Received: 15 August 2025 | Revised: 31 March 2026 | Accepted: 5 April 2026

DOI: 10.1111/aogs.70233

ORIGINAL RESEARCH

Maternal smoking during pregnancy and gestational diabetes mellitus: Interactions and independent associations on pregnancy duration and perinatal outcomes

Lotta S. Holopainen[1] | Hanna H. Tähtinen[1] | Mika Gissler[2,3,4,5] | Päivi E. Korhonen[1] | Mikael O. Ekblad[1]

[1]Department of General Practice, Institute of Clinical Medicine, University of Turku and Turku University Hospital, Turku, Finland

[2]THL Finnish Institute for Health and Welfare, Department of Data and Analytics, Helsinki, Finland

[3]Research Centre for Child Psychiatry, University of Turku, Turku, Finland

[4]Karolinska Institute, Department of Molecular Medicine and Surgery, Stockholm, Sweden

[5]Region Stockholm, Academic Primary Health Care Centre, Stockholm, Sweden

Correspondence
Lotta S. Holopainen, Department of General Practice, University of Turku, Turun yliopisto, Yleislääketiede, 20014 Turun yliopisto, Turku, Finland.
Email: lsholo@utu.fi

Funding information
Juho Vainion Säätiö, Grant/Award Number: 202500230 and 202600492; Turun Yliopistosäätiö, Grant/Award Number: 082078; State research funding, Grant/Award Number: 11142

Abstract

Introduction: To examine the independent and joint associations of maternal smoking during pregnancy and gestational diabetes mellitus (GDM) on the risk of preterm birth and newborn perinatal complications in a large national cohort of primiparous women, with an area of limited existing research.

Material and Methods: This register-based cohort study included 318 783 singleton births among primiparous women in Finland (2004–2018), of which 290 602 were full-term. Data on GDM, smoking status, maternal characteristics, pregnancy duration, newborn hospitalization, and mortality were obtained from the Finnish Medical Birth Register. Associations were examined using linear, logistic, and Poisson regression. Interaction between GDM and maternal smoking was assessed on multiplicative and additive scales.

Results: GDM and continued smoking were independently associated with shorter pregnancy duration and an increased risk of newborn hospitalization beyond 1 week. Continued smoking also increased the risks of preterm birth and perinatal mortality. On the additive scale, combined exposure to GDM and maternal continued smoking produced higher absolute risks than expected from either exposure alone. Additive interaction was observed for preterm birth (RERI = 0.44, 95% CI: 0.16–0.67), gestational duration (RERI = 2.05 days, 95% CI: 1.07–3.04), and delayed hospital discharge (RERI = 0.36, 95% CI: 0.27–0.39). On the multiplicative scale, interaction was detected only for gestational duration ($p = 0.008$).

Conclusion: Both GDM and maternal smoking contribute independently to adverse perinatal outcomes, but their combined exposure elevates absolute risks more than either factor alone, particularly for reduced gestational length, preterm birth, and delayed newborn discharge. These findings highlight the importance of

Abbreviations: BMI, body mass index; GDM, gestational diabetes mellitus; ICD, international classification of diseases; OGTT, oral glucose tolerance test; RERI, the relative excess risk due to interaction.

addressing both smoking and GDM in prenatal care, even among generally low-risk primiparous women.

KEYWORDS
gestational diabetes, perinatal mortality, perinatal risk, pregnancy, preterm birth, smoking

1 | INTRODUCTION

Maternal smoking during pregnancy and gestational diabetes mellitus (GDM) are major risk factors for adverse perinatal outcomes, including preterm birth, neonatal morbidity, and perinatal mortality.[1,2] Both conditions share common pathophysiological pathways, such as placental dysfunction, oxidative stress, and inflammation,[3,4] potentially amplifying their adverse effects when coexisting.

Both maternal smoking and GDM are individually associated with reduced pregnancy duration and an increased risk of preterm birth as well as perinatal mortality, encompassing stillbirth and neonatal death.[5–8] Maternal smoking during pregnancy and GDM also contribute to prolonged hospitalization due to metabolic instability and feeding difficulties.[2,9] Newborns exposed to maternal smoking often require extended monitoring for impaired metabolic adaptation,[6] while those affected by GDM are at increased risk of hypoglycemia and respiratory distress, possibly leading to longer stays in the neonatal intensive care unit (NICU).[10]

Despite the well-documented independent risks, the interaction and combined impact of maternal smoking and GDM on perinatal outcomes remains insufficiently studied. Recent findings indicate that smoking throughout pregnancy compromises the newborn's head growth and is associated with smaller newborn's birth weight in women both with and without GDM.[11] Another study showed that smoking among women with hyperglycemia first diagnosed during pregnancy could mask the risk of maternal hyperglycemia for newborns who are large for gestational age.[12] Further, a study from the United States showed that maternal smoking and GDM each increased the risk of cesarean delivery, with a synergistic interaction between the two further elevating the likelihood.[13] Previous literature raises the concern that other adverse outcomes might be more prevalent during perinatal period when maternal smoking and GDM are coexisting. Shared mechanisms suggest a possible interaction, necessitating further investigation into their combined effect on preterm birth, perinatal mortality, and hospitalization duration.

Previous studies have shown independent effects of GDM and maternal smoking on perinatal outcomes, but evidence for their combined effect is limited. Our analyses aim to both replicate established findings in a large population and assess whether clinically relevant combined associations exist. Using registry-based longitudinal cohort data, we assess these outcomes in a population of healthy primiparous and term newborns.

Key message

Combined exposure to GDM and continued smoking increased absolute risks of shorter gestation, preterm birth, and delayed newborn discharge, while both exposures also showed independent adverse associations. These risks were evident even in a largely low-risk population.

2 | MATERIAL AND METHODS

2.1 | Data sources

The research data on newborn and maternal characteristics were derived from the Finnish Medical Birth Register and the Finnish Hospital Discharge Register which are currently maintained by the Finnish Institute of Health and Welfare (THL). The Medical Birth Register is considered a complete register of all births and newborns in Finland. The register data include all live births and stillborn fetuses with a gestational age of at least 22 weeks or with a birth weight of at least 500 grams. Register data are collected from all maternity hospitals (hospital births), auxiliary health care personnel (home births), the Central Population Register (missing live births), and the Cause of Death Register (missing stillbirths and neonatal deaths). The register contains information about the mother's and newborn's personal identification number; the mother's background information, previous pregnancies and deliveries, as well as health care visits and interventions during pregnancy and delivery; and newborn outcome up to 7 days of age. According to data quality studies, most of the content of the register data corresponds well or satisfactorily to the information in the hospital records.[14]

The Hospital Discharge Register includes information on all episodes of inpatient care, including all inpatient stays in public and private hospitals since 1969 and outpatient visits in public hospitals since 1998. The register contains information on the patient's background, procedures, hospital stays and diagnoses according to the Tenth Revision of International Classification of Diseases (ICD) since 1996. ICD-10 classification was used throughout the study period. A systematic review revealed that the completeness and accuracy of the register range from satisfactory to very good.[15]

2.2 | Study sample

The original study sample comprised 835 551 pregnancies in Finland between 2004 and 2018. We excluded multiparous pregnancies ($n = 487\,928$), pregnancies with pregestational diabetes (ICD-10 O24.0–O24.3; $n = 2685$), insulin-treated diabetes during pregnancy ($n = 4535$), and observations with missing maternal anthropometrics ($n = 15\,321$) or missing smoking information ($n = 5472$).

The final study population included 318 783 singleton births from primiparous women, of which 15 733 were preterm (<37 + 0 weeks) and 12 448 were post-term (>42 + 0 weeks). Full-term births ($n = 290\,602$) formed the main analytic cohort, representing 91.2% of eligible cases. In sensitivity analyses, the cohort was stratified by gestational age category to evaluate whether the main associations were consistent across different birth-timing groups.

2.3 | Variables

Information on newborn and maternal background factors was obtained from the Finnish Medical Birth Register. Smoking status was self-reported and documented in a structured form at the delivery hospital. Smoking was categorized into three classes: (1) did not smoke during pregnancy, (2) quit during the first trimester, and (3) continued smoking after the first trimester. GDM was identified using ICD-10 codes O24.4 and O24.9.

Preterm birth was defined as delivery before 37 completed weeks of gestation (yes/no). Perinatal mortality was analyzed as a dichotomous variable and defined in accordance with the Finnish Medical Birth Register to include both stillbirths (≥22 + 0 gestational weeks or birthweight ≥500 g) and early neonatal deaths. To complement the binary preterm outcome, pregnancy duration was analyzed as a continuous variable in days (with 40 + 0 weeks = 280 days). Age at discharge was analyzed both continuously (days) and dichotomously as >7 days vs. ≤ 7 days.

2.4 | Statistical analysis

Logistic regression models were used to estimate the association between GDM, smoking, and the following outcomes: preterm birth, perinatal mortality, and delayed hospital discharge. Linear regression model was used to estimate the association between GDM, smoking, and duration of pregnancy, while Poisson regression model was applied to assess their association with age at discharge from the hospital. Beta in the results, regarding duration of pregnancy and age at discharge from the hospital, indicates differences between the groups in days. The main analyses were conducted using a population of only full-term newborns ($n = 290\,602$), while the analyses regarding the risk of preterm birth were performed using the entire study population ($n = 306\,335$).

We analyzed associations between maternal smoking, GDM, and perinatal outcomes using multivariable logistic regression. The first model was fitted separately for each perinatal outcome, with the outcome as the dependent variable and maternal smoking, GDM, and covariates as independent variables. Maternal age was modeled continuously and pre-pregnancy BMI categorically. In the second model, we added a multiplicative interaction term (maternal smoking × GDM) and evaluated its statistical significance using Wald χ^2 tests. When interactions were significant, we derived stratum-specific adjusted odds ratios with 95% confidence intervals using model-based linear combinations. To improve interpretability, we additionally assessed additive effect using established measure: the relative excess risk due to interaction (RERI).[16] RERI was calculated from adjusted odds ratios, with confidence intervals estimated using the delta method. Additive-scale models were adjusted for the same covariates as the multiplicative models. For the additive interaction analyses, maternal smoking was additionally recoded into two contrast variables to reflect clinically meaningful exposure contrasts: (i) any prenatal maternal smoking (women who quit during the first trimester plus women who continued after the first trimester) vs non-smoking, and (ii) continued smoking after the first trimester vs all others. This specification allowed quantification of departure from additivity for both "any prenatal maternal smoking" and "continued maternal smoking" in combination with GDM, using the same covariate set as in the multiplicative models.

Information on socioeconomic status was available for only 53.4% of the population and was therefore not included in the adjusted models; its implications are addressed in the discussion. Model assumptions were evaluated using studentized residuals. Sensitivity analyses were performed using the full gestational age range to assess robustness and examine whether conditioning on term births influenced estimates.

All statistical analyses were conducted using SAS version 9.4 (SAS Institute Inc., Cary, NC). Statistical significance was defined as two-sided $p < 0.05$ and 95% confidence intervals.

3 | RESULTS

Table 1 presents the characteristics of the term pregnancies ($n = 290\,602$) according to GDM diagnoses and maternal smoking status. Continued smoking after the first trimester of pregnancy was reported in 9.9% ($n = 28\,761$) of cases, while 8.0% ($n = 23\,302$) of women quit smoking during the first trimester, and 82.1% ($n = 238\,539$) reported no smoking. Smoking was more common among younger women and those with lower socioeconomic status. GDM was diagnosed in 8.9% ($n = 25\,948$) of pregnancies. The prevalence of smoking only during the first trimester of pregnancy was slightly higher among women with GDM compared with those without GDM (9.8% vs. 7.8%, respectively), while rates of continued smoking were nearly identical (9.86% vs. 9.90%, respectively). Women with GDM were older (mean 29.4 years vs. 27.6 years) and had higher BMI (27.6 vs. 23.5) than those without GDM.

TABLE 1 Background characteristics of the study population by GDM and maternal smoking status.

	GDM, *n* (%)[a]			Smoking status, *n* (%)				
	No	Yes	*p*-value	No smoking	Quit smoking	Continued smoking	*p*-value	Total, *n* (%)[a]
Total, *n* (%)	264 654 (91.07)	25 948 (8.93)		238 539 (82.08)	23 302 (8.02)	28 761 (9.90)		2,90 602
Maternal age, mean (SD)	27.60 (5.16)	29.36 (5.43)	<0.0001	28.36 (5.00)	25.77 (5.05)	24.31 (5.22)	<0.0001	27.75 (5.20)
Marital status, *n* (%)			<0.0003				<0.0001	
Single	19 090 (7.21)	1595 (6.15)		12 608 (5.29)	2454 (10.53)	5623 (19.55)		20 685 (7.12)
Cohabiting/married	228 026 (86.16)	22 648 (87.28)		211 397 (88.62)	18 896 (81.09)	20 381 (70.86)		250 674 (86.26)
Unknown	17 538 (6.63)	1705 (6.57)		14 534 (6.09)	1952 (8.38)	2757 (9.59)		19 243 (6.62)
Smoking status, *n* (%)			<0.0001					
No smoking	217 693 (82.26)	20 846 (80.34)						238 539 (82.08)
Quit smoking	20 759 (7.84)	2543 (9.80)						23 302 (8.02)
Continued smoking	26 202 (9.90)	2559 (9.86)						28 761 (9.90)
GDM, *n* (%)							<0.0001	
No				217 693 (91.26)	20 759 (89.09)	26 202 (91.10)		264 654 (91.07)
Yes				20 846 (8.74)	2543 (10.91)	2559 (8.89)		25 948 (8.93)
BMI, mean (SD)	24.49 (4.16)	27.55 (6.10)	<0.0001	23.74 (4.83)	24.41 (4.98)	24.30 (5.71)	<0.0001	23.85 (4.52)
BMI categories, *n* (%)							<0.0001	
<20	43 958 (16.61)	1649 (6.36)		36 712 (15.39)	3580 (15.36)	5315 (18.48)		45 607 (15.69)
20–24.9	150 736 (56.96)	8704 (33.54)		134 478 (56.38)	11 468 (49.21)	13 494 (46.92)		159 440 (54.87)
25–29.9	49 496 (18.70)	7837 (30.20)		45 947 (19.26)	5268 (22.61)	6118 (21.27)		57 333 (19.73)
30–34.9	14 967 (5.66)	4541 (17.50)		14 969 (6.28)	2005 (8.60)	2534 (8.81)		19 508 (6.71)
35 or more	5497 (2.08)	3217 (12.40)		6433 (2.70)	981 (4.21)	1300 (4.52)		8714 (3.00)
Socioeconomic status, *n* (%)			<0.0001				<0.0001	
Upper white-collar	40 139 (15.17)	3074 (11.58)		40 715 (17.07)	1539 (6.60)	959 (3.33)		43 213 (14.87)
Lower white-collar	72 980 (27.58)	7536 (29.04)		66 979 (28.08)	6916 (29.68)	6621 (23.02)		80 516 (27.71)
Blue-collar	28 600 (10.81)	2990 (11.55)		22 055 (9.52)	3771 (16.19)	5771 (20.07)		31 597 (10.87)
Other/unknown	122 935 (46.45)	12 341 (47.56)		108 790 (45.61)	11 076 (47.53)	15 410 (53.58)		135 276 (46.55)

Abbreviations: BMI, body mass index; GDM, gestational diabetes mellitus; SD, standard deviation.

[a]If not stated otherwise.

3.1 | Preterm birth and pregnancy duration

Continued maternal smoking was associated with a higher risk for preterm birth (OR = 1.20, 95% CI: = 1.13–1.26) compared with non-smoking. GDM was not associated with higher risk for preterm birth (OR = 0.98, 95% CI: = 0.92–1.03). The multiplicative interaction of GDM and maternal smoking on preterm birth was not significant ($p = 0.49$). Additive interaction analyses showed significant results for preterm birth in the group of women of any smoking during pregnancy (RERI = 0.24, 95% CI: = 0.05–0.44) and smoking after the first trimester (RERI = 0.44, 95% CI: = 0.16–0.67). The detailed results regarding interaction are presented in Table 2.

Both GDM (b = −1.20, 95% CI: = −1.30, −1.09) and continued maternal smoking (b = −0.29, 95% CI = −0.41, −0.17, respectively) were associated with shorter pregnancy duration. The multiplicative interaction of GDM and maternal smoking was significant for shorter pregnancy duration by days ($p = 0.008$), such that GDM was associated with a shorter pregnancy duration regardless of smoking, whereas smoking was associated with pregnancy duration only in those without GDM. Figure 1 illustrates the multiplicative interaction of GDM and maternal smoking on gestational duration (in days) among full-term newborns.

3.2 | Perinatal mortality

Continued maternal smoking was associated with a higher risk for perinatal mortality (OR = 1.38, 95% CI = 1.01–1.88) compared with non-smoking. Smoking during only the first trimester was not associated with perinatal mortality. A higher risk for perinatal mortality was not observed with GDM (OR = 0.80, 95% CI = 0.56–1.14) compared with newborns of women without GDM. No significant multiplicative or additive interactions were observed between GDM and maternal smoking on perinatal mortality (Table 2).

3.3 | Delayed hospital discharge

Both GDM (OR = 1.25, 95% CI = 1.16–1.33) and continued maternal smoking (OR = 1.41, 95% CI = 1.32–1.51) were associated with a higher risk of the dichotomized outcome of hospitalization beyond 1 week. No significant multiplicative interactions were observed between GDM and maternal smoking on delayed hospital discharge of the newborn ($p = 0.80$). A significant additive interaction was observed for delayed hospital discharge in the group of women smoking after the first trimester (RERI = 0.36, 95% CI: 0.27–0.39). Detailed interaction results are presented in Table 2.

Figure 2 illustrates the multiplicative interaction of GDM and maternal smoking on the age of newborn at hospital discharge by days among full-term newborns. The mean age of newborn at hospital discharge was among newborns exposed to no smoking 3.59 days (95% CI: 3.58–3.61), quit smoking 3.50 days (95% CI: 3.48–3.53), and continued smoking 3.69 days (95% CI: 3.66–3.71, $p < 0.0001$). The mean age of newborn at hospital discharge was among women without GDM 3.55 days (95% CI: 3.54–3.57) and with GDM 3.63 days (95% CI: 3.61–3.66, $p < 0.001$). The multiplicative interaction of maternal smoking and GDM on the age at hospital discharge by days was statistically insignificant ($p = 0.36$).

3.4 | Supporting information

We performed sensitivity analyses on the characteristics of the study population and interaction models of maternal smoking and GDM on the perinatal outcomes with the entire study population ($n = 318\,783$), including also preterm ($n = 15\,733$, 4.93%) and post-term ($n = 12\,448$, 3.90%) pregnancies (Tables S1 and S2; Figures S1 and S2). The primary observed results remained statistically significant and valid.

4 | DISCUSSION

This study examined the independent and joint associations of GDM and maternal smoking during pregnancy with perinatal outcomes in a large national cohort of primiparous women. GDM and continued smoking were each associated with shorter pregnancy duration, a higher age of the newborn at discharge, and an increased risk of hospitalization lasting longer than 1 week. Continued maternal smoking was also associated with higher odds of preterm birth and perinatal mortality, consistent with earlier research identifying smoking as one of the most important preventable risk factors for adverse pregnancy outcomes.[9]

A key aim of the study was to assess whether GDM and maternal smoking have an interaction effect on perinatal risk factors. On the multiplicative scale, the only interaction was detected for gestational duration, where GDM was consistently associated with moderate shorter pregnancy duration, regardless of smoking status, whereas continued smoking was associated with shorter pregnancy duration only in pregnancies without maternal GDM. Multiplicative interactions were not observed for preterm birth, perinatal mortality, or prolonged hospitalization, suggesting that smoking did not modify the relative associations between GDM and these outcomes.

However, on the additive scale – more relevant for public-health impact—important joint effects were observed. Additive interaction analyses showed that the combined exposure to GDM and maternal smoking was associated with a higher absolute risk of preterm birth than would be expected from their individual effects. These findings indicate that women exposed to both GDM and smoking face a higher absolute risk of preterm birth than would be expected from either exposure alone.

Additive interaction was also observed for gestational duration, where the combined exposure resulted in a greater reduction in pregnancy length than anticipated from the independent effects. These results suggest that the coexistence of GDM and smoking

TABLE 2 Results from multivariable logistic regression quantifying multiplicative and additive interaction between maternal smoking and gestational diabetes on the risk of preterm birth, perinatal mortality, delayed hospital discharge.

	No.	Incidence (per 1000)	Standard model		Multiplicative interaction model		Additive interaction model	
			OR (95% CI)	*p*	OR (95% CI)	*p*	Exposure category	RERI (95% CI)
Preterm birth								
Smoking status								
No smoking	12881	49.2	1 (ref)					
Quit smoking	1150	45.3	0.97 (0.91–1.03)	0.29		0.32		
Continued smoking	1704	53.7	1.20 (1.13–1.26)	<0.0001		<0.0001		
Total	15735	49.4						
GDM								
No	14215	49.0	1 (ref)					
Yes	1520	53.5	0.98 (0.92–1.03)	0.38		0.65		
Total	15735	59.4						
Interaction model SDP × GDM						0.49		
GDM yes vs. no at no smoking					0.99 (0.93–1.05)		Any smoking during pregnancy	0.24 (0.05–0.44)
GDM yes vs. no at quit smoking					0.99 (0.82–1.19)		Smoking after the 1st trimester	0.41 (0.16–0.67)
GDM yes vs. no at continued smoking					0.88 (0.75–1.05)			
Perinatal mortality								
Smoking status								
No smoking	323	1.4	1 (ref)					
Quit smoking	29	1.2	0.97 (0.66–1.43)	0.89		0.65		
Continued smoking	48	1.7	1.38 (1.01–1.88)	0.46		0.48		
Total	400	1.4						
GDM								
No	365	1.4	1 (ref)					
Yes	35	1.3	0.80 (0.56–1.14)	0.21		0.31		
Total	400	1.4						

TABLE 2 (Continued)

	No.	Incidence (per 1000)	Standard model		Multiplicative interaction model		Additive interaction model	
			OR (95% CI)	*p*	OR (95% CI)	*p*	Exposure category	RERI (95% CI)
Interaction model SDP × GDM						0.68		
GDM yes vs. no at no smoking					0.81 (0.54–1.21)		Any smoking during pregnancy	0.63 (−0.53–1.78)
GDM yes vs. no at quit smoking					1.06 (0.37–3.05)		Smoking after the 1st trimester	1.44 (−0.66–3.54)
GDM yes vs. no at continued smoking					0.52 (0.16–1.69)			
Delayed hospital discharge								
Smoking status								
No smoking	6753	28.3	1 (ref)					
Quit smoking	606	26.0	0.94 (0.83–1.02)	0.15		0.87		
Continued smoking	1067	37.1	1.41 (1.32–1.51)	<0.0001		0.53		
Total	8426	29.0						
GDM								
No	7346	27.8	1 (ref)					
Yes	1080	41.6	1.25 (1.16–1.33)	<0.0001		<0.0001		
Total	8426	29.0						
Interaction model SDP × GDM						0.80		
GDM yes vs. no at no smoking					1.25 (1.16–1.35)		Any smoking during pregnancy	0.039 (−0.21–0.28)
GDM yes vs. no at quit smoking					1.28 (1.02–1.60)		Smoking after the 1st trimester	0.36 (0.027–0.39)
GDM yes vs. no at continued smoking					1.18 (0.98–1.42)			

Note: Adjusted by maternal age, marital status, BMI, and socioeconomic status.

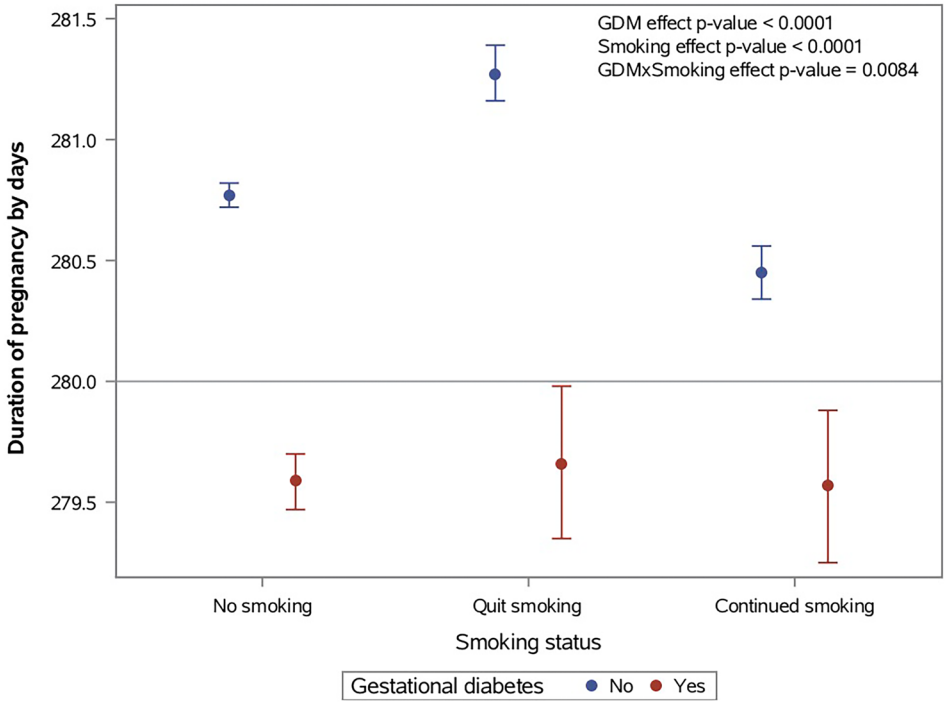

FIGURE 1 The association of GDM and maternal smoking on the duration of pregnancy by days among full-term newborns. The figure presents β-estimates (days) and 95% CI for each exposure group.

accelerates the timing of delivery to a degree that reflects more than the sum of their separate associations.

Previous studies have consistently reported an increased risk of preterm birth among women with GDM, potentially reflecting metabolic disturbances, co-morbidities, or suboptimal glycemic control.[2,5,7,8] In our study, however, GDM was not associated with elevated odds of preterm birth. While the Finnish GDM care model—based on early identification and dietary management—may contribute to lower preterm birth risk, this remains speculative.[17] Several methodological considerations must also be acknowledged. First, misclassification of GDM is possible because diagnoses were based solely on ICD codes, and individual oral glucose tolerance test (OGTT) laboratory values or detailed measures of glycemic control were not available. Second, variation in GDM severity may have influenced the findings, particularly since insulin-treated pregnancies were excluded, limiting generalizability to milder cases. Third, residual confounding by unmeasured lifestyle, metabolic, or clinical factors cannot be excluded. Future studies with more detailed metabolic data, including OGTT values or severity indicators, may clarify these associations further.

In contrast, continued maternal smoking was associated with 20% higher odds of preterm birth, consistent with earlier literature identifying smoking as a primary contributor to spontaneous preterm labor, likely mediated through placental insufficiency, chronic fetal hypoxia, and systemic inflammation.[18,19]

A significant multiplicative interaction between GDM and maternal smoking was observed for pregnancy duration. Duration of pregnancy in full-term pregnancies was on average 1.3 days shorter in women with GDM, regardless of maternal smoking status. This reduction is minor and likely of limited clinical significance, but it may reflect obstetric management practices such as earlier induction or planned cesarean section—information that was not available in the register data. In contrast, in women without GDM, smoking was associated with shorter duration of pregnancy, consistent with findings from previous studies.[8,18,19] While preterm birth is a well-established risk factor for neonatal morbidity and mortality, recent evidence suggests that even modest reductions in gestational age within the term range (37–38 weeks) are associated with increased risks of respiratory distress, hypoglycemia, jaundice, and feeding difficulties.[20,21] These risks are particularly relevant in pregnancies affected by GDM or maternal smoking, where fetal metabolic regulation and placental function may already be compromised. In our study, the gestational age was also analyzed as a continuous variable (days) to capture subtle differences in pregnancy duration within the term range. Thus, maintaining optimal gestational length is essential not only for preventing preterm birth but also for reducing newborn complications among early term deliveries.

For delayed hospital discharge, additive interaction was seen in the group of women who continued smoking after the first trimester. This indicates that infants born to women with both exposures have an increased absolute likelihood of requiring prolonged hospital care. Both smoking and GDM contribute to prolonged hospitalization for example due to metabolic instability and feeding difficulties. Newborns exposed to maternal smoking often require extended monitoring for impaired metabolic and respiratory adaptation,[6,22] while those affected by GDM are at increased risk of hypoglycemia and NICU days due to respiratory distress.[23] Our findings were consistent with prior research, showing that GDM and maternal smoking each significantly

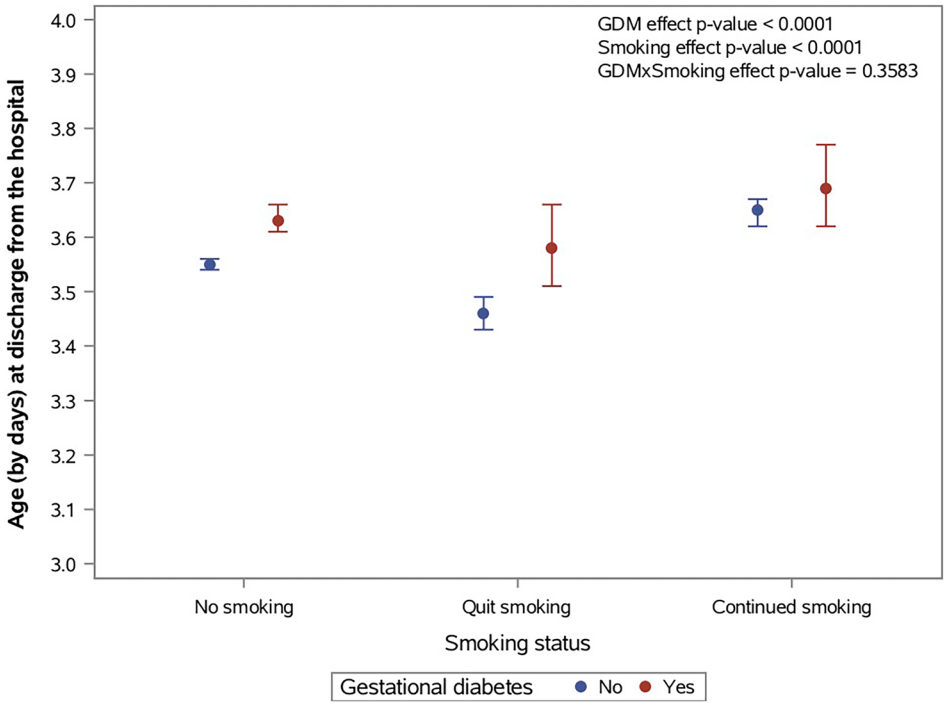

FIGURE 2 The association between GDM and maternal smoking on the age at hospital discharge by days among full-term newborns. The figure presents β-estimates (days) and 95% CI for each exposure group.

were associated with increased odds of newborn hospitalization beyond 1 week and with slightly higher mean newborn age at hospital discharge. These findings underline the clinical relevance of considering combined maternal risk profiles in early postnatal care planning.

Perinatal mortality is most commonly linked to preterm birth, but it also occurs among term newborns[24] and remains a meaningful contributor to newborn mortality in high-income countries.[25] Among term births, perinatal death is often related to intrapartum complications, unrecognized fetal growth restriction, placental insufficiency, or maternal conditions such as hypertension, obesity, and smoking.[24,26] Smoking during pregnancy is a well-established modifiable risk factor for stillbirth and neonatal death, even in otherwise low-risk term pregnancies.[25,27] In our study of healthy primiparous women, continued smoking was associated with 38% higher odds in perinatal mortality, underscoring its importance as a preventable risk factor. In contrast, GDM alone did not increase mortality among term newborns, suggesting that well-managed GDM may not substantially elevate risk. The absence of interaction associations between smoking and GDM on perinatal mortality may reflect methodological and biological factors, including measurement limitations, systematic screening and proactive management, and limited statistical power for rare outcomes.[16]

A major strength of this study is the use of comprehensive national register data covering 88% of all primiparous singleton births over a 14-year period, providing a large and population-based cohort with detailed information on maternal characteristics and key preexisting conditions. Excluding women with pregestational diabetes strengthened internal validity by clearly separating gestationally acquired hyperglycemia.

However, several limitations must be acknowledged. Smoking data were self-reported and therefore vulnerable to underreporting[28–30] and information on the amount of smoking or use of newer nicotine products, such as e-cigarettes or nicotine pouches, was not available. Although these products were uncommon in Finland during the study years, the lack of detailed tobacco exposure data may lead to underestimation of nicotine-related risks. Paternal smoking was also unavailable despite its potential relevance through secondhand exposure.

For GDM, diagnostic detail was limited because the Medical Birth Register does not include OGTT laboratory values, fasting glucose measurements, or individual-level treatment information. Information on GDM treatment was limited to aggregate data from a survey conducted by the Finnish Diabetes Association.[31] According to the survey, women with GDM, 82% were treated with diet alone, while 8% received metformin, 11% insulin, and 8% a combination of insulin and metformin. Despite potential treatment, women diagnosed with GDM in our study showed statistically significant differences in pregnancy duration and perinatal outcomes compared with those without GDM. Unfortunately, the Medical Birth Register does not include information on maternal weight gain, dietary intake, or physical activity during pregnancy—factors that would provide more comprehensive insight into modifiable risks for GDM.

The study also lacks information on whether women received treatment to prevent preterm birth or on specific delivery details, such as the proportion of induced births or elective vs. emergency cesarean sections. Furthermore, reasons for prolonged newborn hospitalization were not available, which limits the interpretation of

these outcomes. For example, newborns of women with GDM are at increased risk of hypoglycemia, which frequently requires admission to the NICU.[32,33]

Residual confounding remains possible because socioeconomic status, lifestyle factors, and other potential confounders were incompletely captured. The primary analyses focused on term births to reduce heterogeneity but restricting analyses to full-term infants may introduce collider bias, as both smoking and GDM influence the likelihood of preterm delivery. Sensitivity analyses including all gestational ages supported the robustness of the findings, although some bias cannot be entirely excluded.

Overall, these limitations should be considered when interpreting the results, and future studies would benefit from more detailed clinical measures—particularly OGTT values, maternal lifestyle factors, and comprehensive assessments of tobacco and nicotine exposure.

5 | CONCLUSION

In our study, interaction analyses showed that combined exposure to GDM and maternal smoking—particularly continued smoking after the first trimester—was associated with higher absolute risks than expected from either exposure alone, including shorter gestation, increased risk of preterm birth, and delayed newborn discharge. Our findings also confirm patterns reported in earlier literature; independent associations with GDM and SDP on perinatal outcomes were observed concerning shorter pregnancy duration and increased risk of prolonged newborn hospitalization above 1 week. Maternal smoking was also associated with higher risk of preterm birth and perinatal mortality. These findings demonstrate that clinically meaningful perinatal risks are evident even in low-risk pregnancies and underline the importance of addressing both maternal smoking and GDM in prenatal care, with particular focus on women exposed to both risk factors.

AUTHOR CONTRIBUTIONS

All authors contributed to the study conception and design. Material preparation, data collection, and analysis were performed by Mikael O. Ekblad and Mika Gissler. The first draft of the manuscript was written by Lotta S. Holopainen. Holopainen and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

ACKNOWLEDGEMENT

Open access publishing facilitated by Turun yliopisto, as part of the Wiley - FinELib agreement.

FUNDING INFORMATION

L. S. Holopainen reports on a grant awarded to write an article by the Juho Vainio Foundation (grant numbers 202500230 and 202600492) and Turku University Foundation (grant number 082078). This research was funded by the State Research Funding (grant number 11142).

CONFLICT OF INTEREST STATEMENT

The authors declare that they have no conflict of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from Findata. Restrictions apply to the availability of these data, which were used under license for this study. Data are available from https://www.findata.fi with the permission of Findata.

ETHICS STATEMENT

Our research does not require a separate permission from the ethics committee, because the material is based on anonymous or pseudonymized material and data subjects are not contacted. As our study used routinely recorded administrative health records, informed consent was not required. THL Finnish Institute for Health and Welfare performed the ethical review and granted the permission to use its confidential register data.

ORCID

Lotta S. Holopainen https://orcid.org/0000-0003-2138-4878
Hanna H. Tähtinen https://orcid.org/0000-0002-1912-4877
Mika Gissler https://orcid.org/0000-0001-8254-7525
Päivi E. Korhonen https://orcid.org/0000-0002-5614-6442
Mikael O. Ekblad https://orcid.org/0000-0001-8369-4359

REFERENCES

1. Castles A, Adams EK, Melvin CL, Kelsch C, Boulton ML. Effects of smoking during pregnancy. *Am J Prev Med*. 1999;16(3):208-215. doi:10.1016/S0749-3797(98)00089-0
2. HAPO - Metzger et al. Hyperglycemia and adverse pregnancy outcome (HAPO) study. *Diabetes*. 2009;58(2):453-459. doi:10.2337/db08-1112
3. Zhou X, Zhang H, Wei L, et al. Oxidative stress, mitochondrial dysfunction, and ferroptosis in the placenta of gestational diabetes mellitus. *J Mol Med*. 2026;104(1):8. doi:10.1007/s00109-025-02629-7
4. Stone WL. The pathophysiology of smoking during pregnancy a systems biology approach. *Front Biosci*. 2014;6(2):318-328. doi:10.2741/e708
5. Preda A, Iliescu DG, Comănescu A, et al. Gestational diabetes and preterm birth: what do we know? Our experience and mini-review of the literature. *J Clin Med*. 2023;12(14):4572. doi:10.3390/jcm12144572
6. Yang L, Yang L, Wang H, et al. Maternal cigarette smoking before or during pregnancy increases the risk of severe neonatal morbidity after delivery: a nationwide population-based retrospective cohort study. *J Epidemiol Community Health*. 2024;78(11):690-699. doi:10.1136/jech-2024-222259
7. Zhang T, Tian M, Zhang P, et al. Risk of adverse pregnancy outcomes in pregnant women with gestational diabetes mellitus by age: a multicentric cohort study in Hebei, China. *Sci Rep*. 2024;14(1):807. doi:10.1038/s41598-023-49916-2
8. Goldenberg RL, Culhane JF, Iams JD, Romero R. Epidemiology and causes of preterm birth. *Lancet*. 2008;371(9606):75-84. doi:10.1016/S0140-6736(08)60074-4
9. Tarasi B, Cornuz J, Clair C, Baud D. Cigarette smoking during pregnancy and adverse perinatal outcomes: a cross-sectional study over 10 years. *BMC Public Health*. 2022;22(1):2403. doi:10.1186/s12889-022-14881-4

10. ACOG Practice Bulletin No. 190. Gestational diabetes mellitus. *Obstet Gynecol*. 2018;131(2):e49-e64. doi:10.1097/AOG.0000000000002501
11. Holopainen LS, Tähtinen HH, Gissler M, Korhonen PE, Ekblad MO. Interaction of maternal smoking and gestational diabetes mellitus on newborn head circumference and birthweight. *Acta Obstet Gynecol Scand*. 2024;103(9):1859-1867. doi:10.1111/aogs.14920
12. Cosson E, Carbillon L, Tatulashvili S, et al. Antagonistic effects of smoking and maternal glycemia on fetal growth: a retrospective study among 13,958 pregnant French women. *Front Endocrinol*. 2025;16:1527358. doi:10.3389/fendo.2025.1527358
13. Song J, Cai R. Interaction between smoking during pregnancy and gestational diabetes mellitus and the risk of cesarean delivery: evidence from the National Vital Statistics System 2019. *J Matern Fetal Neonatal Med*. 2023;36(2):2259048. doi:10.1080/14767058.2023.2259048
14. Gissler M, Teperi J, Hemminki E, Meriläinen J. Short communication: data quality after restructuring a National Medical Registry. *Scand J Soc Med*. 1995;23(1):75-80. doi:10.1177/140349489502300113
15. Sund R. Quality of the Finnish hospital discharge register: a systematic review. *Scand J Public Health*. 2012;40(6):505-515. doi:10.1177/1403494812456637
16. VanderWeele TJ, Knol MJ. A tutorial on interaction. *Epidemiol Methods*. 2014;3(1):33-72. doi:10.1515/em-2013-0005
17. Gestational diabetes. *Current Care Guidelines. Working group set up by the Finnish Medical Society Duodecim and the Finnish Diabetes Medical Association and the Finnish Gynecological Association working group*. Finish Medical Society Duodecim; 2022. Accessed August 8, 2025. www.kaypahoito.fi
18. Shah NR, Bracken MB. A systematic review and meta-analysis of prospective studies on the association between maternal cigarette smoking and preterm delivery. *Am J Obstet Gynecol*. 2000;182(2):465-472. doi:10.1016/S0002-9378(00)70240-7
19. Ion R, Bernal AL. Smoking and preterm birth. *Reprod Sci*. 2015;22(8):918-926. doi:10.1177/1933719114556486
20. Engle WA, Kominiarek MA. Late preterm infants, early term infants, and timing of elective deliveries. *Clin Perinatol*. 2008;35(2):325-341. doi:10.1016/j.clp.2008.03.003
21. Shapiro-Mendoza CK, Tomashek KM, Kotelchuck M, et al. Effect of late-preterm birth and maternal medical conditions on newborn morbidity risk. *Pediatrics*. 2008;121(2):e223-e232. doi:10.1542/peds.2006-3629
22. Ueda Y, Stick SM, Hall G, Sly PD. Control of breathing in infants born to smoking mothers. *J Pediatr*. 1999;135(2):226-232. doi:10.1016/S0022-3476(99)70026-0
23. Yang F, Liu H, Ding C. Gestational diabetes mellitus and risk of neonatal respiratory distress syndrome: a systematic review and meta-analysis. *Diabetol Metab Syndr*. 2024;16(1):294. doi:10.1186/s13098-024-01539-x
24. Lawn JE, Cousens S, Zupan J. 4 million neonatal deaths: when? Where? Why? *Lancet*. 2005;365(9462):891-900. doi:10.1016/S0140-6736(05)71048-5
25. Flenady V, Koopmans L, Middleton P, et al. Major risk factors for stillbirth in high-income countries: a systematic review and meta-analysis. *Lancet*. 2011;377(9774):1331-1340. doi:10.1016/S0140-6736(10)62233-7
26. Gardosi J, Madurasinghe V, Williams M, Malik A, Francis A. Maternal and fetal risk factors for stillbirth: population based study. *BMJ*. 2013;346(3):f108. doi:10.1136/bmj.f108
27. Salihu HM, Shumpert MN, Aliyu MH, Kirby RS, Alexander GR. Smoking-associated fetal morbidity among older gravidas: a population study. *Acta Obstet Gynecol Scand*. 2005;84(4):329-334. doi:10.1111/j.0001-6349.2005.00552.x
28. Dietz PM, Homa D, England LJ, et al. Estimates of nondisclosure of cigarette smoking among pregnant and nonpregnant women of reproductive age in the United States. *Am J Epidemiol*. 2011;173(3):355-359. doi:10.1093/aje/kwq381
29. Shipton D, Tappin DM, Vadiveloo T, Crossley JA, Aitken DA, Chalmers J. Reliability of self reported smoking status by pregnant women for estimating smoking prevalence: a retrospective, cross sectional study. *BMJ*. 2009;339(1):b4347. doi:10.1136/bmj.b4347
30. England L, Grauman A, Qian C, et al. Misclassification of maternal smoking status and its effects on an epidemiologic study of pregnancy outcomes. *Nicotine Tob Res*. 2007;9(10):1005-1013. doi:10.1080/14622200701491255
31. Koski S, Koivusilta K. *Raskausdiabetesselvitys 2019*. Finnish Diabetes Association. 2019; Accessed August 8, 2025: Available from: https://www.diabetes.fi/files/10918/Raskausdiabetesselvitys_2019.pdf
32. McKinlay CJD, Alsweiler JM, Ansell JM, et al. Neonatal Glycemia and neurodevelopmental outcomes at 2 years. *N Engl J Med*. 2015;373(16):1507-1518. doi:10.1056/NEJMoa1504909
33. Stanley CA, Rozance PJ, Thornton PS, et al. Re-evaluating "transitional neonatal hypoglycemia": mechanism and implications for management. *J Pediatr*. 2015;166(6):1520-1525.e1. doi:10.1016/j.jpeds.2015.02.045

SUPPORTING INFORMATION

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

How to cite this article: Holopainen LS, Tähtinen HH, Gissler M, Korhonen PE, Ekblad MO. Maternal smoking during pregnancy and gestational diabetes mellitus: Interactions and independent associations on pregnancy duration and perinatal outcomes. *Acta Obstet Gynecol Scand*. 2026;00:1-11. doi:10.1111/aogs.70233