ORIGINAL ARTICLE



Maternal characteristics as indications for routine induction of labor: A nationwide retrospective cohort study

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Abstract

Background: Maternal characteristics, such as parity and age, are increasingly considered indications for routine induction of labor of otherwise healthy women to prevent fetal and neonatal mortality. To fully balance the risks and benefits of induction of labor, we examined the association of additional relevant maternal characteristics and gestational age with fetal and neonatal mortality.

Methods: We conducted a nationwide retrospective cohort study among a healthy Dutch population consisting of all singleton pregnancies in midwife-led care after 37 weeks of gestation in the period 2000-2018. We examined the association of maternal ethnicity, age, parity, and socioeconomic status with fetal and neonatal mortality, stratified by gestational age. The association of single characteristics was examined using descriptive statistics, and univariable and multivariable logistics regression analyses. The associations of multiple characteristics were examined using inter-categorical analyses and using interaction terms in the multivariable logistic regression analyses.

Results: The results showed that ethnicity, age, parity, socioeconomic status, and gestational age did not act as single determinant of fetal and neonatal mortality. The probability of fetal and neonatal mortality differed among subgroups of women depending on which determinants were considered and the number of determinants included.

Conclusions: Decision-making about induction of labor to prevent fetal and neonatal mortality based on a single determinant may lead to overuse or underuse of IOL. A value-based health care strategy, addressing social inequity, and investing in better screening and diagnostic methods that employ an individualized and multi-determinant approach may be more effective at preventing fetal and neonatal mortality.

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KEYWORDS

age, decision-making, ethnicity, induction of labor, maternal characteristics, parity, risk, risk selection, socioeconomic status

1 | INTRODUCTION

Maternal characteristics, such as parity and age, are increasingly considered indications for induction of labor (IOL) of healthy women (when we use the term "woman," we also refer to individuals with a uterus who are not woman identified, including trans and non-binary individuals). Nulliparity and advanced maternal agegenerally defined as 35 years or older¹–are associated with a higher probability of fetal and neonatal mortality (FM and NM).^{2,3} To prevent FM and NM, a growing number of healthy nulliparous women and women at advanced age are routinely offered IOL at 39 weeks of gestation.⁴

Although medically indicated IOL can prevent FM and NM, routine IOL may lead to unnecessary harm to women and their children. IOL is associated with harmful side effects, including suboptimal fetal brain development,⁵ uterine rupture, ⁶ severe postpartum haemorrhage, ⁷ severe perineal lacerations, and negative birth experiences due to reduction of choice in care provider and birth place, restricted mobility, and feeling of loss of control.9 A recent study into short-term and long-term outcomes of IOL in a healthy population found that IOL for non-medical reasons was associated with higher birth interventions and adverse maternal, neonatal, and child outcomes. 10 Therefore, it is argued that IOL should only be used if the expected benefits of IOL outweigh its potential harms and the disadvantage of waiting for spontaneous onset of labor. 11

To fully balance the risks and benefits of IOL for maternal characteristics such as parity and advanced maternal age, and to more accurately identify those births which would benefit from IOL, additional relevant maternal characteristics and gestational age should be taken into account in the risk selection process. Maternal characteristics such as ethnicity¹² and socioeconomic status (SES)¹³ are also associated with an increased probability of FM and NM. Furthermore, the probability of FM and NM differs across the term period.¹⁴ Nevertheless, most studies focus on the association between single determinants and FM and NM, and apply statistical adjustments.^{3,14}

The aim of this study is to gain more insight into the association and interaction between maternal characteristics, gestational age, and FM and NM among healthy women giving birth to a single child at term. Therefore, we examined FM and NM rates for each term gestational week, by maternal ethnicity, age, parity, and SES, and for

the interaction between these characteristics in a healthy Dutch population.

2 | METHODS

2.1 Study design

In this nationwide longitudinal retrospective cohort study, we used data from the Netherlands Perinatal Registry (Perined). Perined includes data from almost all pregnancies and births in primary midwife-led care, secondary obstetrician-led care and pediatric care. Midwives, obstetricians, and pediatricians obtained women's consent for data registration in Perined and the use of their data for research purposes. For the purpose of this study, all data were anonymized. We analyzed the data for the years 2000-2018 (19 years) to show the time trend in fetal mortality (FM), neonatal mortality (NM), and total mortality (TM), and performed a sub-analysis for the years 2012-2018 (7 years), to examine the most recent associations and interactions between single and multiple maternal characteristics and PM.

2.2 | Study population

In the Netherlands, healthy women are cared for by independent midwives in primary midwife-led care in community practices. When the risks of adverse outcomes increase or complications develop, women are referred to obstetrician-led care in the hospital. To study TM in a healthy population, we included all singleton pregnancies in midwife-led care giving birth from 37 weeks of gestation onwards. We excluded cases with missing information on gestational age-including abortions-and multiple gestation, and all cases with a registered medical indication for referral to obstetrician-led care before the onset of labor, including cardiac diseases, respiratory disorders, thromboembolic disorders, hypertensive disorders, diabetes, hematological disorders, neurological disorders, gynecological diseases, use of medicines, drugs or alcohol, blood group antagonism, lethal fetal congenital malformations, cervical insufficiency, caesarean section, infection, fetal heart arrhythmia, suspected fetal growth restriction, suspected macrosomia, non-cephalic presentation, placenta previa, and lack of antenatal care (Figure 1).

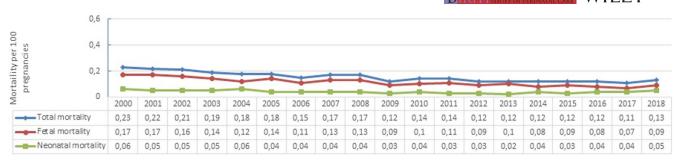


FIGURE 1 The trend in fetal, neonatal and total mortality (%) among women pregnant at 37+0 weeks specified by year for the years 2000-2018

2.3 Determinants

The following determinants were examined: maternal ethnicity, age, parity, SES, and gestational age. These determinants have been shown in previous studies to be associated with TM. Maternal age was categorized in 5 years intervals ranging from "younger than 25 years" up to "40 years and older." Parity was defined in Perined as birth after the gestational age of 16 weeks. Parity was categorized as "P0" (no history of birth), "P1" (history of one birth), "P2" (history of two births), and "P3+" (history of three or more births). Ethnicity was assigned by the woman's care provider, usually based on appearance, name and information provided, and registered according to the following categories: Dutch, North African, African other, Asian other, Latin American, Turkish, and Hindustani. We combined these categories and defined ethnicity as "Dutch" and "non-Dutch." SES is a score provided by The Netherlands Institute for Social Research, based on the average income, educational level and type of employment in a residential postal code area. We categorized SES as "low," "medium," and "high," using the 25th and 75th percentile cutoff points. Cutoff points were calculated with the SES score and the number of inhabitants per residential postal code area, based on the cutoff points in the general Dutch population provided by the Dutch national statistical office, Statistic Netherlands. Gestational age was categorized in weeks, starting from "pregnant at 37 + 0 weeks" up to "pregnant at 42 + 0 weeks."

The following primary outcomes were examined: TM, FM, and NM. 17,18 For the analyses of mortality, we applied an at-risk approach, dividing the number of deaths in a specific week by the number of women still pregnant at the onset of the same week. 19 For the analyses of NM, we excluded women with a fetal loss. 17 TM was defined as the sum of FM and NM. FM was defined as death occurring before birth. For example, to calculate the FM in week 39, we divided the number of stillbirths at 39 + 0 to 39 + 6 weeks by the number of women still pregnant at 39 + 0 weeks. NM was defined as death up to 28 days after

birth among neonates born alive. For example, to calculate NM in week 41, we divided the number of neonatal deaths at 41 + 0 to 41 + 6 weeks by the number of live births among women still pregnant at 41 + 0 weeks.

2.4 | Statistical analyses

We used descriptive statistics to report the time trend in single determinants and the rate of TM, FM, and NM in the period 2000-2018. We used descriptive and logistic regression analyses to examine the association between single and multiple determinants and TM in the period 2012-2018. Univariable logistic regression analyses were conducted to calculate crude odds ratio (OR) and 95% confidence intervals (CI). Multivariable logistic regression analyses were conducted to determine ORs adjusted for the other maternal characteristics as potential confounders (aOR). We used seven models. For model 1, we included all women in the study. For models 2-7, results were stratified by gestational week starting from women still pregnant at 37 + 0 weeks up to women still pregnant at 42 + 0 weeks to calculate TM in a specific week among women still pregnant at the start of the week. Collinearity was tested by entering the determinants in the multivariable logistic regression models using a manual stepwise forward-backward method.

Inter-categorical analysis was conducted to study the association between multiple maternal characteristics and PM.^{20,21} The maternal characteristics were entered as interaction terms in the multivariable analysis using a manual stepwise forward–backward method. *P*-values of <0.05 were considered significant.

For some of the analyses, we combined categories because of small sample sizes. For the time trend analyses, we combined the parity categories "P2" and "P3+" and used the categories "younger than 25 years," "25-34 years," and "35 years and older" for age. We did not include model 7– "pregnant at 42 + 0 weeks" –in the regression analyses because of low numbers. The intercategorical analyses were only conducted for model 1, for

the whole study population. Statistical analyses were conducted using STATA software. ²²

3 RESULTS

3.1 | Study population characteristics and trend analyses 2000-2018

For the study period 2000-2018, Perined contained data of 3 700 336 pregnancies. After applying the exclusion criteria, 1 734 139 pregnancies of healthy women remained for the trend analyses (Figure 1). The trend in TM, FM, and NM rate is shown in Figure 1. The TM rate has declined steadily in the past two decades. The decline was predominantly the result of declining FM, which had almost halved in 2018 compared with 2000. Figures S1-S4 show the trend in TM specified for ethnicity, parity, age, and SES. The TM among nulliparous women and women aged ≥40 years showed the largest decline. In 2000, nulliparous women and women aged ≥40 years had the highest TM rate compared with other parity and age subcategories, 0.3% and 0.64%, respectively. In 2018, the TM rate had declined to 0.13% for nulliparous women, and to 0.16% for women aged ≥40 years, resulting in one of the lowest TM rates compared with other parity and age subcategories. For ethnicity, the TM rate declined among both Dutch and non-Dutch women, but remained overall

higher for non-Dutch women. The trend analyses specified by FM and NM showed a similar trend and are therefore not shown.

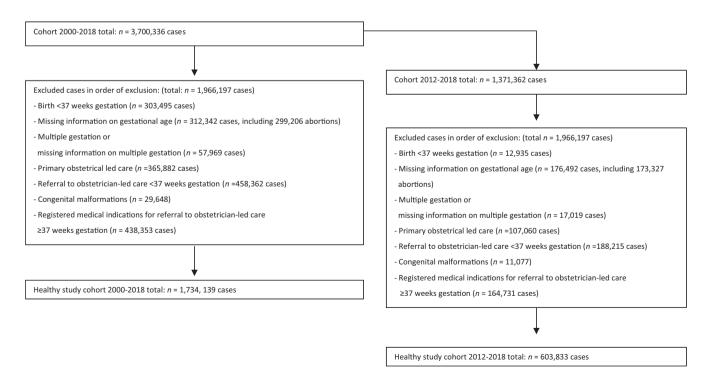
3.2 Study population characteristics and sub-analyses 2012-2018

In the study period 2012-2018, Perined contained data of 1 371 362 pregnancies. After applying the exclusion criteria, 603 833 pregnancies of healthy women were included for the analyses (Figure 2). The demographic characteristics of the population are shown in Figure S5. The absolute number of pregnancies and the absolute number of fetal and neonatal deaths decreased with advancing gestational week because only women still pregnant at the onset of the gestational period were included.

3.3 Descriptive analyses

3.3.1 | Association between single determinants and total mortality

Table 1 presents the associations between single maternal characteristics and TM, stratified by gestational week for the years 2012-2018. The TM rate among women pregnant at the start of the gestational period increased



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	Total mortality among women pregnant at 37 + 0 weeks (model 1)	ımong t at odel 1)	Mortality in week 37 among women pregnar at 37 + 0 weeks (model 2)	Mortality in week 37 among women pregnant at 37 + 0 weeks (model 2)	Mortality in week 38 among women pregnant at 38 + 0 (model 3)	ong gnant odel	Mortality in week 39 among women pregnant at 39 + 0 weeks (model 4)	n odel	Mortality in week 40 among women pregnant at 40 + 0 weeks (model 5)		Mortality in week 41 among women pregnant at 41 + 0 weeks (model 6)		Mortality in week 42 among women pregnant at 42 + 0 weeks (model 7)
	n (column %)	%	u	%	u	%	% u	,0	% u		% u	<u>_</u>	%
Ethnicity													
Dutch	507 (77.85)	0.11	63	0.01	94	0.02	121 0.	0.03	124 0.04		97 0.09	∞	0.10
Non-Dutch	207 (22.15)	0.16	31	0.02	34	0.03	48 0.	0.04	56 0.07		34 0.12	4	0.15
Parity													
P0	375 (45.46)	0.14	42	0.02	56	0.02	85 0.	0.04	90.0 0.06		95 0.14	7	0.10
P1	190 (36.20)	0.09	27	0.01	45	0.02	45 0.	0.02	48 0.04		22 0.05	8	0.14
P2	94 (13.01)	0.12	13	0.02	17	0.02	27 0.	0.04	27 0.06		9 0.05	1	0.10
P3+	64 (5.34)	0.20	12	0.04	11	0.04	14 0.	0.05	17 0.09		8 0.11	2	0.34
Age													
<25 years	78 (10.36)	0.12	17	0.03	19	0.03	15 0.	0.03	16 0.05		10 0.08	1	0.11
25-29 years	219 (32.35)	0.11	27	0.01	44	0.02	50 0.	0.03	58 0.05		39 0.09	1	0.03
30-34 years	272 (39.26)	0.11	28	0.01	46	0.02	70 0.	0.03	71 0.05		51 0.09	9	0.14
35-39 years	123 (15.75)	0.12	20	0.02	17	0.02	27 0.	0.03	31 0.05		25 0.10	3	0.04
≥40 years	30 (2.27)	0.22	2	0.01	3	0.02	9 0.	80.0	0.07		8 0.22	2	0.53
Socioeconomic status	sn												
Low	207 (25.76)	0.13	31	0.02	3	0.02	48 0.	0.04	56 0.06		37 0.11	в	В
Medium	347 (47.82)	0.12	46	0.02	99	0.02	76 0.	0.03	90 0.05		62 0.09	7	0.13
High	160 (26.41)	0.10	15	0.01	27	0.02	44 0.	0.03	34 0.04		34 0.09	9	0.21

^aNo mortality.

with advancing gestational week. NM contributed more to the increased TM rate compared with FM (Figure S6). In the whole population, non-Dutch women, women with ≥ 3 previous births, women aged ≥ 40 years, and low-SES women had the highest rate of PM. Although the TM rate increased with advancing gestational week, the degree of increase differed between subcategories. The trend analyses specified by FM and NM showed a similar trend and are therefore not shown.

3.3.2 | Association between multiple determinants and total mortality

Table 2 shows the absolute number and rate of TM for the interaction between two maternal characteristics in the whole study population (model 1). The TM rate associated with single maternal characteristic (Table 1) differed for subcategories when taking a second maternal characteristic into account. The absolute number of TM in the 8-year study period was very low for many subcategories. The TM rate was higher among low-SES women but only for non-Dutch and not for Dutch women. Among Dutch women, the TM rate increased from 40 years and from ≥3 previous births and among non-Dutch women from 35 to 39 years and from ≥2 previous births. Among women aged ≥40 years, primiparous women and high-SES women had the highest rate of PM.

3.4 | Logistic regression analyses

3.4.1 | Association between single determinants and total mortality

The results of the univariable and multivariable logistic regression analyses for TM are shown in Figure S7. In the whole population, the OR for TM was the highest for non-Dutch women and women aged ≥40 years compared with reference categories, and remained significant after adjustment for other maternal characteristics. Low-SES women had the highest OR for TM compared with other SES categories, although not significantly different from the reference category after adjustment for other maternal characteristics. Among parity categories, the OR for TM was the lowest for primiparous women compared with nulliparous women, and remained significantly different after adjustment for other maternal characteristics. Women with ≥3 previous births had higher OR than primiparous women compared with nulliparous women, but this difference was not significant after adjustment for other maternal characteristics.

After stratification by gestational week, the OR for TM remained significant compared with reference categories after adjustment for other maternal characteristics for non-Dutch women pregnant at 40 + 0 weeks, primiparous women pregnant at 39 + 0 weeks, 40 + 0 weeks and 41 + 0 weeks, women with ≥ 3 previous birth and women aged <25 years pregnant at 37 + 0 weeks, and women with ≤2 previous births and women aged ≥40 years pregnant at 41 + 0 weeks. The aOR for TM for non-Dutch women pregnant at 37 + 0 weeks and women aged ≥40 years pregnant at ≥39 weeks were not significant compared with the reference categories. The differences in aOR between the parity subcategories were the largest among women pregnant at 37 + 0 weeks and the smallest among women pregnant at 41 + 0 weeks. The difference in aOR between women aged <25 years and 25-29 years was largest for women pregnant at 37 + 0 weeks and the smallest for women pregnant at 41 + 0 weeks.

3.4.2 | Association between multiple determinants and total mortality

Interaction between two maternal characteristics in the whole study population was examined by entering a second maternal characteristic as interaction term in the multivariable regression analysis of model 1. When a second maternal characteristic was taken into account, the aOR for TM associated with a single maternal characteristic differed for subcategories.

First, we tested differences between subcategories. The interaction between ethnicity and SES and between parity and age showed significant differences in TM between subcategories after adjustment for other maternal characteristics (Figure S7). To examine the specific direction of the interaction effect, different interactions between ethnicity and SES, and between parity and age were tested (Figures S8-S11). Significant aOR are listed in Table 3. Among low-SES women compared with high-SES women, the aOR for TM increased from 1.37 [CI 1.16-1.62] in the whole study population to 1.76 [1.33-2.33] for non-Dutch women compared with Dutch women. Among women aged ≥35-39 years compared with women aged 25-29 years, the aOR for TM was increased for nulliparous women, respectively, from 1.15 [0.95-1.51] to 1.47 [1.04-2.07] for women aged 35-39 years, and from 1.82 [1.23-2.72] to 3.99 [CI 2.37-6.72] for women aged \geq 40 years.

Three-way interaction with ethnicity and SES were tested and found not significant for parity and not feasible due to insufficient power for age. Three-way interactions with parity and age were tested and found not feasible due to insufficient power.

TABLE 2 Total mortality (n, %) for the interaction between two maternal characteristics, results for the whole study population (model 1)

	Parity	ty.							Age										Socioe	Socioeconomic status	ic stat	sn		
	P0		P1		P2		P3+		<25	<25 years	25-29	25-29 years	30-34 years	years	35- 39 years	ars	≥40 years	ears	Low		Medium	un	High	
	l u	%	u	%	l u	%	l u	%		%	l u	%	l a	. %	. u	%	u u	%	l u	%	l u	%	n u	%
Ethnicity																								
Dutch	272	0.13	142	0.13 142 0.08	57	0.10	36	0.17	49	0.12	155	0.10	210	0.11	79	0.11	23	0.23	86	0.10	274	0.12	127	0.10
Non-Dutch	66	0.16	45	0.11	45	0.18	28	0.26	29	0.14	63	0.15	99	0.15	42	0.21	7	0.19	107	0.19	29	0.14	32	0.12
Parity																								
P0									99	0.12	135	0.12	122	0.13	45	0.18	17	0.51	110	0.15	170	0.13	68	0.13
P1									18	0.13	48	0.07	87	60.0	33	0.09	4	60.0	51	0.10	94	60.0	42	0.07
P2									ю	0.13	26	0.16	42	0.12	21	0.10	1	0.04	23	0.12	51	0.14	19	0.09
P3+									1	0.29	∞	0.23	16	0.18	13	0.18	3	0.19	22	0.23	32	0.20	10	0.16
Age																								
<25 years																			35	0.15	34	0.12	6	0.10
25-29 years																			72	0.13	101	0.10	43	0.10
30-34 years																			58	0.11	139	0.12	70	0.10
35-39 years																			38	0.19	58	0.14	27	0.09
≥40 years																			4	0.13	14	0.23	11	0.25

Note: Perinatal mortality rates obtained from the result about the whole study population (model 1) shown in Table 1.

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TABLE 3 Univariable and multivariable logistic regression analyses (OR, aOR) for the associations between single (models 1-7) and multiple (model 1) maternal characteristics and total mortality for the years 2012-2018

pregnant at 41 + 0 wks aOR [95% 1.30 [0.87-0.34 [0.21-0.26 [0.12-0.54 0.56Mortality in week 41 among women 1.0 1.0 (model 6) 1.32 [0.90-0.36 [0.22-0.38 [0.19-0.74]* 0.57OR [95% CI 1.0 1.0 1.02 [0.65aOR [95% 1.57 [1.13-0.69 [0.48-2.1940 + 0 wks (model 5) 0.99 [1.59]Mortality in week 40 among women 1.0 1.0 pregnant at 1.68 [1.23-0.68 [0.48-1.03 [0.67-2.31]* *[96.0 OR [95% 1.58 CI 1.0 1.0 aOR [95% CI] 0.61 [0.42-1.04 [0.66-1.38 [0.97-0.89 39 + 0 wks (model 4) [1.63][1.95]Mortality in week 39 among women 1.0 1.0 pregnant at 0.65 [0.45-1.42 [0.02-1.08 [0.70-0.94]* OR [95% [1.98]1.67CI 1.0 1.0 1.22 [0.69-1.16 [0.77-1.09 [0.73aOR [95% 1.642.15] 1.75 Mortality in week pregnant at 38 + 0 38 among women 1.0 1.0 (model 3) [0.61-OR [95% [0.86--79.01.48 1.88[1.80]1.00 1.05 1.27 1.0 1.0 pregnant at 37 + 0 wks 0.94 [0.57-1.23 [0.64aOR [95% 1.50 [0.92-2.36 2.91] 1.56Mortality in week 37 among women CI 1.0 1.0 (model 2) 1.73 [1.13-0.81 [0.50-1.08 [0.58-2.66]*OR [95% 1.31 2.02 1.0 1.0 $[1.16-1.62]^*$ [1.33-2.33]*[0.52 - 0.75]*[0.50 - 0.88]* [0.32-0.79] [0.34-0.95] [0.01-0.56][0.06-0.58][0.66-1.05]aOR^a [95% x Low-SES Fotal mortality among x 35-39 y x 30 - 34 yx 35-39 y $x \ge 40 y$ $x \ge 40 y$ 37 + 0 wks (model 1) women pregnant at 0.19 0.83 0.57 1.76 0.67 0.50 0.63 CI 1.0 1.0 1.44 [1.22-0.64 [0.53-0.88 [0.70-0.76 1.69]*OR [95% 1.101.0 1.0 Dutch (reference P0 (reference Non-Dutch group) group) Ethnicity Parity P2 P1

	Total mort women pre 37 + 0 wks	Fotal mortality among women pregnant at 57 + 0 wks (model 1)	Mortality in week 37 among women pregnant at 37 + 0 (model 2)	Mortality in week 7 among women regnant at 37 + 0 wks model 2)	Mortality in week 38 among women pregnant at 38 + 0 (model 3)	in week women it 38 + 0	Mortality in week 39 among women pregnant at 39 + 0 wks (model	Mortality in week 39 among women pregnant at 39 + 0 wks (model 4)	Mortality in week 40 among women pregnant at 40 + 0 wks (model 5)	in week women tt (model 5)	Mortality in week 41 among women pregnant at 41 + 0 (model 6)	Mortality in week 41 among women pregnant at 41 + 0 wks (model 6)
	OR [95% CI]	OR [95% aOR ^a [95% CI]	OR [95% CI]	aOR [95% CI]	OR [95% CI]	aOR [95% CI]	OR [95% CI]	OR [95% aOR [95% CI]	OR [95% CI]	OR [95% aOR [95% CI]	OR [95% CI]	aOR [95% CI]
P3+	1.45 [1.12- 1.27 1.90]* [[5 [1.12- 1.27 2.43 [1.28 1.90]* [0.96-1.69] 4.62]*	2.43 [1.28- 4.62]*	2.53 [1.36- 1.66 5.11]* [0.87- 3.17]	1.66 [0.87- 3.17]	1.96 [0.99- 3.89]		1.40 [0.79- 1.21 [0.67- 1.62 [0.96- 1.44 [0.83- 2.46] 2.21] 2.72] 2.50]	1.62 [0.96- 2.72]	1.44 [0.83-2.50]	0.78 [0.34-	0.58 [0.27-
Age												

TABLE 3 (Continued)

	0.70 [0.35- 1.40]			1.45 [0.86- 2.44]	3.08 [1.41-6.72]*		1.12 [0.73-	1.0	0.96 [0.63- 1.46]
	0.84 [0.42- 1.69]	1.0	1.00 [0.67-	1.12 [0.68-	2.40 [1.12- 5.13]*		1.16 [0.77-1.75]		0.96 [0.63- 1.46]
	0.81 [0.46- 1.42]	1.0	1.00 [0.70-	1.07 [0.68-	1.29 [0.54- 3.04]		1.10 [0.78-	1.0	0.67 [0.45- 0.69 [0.46- 0.99] 1.02]
	0.90 [0.52- 1.56]	1.0	0.97 [0.68- 1.34]	1.03 [0.67- 1.59]	1.38 [0.59- 3.19]		1.20 [0.86-	1.0	0.67 [0.45-0.99]
	0.87 [0.49- 1.56]	1.0	1.11 [0.7- 1.62]	1.09 [0.67-	2.07 [0.96- 4.47]		1.13 [0.78- 1.65]	1.0	1.05 [0.72- 1.53]
	0.96 [0.54- 1.70]	1.0	1.13 [0.79- 1.63]	1.09 [0.68-1.73]	2.52 [1.24- 5.12]*		1.19 [0.83-	1.0	1.04 [0.72- 1.50]
	1.44 [0.83- 2.49]	1.0	0.87 [0.57- 1.33]	0.75 [0.42-	0.84 [0.26-2.78]		0.89 [0.58-	1.0	0.78 [0.49-
	1.36 [0.79- 2.32]	1.0	0.86 [0.57- 1.29]	0.79 [0.45- 1.38]	0.96 [0.30- 3.11]		1.00 [0.65- 1.49]	1.0	0.74
	1.93 [1.04- 3.60]*	1.0	0.85 [0.49-	1.41 [0.76-2.61]	0.83 [0.19- 3.38]		1.08 [0.67-	1.0	0.62 [0.34-1.11]
	1.97 [1.07- 3.61]*	1.0	0.85 [0.50- 1.45]	1.52 [0.85- 2.71]	1.05 [0.25- 4.43]		1.25 [0.79- 1.97]	1.0	0.59 [0.33-
	1.02 [0.79-1.33]	1.0	1.07 [0.89-1.28]	1.20 [0.95-1.51] $x P0 1.47$ [1.04-2.07]*	1.82 [1.23-2.72]* x P0 3.99 [2.37-6.72]*		1.03 [0.86-1.23]	1.0	0.84 [0.69-1.01]
	1.11 [0.86- 1.44]	1.0	1.02 [0.86- 1.22]	1.15 [0.92- 1.44]	1.95 [1.22- 2.86]*		1.11 [0.93- 1.32]	1.0	0.83 [0.69- 1.01]
Age	<25 y	25-29 y(reference group)	30-34 y	35-39 y	≥40 y	Socioeconomic status	Low	Medium (reference group)	High

^aAdjusted for the other maternal characteristics as potential confounders.

[0.47-1.15]

*P value <0.05.

4 | DISCUSSION

4.1 The complexity of risk selection

This nationwide longitudinal retrospective cohort study in a healthy Dutch pregnant population offers novel insights into the associations between maternal characteristics, gestational age, and PM. The absolute number of fetal and neonatal death and the probability of TM was low. The differences between subgroups of women have declined substantially over the past two decades. In most subcategories, the increase in TM rate with advancing gestational age was minimal. Overall, we observed the highest probability of TM among non-Dutch women, women with ≥3 previous births, women aged ≥40 years, and low-SES women. However, interaction analyses showed that the probability of TM differed among subgroups of women when taking a second maternal characteristic into account. We observed a higher probability of TM among low-SES women but only for non-Dutch and not for Dutch women. We observed the highest probability of TM among non-Dutch low-SES women, nulliparous women aged ≥40 years, and women aged up to 29 years with ≥3 previous births.

4.2 | The limitations of a routine approach

Currently, in some countries, shared decision-making is used to offer healthy nulliparous women and women at advanced age IOL at term. Women are informed about the probability of TM associated with their parity or age and the benefits and harmful side effects of IOL. These harmful side effects have not been found in randomized controlled trials,²³ which may be due to the low incidence of these side effects, and the non-representative samples in these studies.²⁴ Furthermore, some consequences of IOL have been examined insufficiently, such as the longterm care outcomes for the mother and child and maternal experiences. 11 It is presumed that women can make a well-informed decision about IOL based on the information about the benefits and harmful side effects of IOL. However, studies show that women often feel insufficiently involved and informed in the decision-making process regarding IOL, and women's choice is led by the presented information which is focused on concerns for their child's short-term outcomes.^{25,26}

The results of this study do not support routinely offering women IOL based on the probabilities of TM associated with a single maternal characteristic. Furthermore, this is a sliding scale approach: because the probability of TM is never zero; ultimately, all healthy women should be informed about their risk of TM and be offered the choice of

IOL. Also, care providers are not obliged to inform women about every very small risk inherent to healthy pregnancy and birth.²⁷ More importantly, the results of this study indicate that using single determinants as indications for IOL has poor predictive value. ^{28,29} Our study results point to the difficulty of distinguishing which women would benefit from IOL. Interventions for which the balance between benefits and harms varies substantially among subgroups are also referred to as "gray zone" interventions. 30,31 Brownlee and colleagues (2017) emphasize that for gray zone interventions, "even when robust consensus has established criteria defining the appropriateness of tests and treatments [...], appropriateness can remain uncertain in many individual cases." 30 (p157) Risk selection regarding gray zone interventions is associated with professional bias, and overuse or underuse of care. 30,31

Lastly, to prevent one case of TM, hundreds of healthy women and children who will not experience TM if labor is not induced will be needlessly exposed to the discomfort and disadvantages of IOL.4 Thus, applying a routine approach to IOL based on single maternal characteristics might result in underestimation or overestimation of probabilities of TM, leading to overuse or underuse of care. 11 This approach also disproportionately puts the focus on mortality risks, causes fear, and shifts the responsibility for outcomes to women.^{4,32} However, it does not mean that TM risks should be ignored. Childbearing women need a high value care system that not only provides timely intervention using and allocating resources optimally, but also helps them stay safe and healthy by preventing unnecessary medical interventions. 11

4.3 | Toward value-based health care

The results of this study call for a comprehensive approach, in which women are individually assessed within their own context to better identify those women who would benefit from IOL while preventing inappropriate care. This requires further understanding of the interaction between maternal characteristics, gestational age and TM and the differences in TM between subgroups, which has been identified as one of the top research priorities necessarv to improve risk selection. ^{28,29} Furthermore, there is a call to expand the contemporary research focus on individual risk and include the social context as well.^{33,34} We recommend a value-based health care (VBHC)³⁵ strategyforegrounding women centered, evidence-based, appropriate, cost-effective, accessible, and equitable care-by investing in better screening and diagnostic methods, 11 addressing social inequities, 33,36 and using a multideterminant approach in research and practice. 20,21,28,29

The transition to VBHC would benefit from investing in the prevention of known causes of TM. For example, the majority of TM at term is associated with fetal growth restriction. ^{2,37,38} Current screening and diagnostic methods fail to accurately differentiate between fetuses and newborns with unreached growth potential and those constitutionally small but healthy. ³⁸ More importantly, current methods do not address structural social causes of growth restriction, which have been identified as the primary drivers of fetal growth restriction. ³⁷

Primary prevention by addressing social drivers of TM is the most sustainable approach toward reducing PM. Consistent with previous studies, our study showed an association between TM and non-Dutch ethnicity and low SES. 12,13 This finding may convey the impression that non-Dutch and low-SES women are more likely to benefit from routine IOL. However, studies show that the associations between ethnicity and SES with TM is based on social drivers. Conditions in which people are born, grow, live, work, and age, shape health in powerful ways. 39,40 It has been argued that ethnicity and SES act as proxies for complex societal processes, 41 and that the association with TM is mediated by discrimination and inequity.²⁹ (p247),42 Thus, the extent to which medical interventions, such as IOL, can intervene upon these social processes is limited.40 Nevertheless, often, social determinants of health are used as biological or genetic determinants, and differences between subgroups are medicalized. Consequently, efforts to reduce TM predominantly focus on improving and using medical interventions instead of addressing underlying societal processes. A recent example is the revised National Institute for Health and Care Excellence IOL guideline's recommendation to induce labor at 39 weeks of women with otherwise uncomplicated pregnancies and a black, Asian and minority ethnic background, because they are two to four times as likely to die during pregnancy and birth. 43 This strategy adds the additional risks of IOL without addressing root causes of the adverse outcomes. 44 A value-based approach is primary prevention of TM by systematically addressing institutional discrimination and inequity in society. 33,41 Further research into the underlying causes of the differences in TM between the ethnic and SES categories is necessary.34

Like previous studies, our study indicates that a multideterminant approach contributes to a better identification of women that would benefit from IOL.^{28,29} A recent review identified over 60 determinants of stillbirth, including maternal and medical characteristics and biomarkers.²⁹ A multi-determinant approach can offer the possibility to study the dynamic interaction between mutually constituting social and biomedical drivers doing more justice to the complexity of pregnancy and birth. 33,41 This approach includes considering multiple determinants and measuring effect modification. 20,28,29,41

4.4 | Strengths and limitations

To our knowledge, this study is the first to examine the association between multiple maternal characteristics and TM in different gestational weeks at term in a healthy population. The data set used in this study is unique in size and population, which provided us with the power necessary to study TM in a healthy population. However, the use of registration data also had disadvantages. First, despite the size of the database, in some subgroups, the incidence of TM was very low or zero, resulting in fluctuating outcomes. Also, they were not able to specify the analyses for all subcategories. This would be possible by combining data sets internationally, requiring high-quality data registration and collection, and comparable registration systems. Second, we were unable to include other relevant maternal characteristics associated with TM because they are not registered routinely, such as BMI and cigarette smoking, which are also associated with ethnicity and SES. ^{2,28,29} This may have impacted the outcomes of this study. Third, we were unable to study TM in different ethnic categories because ethnicity is registered imprecisely and inconsistently in Perined. The Perined categories for ethnicity consisted of countries, continents, and racial groups. Therefore, we used a binary construction of ethnicity. This may have conveyed the impression that these groups are homogeneous. However, ethnic categories are diverse and dynamic because they are socially constructed.⁴⁵ For example, in Perined, ethnicity is assigned by women's care provider, usually based on appearance, name, and/or information provided by women. However, ethnicity depends on an individual's and their family's country of birth, migration history, genealogy, 46 and whether ethnicity is self-assigned or socially assigned. 47 This makes the categorization of individuals into ethnic categories difficult. 48 Furthermore, the definition of ethnic categories changes over time and differs between settings. 45 Like ethnicity, SES categories are also socially constructed. 49 Caution should be taken when using ethnic or SES categories in research and practice as biogenetic determinants of health outcomes.34,50 To be able to use ethnicity and SES in a more meaningful way as a social determinant in future research, underlying categories should be registered.³⁴ Fourth, because the moment of fetal and neonatal death was not registered, we used moment of birth as inclusion criterion, assuming fetal death and birth occurred, at most, a few days apart. Last, this study included data

from a time period in which the IOL rate has increased, which may have impacted the outcomes of this study.

4.5 | Conclusions

This nationwide longitudinal retrospective cohort study in a healthy Dutch pregnant population showed that the probability of TM differed among subgroups of women depending on which determinants were considered and the number of determinants included. These results indicate that a routine approach using single determinants may result in underestimation or overestimation of probabilities of TM, leading to overuse or underuse of IOL. A VBHC strategy, addressing social inequity, and investing in better screening and diagnostic methods that employ an individualized and multi-determinant approach may be more effective at preventing fetal and neonatal mortality.

ETHICAL APPROVAL

Ethical approval was requested from the Medical Ethics Review Committee of VU University Medical Centre. The approval was waived because the Medical Research Involving Human Subjects Act did not apply to this study (reference number 2020140).

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from Perined. Restrictions apply to the availability of these data, which were used under license for this study. Data are available from the author(s) with the permission of Perined.

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