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# BMI, overweight and obesity in Swedish women born post-term

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## ABSTRACT

**Background:** There is increasing evidence that post-term birth ( $\geq 42$  weeks of gestation) is associated with adverse long-term outcomes. We assessed whether women born post-term displayed increased risk of overweight and obesity in adulthood.

**Methods:** Data were collected at first antenatal visit (~10–12 weeks of gestation) on singleton Swedish women aged  $\geq 18$  years in 1991–2009 (mean age 26.1 years), who were born post-term ( $n=27,153$ ) or at term (37–41 weeks of gestation;  $n=184,245$ ). Study outcomes were evaluated for continuous associations with gestational age. Stratified analyses were carried out comparing women born post-term or at term. Analyses were also run with a 2-week buffer between groups to account for possible errors in gestational age estimation, comparing women born very post-term ( $\geq 43$  weeks of gestation;  $n=5,761$ ) to those born within a narrower term window (38–40 weeks of gestation;  $n=130,110$ ).

**Results:** Increasing gestational age was associated with greater adult weight and BMI. Stratified analyses showed that women born post-term were 0.5 kg heavier and had BMI 0.2 kg/m<sup>2</sup> greater than those born at term. Differences were more marked between women born very post-term ( $\geq 43$  weeks) versus a narrower term group (38–40 weeks): 1.0 kg and 0.3 kg/m<sup>2</sup>. The adjusted relative risks of overweight/obesity and obesity in women born very post-term were 1.13 and 1.12 times higher, respectively, than in those born at term

**Conclusions:** Post-term birth is associated with greater BMI and increased odds of overweight

and obesity in adulthood, particularly among women born  $\geq 43$  weeks of gestation.

**Keywords:** adult; body mass index; females; gestational age; obesity; overweight; prolonged gestation

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## INTRODUCTION

Marked physiological stress during pregnancy is commonly associated with a pattern of adverse metabolic sequelae in the offspring, which can be detected in childhood. This is principally manifested as adverse effects on insulin sensitivity, which has been shown to be reduced in children born too small<sup>1</sup>, too large (from diabetic mothers)<sup>2</sup>, or too early (preterm)<sup>3</sup>.

Recently, it was observed that prepubertal children born post-term ( $\geq 42$  weeks of gestation) had a 34% reduction in insulin sensitivity, as well as increased body fat and abdominal adiposity<sup>4</sup>. Further, longitudinal data from Sweden showed that males born post-term had accelerated weight gain during childhood and an associated increased risk of obesity in adolescence<sup>5</sup>. Thus, it was of interest to examine whether adverse outcomes seen in childhood and adolescence persist into adulthood. We aimed to assess whether women born post-term displayed

increased risk of overweight and obesity in a large cohort of mothers with data from early pregnancy.

## METHODS

In Sweden, information is collected prospectively during pregnancy from the first antenatal visit and is subsequently forwarded to the Swedish Birth Register, which was established in 1973 and contains data on >99% of births in the country<sup>6</sup>. This study was approved by the Regional Ethical Review Board in Uppsala.

We examined data from the first antenatal visit (mostly 10–12 weeks of gestation) on all singleton Swedish women aged  $\geq 18$  years in 1991–2009. Exclusion criteria were birth to non-Nordic mothers, congenital malformations, or preterm birth (<37 weeks of gestation). Further, women were only included if also born to a singleton mother aged  $\geq 18$  years at their first antenatal visit.

Gestational age (extracted from the Swedish Birth Register) was mostly based on maternal report of last menstrual period, otherwise determined from ultrasound scans. We compared women born post-term ( $\geq 42$  weeks of gestation) versus those born at term (37–41 weeks of gestation). However, due to potential inaccuracies associated with gestational age estimation in the second trimester<sup>7</sup>, it is very likely that a number of women born at term would have been misclassified as post-term. As a result, we also examined differences in the two groups with a 2-week buffer between them, comparing women born very post-term ( $\geq 43$  weeks of gestation) to those born within a narrower term window (38–40 weeks of gestation).

Weight was measured and current height was self-reported or measured, with body mass index (BMI) being subsequently calculated. Overweight/obesity was defined as BMI  $\geq 25.0$  kg/m<sup>2</sup> and obesity as  $\geq 30.0$  kg/m<sup>2</sup>.

Study outcomes (i.e. anthropometry) were evaluated for continuous associations with gestational age, while stratified analyses were

also carried out comparing the above-described groups. Analyses were performed using general linear regression models, accounting for a number of confounding factors: sibship size (i.e. total number of siblings), birth order, age, year of birth, SGA status (SGA by birthweight and/or length vs not SGA), maternal smoking during pregnancy, and family situation (two-parent family vs other arrangements). Generalized linear models with a similar construction were run to evaluate binary outcomes (e.g. obesity risk). Statistical analyses were carried out in SAS v.9.4 (SAS Institute, Cary, NC, USA). Where applicable, results are expressed as adjusted relative risks (aRR) or  $\beta$  coefficients with associated 95% confidence intervals.

## RESULTS

There were 303,301 Swedish women who were born in 1973–1988 and gave birth to a child in 1991–2009. A total of 65,298 failed to meet inclusion criteria and a further 26,605 women had incomplete anthropometric data in early pregnancy. Thus, we examined data on 211,398 women at an average of 26.1 years of age (range 18–36 years), including 27,153 born post-term and 184,245 born at term.

### *Continuous associations*

Increasing gestational age was associated with greater adult weight [in kg,  $\beta=0.127$  (0.087–0.166)] and BMI [ $\beta=0.030$  (0.016–0.043)] in women. Weight and BMI were lowest in women born at 39 weeks of gestation, progressively increasing with greater gestational age (Figure 1).

### *Stratified analyses*

Women born post-term were 0.5 kg heavier and had BMI that was 0.2 kg/m<sup>2</sup> greater than those born at term (Table 1). Women born post-term also had a slightly greater risk of being overweight/obese (aRR 1.04) or obese (aRR 1.05) (Table 1).

However, when a 2-week buffer was applied between groups, differences were more marked. Women born very post-term ( $\geq 43$  weeks of

gestation) were 1.0 kg heavier and had BMI 0.3 kg/m<sup>2</sup> greater than those born within a narrower term window (38–40 weeks) (Table 2). The adjusted relative risk of overweight/obesity was 1.13 and of obesity 1.12 times higher in women born very post-term (Table 2).

## DISCUSSION

This study shows that women born post-term were heavier, had greater BMI, and had increased odds of overweight and obesity early in pregnancy. Notably, there was a progressive increase in BMI with increasing gestational age from a nadir at 39 weeks of gestation, so that the risk of overweight and obesity was particularly higher in those born very post-term ( $\geq 43$  weeks of gestation).

Despite changes in obstetric practice and lack of data for many countries, there is still great variation in rates of post-term births across the world. It has been estimated that post-term births account for as few as 0.4% of live births in Austria to as many as 8.1% in Denmark<sup>8</sup> and 5.5% in the USA<sup>9</sup>. Thus, individuals born post-term are a relatively common group in some countries. However, post-term birth had not been identified as a risk factor for adverse metabolic outcomes until very recently<sup>4,5</sup>. Apart from these studies in childhood and adolescence<sup>4,5</sup>, it seems that the possible effects of post-term birth on anthropometry and metabolism in adulthood have not been examined<sup>10</sup>. Thus, our findings are of interest, as the observed increased risk of overweight and obesity in adult women born post-term may be also associated with greater cardio-metabolic risk. Although the proportion of infants born at 43 weeks and beyond seems to be much reduced (maybe 0.1 to 1.5% of all births in Europe<sup>8</sup> and 21.2% of all post-term births in our study), our findings suggest that this group may be particularly at risk of adverse outcomes.

Notably, sexual dimorphism has been commonly observed in studies examining the effects of early life programming on long-term health<sup>11</sup>. Mathai et al. showed in a small New Zealand study that men born preterm were heavier and had greater BMI than term counterparts in their mid-thirties, while these parameters were similar amongst

women<sup>12</sup>. For those born at the other end of the gestational age spectrum, Beltrand et al. observed that the adverse effects of post-term birth were markedly greater among male adolescents<sup>5</sup>. As a result, the magnitude of the associations observed in women born post-term cannot be automatically extrapolated to men due to possible sexual dimorphism, and it would be important to evaluate whether there are more marked associations among men born post-term.

The factors underpinning the metabolic programming in children and adults born post-term are unclear, but may be associated with genetic inheritance or an adverse fetal environment in late gestation<sup>4</sup>. It is possible that post-term infants may be exposed to physiological stress due to an abnormally long gestation or late pregnancy utero-placental insufficiency. Placentae from post-term pregnancies have abnormal histological features that are similar to placentae of babies born small-for-gestational-age, including apoptotic changes, diffuse calcifications, chorionic villus degeneration, infarcts, increased necrosis, and decreased perfusion surface<sup>10,13,14</sup>. However, under-nutrition *in utero* is unlikely to occur in most prolonged pregnancies, since post-term and term infants have comparable ponderal indices and adjusted birth weights<sup>4</sup>. Thus, adverse outcomes may not be necessarily associated with the extended period *in utero per se*<sup>10</sup>. There may be underlying genetic or epigenetic mechanisms determining both the prolonged gestation and the associated metabolic programming<sup>10</sup>.

The limitations of our study include the lack of data on socioeconomic status and other potential confounding factors, particularly maternal BMI. In Sweden, the odds of post-term delivery among obese women are 1.63 times higher than in normal-weight women<sup>15</sup>. Therefore, one cannot discard the possibility that maternal overweight/obesity may be an important factor underpinning increased BMI among women born post-term. In addition, there are inaccuracies associated with gestational age estimation using the date of last menstrual period, which are less precise than early ultrasound scans and overestimate the number of post-term births<sup>7</sup>. The misclassification of women born at term as

post-term could have masked stronger associations between post-term birth and risks of overweight and obesity in adulthood. This also highlights the importance of our stratified analyses including a 2-week buffer between groups to account for possible errors in gestational age estimation. Another limitation was our relatively homogenous population of Nordic women, so that findings may not be readily extrapolated to other ethnic groups.

In conclusion, post-term birth was associated with greater BMI and increased odds of overweight and obesity in adult women. However, the relevance of these findings for later cardiovascular and metabolic risks is unclear. Further, other studies need to identify whether or not maternal overweight/obesity is an important driver of the observed associations. Future studies should also assess whether the pattern and magnitude of such associations differ in adult men born post-term.

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**Table 1.** Anthropometric data recorded early in pregnancy (10–12 weeks of gestation) among Swedish women born post-term ( $\geq 42$  weeks of gestation) or at term (37–41 weeks of gestation).

	Unadjusted			Adjusted		
	Term	Post-term	P-value	Term	Post-term	P-value
<b>n</b>	184,245	27,153		184,245	27,153	
<b>Age (years)</b>	26.1 $\pm$ 3.9	26.3 $\pm$ 3.9	<0.0001			
<b>Height (cm)</b>	167.2 $\pm$ 6.0	167.3 $\pm$ 5.9	0.05	164.7 (164.6–164.9)	164.9 (164.7–165.1)	0.21
<b>Weight (kg)</b>	67.4 $\pm$ 12.8	67.8 $\pm$ 12.9	<0.0001	65.3 (64.9–65.7)	65.8 (65.4–66.2)	<0.0001
<b>BMI (kg/m<sup>2</sup>)</b>	24.1 $\pm$ 4.3	24.2 $\pm$ 4.3	<0.0001	24.0 (23.9–24.2)	24.2 (24.0–24.3)	<0.0001
<b>Overweight/obese (BMI <math>\geq 25.0</math> kg/m<sup>2</sup>)</b>	31.5%	32.8%	<0.0001			
	1.00	1.04 (1.02–1.06)	<0.0001	1.00	1.05 (1.03–1.07)	<0.0001
<b>Obese (BMI <math>\geq 30.0</math> kg/m<sup>2</sup>)</b>	9.5%	10.0%	0.020			
	1.00	1.05 (1.01–1.09)	0.02	1.00	1.08 (1.04–1.12)	<0.001

Unadjusted data are percentages, means  $\pm$  standard deviations, or relative risks and 95% confidence intervals. Adjusted data are means or relative risks with respective 95% confidence intervals, adjusted for confounding factors (i.e. sibship size, birth order, age, year of birth, family situation, SGA status, and maternal smoking during pregnancy).

**Table 2.** Anthropometric data recorded early in pregnancy (10–12 weeks of gestation) among Swedish women born very post-term ( $\geq 43$  weeks of gestation) or at a narrower term window (38–40 weeks of gestation).

	Unadjusted			Adjusted		
	Term	Very post-term	P-value	Term	Very post-term	P-value
<b>n</b>	130,110	5,761		130,110	5,761	
<b>Age (years)</b>	26.0 $\pm$ 3.9	26.5 $\pm$ 4.0	<0.0001			
<b>Height (cm)</b>	167.2 $\pm$ 6.0	167.2 $\pm$ 5.9	0.83	164.7 (164.5–164.9)	164.8 (164.6–165.1)	0.07
<b>Weight (kg)</b>	67.3 $\pm$ 12.7	68.0 $\pm$ 13.1	<0.0001	65.2 (64.7–65.6)	66.2 (65.6–66.7)	<0.0001
<b>BMI (kg/m<sup>2</sup>)</b>	24.1 $\pm$ 4.3	24.3 $\pm$ 4.3	<0.0001	24.0 (23.8–24.1)	24.3 (24.1–24.5)	<0.0001
<b>Overweight/obese (BMI <math>\geq 25.0</math> kg/m<sup>2</sup>)</b>	31.3%	34.6%	<0.0001			
	1.00	1.11 (1.07–1.15)	<0.0001	1.00	1.13 (1.09–1.17)	<0.0001
<b>Obese (BMI <math>\geq 30.0</math> kg/m<sup>2</sup>)</b>	9.4%	10.1%	0.08			
	1.00	1.07 (0.99–1.16)	0.08	1.00	1.12 (1.03–1.21)	0.006

Unadjusted data are percentages, means  $\pm$  standard deviations, or relative risks and 95% confidence intervals. Adjusted data are means or relative risks with respective 95% confidence intervals, adjusted for confounding factors (i.e. sibship size, birth order, age, year of birth, family situation, SGA status, and maternal smoking during pregnancy).

**Figure 1.** Body mass index (BMI) early in pregnancy (10–12 weeks of gestation) among 211,398 Swedish women, according to their gestational age at birth. Data are means and 95% confidence intervals, adjusted for confounding factors (i.e. sibship size, birth order, age, year of birth, family situation, SGA status, and maternal smoking during pregnancy).

