

# Maternal and fetal characteristics affect discrepancies between pregnancy-dating methods: a population-based cross-sectional register study

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## Key words

Pregnancy dating, pregnancy, gestational age, ultrasonography, prenatal, menstruation, female, humans

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## Conflict of interest

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

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## Abstract

**Introduction.** Gestational age is estimated by ultrasound using fetal size as a proxy for age, although variance in early growth affects reliability. The aim of this study was to identify characteristics associated with discrepancies between last menstrual period-based (EDD-LMP) and ultrasound-based (EDD-US) estimated delivery dates. **Material and methods.** We identified all singleton births ( $n = 1\,201\,679$ ) recorded in the Swedish Medical Birth Register in 1995–2010, to assess the association between maternal/fetal characteristics and large negative and large positive discrepancies (EDD-LMP earlier than EDD-US and 10th percentile in the discrepancy distribution vs. EDD-LMP later than EDD-US and 90th percentile). Analyses were adjusted for age, parity, height, body mass index, smoking, and employment status. **Results.** Women with a body mass index  $>40\text{ kg/m}^2$  had the highest odds for large negative discrepancies ( $-9$  to  $-20$  days) [odds ratio (OR) 2.16, 95% CI 2.01–2.33]. Other factors associated with large negative discrepancies were: diabetes, young maternal age, multiparity, body mass index between 30 and  $39.9\text{ kg/m}^2$  or  $<18.5\text{ kg/m}^2$ , a history of gestational diabetes, female fetus, shorter stature ( $<-1$  SD), a history of preeclampsia, smoking or snuff use, and unemployment. Large positive discrepancies ( $+4$  to  $+20$  days) were associated with male fetus (OR 1.80, 95% CI 1.77–1.83), age  $\geq 30$  years, multiparity, not living with a partner, taller stature ( $>+1$  SD), and unemployment. **Conclusions.** Several maternal and fetal characteristics were associated with discrepancies between dating methods. Systematic associations of discrepancies with maternal height, fetal sex, and partly obesity, may reflect an influence on the precision of the ultrasound estimate due to variance in early growth.

**Abbreviations:** BMI, body mass index; CI, confidence interval; EDD, estimated delivery date; GA, gestational age; LMP, last menstrual period; OR, odds ratio; US, ultrasound.

## Introduction

The method of estimating gestational age (GA) by ultrasound (US), using fetal size as a proxy for age, is usually more precise than the method based on the last menstrual period (LMP). However, there is variance in early growth, which may affect the reliability of the US-based

## Key Message

Variance in early fetal growth can bias ultrasound-based pregnancy dating. Maternal obesity, height, and fetal sex may partly explain large discrepancies between pregnancy-dating methods.

estimate that is used for clinical decision-making (1,2). For example, early discrepancies between expected and actual fetal size can be detected in assisted reproductive technology pregnancies and are associated with maternal obesity and the birth of small-for-gestational-age infants (1). In addition, fetal sex, by association with size, affects the accuracy of US pregnancy dating. Male fetuses have on average a 1-mm larger biparietal diameter early in the second trimester, corresponding to about one day in growth (2).

Average differences between LMP- and US-based estimated delivery dates (EDD) are small, with LMP estimates of one to three days more advanced pregnancy length than US estimates (3). Nevertheless, the choice of method affects the rates of preterm and post-term deliveries, as well as neonatal outcomes, which is probably related to correction of EDD in pregnancies with large discrepancies between dating methods (4,5).

Maternal and fetal characteristics associated with discrepancies between EDD-LMP and EDD-US estimates include maternal age, parity, smoking, obesity, diabetes, maternal height, educational level, fetal sex, malformations, and small-for-gestational-age infants (1,6–9). Large discrepancies between methods have clinical implications through association with adverse outcomes (6,10).

Because mean differences in early fetal growth are small, and adverse outcomes are thought to occur predominantly in pregnancies with a large deviation from average growth, the aim of this study was to identify characteristics, present at the time of pregnancy dating, associated with large discrepancies between EDD-LMP and EDD-US in a population-based sample of Swedish pregnancies.

## Material and methods

Data were obtained from the Swedish Medical Birth Register and the Swedish Patient Register. We included all singleton births in Sweden from 1995 to 2010, with valid documentation of EDD based on both LMP and US. To avoid data entry errors, and larger discrepancies because of reasons other than variation in early growth, pregnancies with discrepancies >20 days were excluded. The Medical Birth Register contains information on more than 99% of all births in Sweden since 1973, including maternal sociodemographic characteristics and prospectively collected information during pregnancy, delivery, and the neonatal period (11). The register has been found reliable for research purposes, with good internal validity (12). Since 1990, US scanning has been offered to all pregnant women with more than 95% acceptance. Since 1995, nearly all clinics have used EDD-US (11).

Variables from the Medical Birth Register included maternal age, parity, height, weight, smoking and snuff (smokeless tobacco) use at first antenatal visit, family situation, occupational status, LMP, EDD-LMP, EDD-US, and infant sex (Table 1).

Maternal height was defined as shorter stature if height was below 1 standard deviation (SD) from the mean, and taller stature was defined as above 1 SD from the mean. Maternal body mass index (BMI) was calculated based on height and weight, and categorized according to the World Health Organization classification as underweight <18.5 kg/m<sup>2</sup>, normal weight 18.5–24.9 kg/m<sup>2</sup>, pre-obesity 25.0–29.9 kg/m<sup>2</sup>, obesity class I (30.0–34.9 kg/m<sup>2</sup>), obesity class II (35.0–39.9 kg/m<sup>2</sup>), and obesity class III (>40 kg/m<sup>2</sup>) (13).

Information on maternal diagnoses, from five years before until nine months (EDD-US minus 280 days) before delivery, was collected from the Swedish Patient Register. In the inpatient setting, diagnoses were included if they appeared once. In the outpatient setting, diagnoses would have to be registered twice to avoid any preliminary diagnoses. Inpatient diagnoses were retrieved for the whole study period, and outpatient diagnoses were retrieved from 2001. Diagnoses that theoretically could affect early fetal growth were chosen, and included diabetes, gestational diabetes in a former pregnancy, hypertensive disorders, preeclampsia in a former pregnancy, hypothyroidism, systemic lupus erythematosus, inflammatory bowel disease (Crohn's disease and ulcerative colitis), depressive-affective disorders, and phobias and anxiety disorders.

Discrepancy was defined as EDD-LMP minus EDD-US, corresponding to the difference in days between the two pregnancy-dating methods as recorded in the Medical Birth Register. *Negative discrepancy* corresponds to EDD-LMP earlier than EDD-US, reflecting a more advanced GA by LMP estimation than by US estimation, i.e. the fetus was smaller than expected when dated by US and EDD was postponed. *Positive discrepancy* was defined as EDD-LMP later than EDD-US, corresponding to a less advanced GA by LMP-estimation than the GA estimated by US-examination, i.e. the fetus was larger than expected when dated by US and EDD was moved to an earlier date.

Discrepancies of interest were defined as those below the 10th percentile (large negative discrepancy) and above the 90th percentile (large positive discrepancy) in the discrepancy distribution, and the reference category was defined as discrepancies within 2 days of the median. Remaining pregnancies, not corresponding to the large discrepancy categories or the reference category, were excluded from further analyses. Analyses were conducted with the purpose of assessing to what extent maternal

**Table 1.** Correlates of large discrepancies between pregnancy dating methods. Odds ratios (OR) with 95% confidence intervals (95% CI) for large negative discrepancy (below the 10th percentile in the discrepancy distribution; -9 to -20 days) and large positive discrepancy (above the 90th percentile in the discrepancy distribution; +4 to +20 days) between EDD-LMP and EDD-US<sup>a</sup> in association with maternal characteristics at the first antenatal visit, fetal sex, and maternal medical history variables.

	Large negative discrepancies					Large positive discrepancies								
	n	Neg (%) <sup>b</sup>	Ref (%) <sup>c</sup>	cOR	95% CI	aOR <sup>e</sup>	95% CI	n	Pos (%) <sup>b</sup>	Ref (%) <sup>c</sup>	cOR	95% CI	aOR <sup>e</sup>	95% CI
<b>Age at delivery (years)</b>														
<20	18 662	5	3	1.84	1.78-1.90	1.79	1.71-1.86	15 712	3	3	1.14	1.09-1.19	1.05	1.00-1.11
20-24	109 111	24	16	1.42	1.40-1.44	1.40	1.37-1.43	96 840	14	16	1.00	0.98-1.03	1.00	0.97-1.02
25-29	226 304	38	35	1.00	-	1.00	-	217 512	32	35	1.00	-	1.00	-
30-34	198 848	25	33	0.71	0.69-0.72	0.68	0.67-0.70	206 725	33	33	1.11	1.09-1.13	1.12	1.10-1.14
35-39	73 707	7	13	0.54	0.53-0.56	0.49	0.48-0.50	81 893	15	13	1.30	1.28-1.33	1.29	1.26-1.32
>40	10 300	1	2	0.46	0.43-0.49	0.38	0.35-0.40	12 211	3	2	1.60	1.53-1.67	1.57	1.50-1.65
Total	636 932	100	100					630 893	100	100				
<b>Height (cm)</b>														
<160	119 842	22	18	1.22	1.21-1.24	1.17	1.15-1.20	113 261	17	18	0.98	0.96-1.00	0.96	0.94-0.98
160-172 <sup>f</sup>	412 279	64	65	1.00	-	1.00	-	407 312	63	65	1.00	-	1.00	-
>172	104 811	14	17	0.82	0.81-0.84	0.86	0.84-0.88	110 320	20	17	1.17	1.15-1.19	1.19	1.17-1.21
Total	636 932	100	100					630 893	100	100				
<b>BMI classes according to WHO classification</b>														
Underweight	15 836	3	2	1.36	1.31-1.42	1.18	1.13-1.24	15 049	3	2	1.03	0.98-1.07	1.03	0.98-1.09
Normal range	402 285	60	64	1.00	-	1.00	-	404 877	65	64	1.00	-	1.00	-
Pre-obese	153 378	24	24	1.08	1.06-1.09	1.07	1.05-1.08	151 804	24	24	0.98	0.97-1.00	0.97	0.95-0.98
Obese class I	47 165	9	7	1.39	1.36-1.42	1.34	1.30-1.37	43 689	7	7	0.91	0.89-0.94	0.90	0.87-0.92
Obese class II	13 860	3	2	1.74	1.68-1.81	1.70	1.63-1.78	11 950	2	2	0.83	0.79-0.87	0.80	0.76-0.85
Obese class III	4408	1	1	2.18	2.05-2.33	2.16	2.01-2.33	3524	1	1	0.78	0.71-0.86	0.74	0.66-0.82
Total	636 932	100	100					630 893	100	100				
<b>Living with partner</b>														
Yes	599 095	93	94	1.00	-	1.00	-	593 478	93	94	1.00	-	1.00	-
No	30 259	6	5	1.23	1.20-1.27	0.99	0.95-1.02	30 030	6	5	1.25	1.22-1.29	1.21	1.17-1.25
Missing	7578	1	1					7385	1	1				
Total	636 932	100	100					630 893	100	100				
<b>Employed</b>														
Yes	461 462	68	74	1.00	-	1.00	-	461 500	71	74	1.00	-	1.00	-
No	113 304	21	17	1.32	1.30-1.34	1.09	1.07-1.11	109 636	19	17	1.12	1.10-1.14	1.16	1.14-1.19
Missing	62 166	12	9					59 757	10	9				
Total	636 932	100	100					630 893	100	100				
<b>Smoking at first antenatal visit</b>														
No	568 365	87	90	1.00	-	1.00	-	565 880	89	90	1.00	-	1.00	-
Yes	59 502	12	9	1.35	1.33-1.38	1.13	1.11-1.16	56 077	9	9	1.04	1.02-1.07	1.04	1.02-1.07
Missing	9065	2	1					8936	1	1				
Total	636 932	100	100					630 893	100	100				

Table 1. Continued

	Large negative discrepancies					Large positive discrepancies								
	n	Neg (%) <sup>b</sup>	Ref (%) <sup>c</sup>	cOR	95% CI	aOR <sup>e</sup>	95% CI	n	Pos (%) <sup>d</sup>	Ref (%) <sup>c</sup>	cOR	95% CI	aOR <sup>e</sup>	95% CI
<b>Snuff use at first antenatal visit<sup>g</sup></b>														
No	483 073	73	77	1.00	-	1.00	-	481 672	75	77	1.00	-	1.00	-
Yes	5844	1	1	1.16	1.09–1.24	1.12	1.05–1.20	5670	1	1	1.01	0.94–1.08	1.01	0.94–1.09
Missing	148 015	26	23					143 551	24	23				
Total	636 932	100	100					630 893	100	100				
<b>Parity</b>														
0-parous	280 971	45	44	1.00	-	1.00	-	276 029	43	44	1.00	-	1.00	-
1-parous	236 861	36	38	0.92	0.91–0.93	1.05	1.03–1.07	233 995	35	38	0.94	0.93–0.96	0.91	0.89–0.92
2-parous	85 121	13	13	0.94	0.92–0.95	1.20	1.17–1.24	86 219	15	13	1.10	1.08–1.12	1.02	0.99–1.04
3-parous	22 807	4	4	1.04	1.00–1.07	1.40	1.34–1.46	23 246	4	4	1.25	1.21–1.29	1.13	1.08–1.17
4-parous or more	11 172	2	2	1.24	1.19–1.30	1.77	1.67–1.87	11 404	3	2	1.49	1.43–1.56	1.29	1.23–1.37
Total	636 932	100	100					630 893	100	100				
<b>Fetal sex</b>														
Male	319 057	44	52	1.00	-	1.00	-	340 140	65	52	1.76	1.74–1.78	1.80	1.77–1.83
Female	317 875	56	49	1.34	1.33–1.36	1.36	1.34–1.38	290 753	35	49	1.00	-	1.00	-
Total	636 932	100	100					630 893	100	100				
<b>Medical history variables<sup>h</sup></b>														
<b>Diabetes mellitus</b>														
No	635 613	100	100	1.00	-	1.00	-	629 860	100	100	1.00	-	1.00	-
Yes	1319	0	0	2.15	1.91–2.41	1.95	1.69–2.25	1033	0	0	0.78	0.65–0.92	0.86	0.70–1.04
Total	636 932	100	100					630 893	100	100				
<b>Gestational diabetes in a former pregnancy<sup>i</sup></b>														
No	353 236	99	99	1.00	-	1.00	-	353 236	99	100	1.00	-	1.00	-
Yes	2725	1	1	1.61	1.48–1.75	1.47	1.38–1.63	2725	1	0	0.75	0.67–0.85	0.74	0.65–0.84
Total	355 961	100	100					355 961	100	100				
<b>Hypertensive disorders</b>														
No	636 565	100	100	1.00	-	1.00	-	630 560	100	100	1.00	-	1.00	-
Yes	367	0	0	1.37	1.08–1.74	1.26	0.94–1.68	333	0	0	0.88	0.66–1.18	0.76	0.54–1.07
Total	636 932	100	100					630 893	100	100				
<b>Preeclampsia in a former pregnancy<sup>j</sup></b>														
No	345 235	96	97	1.00	-	1.00	-	345 235	98	97	1.00	-	1.00	-
Yes	10 726	4	3	1.22	1.17–1.28	1.16	1.09–1.23	10 726	2	3	0.86	0.82–0.91	0.92	0.86–0.98
Total	355 961	100	100					355 961	100	100				
<b>Hypothyroidism</b>														
No	635 635	100	100	1.00	-	1.00	-	629 595	100	100	1.00	-	1.00	-
Yes	1297	0	0	0.91	0.78–1.05	0.97	0.82–1.14	1298	0	0	0.96	0.83–1.11	0.85	0.72–1.01
Total	636 932	100	100					630 893	100	100				

**Table 1.** Continued

	Large negative discrepancies					Large positive discrepancies								
	n	Neg (%) <sup>b</sup>	Ref (%) <sup>c</sup>	cOR	95% CI	aOR <sup>e</sup>	95% CI	n	Pos (%) <sup>d</sup>	Ref (%) <sup>c</sup>	cOR	95% CI	aOR <sup>e</sup>	95% CI
<b>Systematic lupus erythematosus</b>														
No	636 720	100	100	1.00	–	1.00	–	630 695	100	100	1.00	–	1.00	–
Yes	212	0	0	1.17	0.84–1.63	1.24	0.83–1.84	198	0	0	0.85	0.58–1.25	0.79	0.50–1.24
Total	636 932	100	100					630 893	100	100				
<b>Ulcerative colitis</b>														
No	636 163	100	100	1.00	–	1.00	–	630 101	100	100	1.00	–	1.00	–
Yes	769	0	0	0.76	0.62–0.92	0.82	0.64–1.04	792	0	0	0.96	0.80–1.15	1.09	0.89–1.34
Total	636 932	100	100					630 893	100	100				
<b>Crohn's disease</b>														
No	636 174	100	100	1.00	–	1.00	–	630 124	100	100	1.00	–	1.00	–
Yes	758	0	0	0.92	0.77–1.11	0.92	0.73–1.14	769	0	0	1.05	0.88–1.26	1.17	0.96–1.44
Total	636 932	100	100					630 893	100	100				
<b>Depressive disorders</b>														
No	634 329	100	100	1.00	–	1.00	–	628 468	100	100	1.00	–	1.00	–
Yes	2603	1	0	1.26	1.15–1.38	1.09	0.98–1.21	2425	0	0	0.92	0.83–1.03	0.91	0.81–1.03
Total	636 932	100	100					630 893	100	100				
<b>Anxiety disorders and phobias</b>														
No	635 326	100	100	1.00	–	1.00	–	629 406	100	100	1.00	–	1.00	–
Yes	1606	0	0	1.30	1.16–1.47	1.14	1.00–1.30	1487	0	0	0.93	0.81–1.07	0.92	0.79–1.07
Total	636 932	100	100					630 893	100	100				

<sup>a</sup>Estimated due date based on the date of the last menstrual period (EDD-LMP) and estimated due date based ultrasound biometry (EDD-US).

<sup>b</sup>Pregnancies with negative discrepancy below the 10th percentile (–9 to –20 days), n = 119 275 births.

<sup>c</sup>Reference category is median discrepancy ±2 days (–1 to +3 days), n = 517 657 births.

<sup>d</sup>Pregnancies with positive discrepancy above the 90th percentile (+4 to +20 days), n = 113 236 births.

<sup>e</sup>Adjusted, as appropriate, for age, parity, height, BMI, smoking at first antenatal visit, and employment status.

<sup>f</sup>Mean ± 1 SD.

<sup>g</sup>Variable available for analyses for births in years 2000–2010.

<sup>h</sup>Inpatient diagnoses registered at least once from 5 years to 9 months before registered birth.

<sup>i</sup>Analyses excluding 0-parous women.

[Correction added on 23 December 2016 after online publication: In Table 1, the values of Male and Female Fetal Sex under Large positive discrepancies have been corrected.]

characteristics, disease, and fetal sex were associated with large discrepancies in days between EDD-LMP and EDD-US. Multiple logistic regression analyses were used to calculate odds ratios (OR) and 95% confidence intervals (95% CI) for large positive or negative discrepancy, in association with maternal characteristics, disease, and fetal sex.

Analyses were restricted to births with maternal height 140–189 cm and maternal weight 35–139 kg, to reduce data entry errors. Analyses of diagnoses in former pregnancies were restricted to parous women. All models were adjusted for age, parity, height, BMI, smoking in early pregnancy, and employment status, as appropriate. Analyses were further adjusted for maternal comorbidity, which was a composite variable defined as the woman having one of the selected diagnoses recorded at least once. Statistical analyses were conducted using the statistical software R version 3.1.3, R Core Team (2015).

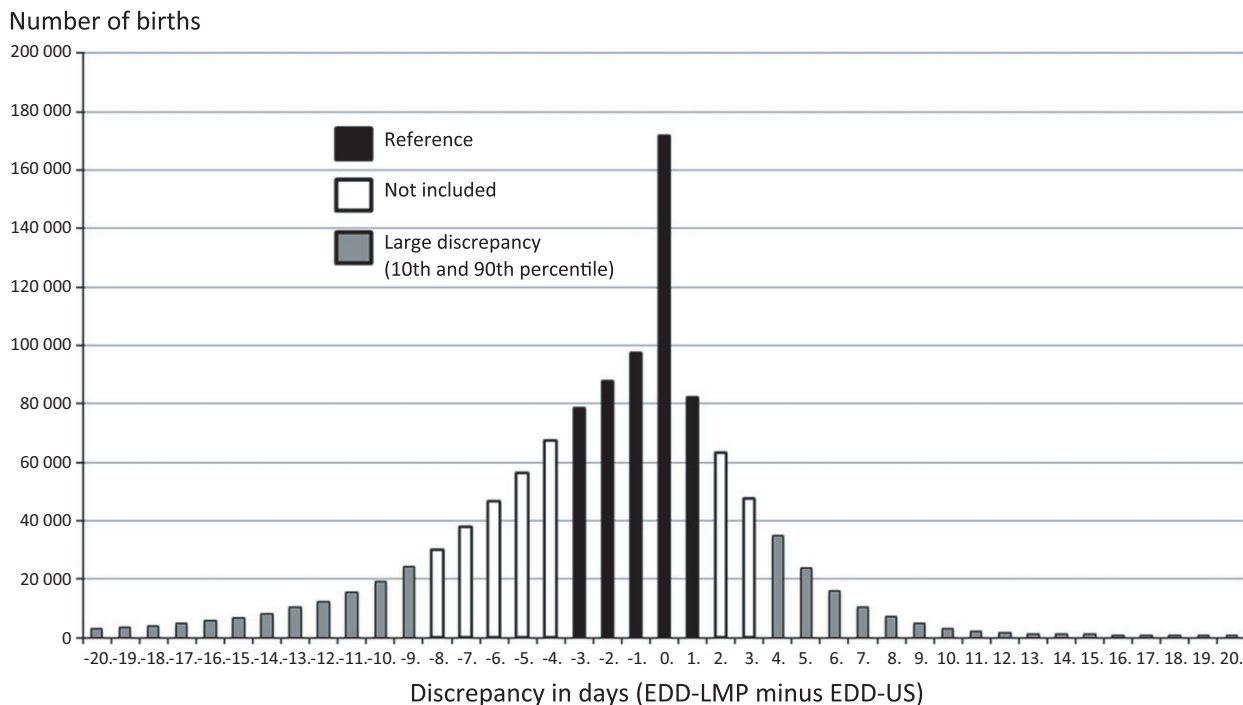
The Regional Ethical Review Board in Uppsala, Sweden, approved the study protocol reference number 2012/412, 19 December 2012.

## Results

The total number of births in the study population was 1 201 679. Mean maternal age was 30 years (SD = 5 years), mean height was 166 cm (SD = 6 cm), and mean

BMI was 24 kg/m<sup>2</sup> (SD = 4 kg/m<sup>2</sup>). Most commonly, there was no (16%) or only a few days' discrepancy between EDD-LMP and EDD-US (Figure 1). Mean discrepancy was +2 days, and the median discrepancy was +1 day. A large negative discrepancy, below the 10th percentile, corresponded to −9 to −20 days, whereas a large positive discrepancy, above the 90th percentile, corresponded to +4 to +20 days. Information on maternal height or weight was missing in 101 630 births (8.5%). A total of 1 100 049 births had valid documentation for maternal height and weight: large negative discrepancies ( $n = 119\,275$ ), reference category (discrepancy −1 to +3 days,  $n = 517\,657$ ), and large positive discrepancies ( $n = 113\,236$ ).

For large negative discrepancies, the strongest association was observed for obesity class III (OR 2.16, 95% CI 2.01–2.33). Other factors associated with large negative discrepancies were: diabetes (OR 1.95, 95% CI 1.69–2.25), maternal age <20 years (OR 1.79, 95% CI 1.71–1.86), being four-parous or more (OR 1.77, 95% CI 1.67–1.87), and obesity class II, a history of gestational diabetes, age 20–24 years, three-parous, female fetus, obesity class I, underweight, shorter stature, a history of preeclampsia, smoking, snuff use, unemployment, pre-obesity, or primiparity (Table 1). Women who had a taller stature or were aged 30 years or above were less likely to have large negative discrepancies.



**Figure 1.** Number of births and discrepancy in days between ultrasound (US)-based and last menstrual period (LMP)-based estimated delivery date (EDD).

For large positive discrepancies, the strongest association was observed for pregnancies with a male fetus (OR 1.80, 95% CI 1.77–1.83). Other factors associated with large positive discrepancies were: age 40 years or above (OR 1.57, 95% CI 1.50–1.65), 35–39 years (OR 1.29, 95% CI 1.26–1.32), being four-parous or more (OR 1.29, 95% CI 1.23–1.37), not living with a partner, taller stature, unemployed, being three-parous, 30–34 years, or smoking (Table 1). Women who were overweight, obese, had gestational diabetes or preeclampsia, were primiparous, or had a shorter stature were less likely to have large positive discrepancies.

When outpatient diagnoses were included in the adjusted analyses, possible for the years 2006–2010, there were higher odds for large negative discrepancies in association with depressive disorder OR 1.11 (95% CI 1.02–1.21) and higher odds for large positive discrepancies with Crohn's disease (OR 1.36, 95% CI 1.10–1.67). There were lower odds for large positive discrepancies with diabetes (OR 0.79, 95% CI 0.66–0.94), hypothyroid disease (OR 0.85, 95% CI 0.73–0.99), and depressive disorders (OR 0.85, 95% CI 0.78–0.94). Adjusting for maternal comorbidity only marginally affected the estimates.

## Discussion

This study confirmed previously reported associations of discrepancies between pregnancy-dating methods and characteristics such as obesity, maternal age, parity, fetal sex, maternal height, smoking, and diabetes (6,8,9). Our study population was partly overlapping with the populations in two of the studies (8,9). However, we included a more recent and longer time period and also assessed other possible risk factors for discrepancies in dating methods, such as snuff use, unemployment, living without a partner, and preeclampsia in a former pregnancy.

Discrepancies could be the result of variation in menstrual cycles or difficulties recalling the LMP, as well as differences in early fetal growth and technical issues in US biometry (1,2). In most situations, it may be difficult to determine which of the estimates is biased. However, the systematic effect of both fetal sex, attributable to the smaller size of female fetuses, and maternal height, because of genetic influence on fetal growth, is not likely to be explained by unreliable LMP.

Only small average discrepancies between LMP-based and US-based methods are expected because both methods predict EDD relatively well; US is the preferred method, being more precise in the general population (14). However, as average differences may not be clinically meaningful, we compared pregnancies where a substantial difference was observed to those with minimal differences. In this study, discrepancies exceeded one

week in more than one of six pregnancies (14% with negative and 4% with positive discrepancies). In addition, large negative discrepancies were associated with obesity and diabetes. These conditions, as well as large negative discrepancies between pregnancy-dating methods, have been associated with adverse outcomes (1,6,10,15,16). The reason for the association between large negative discrepancies between the dating methods and adverse outcomes may be misclassifications of GA, resulting for example in delayed post-term inductions (6,10). Another reason is that a smaller-than-expected fetus at the time of US pregnancy dating may be growth-restricted (1,10).

Maternal age >30 years was associated with larger fetuses than expected at the US scan, and a similar effect of maternal age has been reported earlier (6). This is consistent with another study relating maternal age to increasing embryonic growth trajectories (17). However, the follicular phase can be one day shorter in women from 35 years of age, which could increase the probability of earlier conception and a large-than-expected fetus at the US scan (18). Tunón *et al.* found that maternal age affected the precision of EDD-US estimates but not of EDD-LMP estimates, indicating an effect on fetal growth (19). Age below 25 years was associated with higher odds for both negative and positive large discrepancies, hypothetically because of greater LMP uncertainty.

Maternal height systematically affected the odds for large discrepancies; taller mothers were more likely to have larger fetuses and shorter mothers to have smaller fetuses than expected according to EDD-LMP. The effect of height was expected, based on genetic influence rather than menstrual cycle differences (5,20).

Obesity class III had the largest effect on large negative discrepancies. Every increase in BMI class above the normal range increased the odds for large negative discrepancies, and decreased the odds for large positive discrepancies. It could be hypothesized that obese women would have larger fetuses than expected at the US scan because of associated macrosomia. The association between high maternal BMI and negative discrepancies is, however, in accordance with results of earlier studies (6,9). In particular, in another study based on data from the Swedish Medical Birth Register between 1992 and 2005, EDD was more often postponed among overweight and obese women (9). One explanation could be prolonged menstruation cycles associated with obesity (21,22). Other reasons might be due to the accuracy of the US measurements of fetal size when examining obese women, or a possible repressive influence of obesity on early fetal growth. According to a study on assisted reproductive technology pregnancies, there is a risk of underestimating the GA when it is based on US examination in obese women (1). In Sweden, 13% of pregnant women in

2010 were obese (6,10,23). Both maternal obesity and negative discrepancies are known to be associated with adverse pregnancy outcomes (6,10). Underweight women were also at higher odds for large negative discrepancies, as expected based on a higher risk for small-for-gestational-age infants and delayed ovulations (22,24).

Of the socioeconomic factors that were assessed, living without a partner and being unemployed increased odds for both negative and positive discrepancies. However, the association between living without a partner and a negative discrepancy was not significant after adjustment. Even though Sweden offers free antenatal care for all pregnant women, and living without a partner is a socially accepted family structure, this group differs from the rest of the population in terms of risk for discrepancies for mostly unknown reasons.

Smoking and snuff tobacco use were associated with higher odds for large negative discrepancies. There is a well-known repressive effect on fetal growth caused by smoking, with linear dose–response curves for increased smoking in relation to shorter biparietal diameter and femur length in the third trimester (25). Our results suggested an effect of smoking also on early fetal growth, which was in line with another study, where fetal crown rump length was found to be shorter in women who smoked 10 or more cigarettes per day as compared with non-smokers (26).

Advanced parity increased the odds for large discrepancies. These results are in line with a previous Swedish study with data partly overlapping those included in this study (8). The effect estimates in the current study remained significant for large negative discrepancies after adjustments; however, the associations with large positive discrepancies were weaker after adjustments, strengthening the notion of a more complex association.

Fetal sex had a systematic effect on discrepancies. The odds for large negative discrepancies were higher for female fetuses, whereas the odds for large positive discrepancies were higher for male fetuses. This could be attributed to the smaller average size of female fetuses in early pregnancy, and confirms results from earlier studies (2,8,27). Although most fetuses are mildly misclassified, a number of fetuses are misclassified by more than a week because they are considerably larger (more often males) or smaller (more often females) than the mean. This is reflected in adversely affected odds for postmaturity-related morbidity and mortality in post-term female infants in a Swedish register study after introduction of – predominantly second trimester – US pregnancy dating, and also reflected in a successively increasing male-to-female birth ratio in gestational weeks 41, 42, and 43 (28,29). According to a Norwegian study, this increased post-term male–female ratio is normalized when estimates

are based on LMP or first trimester instead of second trimester US (27).

The association of maternal diabetes with negative discrepancies confirms the results of other studies (6,30). In a Norwegian study, women with type 1 diabetes had negative discrepancies of seven or more days in 25% of pregnancies, and 14 or more days in 10% of pregnancies, compared with a certain LMP date, with a risk of going beyond the optimal pregnancy length because of systematic postponement of EDD-US (30).

Odds of negative discrepancies for those with a history of hypertensive disease were not significant after adjustments, which could indicate that the effect on fetal growth occurs later in pregnancy, although hypertension has also been associated with shorter crown rump length measurements (7). A history of preeclampsia in former pregnancy was associated with higher odds for negative discrepancies and lower odds for positive discrepancies. This is in accordance with the higher risk among these women, also in the currently studied pregnancy, for preeclampsia and intrauterine growth retardation, which can be of early onset (31).

A history of anxiety disorders was associated with higher odds for negative discrepancies. However, there were no statistically significant associations with large negative or large positive discrepancies when having a history of hypothyroidism, systemic lupus erythematosus, ulcerative colitis, Crohn's disease or depressive disorders, which could be the result of a later effect on growth.

The present large register-based cohort, which could be considered population-based as more than 99% of all births were registered, allowed for high external validity compared with an earlier hospital-based study (6). In comparison with two earlier Swedish register studies, the current study includes a larger sample, addresses a more recent time period and adds several other characteristics, such as maternal medical history variables (for example preeclampsia and diabetes in an former pregnancy), as well as snuff use, unemployment, and living without a partner (8,9). Detailed information was prospectively recorded, minimizing recall bias. A limitation of the study was that no information of regularity on menstrual cycles was included in the register. There was also some missing information on maternal weight, possibly introducing a degree of inclusion bias.

Large discrepancies between the LMP and US methods are not rare, and clinicians should be aware that one or both methods may be unreliable. This is particularly important in the extremes of pregnancy length, when GA influences clinical decision-making. Early pregnancy dating is preferred – due to increasing growth variance with advancing GA – and is optimally performed at 10 weeks + 0 days to 13 weeks + 6 days according to the



recommendations of the International Society of Ultrasound in Obstetrics and Gynecology (32).

Increased awareness of maternal and fetal characteristics that can bias GA estimates can be helpful in clinical situations when large discrepancies between methods are noted. A large discrepancy combined with characteristics affecting early growth should lead to critical evaluation of the GA estimate based on US, and additional information, such as the date of the LMP or an assumed date of conception, should be considered before decision-making. As large negative discrepancies are associated with adverse outcomes, these pregnancies may benefit from closer monitoring in order to detect intrauterine growth retardation and to avoid post-term pregnancies (14,33).

## Conclusions

Maternal and fetal characteristics affect discrepancies between pregnancy-dating methods based on LMP and US. The US estimate is often regarded as the most reliable method and is used for clinical decision-making. This study indicates that the precision of the US estimate is systematically affected by characteristics such as maternal height and fetal sex, and possibly partly by obesity. In clinical settings, large discrepancies between GA estimates, in combination with certain maternal or fetal characteristics, can help clinicians identify pregnancies with high risk for uncertain dating estimates in order to make appropriate management decisions.

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