Received: 13 May 2022 | Revised: 28 August 2022 | Accepted: 16 September 2022

DOI: 10.1111/aogs.14465

ORIGINAL RESEARCH ARTICLE

Relation between perinatal outcome and gestational duration in term primiparous pregnancies stratified by body mass index

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Funding information
Stig and Ragna Gorthon Fundation

Abstract

Introduction: There is growing evidence that induction of labor at 41 completed weeks improves neonatal outcome, at least among primiparous women. This study was performed to investigate whether maternal body mass index (BMI) should be considered when deciding on timing of intervention in term pregnancies.

Material and methods: The study design was a historical cohort study using data from the Swedish Medical Birth Register, singletons in cephalic presentation with births 39+0 to 41+6 weeks, with available information on maternal BMI 2005–2017 (n = 352 567). Modified Poisson regression analyses were used to investigate the association between gestational duration and stillbirth or death before 45 postmenstrual weeks (primary outcome) and Apgar score <7 at 5 minutes (secondary outcome) by BMI, respectively. Adjustments were made for maternal age, smoking, country of birth and educational level.

Results: The adjusted relative risk (ARR) of stillbirth or death before 45 weeks among infants born at 41+0 to 41+6 vs 40+0 to 40+6 weeks, was 1.26 with a 95% confidence interval (CI) of 1.07–1.48. Among women with BMI ≥30, the offspring mortality risk in pregnancies lasting 39+0 to 39+2 weeks was significantly above the corresponding risk among women of normal BMI who delivered at 41+0 to 41+2 weeks (ARR = 1.95; 95% CI 1.07–3.56) but no statistically significant heterogeneity was found regarding the magnitude of the association between gestational duration and offspring mortality. The ARR, for Apgar <7 at 5 minutes (41+0 to 41+6 vs 40+0 to 40+6 weeks, regardless of BMI), was 1.36 (95% CI 1.27–1.45). The risk for low Apgar score at 41+0 weeks was 1.5% among all children regardless of maternal BMI. Among children to women with BMI ≥30, this magnitude of risk was found already at 39+3 weeks.

Conclusions: In primiparous women with obesity the risk of stillbirth or death before 45 postmenstrual weeks were increased throughout all full-term gestational age categories, compared with women with overweight or normal BMI. Children to obese women had the same risk for Apgar scores <7 at 5 minutes compared with women overall at earlier gestational age. The results suggest that maternal BMI needs to be considered when discussing timing of elective induction in term healthy pregnancies of primiparous women.

Abbreviations: ARR, adjusted risk ratio; BMI, body mass index; CI, confidence interval; RR, risk ratio.

KEYWORDS
Apgar score, body mass index, gestational duration, obesity, overweight, perinatal outcome, stillbirth

1 | INTRODUCTION

Gestational duration and delivery after 42 completed weeks are associated with poor pregnancy outcome.[1–3] Meta-analyses of randomized clinical studies indicate that induction of labor at 41+0 weeks decreases stillbirth and perinatal death rates,[4,5] with the gestational period 41+0 to 41+6 weeks often being referred to as "late term".[6] A Swedish meta-analysis concludes that offering all women induction of labor from 41+0 weeks would significantly improve pregnancy outcome in late term pregnancies compared with expectant management.[4] In a subgroup analysis, the risk of adverse outcome in the induction of labor group was significantly decreased among primiparous but not among multiparous women.[4] This is in line with the findings from an epidemiological cohort study from Sweden which indicated that neonates of primiparous, but not of multiparous women, gained from active management in prolonged pregnancies (≥41+3), especially for neonates of obese women.[7,8] Obesity is a known risk factor for low Apgar score,[9,10] preeclampsia, diabetes, macrosomia and stillbirth during pregnancy.[11–13] High body mass index (BMI) also increases the risks for failed induction, emergency cesarean section, shoulder dystocia and postpartum bleeding >1000 ml.[14,15] Studies on elective induction from 39+0 weeks vs expectant management for women with normal BMI and for obese or severe obese women show results of lower cesarean section rate in the induction group.[16–18] For the neonate there appear to be no advantages from an additional week of expectant management after 39 weeks of gestation.[19] In the latest Cochrane analysis on the subject, the authors conclude that "the optimal timing of offering induction of labor needs further investigation as does further exploration of risk profiles of women".[5] The Swedish recommendation, from autumn 2021, on induction in the late term period, recommends that all Swedish women should be offered elective induction from 41+0 weeks, prioritizing primiparous women, a BMI >30, women born south of Sahara and >40 years old.[20]

Considering the poorer pregnancy outcomes associated with obesity, primiparous women with high BMI belongs to a high-risk group and would possibly gain from an earlier active management at term gestational duration. The aim with the current study was to investigate the combined association of BMI and advancing gestational duration with neonatal outcome among children of primiparous women in pregnancies from 39+0 to 41+6 weeks.

Key message

Children of primiparous obese women benefit from earlier term induction. The results imply that induction after a gestational duration of 39 completed weeks improves Apgar score at 5 minutes and the risk for stillbirth or death before 45 postmenstrual weeks.

2 | MATERIAL AND METHODS

Data were collected from the Swedish Medical Birth Register containing information on 98% of all births in Sweden.[21] The Medical Birth Register is kept by the Swedish National Board of Health and Welfare. Delivery and pediatric units are obligated by law to report information from standardized medical records on maternal and neonatal data. All pregnant women are offered free antenatal care, and a first or second trimester routine ultrasound screening to detect multiple births, fetal abnormalities and to estimate the fetal gestational age. Maternal first trimester smoking habits, height and weight are recorded at the first antenatal midwife appointment. In Sweden, 97% of pregnancies are dated by ultrasound examination using biparietal diameter formulas in weeks 12–14 and biparietal diameter/femur length formulas in week 15–20 scans.[22]

The inclusion criteria in the study were primiparous (no previous birth) women with singletons in cephalic presentation with available information on first trimester BMI and births between 2005 to 2017 in gestational weeks 39+0 to 41+6 (n = 352 567). The exclusion criterion was unknown first trimester BMI. BMI class was constructed as BMI <25, BMI 25–29.9, BMI ≥30. Gestational duration was divided into 3- and 4-day intervals: 39+0 to 39+2, 39+3 to 39+6, 40+0 to 40+2, 40+3 to 40+6, 41+0 to 41+2, 41+3 to 41+6 weeks.

To avoid systematic bias due to gestation-dependent follow-up length, a composite mortality outcome measure was used as the primary outcome measure, consisting of stillbirth at 39+0 to 41+6 weeks, or neonatal death occurring at 39+0 to 44+6 weeks after last menstrual period (ultrasound-adjusted), stillbirth or death before 45 postmenstrual weeks. The secondary outcome measure was Apgar <7 at 5 minutes.

2.1 | Statistical analyses

Chi-square tests were performed to compare descriptive data. The coefficients obtained from modified Poisson regression analyses were used to visualize the association between gestational duration for death at <45 ultrasound-adjusted postmenstrual weeks and for Apgar score <7 at 5 minutes, respectively, by maternal BMI. For Apgar <7, a linear model was used; for the mortality estimates, a third-degree polynomial model was fitted. If not stated otherwise, adjustments were made for maternal age (continuous), smoking (ordinal: 1 = no, 2 = 1–9 cigarettes per day, 3 = 10 or more cigarettes per day), country of birth (classes: 1 = Nordic countries, 2 = Europe/

USA/Canada/Australia/New Zealand, 3 = other), highest educational level achieved (ordinal: 9 years, 10–12, 13–14, ≥15) and gestational duration.

Missing values (for maternal smoking and educational level) were replaced by the overall means. Statistical analyses were performed using SPSS version 25 (IBM Corp., Armonk, NY, USA).

2.2 | Ethics statement

The study was approved at the Research Ethics Committee at Lund University, Sweden (reference 2015/397) on June 25, 2015

3 | RESULTS

Table 1 shows pregnancy duration, maternal characteristics, pregnancy complications and neonatal outcomes by maternal BMI. Women who were overweight or obese were more likely than women with normal BMI to deliver at 41+0 weeks or later. They were also overrepresented among women who were 35 year old or more, smokers, and born outside Europe/USA/Canada/Commonwealth. There was a strong association between low maternal educational level ≤12 years and overweight and (even more pronounced) obesity. Pregnancy complications (preeclampsia, preexisting or gestational diabetes were also more common among women who were overweight or obese than among women with normal weight, as were induction of labor and cesarean section (both elective and emergency). Children of women who were overweight or obese were at higher risk than other children of having low Apgar score, birthweight >4500 g, and/or stillbirth or death before 45 ultrasound-adjusted postmenstrual weeks.

Table 2 shows the risk of stillbirth or death before 45 weeks and low Apgar score by gestational duration (<40+0 or ≥41+0 weeks compared with 40+0 to 40+6 weeks) and by maternal BMI class. For stillbirth or death before 45 ultrasound-adjusted postmenstrual weeks, no protective association of delivery at <40 weeks compared with 40+0 to 40+6 was detected. Adjustment for maternal characteristics changed the estimates marginally. Overall, delivery at 41 completed weeks or more was significantly associated with a higher risk of stillbirth or death before 45 postmenstrual weeks than at 40+0 to 40+6 weeks. No significant heterogeneity between BMI groups was detected, but when stratified by BMI, it was revealed that the increased risk for mortality at 41 weeks compared with 40 weeks was statistically significant only for women with BMI 25.0–29.9. For women with BMI ≥30, an additional analysis comparing 41+0 to 41+6 with 39+0 to 39+6 weeks revealed an increased risk for stillbirth or death before 45 postmenstrual weeks (ARR 1.54; 95% CI 1.06–2.26). Compared with children born at 40+0 to 40+6 gestational weeks, children who were born before 40 completed weeks of pregnancy had a lower risk, and children who were born at or after 41 weeks a higher risk of low Apgar score, respectively. Adjustments for maternal characteristics changed the risk estimates marginally. The lowest point estimate for low Apgar score (RR = 0.67), <40+0 vs 40+0 to 40+6, was found among women with obesity, but no significant heterogeneity over maternal BMI strata was detected.

Figure 1 shows the risk of stillbirth or death before 45 postmenstrual weeks, ultrasound-adjusted. No linear association between mortality risk and gestational duration was indicated; instead, cubic models were applied to fit the data. From the figure it is evident that compared with children of women with normal BMI, the children of women who were overweight or obese were at higher risk of mortality during the entire period of 39+0 to 41+6 weeks. For women with BMI <25, no association between gestational duration and risk of stillbirth or death before 45 postmenstrual weeks was indicated.

Figure 2 shows the risk of Apgar <7 at 5 minutes by gestational age at birth and maternal BMI class. The regression lines were obtained by applying the coefficients retrieved from the Poisson regression analyses and the equations used are displayed in Table S1. Within each BMI class, a linear relation between low Apgar score risk and gestational duration was demonstrated. In the linear model, the crude RR for a 1-day increase of gestational duration within the interval, was 1.043 (95% CI 1.037–1.048) for children of all women, 1040 (95% CI 1.033–1.047) children of women with normal weight, 1.039 (95% CI 1.028–1.050) children of overweight women and 1.047 (95% CI 1.034–1.061) children of obese women. No interaction between maternal BMI and gestational duration in relation to risk of low Apgar scores was detected ($P = 0.737$). The risk of low Apgar score at 41+0 weeks among all women was estimated as 1.50%. Among obese women that risk level corresponded to 39+3 weeks, among overweight women 40+4, and among women with normal BMI 41+4 weeks.

4 | DISCUSSION

Women who were overweight or obese were, throughout the gestational period studied, at increased risk of having a child who died perinatally or had low Apgar score at 5 minutes compared with women with normal weight. No significant interaction between maternal BMI and gestational duration on the risk of adverse outcome was detected.

For stillbirth or death before 45 postmenstrual weeks, no linear association with increasing gestational duration was demonstrated, but an increased risk was detected for children in pregnancies lasting 41+3 weeks or more. When all BMI classes were combined, a linear association was found between risk of low Apgar score and gestational duration in pregnancies of 39+0 to 41+6 weeks among children of primiparous women.

Nevertheless, the results indicate that it is important to study the combined association of BMI and gestational duration with pregnancy outcome. Children born to women with obesity were at substantial risk (1.5%) of having low Apgar score at 39+3 weeks. The corresponding risk among children of overweight women was found at 40+2 weeks. Compared with children of women with normal BMI, children of overweight or obese women were at increased risk of stillbirth or death within 45 postmenstrual weeks

TABLE 1 Study group characteristics by maternal BMI. Primiparous women with singleton pregnancies, cephalic presentations, 2005–2017, *n* = 352 567

	BMI <25 *n* = 238 773		BMI 25–29.9 *n* = 79 313		BMI 30–34.9 *n* = 24 702		BMI ≥35 *n* = 9779		*p*-value
	n	%	*n*	%	*n*	%	*n*	%	χ^2
Gestation duration, weeks+days									<0.001
39+0 to 39+2	28 012	11.7	8561	10.8	2691	10.9	998	10.2	
39+3 to 39+6	47 004	19.7	14 495	18.3	4325	17.5	1632	16.7	
40+0 to 40+2	42 714	17.9	13 695	17.3	4135	16.7	1585	16.2	
40+3 to 40+6	54 678	22.9	18 381	23.2	5630	22.8	2204	22.5	
41+0 to 41+2	34 682	14.5	12 234	15.4	3920	15.9	1607	16.4	
41+3 to 41+6	31 683	13.3	11 947	15.1	4001	16.2	1753	17.9	
Maternal age, years									<0.001
<20	7360	3.1	2229	2.8	754	3.1	257	2.6	
20–34	206 661	86.6	66 917	84.4	20 644	83.6	8280	84.7	
35–39	20 850	8.7	8272	10.4	2610	10.6	969	9.9	
≥40	3902	1.6	1895	2.4	694	2.8	273	2.8	
Maternal smoking									<0.001
Yes	12 034	5.0	5179	6.5	2278	9.2	1095	11.2	
Not known	2128	0.9	715	0.9	227	0.9	86	0.9	
Maternal country of birth									<0.001
Nordic countries	208 433	87.3	68 529	86.4	21 587	87.4	8911	91.1	
Europe/USA/Canada/ Commonwealth	4481	1.9	1128	1.4	301	1.2	85	0.9	
Other	25 859	10.8	9656	12.2	2814	11.4	783	8.0	
Maternal educational level, years									<0.001
≤9	15 387	6.4	5981	7.5	2209	8.9	974	10.0	
10–12	72 244	30.3	28 721	36.2	10 602	42.9	4629	47.3	
13–14	31 313	13.1	10 806	13.6	3287	13.3	1204	12.3	
≥15	108 294	45.4	29 065	36.6	7056	28.6	2364	24.2	
Not known	11 535	4.8	4740	6.0	1548	6.3	608	6.2	
Pregnancy complications									
Preeclampsia	5356	2.2	2997	3.8	1493	6.0	902	9.2	<0.001
Diabetes mellitus	540	0.2	322	0.4	83	0.3	36	0.4	<0.001
Gestational diabetes	1179	0.5	818	1.0	587	2.4	425	4.3	<0.001
Start of labor									<0.001
Induction	21 993	9.2	10 578	13.3	4489	18.2	2317	23.7	
Spontaneous start	213 258	89.3	67 394	85.0	19 723	79.8	7248	74.1	
Elective CS	3609	1.5	1398	1.8	518	2.1	223	2.3	
Delivery mode									<0.001
Emergency CS	20 104	8.4	10 431	13.2	4193	17.0	2050	21.0	
Forceps/VE	32 520	13.6	10 495	13.2	2854	11.6	1052	10.8	
Vaginal, non-instrumental	181 921	76.2	56 822	71.6	17 085	69.2	6436	65.8	
Neonatal outcome									
Apgar score at 5 min <7	2631	1.1	1176	1.5	494	2.0	263	2.7	<0.001
Birthweight >4500 g	3603	1.5	2460	3.1	1094	4.4	609	6.2	<0.001
Stillbirth	302	0.1	209	0.3	98	0.4	59	0.6	<0.001
Stillbirth or death <45 weeks	399	0.2	254	0.3	113	0.5	70	0.7	<0.001

Abbreviations: CS, cesarean section; VE, vacuum extraction.

(Continues)

TABLE 2 Risk ratios (RR) for low Apgar score or stillbirth or death before 45 ultrasound-adjusted postmenstrual weeks, delivery 39+0 to 39+6 or delivery 41+0 to 41+6, weeks, respectively, vs delivery 40+0 to 40+6 weeks, stratified by maternal BMI class. Primiparous women with singleton pregnancies, cephalic presentations, 2005–2017, $n = 352\,567$

		Crude					Adjusted[a]				
		<40+0		40+0 to 40+6	≥41+0		<40+0		40+0 to 40+6	≥41+0	
		RR	95% CI	RR	RR	95% CI	RR	95% CI	RR	RR	95% CI
Apgar score <7 at 5 min											
All		0.80	0.74–0.86	1.00	1.38	1.29–1.47	0.80	0.74–086	1.0	1.36	1.27–1.45
BMI class											
	<25	0.85	0.77–0.93	1.00	1.40	1.28–1.53	0.85	0.77–0.93	1.0	1.37	1.26–1.50
	25–29.9	0.81	0.70–0.94	1.00	1.32	1.16–1.50	0.81	0.70–0.94	1.0	1.30	1.14–1.48
	≥30	0.67	0.55–0.81	1.00	1.28	1.10–1.50	0.66	0.55–0.81	1.0	1.27	1.09–1.48
P-value for heterogeneity		0.107			0.546		0.057			0.627	
Stillbirth or death before 45 postmenstrual weeks											
All		1.14	0.96–1.34	1.00	1.29	1.10–1.52	1.14	0.96–1.34	1.0	1.26	1.07–1.48
BMI class											
	<25	1.14	0.91–1.44	1.00	1.12	0.88–1.42	1.15	0.91–1.45	1.00	1.08	0.85–1.38
	25–29.9	1.43	1.05–1.93	1.00	1.42	1.05–1.92	1.42	1.05–1.92	1.00	1.40	1.04–1.89
	≥30	0.85	0.58–1.25	1.00	1.31	0.94–1.82	0.84	0.57–1.24	1.00	1.30	0.94–1.80
P-value for heterogenicity		0.115			0.459		0.111			0.374	

Abbreviations: CI, confidence interval; RR, relative risk.

[a]Adjusted for maternal age, smoking, educational level and maternal country of birth.

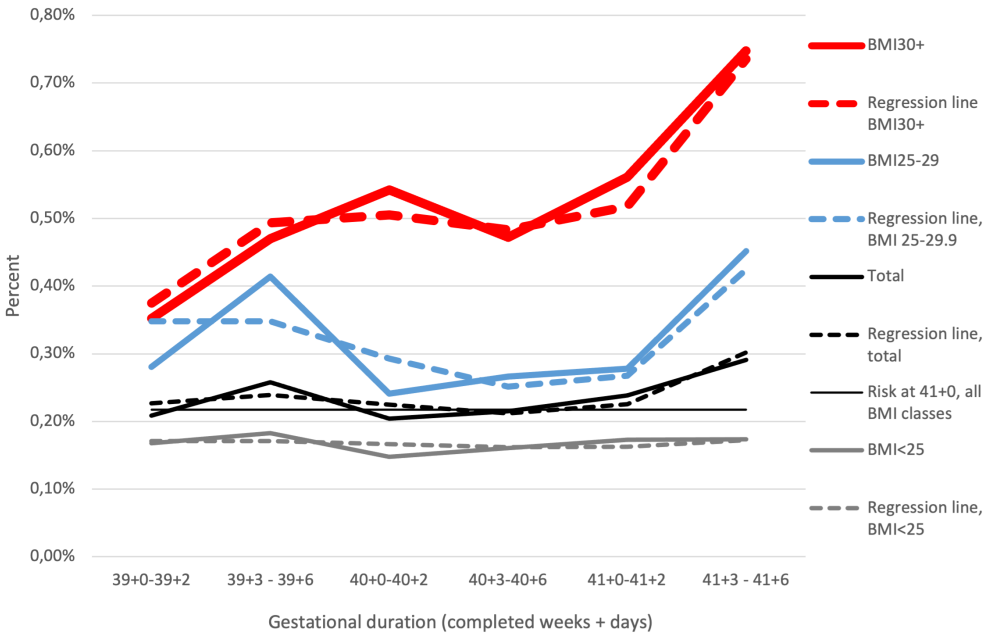

FIGURE 1 Stillbirth or death before 45 ultrasound-adjusted postmenstrual weeks combined with BMI class and gestational duration. The line at 0.22% represents the general incidence at 41+0 weeks for women overall for comparison. Primiparous women with singleton pregnancies, cephalic presentations, 2005–2017, $n = 352\,567$.

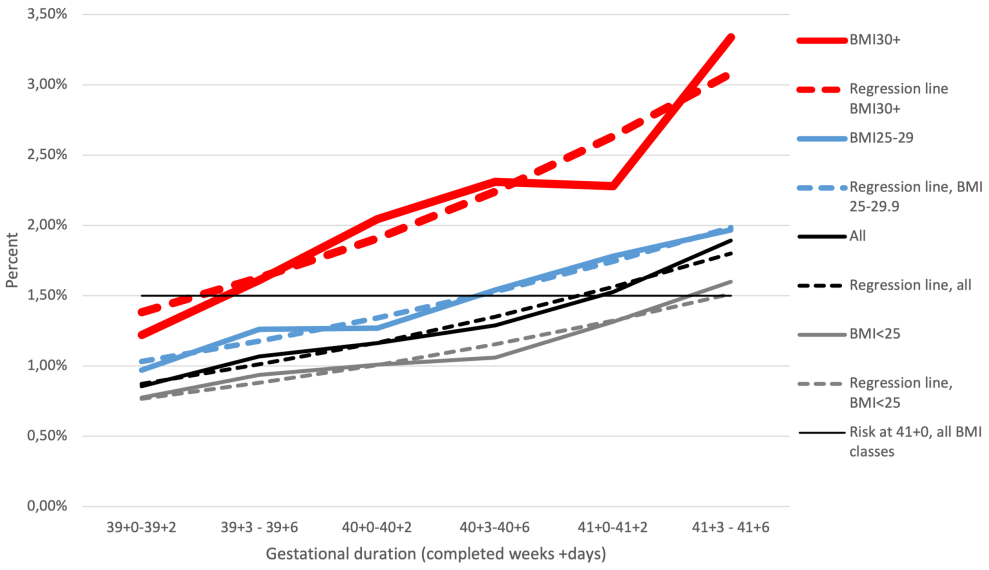

FIGURE 2 Absolute risk of Apgar score <7 at 5 minutes combined with BMI class and gestational duration. The line at 1.5% represents the general incidence at 41+0 weeks for women over all for comparison. Primiparous women with singleton pregnancies, cephalic presentations, 2005–2017, $n = 352\,567$.

throughout the studied gestational period (39+0 to 41+6 weeks). The non-linear association between stillbirth or death within 45 ultrasound-adjusted postmenstrual weeks and gestational duration made it impossible to identify a certain gestational age at which the risks among children of overweight or obese women correspond to that among women with normal BMI at 41+0 weeks. Individualized decisions on labor induction in term pregnancies need to be based on women-specific risk profiles. The results from the current study suggest that maternal BMI among primiparous women is a risk factor to consider.

The current study was performed using a large national cohort with prospectively collected data on maternal BMI, smoking, educational level and maternal country of birth. The data were retrospectively recorded but prospectively collected. Thus information on, for example, maternal smoking and BMI was collected before the outcome of the pregnancy was known, which limits the risk for recall

bias. Furthermore, the high coverage of the mandatory national register ensures that the data represent the whole population giving birth in Sweden. However, even though the initial data base was large, the low mortality rates result in low numbers—especially when the data material was divided by gestational week and maternal BMI class.

When comparing stillbirth rate in relation to gestational duration, it is important to compare the rates for a certain week, not for all children born at a certain week but for all fetuses remaining in utero. In such analyses, children born at early term would be "at risk" for a substantially shorter period than children born at late term. To overcome this type of potential bias, we studied the combined risk of mortality, regardless of type of death (ante-, intra- or postpartum), so that all children were "at risk" for an equal period (from 39+0 to 45+0 post-menstrual weeks).

Even though Apgar score (the sum of scores for neonate heart rate, respiratory effort, muscle tone, reflex irritability and color) is a subjective measure, it is often used in epidemiologic studies in the absence of objective measures of delivery outcomes other than mortality. Apgar score <7 at 5 minutes has proven to be a reliable marker of newborn health.[9,23] It has also been reported to be associated with child health[24,25] as well as school grades and academic achievements at 16 years of age.[26]

The current study included all cephalic presentations in simplex pregnancies lasting 39+0 to 41+6 weeks. Thus, the dataset would be expected to include few very high-risk pregnancies that would be eligible for interventions in early term pregnancy. However, the current study design still has an inherent bias as, at certain observation points, pregnancies with evolving risk conditions will be identified and managed (eg by induction of labor or cesarean section). Inevitably, for each time point, only the healthiest pregnancies would be selected for continuation of pregnancy. This potential bias would result in overestimations of the considered outcomes observed in the 39+0 to 39+6 group, thereby resulting in a lower negative effect of advancing gestational duration on pregnancy outcome than if no interventions had been done. We did not exclude or adjust for possible pregnancy complications that may have appeared after a gestation age of 39+0 weeks, as those complications (especially in prolonged pregnancies in women with high BMI) are part of the outcome spectrum. If we had adjusted (or excluded) these pregnancies, we might have excluded the outcomes that we intended to study.

5 | CONCLUSION

The high absolute risk of stillbirth or death before 45 postmenstrual weeks among children of women with BMI ≥30 at 39 gestational weeks or more may suggest that for these women induction of labor should be considered at 39 weeks, even if it was hard to define the optimal timing. The same conclusion on individualized management based on maternal BMI could be drawn when making decisions to reduce adverse perinatal outcomes manifested by low Apgar scores (in particular perinatal asphyxia) in gestational age from 39+0 to 41+6 weeks.

FUNDING

Stig and Ragna Gorthon Foundation.

CONFLICT OF INTEREST

The authors have stated explicitly that there are no conflicts of interest in connection with this article.

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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: Lindegren L, Stuart A, Herbst A, Källén K. Relation between perinatal outcome and gestational duration in term primiparous pregnancies stratified by body mass index. *Acta Obstet Gynecol Scand*. 2022;101:1414-1421. doi:10.1111/aogs.14465