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Maternal body mass index and the prevalence of spontaneous and elective preterm deliveries in an Irish obstetric population: a retrospective cohort study

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ABSTRACT

Objective To estimate the association between maternal body mass index (BMI) and risk of spontaneous preterm delivery (sPTD) and elective preterm delivery (ePTD) in singleton and multiple pregnancies.

Design Retrospective cohort study.

Setting Electronic records of all deliveries from 2009 through 2013 in a tertiary university hospital were abstracted for demographic and obstetrical information.

Participants A total of 38 528 deliveries were included. Participants with missing data were excluded from the study. BMI was calculated from the measurement of height and weight at the first prenatal visit and categorised. Sonographic confirmation of gestational age was standard.

Outcome measures Primary outcomes, sPTD and ePTD in singleton and multiple pregnancies, were evaluated by multinomial logistic regression analyses, stratified by parity, controlling for confounding variables.

Results Overall rate of PTD was 5.9%, from which 2.7% were sPTD and 3.2% ePTD. The rate of PTD was 50.4% in multiple pregnancies and 5.0% in singleton pregnancies. The risk of sPTD was increased in obese nulliparas (adjusted OR (aOR) 2.8, 95% CI 1.7 to 4.4) and underweight multiparas (aOR 2.2, 95% CI 1.3 to 3.8). The risk of ePTD was increased in underweight nulliparas (aOR 1.8; 95% CI 1.04 to 3.4) and severely obese multiparas (aOR 1.4, 95% CI 1.02 to 3.8). Severe obesity increased the risk of both sPTD (aOR 1.4; 95% CI 1.01 to 2.1) and ePTD (aOR 1.4; 95% CI 1.1 to 1.8) in singleton pregnancies. Obesity did not influence the rate of either sPTD or ePTD in multiple pregnancies.

Conclusion Maternal obesity is an independent risk factor for PTD in singleton pregnancies but not in multiple pregnancies. Obesity and nulliparity increase the risk of sPTD, whereas obesity and multiparity increase the risk of ePTD.

INTRODUCTION

Preterm delivery (PTD), defined as delivery prior to 37 weeks of gestation, is the main cause of perinatal mortality and morbidity worldwide.[1] It is associated with high rates of interventions and specialised obstetrical and neonatal care, and long-term disability of the offspring, which in turn leads to increased emotional costs for families and financial costs for families and society.[2 3]

Evidence from systematic reviews and meta-analyses demonstrates that the risk of PTD is influenced by both individual and socioeconomic factors.[4–14] Among these, the role of maternal body mass index (BMI) in the complex interplay of biological, behavioural and socioeconomic determinants of preterm birth is not fully understood and the debate on the relationship between maternal BMI and spontaneous preterm delivery (sPTD) or elective preterm delivery (ePTD) is ongoing. Both low and increased BMIs have been associated with risk of adverse pregnancy and perinatal outcomes. Whether the continuum of overweight and obesity is associated with increased, decreased or neutral risks on the length of gestation is uncertain.[4 5 15–18] The same holds true for the association between maternal underweight and preterm birth.[5 18] The discordance in opinions may reside with different characteristics of various populations, and with interpretation of the findings, which in most studies is hindered by the uncontrolled or residual confounding such as parity, plurality, socioeconomic and

Strengths and limitations of this study

► This study ascertained obesity-attributable spontaneous and elective preterm deliveries stratified by parity and plurality.
► The study used a large obstetrics cohort representative for the Irish population, inclusive of all socioeconomic strata across the urban-rural divide.
► Increased accuracy and reliability of the data by objective measures of maternal anthropometrics and standard sonographic confirmation of gestational age in all women.
► No detailed information on obstetrical history was available for this study.

smoking status, access to antenatal healthcare, among others.

PTD is common in multiple pregnancies, with 55% of multiple births being delivered before 37 weeks' gestation, compared with the rate of 6%–10% in singleton pregnancies.[19 20] The incidence of multiple pregnancies has increased over past decades, mainly due to increase in assisted reproduction[21]. While multiple factors contribute to the increased rates of PTD in multiple pregnancies, the independent role of maternal obesity as a risk factor for either ePTD or sPTD remains uncertain.[22 23]

The incidence of obesity is increasing among women of childbearing age, approximately 60% of women entering pregnancy being overweight or obese in the USA.[24 25] Similar trends are observed in Ireland,[26 27] where the incidence of overweight and obesity was reported of approximately 44%,[28] with a rate of obesity in first trimester of pregnancy between 19% and 25% at the first prenatal visit.[29 30] With rates of obesity in developed countries continuing to rise, it is imperative to understand the complex patterns of associations between maternal obesity and risk of PTD in nulliparous and multiparous women, singleton and multiple pregnancies, in order to develop targeted, effective lifestyle and therapeutic interventions for women at risk of PTD.

Using the data collected prospectively in the electronic health records from labour and delivery in a tertiary maternity hospital, the aim of this study was to examine the association between maternal BMI and the risk of sPTD and ePTD in singleton and multiple pregnancies, and in nulliparous and multiparous women.

METHODS
Study population
The study included all women who delivered a baby weighing ≥500 g at a tertiary referral university teaching hospital between 1 January 2009 and 31 December 2013. The hospital, Coombe Women and Infants University Hospital Dublin, is one of the largest maternity hospitals in the European Union. The hospital population includes all socioeconomic strata across the urban-rural divide, including women with both public and private health insurance. Data from antenatal care, labour and delivery were collected prospectively and recorded electronically. Anthropometric, sociodemographic and clinical information at the first prenatal visit ('booking visit') was recorded by trained midwives and the information from labour and delivery was abstracted from medical records by administrative staff. Gestational age was confirmed for all women by ultrasound scanning at the booking visit. The use of anonymised data set for research purposes was granted by the Coombe Women and Infants University Hospital Research Ethics Committee (ref 004–013). Accuracy of the data was validated by the IT Department and the Master's Office for the Annual Clinical Report.

Variable definitions
The gestational age at delivery provided in the data set was dichotomised into term and preterm deliveries. The main outcome variable, PTD, was defined as a birth occurring before 36^{+6} weeks' gestation inclusive. Term delivery was defined as a birth occurring between 37^{+0} and 41^{+6} weeks' gestation. Further, PTD was categorised into spontaneous and elective preterm births. An sPTD was defined as a birth in which spontaneous onset of labour was documented. An ePTD was defined as a medically indicated, provider-initiated birth in which the labour was either induced or the woman was delivered by elective caesarean section (CS).

BMI was calculated as the ratio of weight (kg) divided by height squared (m^2) from the standardised measurement of height and weight at the first prenatal appointment (first trimester of pregnancy) by trained midwives. Women were divided into five groups according to the categories defined by the WHO's classification as follows: underweight (BMI≤18.49 kg/m^2), normal weight (BMI 18.50–24.99 kg/m^2), overweight (BMI 25.00–29.99 kg/m^2), obese class I (mildly obese) (BMI 30.00–34.99 kg/m^2), obese class II (moderately obese) (BMI 35.00–39.99 kg/m^2) and obese class III (severely obese) (BMI≥40.00 kg/m^2). For meaningful comparisons, the obesity class II and class III were collapsed in one category of moderately/severely obese women (BMI>35.00 kg/m^2).

All women were offered a routine dating scan at the first prenatal visit to confirm gestational age and to accurately determine the estimated date of confinement.

Attendance for prenatal care was defined as normal attendance for women with early booking for antenatal care (before 10 weeks' gestation) and regular attendance to appointments with the healthcare provider, and poor attendance for women who were late bookers (after 20 weeks' gestation) and/or attended sporadically for their appointments.

Multiparity was defined as women who had a least one previous delivery of a fetus weighing 500 g or more. Multiple pregnancies included twin, triplet and quadruplet pregnancies. Advanced maternal age was considered age ≥35 years at the time of attendance to prenatal care (11). We used self-reported nativity (European (Irish, non-Irish) and non-European (Afro-Caribbean, Asian, Hispanics)) to classify the ethnic and racial origin of women (12).

Study design and methodology
The inclusion criteria for the women in the study were: delivery before 42 weeks' gestation; live infant weighing ≥500 g; singleton or multiple pregnancy. Multiple deliveries were counted once. Data for BMI were missing for 435 women, 318 women in the term deliveries group and 117 women in the preterm group. Women with missing BMI information were excluded from further analyses. Data for gestational age at delivery were missing for 34 women. Information on parity was available for all cases. Women who

delivered at ≥42+0 weeks' gestational age (post-term) were excluded from the study. From 42 362 women in cohort, 2834 (6.6%) were post-term. A total of 39 528 women were included in the study. For women with missing covariate, we handled the missing data by creating a categorical indicator variable (1/0) for missing responses.

Information about pregnancy, labour and delivery was linked to information on newborn infant using unique identifiers (hospital numbers).

The main outcome of the study was PTD, which was examined as a composite variable including all PTD and separately as sPTD and ePTD. The rates of PTD were assessed in nulliparous and multiparous women, and in singleton and multiple pregnancies, stratified by maternal BMI at first antenatal visit, controlling for confounders: maternal age, nativity, maternal occupation, smoking status, parity, attendance to antenatal care, multiples, congenital anomalies.

Statistical analyses

Descriptive statistics were produced for sociodemographic, clinical characteristics and outcome variables for all women. Continuous data were presented as mean±SD. Categorical data were expressed as frequency distributions. Univariate analyses assessed associations between sociodemographic and obstetrical characteristics and perinatal outcomes of interest using χ^2 test and logistic regression. Student's t-test assessed the difference between groups for continuous variables. Multinomial logistic regression analyses were conducted to investigate the association between non-optimal body weight and the subtypes of preterm birth stratifying by parity and type of pregnancy, controlling for the effect of confounders. The statistical models were fitted to the data using a forward stepwise model strategy which introduced a block of demographic variables (maternal age (≤34 years old, >35 years old), nativity (European, non-European), occupation (employed, non-employed), smoking status (smoker, non-smoker)), followed by a block of obstetrical variables (parity (nullipara, multipara), attendance to prenatal care (normal attendance, poor attendance), number of fetuses in the index pregnancy (singleton, multiples), congenital anomalies (yes, no)). The model performance was assessed using goodness of fit, the Cox and Snell, Nagelkerke and McFadden pseudo R2 measures, and the likelihood ratio tests. To assess the effect on PTD of the relationship between the dependent variables BMI, parity and multiples, level of interaction has been tested in the regression models. Additional analyses compared the sociodemographic, lifestyle and clinical characteristics of term and preterm deliveries.

ORs and 95% CIs were calculated for final models. All statistical analyses were performed using the SPSS for Windows package, V.20 (IBM SPSS).

RESULTS

Of the 39 528 deliveries, 37 167 (94.0%) were term and 2361 (5.9%) were preterm. Of the preterms, 209 (8.9%) were extremely preterm (<28+0 weeks' gestation), 342 (14.5%) were very preterm (28+1 to 31+6 weeks' gestation) and 1810 (76.7%) were moderate to late preterm (32+0 to 36+6 weeks). From PTD, 1075 (2.5%) were sPTD and 1286 (3.1%) were ePTD (table 1).

Demographic and obstetrical characteristics of women with term and preterm deliveries, spontaneous and elective, are shown in table 1. When compared with women who delivered at term, women with PTD were more likely to be of non-European nativity, older than 35 years, unemployed, nulliparous, had fertility treatments, or irregular attendance to prenatal care. Women from this group were also more likely to smoke, use illicit drugs and be exposed to domestic violence during pregnancy than women from term delivery group. Women with multiples were 19 times more likely to deliver preterm than women with singleton pregnancies. Women with PTD were five times more likely to deliver by emergency CS but less likely to be induced or have an instrumental vaginal delivery than women who delivered at term. Preterm infants were more likely to have been diagnosed with congenital anomalies.

When further compared the demographic and clinical characteristics between women with sPTD and ePTD, our data showed that women with sPTD were more likely to be younger than 35 years, smoke and use recreational drugs throughout pregnancy, conceive spontaneously, and carry a singleton pregnancy, and less likely to have a planned pregnancy than women with ePTD. Conversely, women with ePTD were more likely to be heavier, undergo fertility treatments, carry multiples, have a planned pregnancy and attend regularly prenatal care appointments than women with sPTD. The occurrence of either sPTD or ePTD was similar in women of European or non-European ancestry, Irish or non-Irish nationality, employed or unemployed. Both sPTD and ePTD occurred with similar frequency in nulliparous (46.0% and 44.4%, respectively) and multiparous (54.0% and 55.6%, respectively) women.

Almost 70% of women with sPTD delivered vaginally, whereas only 20% of women from ePTD group delivered vaginally, with the rest requiring either elective (19.9%) or emergency caesarean (60.0%). As expected, most infants delivered preterm had a birth weight lower than 2500 g (64.2% of sPTD and 77.4% of ePTD). However, the infants from sPTDs were heavier and less likely to be diagnosed with congenital anomalies than babies resulted from ePTDs. More babies were spontaneously delivered by 28 weeks' gestation, whereas more elective deliveries occurred at gestational age of 28–32 weeks.

Table 2 shows the characteristics of women who delivered preterm stratified by BMI at the first antenatal visit. In our study, ePTD was more frequent in overweight (58.3%), moderately (64.4%) and severely obese women (66.7%), whereas sPTD was more frequent in underweight women (58.9%) (p<0.001).

Table 1 Sociodemographic, lifestyle and clinical characteristics of term and preterm deliveries, spontaneous and electives

	All women (N=38 528)*	Term deliveries† (n=37 167)	PTD‡ (n=2361)	OR (95% CI)§	sPTD (n=1075)	ePTD (n=1286)	p Value
Demographic characteristics							
Maternal age							
<35 years old	28655(72.5)	27 034 (72.7)	1621 (68.7)	1.0	810 (75.3)	811 (63.1)	<0.001*
≥35 years old	10873 (27.5)	10133 (27.3)	740 (31.3)	1.2 (1.1 to 1.3)	265 (24.7)	475 (36.9)	0.583
Nativity							
European	33812 812 (86.0)	31857 (86.0)	2033 (86.6)	1.0	926 (87.1)	1107 (86.3)	
Non-European	5499 (14.0)	5168 (14.0)	313 (13.3)	1.1 (1.0 to 1.2)	137 (12.9)	176 (13.7)	
Nationality							
Irish	27657(70.3)	26003 (70.2)	1654 (71.8)	1.0 (0.9 to 1.1)	735 (69.9)	919 (73.4)	0.063
Non-Irish	11672 (29.7)	11022 (29.8)	650 (28.2)	1.0	317 (30.1)	333 (26.6)	
Occupation							
Employed	36988 (94.2)	32236 (87.2)	1903 (82.9)	1.0	849 (81.2)	1054 (84.3)	0.058
Unemployed	2295 (5.8)	4752 (12.8)	392 (17.1)	1.4 (1.2 to 1.5)	196 (18.8)	196 (15.7)	
BMI at first prenatal visit, mean (SD)	25.5 (5.5)	25.5 (5.0)	25.9 (5.4)	<0.001*	24.0 (22.0–28.0)	26.0 (23.0–30.0)	<0.001*
Lifestyle characteristics							
Smoking status							
Current smoker	5880 (14.9)	5390 (14.5)	490 (20.8)	1.4 (1.3 to 1.6)	283 (26.3)	207 (16.1)	<0.001*
Former smoker	12612 (31.9)	11961 (32.2)	651 (27.6)	0.8 (0.8 to 0.9)	276 (25.7)	375 (29.2)	
Never smoke	21036 (53.2)	19816 (53.3)	1220 (51.7)	1.0	516 (48.0)	704 (54.7)	
Alcohol consumption							
>10 units/week	15 (0.0004)	10 (0.03)	5 (0.23)	1.3 (0.9 to 1.9)	4 (0.4)	1 (0.1)	0.269
1–10 units/week	652 (1.8)	623 (1.8)	29 (1.4)	0.1 (0.04 to 0.3)	12 (1.2)	17 (1.4)	
No alcohol	36447 (98.2)	34335 (98.2)	2112 (98.4)	1.0	950 (98.3)	1162 (98.5)	
Illicit drugs							
Yes	2944 (7.5)	2705 (7.3)	239 (10.5)	1.4 (1.2 to 1.7)	140 (13.6)	99 (7.9)	<0.001*
No	36456 (92.5)	34414 (92.7)	2042 (89.5)	1.0	891 (86.4)	1151 (92.1)	
Domestic violence							
Yes	431 (1.1)	393 (1.1)	38 (1.7)	1.5 (1.1 to 2.2)	15 (1.5)	23 (1.8)	0.515
No	38865 (98.9)	36635 (98.9)	2230 (98.3)	1.0	1009 (98.5)	1221 (98.2)	
Clinical characteristics							

Continued

Table 1 Continued

	All women (N=38 528)*	Term deliveries† (n=37 167)	PTD‡ (n=2361)	OR (95% CI)§	sPTD (n=1075)	ePTD (n=1286)	p Value
Parity							
Nulliparous	15699 (39.7)	14633 (39.4)	1066 (45.2)	1.2 (1.1 to 1.3)	495 (46.0)	571 (44.4)	0.430
Multiparous	23829 (60.3)	22534 (60.6)	1295 (54.8)	1.0	580 (54.0)	715 (55.6)	
Planned pregnancy							
Yes	27031 (68.7)	25 566 (68.9)	1465 (63.8)	1.0	613 (58.8)	852 (68.1)	<0.001*
No	12344 (31.3)	11514 (31.1)	830 (36.2)	1.2 (1.1 to 1.3)	430 (41.2)	400 (31.9)	
Treatment for infertility							
Yes	702 (1.8)	578 (1.6)	124 (5.3)	2.8 (2.4 to 3.3)	31 (2.9)	93 (7.2)	<0.001*
No	38826 (98.2)	36589 (98.4)	2237 (94.7)	1.0	1044 (97.1)	1193 (92.8)	
Type of pregnancy							
Singletons	38717 (97.9)	36765 (98.9)	1952 (82.7)	1.0	942 (87.6)	1010 (78.5)	<0.001*
Multiples	811 (2.1)	402 (1.1)	409 (17.3)	19.1 (16.5 to 22.1)	133 (12.4)	276 (21.5)	
Prenatal care attendance							
Regular	31530 (98.5)	29797 (98.8)	1733 (92.8)	1.0	774 (91.1)	959 (94.3)	0.009*
No attendance or irregular	485 (1.5)	351 (1.2)	134 (7.2)	6.5 (5.3 to 8.0)	76 (8.9)	58 (5.7)	
Type of labour							
Spontaneous	21172 (53.6)	20097 (54.1)	1075 (45.5)	1.0	1075 (100.0)	–	
No labour	6612 (16.7)	5638 (15.2)	974 (41.3)	3.2 (2.9 to 3.5)	–	974 (75.7)	
Induction of labour	11744 (29.7)	11432 (30.8)	312 (13.2)	0.5 (0.4 to 0.6)	–	312 (24.3)	
Mode of delivery							
Spontaneous vaginal	22946 (58.1)	21974 (59.1)	972 (41.2)	1.0	750 (69.8)	222 (17.3)	<0.001*
Instrumental vaginal	6013 (15.2)	5874 (15.8)	139 (5.9)	0.5 (0.4 to 0.6)	103 (9.6)	36 (2.8)	
Elective caesarean	5201 (13.2)	4945 (13.3)	256 (10.8)	1.1 (1.0 to 1.3)	0 (0.0)	256 (19.9)	
Emergency caesarean	5367 (13.6)	4373 (11.8)	994 (42.1)	5.1 (4.6 to 5.6)	222 (20.7)	772 (60.0)	
GA, median (IQR), weeks	39.6 (37–41)	–	35 (33–36)	–	33.1 (19–36)	33.3 (23–36)	0.202
Extremely preterm (<28 weeks)	209 (0.5)	–	209 (8.9)	–	122 (11.3)	87 (6.8)	<0.001*
Very preterm (28 to <32 weeks)	342 (0.9)	–	342 (14.5)	–	130 (12.1)	212 (16.5)	
Moderate to late preterm (32 to <37 weeks)	1810 (4.7)	–	1810 (76.7)	–	823 (76.6)	987 (76.7)	

Continued

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Table 1 Continued

	All women (N=38 528)*	Term deliveries[†] (n=37 167)	PTD[‡] (n=2361)	OR (95% CI)[§]	sPTD (n=1075)	ePTD (n=1286)	p Value
Birth weight (g) median (IQR)	3411.0 (598.8)	3471.1 (481.5)	2057.3 (729.0)	<0.001*	2270.0 (1697.5–2665.0)	2020.0 (1485.0–2470.0)	<0.001*
Apgar score							
≥7	37159 (94.2)	35468 (95.4)	1691 (71.1)	1.0	792 (74.3)	899 (69.9)	
<7	2290 (5.8)	1691 (4.6)	661 (28.9)	8.5 (7.5 to 9.4)	274 (25.7)	387 (30.1)	0.019*
Congenital anomalies							
Yes	298 (0.8)	250 (0.7)	48 (2.0)	2.0 (2.2 to 4.1)	17 (1.6)	31 (2.4)	0.188
No	39230 (99.2)	36917 (99.3)	2313 (98.0)	1.0	1058 (98.4)	1255 (97.6)	

Data presented as n (%).
X^2 test assessed the relationship between categorical variables.
Independent sample t-test compared the means of continuous variables.
*May not add to total number due to missing; the analyses excluded 2834 women with post-term pregnancies.
[†]Term deliveries were defined as deliveries between 37^{+0} and 40^{+6} weeks' gestation.
[‡]Preterm deliveries were defined as deliveries before 36^{+6} weeks' gestation.
[§]Unadjusted ORs and 95% CIs of PTD, with term deliveries as reference category.
BMI, body mass index; ePTD, elective preterm delivery; GA, gestational age at delivery; PTD, preterm delivery; sPTD, spontaneous preterm delivery.

Prevalence of PTD was higher in overweight and obese multiparous than nulliparous women. In women with suboptimal BMI, the nulliparous women had a higher rate of PTD than underweight multiparous women. There was no difference in the prevalence of PTD in singleton and multiple pregnancies when stratified by BMI category.

The highest rate of PTD occurred in women in their 30s; 31.1% in women aged 30–34 years, and 24.1% in women aged 35–39 years. In both these age groups, PTD rate was higher in overweight and obese women than in normal weight women. Women younger than 20 had the lowest incidence of PTD (4.1%). In this group, the occurrence of PTD was higher in underweight women (10.7%) than in normal weight women (6.2%). The majority of women who delivered preterm were of Irish ancestry in each BMI category (p<0.05). For the women of non-Irish ancestry who delivered preterm, Asian women were more likely to be underweight whereas Afro-Caribbean women were more likely to be obese (p<0.001). For all BMI categories, the frequency of PTD was higher in women who performed semiskilled or unskilled manual work than in women with skilled manual or managerial jobs (p=0.024).

There was an association between the mode of delivery, Apgar scores and early pregnancy BMI in women who delivered preterm (all p<0.001). Obese women were more likely to deliver by CS, either elective or emergency, and less likely to undergo assisted vaginal delivery before 37 weeks' gestation. There was no difference in the maternal attendance to antenatal care, birth weight, presence of congenital anomalies and admission to intensive care between overweight or obese women and normal weight women who delivered preterm.

Table 3 shows the adjusted risk of sPTD and ePTD in women with non-optimal BMI, stratified by parity and type of pregnancy.

Multinomial analyses stratified by parity showed that in nulliparas, the odds of sPTD were almost threefold higher in moderate/severely obese (adjusted OR (aOR) 2.8, 95% CI 1.7 to 4.4) and 1.5-fold higher in moderately obese women (aOR 1.5, 95% CI 1.08 to 2.3) than in normal weight women. The risk of ePTD was increased by 80% in underweight (aOR 1.8; 95% CI 1.04 to 3.4) as compared to normal weight nulliparas.

In contrast, in multiparous women, moderate/severely obese had a 40% higher risk of ePTD than women with normal weight (aOR 1.4, 95% CI 1.02 to 3.8). Underweight multiparas had twice the risk of sPTD than normal weight women (aOR 2.2, 95% CI 1.3 to 3.8).

In the adjusted model stratified by type of pregnancy, moderate/severe obesity increased the risk of both sPTD (aOR 1.4; 95% CI 1.01 to 2.1) and ePTD (aOR 1.4; 95% CI 1.1 to 1.8) in singleton pregnancies. Obesity did not influence the rate of either sPTD or ePTD in multiple pregnancies.

No interaction was observed between maternal BMI, parity and type of pregnancy, thus there were no additive effects of these variables on PTD.

Table 2 Sociodemographic and obstetric characteristics of preterm deliveries stratified by maternal BMI

	Underweight BMI<18.5 kg/m² n=56	Normal weight BMI 18.5–24.9 kg/m² n=1077	Overweight BMI 25.0–29.9 kg/m² n=660	Mildly obese BMI 30.0–34.9 kg/m² n=295	Moderate/severely obese BMI>35.0 kg/m² n=156	p Value
GA at delivery						
Extremely preterm (<28^{+0} weeks)	5 (8.9)	75 (7.0)	57 (8.6)	35 (11.9)	11 (7.1)	0.242
Very preterm (28^{+1}–31^{+6} weeks)	7 (12.5)	138 (12.8)	97 (14.7)	39 (13.2)	25 (16.0)	
Moderate to late preterm (32^{+0}–36^{+6} weeks)	44 (78.6)	864 (80.2)	506 (76.7)	221 (74.9)	120 (76.9)	
Type of PTD						
sPTD	33 (58.9)	550 (51.1)	275 (41.7)	105 (35.6)	52 (33.3)	<0.001
ePTD	23 (41.1)	527 (48.9)	385 (58.3)	190 (64.4)	104 (66.7)	
Parity						
Nulliparous	29 (51.8)	535 (49.7)	263 (39.8)	122 (41.4)	59 (37.8)	<0.001
Multiparous	27 (48.2)	542 (50.3)	397 (60.2)	173 (58.6)	97 (62.2)	
Type of pregnancy*						
Singleton	51 (91.1)	885 (82.2)	534 (80.9)	252 (85.4)	135 (86.5)	0.108
Multiples	5 (8.9)	192 (17.8)	126 (19.1)	43 (14.6)	21 (13.5)	
Maternal age (year)						
<20	6 (10.7)	67 (6.2)	13 (2.0)	3 (1.0)	3 (1.9)	<0.001
20–24	13 (23.2)	142 (13.2)	64 (9.7)	33 (11.2)	15 (9.6)	
25–29	14 (25.0)	248 (23.0)	115 (17.4)	65 (22.0)	35 (22.4)	
30–34	11 (19.6)	315 (29.2)	221 (33.5)	100 (33.9)	51 (32.7)	
35–39	9 (16.1)	235 (21.8)	190 (28.8)	66 (22.4)	40 (25.6)	
≥40	3 (5.4)	70 (6.5)	57 (8.6)	28 (9.5)	12 (7.7)	
Nativity						
European Irish	35 (63.6)	790 (74.9)	470 (72.8)	191 (65.4)	140 (68.0)	<0.001
European non-Irish	10 (18.2)	177 (16.8)	92 (14.2)	45 (15.4)	24 (15.7)	
Afro-Caribbean	2 (3.6)	26 (2.5)	39 (6.0)	38 (13.0)	20 (13.1)	
Asian	8 (14.5)	61 (5.8)	43 (6.7)	18 (6.2)	5 (3.3)	
Hispanic	0 (0.0)	1 (0.1)	2 (0.3)	0 (0.0)	0 (0.0)	
Maternal occupation						
Professional/managerial	10 (18.5)	233 (21.9)	134 (20.6)	45 (15.6)	24 (15.7)	0.024
Other non-manual/skilled manual	6 (11.1)	168 (15.8)	83 (12.8)	34 (11.8)	15 (9.8)	

Continued

Table 2 Continued

	Underweight BMI<18.5 kg/m² n=56	Normal weight BMI 18.5–24.9 kg/m² n=1077	Overweight BMI 25.0–29.9 kg/m² n=660	Mildly obese BMI 30.0–34.9 kg/m² n=295	Moderate/severely obese BMI>35.0 kg/m² n=156	p Value
Semiskilled/unskilled manual	24 (44.4)	492 (46.2)	328 (50.5)	151 (52.4)	90 (58.8)	
Unemployed	14 (25.9)	172 (16.2)	105 (16.2)	58 (20.1)	24 (15.7)	
Prenatal care						
Regular attendance	45 (93.8)	822 (94.9)	501 (95.4)	207 (96.3)	119 (96.7)	0.809
Poor attendance	3 (6.3)	44 (5.1)	24 (4.6)	8 (3.7)	4 (3.3)	
Mode of delivery						
Elective CS	10 (17.9)	121 (11.2)	69 (10.5)	25 (8.5)	27 (17.3)	<0.001
Emergency CS	16 (28.6)	390 (36.2)	310 (47.0)	149 (50.5)	73 (46.8)	
Assisted vaginal delivery	2 (3.6)	87 (8.1)	28 (4.2)	15 (5.1)	4 (2.6)	
Spontaneous vaginal delivery	28 (50.0)	479 (44.5)	253 (38.3)	106 (35.9)	52 (33.3)	
Birth weight (singletons)						
2500–4500 g	13 (23.2)	318 (29.5)	199 (30.2)	79 (26.8)	54 (34.6)	0.377
<2500 g	43 (76.8)	759 (70.5)	460 (69.8)	216 (73.2)	102 (65.4)	
NICU admission	26 (54.2)	473 (54.6)	310 (59.0)	132 (61.1)	71 (56.8)	0.339
Congenital anomalies†	1 (1.8)	22 (1.8)	12 (2.0)	6 (2.6)	4 (2.0)	0.983

*Includes twin, triplet and quadruplet pregnancies.
†Congenital anomalies include: chromosomal anomaly, cardiac anomaly, cleft palate and/or lip, neural tube defect, diaphragmatic hernia, cystic hygroma, haemangioma.
BMI, body mass index; CS, caesarean section; ePTD, elective preterm delivery; GA, gestational age; NICU, neonatal intensive care unit; PTD, preterm delivery; sPTD, spontaneous preterm delivery.

Table 3 Adjusted OR (aOR, 95% CIs) for the association of sPTD and ePTD and maternal body mass index stratified by parity and number of fetuses in the index pregnancy, with normal weight as reference category

	Underweight BMI<18.5 kg/m^2		Overweight BMI 25.0–29.9 kg/m^2		Mildly obese BMI 30.0–34.9 kg/m^2		Moderate/severely obese BMI>35.0 kg/m^2	
	aOR	95% CI	aOR	95% CI	aOR	95% CI	aOR	95% CI
All women*								
All PTD	1.4	(1.08 to 2.0)	1.07	(0.9 to 1.2)	1.1	(0.9 to 1.3)	1.3	(1.04 to 1.7)
sPTD	1.5	(1.04 to 2.3)	0.9	(0.8 to 1.1)	0.9	(0.7 to 1.2)	1.3	(0.9 to 1.9)
ePTD	1.4	(0.8 to 2.4)	1.1	(0.9 to 1.3)	1.2	(0.9 to 1.4)	1.3	(1.05 to 1.7)
Nulliparas†								
All PTD	1.4	(0.9 to 2.1)	1.07	(0.8 to 1.3)	1.4	(1.1 to 1.8)	1.7	(1.2 to 2.4)
sPTD	0.9	(0.5 to 1.8)	1.06	(0.8 to 1.3)	1.5	(1.08 to 2.3)	2.8	(1.7 to 4.4)
ePTD	1.8	(1.04 to 3.4)	1.07	(0.8 to 1.3)	1.3	(0.9 to 1.8)	1.2	(0.7 to 1.9)
Multiparas†								
All PTD	1.6	(1.04 to 2.6)	1.05	(0.9 to 1.2)	0.9	(0.8 to 1.2)	1.3	(0.9 to 1.7)
sPTD	2.2	(1.3 to 3.8)	0.9	(0.8 to 1.2)	0.8	(0.6 to 1.1)	0.9	(0.6 to 1.5)
ePTD	1.01	(0.4 to 2.4)	1.1	(0.9 to 1.4)	1.09	(0.8 to1.4)	1.4	(1.02 to 1.9)
Singleton‡								
All PTD	1.5	(1.1 to 2.1)	1.09	(0.9 to 1.2)	1.2	(1.0 to 1.4)	1.5	(1.2 to 1.8)
sPTD	1.6	(1.0 to 2.4)	0.9	(0.8 to 1.1)	0.9	(0.7 to 1.3)	1.4	(1.01 to 2.1)
ePTD	1.5	(0.9 to 2.6)	1.1	(0.9 to 1.4)	1.2	(0.9 to 1.5)	1.4	(1.1 to 1.8)
Multiples‡								
All PTD	0.6	(0.1 to 2.8)	1.03	(0.7 to 1.5)	0.7	(0.4 to 1.3)	0.7	(0.3 to 1.6)
sPTD	–	–	0.8	(0.3 to 2.1)	0.3	(0.09 to 1.2)	0.4	(0.1 to 1.7)
ePTD	0.9	(0.2 to 3.9)	0.9	(0.6 to 1.5)	0.9	(0.5 to 1.7)	0.6	(0.2 to 1.7)

*Adjusted for maternal age, nativity, occupation, smoking status, parity, attendance to antenatal care, multiples, congenital anomalies.
†Adjusted for maternal age, nativity, occupation, smoking status, attendance to antenatal care, multiples.
‡Adjusted for maternal age, nativity, maternal occupation, smoking status, parity and attendance to antenatal care.
BMI, body mass index; ePTD, elective preterm delivery; PTD, preterm delivery; sPTD, spontaneous preterm delivery.

DISCUSSION

This large observational study confirms an association between maternal body weight and PTD. The study shows, however, that the relationship between BMI categories and PTD is more complex than hitherto described. We found that sPTD is associated with obesity in nulliparas, ePTD is associated with obesity in multiparas and obesity does not influence the risk of PTD, either sPTD or ePTD, in multiple pregnancies. In addition, we found that being underweight increased the risk of ePTD in nulliparas and increased the risk of sPTD in multiparas, but did not influence the risk of PTD, either sPTD or ePTD, in multiples. As parity and plurality are not modifiable risk factors, the net effect on the rates of PTD is dependent on the balance between the two extremes of the BMI range, underweight and obesity. Thus, while demonstrating an independent association between non-optimal BMI and adverse pregnancy outcomes, our study suggests that more research is needed into understanding the pathophysiological pathways that lead to sPTD, especially in obese women. At the same time, this study suggests that more effective strategies are needed for reduction in medically indicated PTD and optimisation of evidence-based interventions

for pregnancy complications contributing to ePTD. The new information we provide may be helpful in designing targeted future interventions intended to prevent PTD.

In a recent study evaluating the risk factors for spontaneous and provider-initiated preterm births, it was shown that the effect of maternal complications on preterm birth varied between spontaneous and provider-initiated births, as well as among different countries.[31] While exploring one step further, the present findings concur showing that this relationship is modulated by maternal BMI.

Among preterm deliveries, the underweight and socially disadvantaged women were less likely, while obese women, who have higher medical risks, were more likely, to have an ePTD. Although we have not explored the cause of ePTD, from our analyses that controlled for fetal aetiologies, it can be inferred that ePTD may have had medical indications, such as pregnancy complications. Evidence suggests that hypertensive disorders of pregnancy including chronic hypertension and pre-eclampsia/eclampsia increase twofold to fivefold the risk of provider-initiated PTD.[31] There appears to be a linear, 'dose-dependent' relationship between obesity in

pregnancy and the risk of pre-eclampsia, possibly mediated through insulin resistance and dyslipidaemic effects on the cardiovascular system.[32–35] High BMI is associated with increased risk of pre-eclampsia in both nulliparous and multiparous women.[32 36] Thus, the increased risk of ePTD in nulliparas from our study may be due, at least in part, to higher background rates of pre-eclampsia in these women. In a study of the national registry of Scotland, a similar increased risk of ePTD occurred in obese nulliparous women. In that study, 40% of the obese nulliparous women who had an ePTD had been diagnosed with pre-eclampsia, compared with 2.6% incidence of pre-eclampsia in the remainder of the population studied.[37] The positive association between obesity and ePTD in nulliparas that maintained after adjustment for sociodemographic characteristics, pre-eclampsia and other hypertensive disorders in the study from Scotland[37] and a large Chinese study,[38] contrasts with findings from the Danish National Birth Cohort. In the latter, when obesity-related diseases were accounted for, no excess risk of ePTD was seen in obese women.[39] Other studies analysing the relationship between BMI and ePTD did not find an overall association.[40] Variations in sample sizes (from less than 3000 women to more than 350 000 women) and the fact that data for nulliparous and multiparous women were pooled may explain the discrepancies between studies.

The present study provides new insights into the uncertainty around the relationship between obesity in pregnancy and the risk of sPTD. While we found an increase in the risk of sPTD in nulliparous women with increasing BMI, Smith *et al* found a decreased risk of sPTD in a pooled cohort of nulliparous women. When stratified by BMI categories, the authors observed the association in overweight and mildly obese but not in moderate and severely obese women.[37] The probable explanation for this inconsistency is that the information on BMI was self-reported, and the time of assessment was pooled from various resources.

In contrast, a recent systematic review and meta-analysis found that the risk of sPTD did not differ among overweight, obese and very obese women.[5] This meta-analysis, however, analysed the pooled data for multiparous and nulliparous patients, in studies with wide heterogeneity of design and analytical measures. For instance, the vast majority of the studies assessed BMI by self-reporting, did not report the timing of BMI measurements and had small sample sizes. Thus, it is important that future studies clarify the contribution of artefactual differences owing to measurement in evaluation of the relationship between PTD and obesity.

The association between PTD and parity has been previously explored, yielding mixed results.[14] Two large-scale retrospective cohort studies found that obese nulliparas were at increased risk of extreme preterm delivery and elective preterm birth, whereas obese multiparas were not.[37 41] Several other studies reported increased rates of PTD, low birth weight and neonatal mortality among nulliparas, particularly when women

were young.[42–45] A recent meta-analysis of the association between parity and preterm birth found only a weak association between parity ≥3 and the risk of preterm birth, but failed to demonstrate a dose–response relationship for parity ≥5.[46] The lack of change in risk of preterm birth with increasing parity suggests confounders that have not been captured. The present study suggests that maternal BMI is a covariate that has the potential to alter these findings by changing the magnitude of the association between parity and preterm birth and should be considered in future studies.

Our study reports, unsurprisingly, a different baseline risk for prematurity in multiple pregnancies as compared with singleton pregnancies (60% vs 5%). Consistent with other reports, we show that PTD in multiples is predominantly provider-initiated preterm birth.[22] These findings suggest that more aggressive management of multiples may be associated with changes in birth outcomes in this population.[47] We show, however, that obesity-attributable adverse birth outcomes are lower in multiples compared with singletons. The fact that there was no association between maternal BMI and the risk of ePTD points to a more intensive prenatal care utilisation in these patients regardless of body weight, which may lead to increase in medical interventions in the management of multiples, and respectively, more preterm births.

Numerous studies have explored causal inference between social determinants and pregnancy health.[48–50] Birth outcomes such as PTD are widely accepted key indicators of population health, social development and economic change.[51] Wide variations in the prevalence of PTD observed between and within countries,[52–54] including developed nations,[55 56] may be explained, at least in part, by the dynamic interplay between contextual, societal determinants of health and individual level biological, behavioural and psychosocial factors.[12 57] Our study supports these assumptions, the analyses demonstrating that maternal nativity, smoking and occupation, as a proxy for level of education and income, are independent factors associated with sPTD.[58 59] While ethnic disparities, maternal health behaviours and psychosocial stress contribute to differential pregnancy outcomes, socioeconomic disparities in birth outcomes are additionally pervasive.[11–13 60]

Strengths and limitations of the study
This is the first study, to our knowledge, to analyse the risk of PTD stratifying by BMI category, parity and type of pregnancy, factors that each individually are known health determinants of PTD. The vast majority of prior studies include both variables either as confounders or perform the analyses in selected populations. Analysis of a large, nationally representative cohort of women who delivered in a single maternity hospital over a short time frame is another major strength of this study.[26] In addition, all women were offered sonographic dating at the ultrasound department at their first antenatal visit. The precise estimation of gestational age is paramount for the

accurate diagnosis of preterm birth. This has implications for evaluation of the statistical indicators that gauge the health status of populations and research, and for the management of the pregnancy and newborn infants,[61] gestational age being a proxy for the extent of fetal development, chances for survival at birth, and the likelihood of developing complications.[62]

Furthermore, BMI was calculated based on the measurement of maternal weight and height at the first prenatal visit and not from maternal self-report, which is known to introduce under-reporting bias and to exaggerate the epidemiological risks of obesity.[63–65] This translates in increased accuracy and reliability of our data. Statistical analysis has adjusted for confounding variables which is critical for any epidemiological study on PTD.[48] Although the study was retrospective, data extracted from a single tertiary care centre assured consistent prenatal care with regular antenatal clinic visits, ultrasound assessment for cervical assessment and monitoring of fetal growth, and standardised, high-quality recording of demographic and clinical data for all patients.

Despite its strengths, our study has limitations. First, the overall rate of PTD was small and resulted in a small sample size for the severely obese women and the need to collapse the BMI moderate and severe categories for meaningful statistical comparisons. However, the PTD rate in our study is comparable with other European countries and may reflect contextual differences such as advances in healthcare, affordability and accessibility to specialised prenatal care. Thus, our results, while representative of western populations, may not be reproducible in developing countries. Additional studies with higher sample sizes of class III obesity are warranted to confirm our findings for severe obesity. Second, we report on BMI at the first prenatal visit in the maternity unit, in contrast with the vast majority of previous studies reporting on pre-pregnancy BMI. However, a potential bias that may be introduced by the time of the onset of prenatal care and BMI recording in pregnancy is unlikely for this study for several reasons. Women from our cohort received prenatal care through the prenatal clinics of the maternity unit from the first trimester of pregnancy. Together with BMI measurement and dating scan, this represents the standard of prenatal care in Ireland. In addition, we controlled in the analyses for the late bookers and those women with poor attendance (less than 0.2% of the population), as it is well known that late initiation of antenatal care is associated with PTD. Furthermore, previous reports, including from our research group, suggest minimal weight gain (<2.0 kg) or no increase in average maternal weight or body composition before 18 weeks' gestation.[25 30 66] As such, our measurements of body weight in the first trimester reflect with accuracy the baseline BMI in pregnancy. Third, no detailed information on obstetrical history was available for this study. Therefore, we were not able to appreciate the rate of recurrent second trimester miscarriage or preterm birth in our cohort and its relationship with maternal body composition. In addition, our sample of multiples was relatively small, which may potentially explain why no association was observed between BMI and PTD multiples. However, the decision of delivery in multiples is frequently a trade-off between benefits and harm, being based on chorionicity, complications of pregnancy and assessment of fetal well-being. Hence, decisions based on clinical protocols and guidelines for time of delivery in multiples may as well explain the lack of association between BMI and PTD in this group. Furthermore, we had no information on the indications of ePTD. However, it is likely that pregnancy complications of either maternal or fetal aetiology may have decided on optimal time of delivery. We also acknowledge that a relatively small sample of multiples was included in this study, which may contribute to explain the lack of association observed between BMI and PTD in this group.

Significance and implications for clinical practice

In summary, our study highlights the complex nature of the influence of maternal BMI on pregnancy outcomes. Although our study does not prove causality, the present findings suggest that shared factors, such as maternal and pregnancy characteristics, may modulate the obesity-attributable risk of PTD. We found that parity has a complex influence on the relationship between PTD, either spontaneous or elective, and maternal BMI and that obesity-attributable adverse outcomes such as sPTD or ePTD were lower in multiple pregnancies compared with singleton pregnancies.

As PTD is a key determinant of perinatal morbidity and mortality, our study indicates that strategies for reducing PTD rates should focus on underweight women throughout pregnancy and preventing maternal obesity at the onset of pregnancy. Provision of adequate obstetric care, especially to the socially disadvantaged, corroborated with well-balanced decision-making on optimal timing for delivery in high-risk pregnancies could improve pregnancy outcomes. Most importantly, our study points to a largely neglected risk factor for preterm birth that is maternal BMI. While various national and international bodies, including the WHO, have published guidelines for antenatal care in obese women, no recommendations include clear guidance for management of maternal obesity.[67–69] Most of the interventions to date target the preconception period, while the level of interventions and their efficacy during pregnancy is less clear. Thus, while there is growing evidence showing that maternal obesity may influence pregnancy outcomes, additional studies should decipher in depth this complex relationship in order to develop targeted and efficient interventions that would improve perinatal outcomes in women with non-optimal BMI.

data set, defined and classified the variables; SS: provided clinical governance and oversaw data collection. All authors provided feedback on the manuscript drafts and approved the final version.

Competing interests None declared.

Patient consent Detail has been removed from this case description/these case descriptions to ensure anonymity. The editors and reviewers have seen the detailed information available and are satisfied that the information backs up the case the authors are making.

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