TABLE 5 Unadjusted and adjusted associations between childbirth interventions and PPH and MROP for multiparous women.

	PPH ($n = 1{,}273{,}102$)				MROP[c] ($n = 1{,}107{,}884$)			
Birth interventions	**Total, *n* (%)**	**OR (95% CI)**	**aOR[a] (95% CI)**	**aOR[b] (95% CI)**	**Total, *n* (%)**	**OR (95% CI)**	**aOR[a] (95% CI)**	**aOR[b] (95% CI)**
Induction of labor								
No	41,880 (4.0)	1.0	1.0	1.0	16,494 (1.8)	1.0	1.0	1.0
Yes	12,677 (6.2)	1.60 (1.57–1.63)	1.46 (1.43–1.49)	1.34 (1.31–1.37)	6366 (3.4)	1.92 (1.87–1.98)	1.68 (1.63–1.73)	1.49 (1.45–1.54)
Induction with oxytocin	9857 (6.7)	1.73 (1.69–1.77)	1.54 (1.51–1.58)	1.41 (1.37–1.44)	5053 (3.7)	2.12 (2.05–2.18)	1.81 (1.75–1.87)	1.60 (1.54–1.66)
Induction without oxytocin	2820 (4.9)	1.25 (1.21–1.30)	1.24 (1.19–1.29)	1.16 (1.11–1.21)	1,313 (2.5)	1.42 (1.35–1.51)	1.31 (1.24–1.39)	1.20 (1.13–1.28)
Missing	*14,969 (1.5)*							
Augmentation after spontaneous onset of labor								
No	29,160 (3.5)	1.0	1.0	1.0	12,251 (1.5)	1.0	1.0	1.0
Yes	8502 (6.3)	1.86 (1.81–1.90)	1.54 (1.50–1.58)	1.38 (1.34–1.43)	4333 (3.7)	2.47 (2.39–2.56)	2.14 (2.06–2.22)	1.87 (1.79–1.95)
Missing	*9470 (1.2)*							
Mode of birth								
Spontaneous	44,381 (4.1)	1.0	1.0	1.0	21,540 (2.0)	1.0	1.0	1.0
Assisted vaginal birth	2633 (6.3)	1.57 (1.51–1.63)	1.46 (1.40–1.53)	1.27 (1.21–1.32)	1437 (3.5)	1.75 (1.66–1.85)	1.60 (1.51–1.70)	1.17 (1.10–1.24)
Intrapartum CS	3365 (5.6)	1.39 (1.34–1.44)	1.19 (1.14–1.24)	1.06 (1.02–1.10)	—	—	—	—
Prelabor CS	4256 (4.7)	1.13 (1.10–1.17)	0.97 (0.93–1.00)	1.18 (1.14–1.23)	—	—	—	—
Missing	*17,054 (1.7)*							
Pain medication during labor[d]								
No	42,701 (4.0)	1.0	1.0	1.0	17,174 (1.8)	1.0	1.0	1.0
Epidural analgesia	4727 (7.1)	1.75 (1.70–1.80)	1.49 (1.44–1.53)	1.14 (1.10–1.18)	2200 (4.0)	2.08 (1.99–2.18)	1.72 (1.64–1.81)	1.20 (1.14–1.26)
Other pharmacological pain relief	7566 (5.9)	1.46 (1.43–1.50)	1.32 (1.28–1.35)	1.06 (1.03–1.09)	3736 (3.2)	1.67 (1.61–1.73)	1.48 (1.43–1.54)	1.11 (1.07–1.16)
Missing	*18,753 (1.8)*							
Episiotomy								
No	35,232 (3.7)	1.0	1.0	1.0	17,848 (1.9)	1.0	1.0	1.0
Yes	11,996 (6.9)	1.81 (1.77–1.85)	1.74 (1.70–1.78)	1.66 (1.62–1.70)	5082 (3.0)	1.56 (1.51–1.61)	1.45 (1.40–1.50)	1.27 (1.22–1.31)
Missing	*3652 (0.4)*							

[a]Adjusted for characteristics (maternal age, ethnic background, socioeconomic status, hypertension, coagulation disorders, previous CS, previous PPH, previous MROP, and birth weight) and year of birth.

[b]Adjusted for characteristics, year of birth, and interventions in the table (induction of labor, augmentation after spontaneous onset of labor, mode of birth, pain medication during labor, and episiotomy). Induction and augmentation are combined due to collinearity; adjustment for episiotomy was not conducted for the outcome of cesarean section.

[c]Data for MROP are shown for women with a vaginal birth only.

[d]Pain medication during labor: total numbers exceed the total number of women in the study because more than one method can be used.

suggesting an increase in mild cases of PPH, but a decrease in severe PPH.[2] However, other studies show increasing incidences of severe cases of PPH in other high-income countries,[21,22] and the rate of blood transfusion is largely influenced by local or national policies and guidelines.[24,25]

There are many possible explanations for the rise in PPH and MROP. First, although studied changes in population characteristics over the years were not associated with the rising trend in PPH and MROP, variables such as maternal body mass index and birth characteristics such as the duration of labor, may have been contributors to the rising trend.[26] Second, although the rising incidences in induction or augmentation of labor, pain medication, and CS were not associated with the rising trend in PPH, rising incidences in induction or augmentation of labour and pain medication were associated with the rising trend in MROP to some extent. Previous studies indicate that some childbirth interventions may increase the risk of PPH.[10,11,20,22,27–34] Graugaard and Maimburg (2021) found an increased risk of PPH among women receiving oxytocin during induction or augmentation of labor, also after adjustments for population characteristics, pain medication, and assisted vaginal birth, which is consistent with our findings. Comparable to our results, after adjustments for other interventions, the association between epidural analgesia and PPH was no longer significant,[27] suggesting that the higher risk of PPH after epidural analgesia is mediated by other childbirth interventions.[35] However, a positive association between epidural analgesia and MROP was established after adjustments for other interventions in two cohort studies in Israel.[20,28] A positive association between induction or augmentation of labor and PPH or MROP has been found in many other cohort studies,[10,11,20,28–33] but the association between induction of labor and PPH is not consistent with several randomized controlled trials.[36–38] Although randomized controlled trials are the only design to establish causality, they were limited by selective populations as 34%–73% of women refused participation. Childbirth interventions are very important in reducing maternal and neonatal morbidity and mortality.[39] However, they are, as with every intervention and treatment, accompanied by side effects. An increase in the use of interventions without indication results in too many women being exposed to the disadvantages of these interventions.[40] It is important to find a balance between 'too little, too late' and 'too much, too soon' in the administration of oxytocin during labor and to use it only among women with a clear medical indication.[40]

The literature is not consistent on the association between CS and PPH.[22,33,41] A meta-analysis of eight studies showed a lower incidence of PPH >1000 mL among women with a CS without medical indication, but no difference in the blood transfusion rate.[41] Other studies described higher incidences of blood transfusion.[42,43] Most studies did not stratify by parity. Our results showed a lower incidence of PPH after CS among nulliparous women, but a higher incidence among multiparous women. Women with a previous CS have an increased risk of repeat CS. This might explain the higher rate of PPH among multiparous women, due to a higher risk of abnormal placentation among women with a scarred uterus,[27] which is underpinned by studies showing a positive association between previous CS and MROP after vaginal birth.[20,28] Another explanation for the conflicting findings may be that women with a PPH during CS more often have a very severe PPH, but less frequently a PPH of just more than 1000 mL.[21] In our study, we were not able to distinguish the severity of blood loss over 1000 mL.

A third explanation may be the increased awareness by care providers of the subjectivity of estimating blood loss postpartum leading to underestimation. This has led to recommendations of weighing blood loss which may have led to more cases of PPH being diagnosed.[44] However, this awareness already exists for several years and PPH rates are still rising. Equally, recommendations on management of the third stage of labor have changed in many countries. In the Netherlands, the recommended timing to initiate MROP changed from a third-stage duration of 60 min or more in 2004[45] to 30 min in 2015.[10] The World Health Organization defines a retained placenta as a third stage lasting more than 30 min. The World Health Organization advises to manually remove the placenta at this stage if bleeding occurs.[46] The change in recommendations may be an explanation for the risen MROP rates. However, despite these recommendations and increased interventions in the third stage of labor, the incidence of PPH has increased rather than decreased from 2003 onwards. Randomized controlled trials on the optimal timing for intervention are lacking and it is, therefore, unknown what the effect of different time intervals is on the incidence of PPH in high-income countries.[47–49]

Furthermore, routine use of oxytocin is recommended during the third stage of labor and its use has increased in the Netherlands between 1995 and 2011 in both obstetrician-led care and midwife-led care.[50] However, in the Netherlands, this has not led to a decrease in PPH and MROP. This supports findings from the Cochrane review of Begley et al. (2019) that the evidence for active management of the third stage among low-risk women in high-income countries is unclear.[19,49]

Clinical studies are needed to examine the effects of different types of management during the third stage of labor, and more research is needed to show how this has changed over the years, as well as to re-evaluate current recommendations of management during the third stage of labor.

5 | CONCLUSIONS

PPH and MROP rates have increased, both among medium- and high-risk women in obstetrician-led care and among low-risk women in midwife-led care. Rising PPH rates were not associated with changes in studied population characteristics and childbirth intervention rates. Rising MROP rates were to some extent associated with rising incidences of induction and augmentation of labor and pain medication. More research is needed to explain rising trends and to evaluate current recommendations of management in the third stage of labor with additional clinical studies. Besides, more research is needed to investigate the influence of changes in body mass index, which could not be assessed in the current study.

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CONFLICT OF INTEREST STATEMENT

The authors have declared that no competing interests exist.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from Perined (contact through info@perined.nl) for researchers who meet the criteria for access to confidential data, and if Perined gives permission. Restrictions apply to the availability of these data, which were used under license for this study. Data are available from the Department of Midwifery Science of Amsterdam UMC, location VUmc. with the permission of Perined.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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