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Discrepancy between pregnancy dating methods – correlates and outcomes

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Abstract
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With the introduction of obstetric ultrasound there has been a shift from last menstrual period-based to ultrasound-based estimation of gestational age. The choice of the method and timing of pregnancy dating is important because it can affect dating precision and perinatal outcomes.

First, when comparing two large population-based cohorts from the Medical Birth Register, from before and after the introduction of ultrasound-based pregnancy dating, male infants on the edge of prematurity did not benefit from progress in medical care as much as female infants in terms of prematurity-related outcomes. This might reflect a bias introduced by the ultrasound-based pregnancy dating method, because of a tendency to overestimate gestational age in pregnancies with a male fetus.

Second, in a large population-based cross-sectional study, the associations of discrepancies between last menstrual period-based and ultrasound-based estimates with variables such as fetal sex and maternal height, indicated that ultrasound-based pregnancy dating introduced systematic errors presumably related to the method's use of fetal size as a proxy for gestational age. The largest effect estimates were found for maternal obesity in cases of large negative discrepancies.

Third, in a large population-based cohort study, discrepancies between last menstrual period-based and ultrasound-based estimates were associated with several adverse pregnancy, delivery, and neonatal outcomes. Most importantly, a large negative discrepancy was associated with higher odds for neonatal and intrauterine fetal death, as well as for an infant being small for gestational age.

Fourth, in a survey study there was overall good adherence to national guidelines, except for early pregnancy dating. However, the management of discrepancies between methods for pregnancy dating varied widely in clinical practice, which may be due to the lack of national guidelines.

In summary, ultrasound-based dating can be biased by maternal or fetal characteristics. Discrepancies between methods for pregnancy dating may indicate a need for closer monitoring to optimize perinatal care during pregnancy and childbirth.

Keywords: pregnancy, gestational age, ultrasound, last menstrual period

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To the miracle of life – through pregnancy and childbirth

List of Papers

This thesis is based on the following papers, which are referred to in the text by their Roman numerals.

I Kullinger, M., Haglund, B., Kieler, H., Skalkidou, A. Effects of ultrasound pregnancy dating on neonatal morbidity in late preterm and early term male infants: a register-based cohort study. *BMC Pregnancy and Childbirth 2016:16*

II Kullinger, M., Wesström, J., Kieler, H., Skalkidou, A. Maternal and fetal characteristics affect discrepancies between pregnancy dating methods: a population-based cross-sectional register study. *Acta Obstetricia et Gynecologica Scandinavica 2017:96(1):86–95.*

III Kullinger, M., Granfors, M., Kieler, H., Skalkidou, A. Discrepancy between pregnancy dating methods affects obstetric and neonatal outcomes: a population-based register cohort study. *Submitted.*

IV Kullinger, M., Granfors, M., Kieler, H., Skalkidou, A. Adherence to Swedish national pregnancy dating guidelines and management of discrepancies between pregnancy dating methods. *Submitted.*

Contents

Abbreviations

LMP	Last menstrual period
EDD	Estimated date of delivery
CRL	Crown-rump-length
BPD	Biparietal diameter
SGA	Small-for-gestational-age
LGA	Large-for-gestational-age
ICD	International classification of disease
OR	Odds ratio
CI	Confidence interval
CR	Cohort ratio
BMI	Body mass index

Introduction

"When will the baby be born?"

This question is one of the first things that future parents will ask themselves. However, the response to this question varies according to the method used to estimate the date of delivery.

Generally, when predicting the date when childbirth is most likely to occur, the first method is to count the time since the first day of the last menstrual period (LMP). For cases of spontaneous pregnancy, that date may later be changed to a more probable one after use of a method based on fetal measurements in an ultrasound examination in the first half of pregnancy.

Methods for pregnancy dating may give similar results, with high precision, when evaluated at group level, although maternal or fetal characteristics can affect their precision at the individual level. This is because the ultrasound method is based on the fact that fetuses grow at similar speed during the first half of pregnancy, so their size can be converted into an estimate of their age. However, there will always be some fetuses that are smaller or larger than others at the same age.

The choice of method may affect clinical judgments and interventions during pregnancy and childbirth. In most pregnancies, the exact definition of gestational age is not crucial to the outcome because a normal pregnancy will proceed without the need for interventions, and delivery will begin spontaneously at the right time. However, at the limit of viability for an extremely preterm infant, one day could mean the difference between offering no life support or the possibility of very advanced intensive care. At the other extreme, there is one day of difference between defining a delivery as low risk because of a normal pregnancy length or scheduling induction of labor because a postterm delivery is defined as high risk.

To care for the pregnant woman and fetus, clinicians need to know how far the pregnancy has advanced and in what situations the methods for pregnancy dating can be less reliable. This information can be useful for identifying and preventing risks such as fetal growth restriction and the danger of going beyond an optimal pregnancy length.

Methods for pregnancy dating

Last menstrual period

Women's knowledge of when childbirth is likely to occur has been closely related to lunar cycles, 13 per solar year (Figure 1)[1]. The human pregnancy length, equivalent to 10 lunar cycles of amenorrhea, corresponds to 9⅓ calendar months.

Figure 1. The Venus of Laussel (Venus with horn) from around 25,000 B.C. represents a pregnant woman, her left hand placed on her stomach and her right hand holding a bison's horn with 13 carved lines, which has been thought to represent the 13 cycles of the moon and the menstruations over 1 year. Musée d'Aquitaine, Bordeaux, France. Printed with permission from the Granger Collection.

Naegele's rule is often used to calculate the estimated date of delivery (EDD) based on the date of the LMP (Figure 2). This method was first introduced by Professor Hermann Boerhaave (1668–1738), whose lectures were published after his death, who wrote, "Women for the most part are impregnated after the end of their period. Numerous experiments undertaken in France confirm this. For one hundred births altogether, ninety-nine came about in the ninth month after the last menstruation by counting one week after the last period and by reckoning the nine months of gestation from that time. For, at that time the uterus is purged and empty, and the plethora are drained out ..."[2].

Professor Franz Carl Naegele (1778–1851) quoted this passage and observed, "According to experience, the woman in her reproductive phase does not always have the same capacity to conceive. The time the woman is most likely to conceive is immediately after menstruation," and "The usual calculation of the duration of pregnancy, namely, starting from the last menstruation, is correct in most instances; and conception within the last third of the cycle or in the second half between two periods is unusual and an exception to the rule"[2].

It has been argued that the correct interpretation of Naegele's rule would be to calculate from the end of the LMP[2]. In modern use, the EDD is calculated from the first day of the last menstruation. Because Naegele's rule underestimates the average pregnancy length, it has been suggested that adding 3 days to the formula would correct for this interpretation error. This would correspond to an observed model pregnancy length of 283 days instead of the proposed 280 days[3,4]. A modified rule has also been proposed to correct for irregular menstrual cycles[5].

$$EDD = LMP + 9 \text{ months} + 7 \text{ days} = LMP - 3 \text{ months} + 7 \text{ days} + 1 \text{ year}$$

$$EDD_{modified} = LMP + 9 \text{ months} + (\text{duration of previous cycles} - 21 \text{ days})$$

Figure 2. Estimated delivery date (EDD) based on the date of the last menstrual period (LMP) according to Naegele's rule, and its modification for irregular menstrual cycles.

Ultrasound

Ultrasound is energy in the form of high-frequency sound waves that are transmitted through the body and partially reflected, depending on the tissue type, during their trajectory. The analysis of the reflected sound waves constitutes the basis for the creation of a computerized real-time image. For obstetric purposes, both fetal soft tissue and skeletal structures can be visualized, assessed, and measured (Figure 3).

Figure 3. Fetus in sagittal position at gestational age 20 weeks + 6 days. Image by the author.

As the ultrasound technique evolved, in addition to assessing multiple gestations and the fetal position, it became evident that the association between fetal size and pregnancy length could be used for pregnancy dating in clinical practice[6]. The opportunity to use fetal size as a proxy for gestational age in the first half of pregnancy is based on the assumption that the variation in early fetal growth is very small[7,8]. For this purpose, reference charts have been introduced based on measurements made of populations of spontaneously pregnant women with regular menstrual cycles or of women who were pregnant after intervention with an artificial reproduction technique[9–13].

Measurements of a wide range of fetal structures can be related to gestational age. In the embryonic and early fetal period, gestational age can be assessed by its correlation with the total embryonic length or fetal crown–rump length (CRL)[9,12]. With advancing gestational age, the CRL becomes more unreliable as the fetus can flex and extend from its neutral position, and measurements of skeletal structures are therefore preferred because of the smaller variability. Apart from skeletal structures, such as the fetal head or femur, also soft tissue structures, such as the fetal cerebellum, can be used for pregnancy dating. Fetal head measurements are often used, and reference charts are based on the biparietal diameter (BPD) from the outer to inner cranial edge, from the outer to outer cranial edge, or the head circumference (Figure 4) [10,11,13]. Estimation of gestational age is less precise in some studies when based on combined measurements and formulae, for example, measurement of BPD combined with femur length[10,14]. As the pregnancy proceeds, there is greater individual variation in fetal growth and, therefore, fetal size becomes a less reliable proxy for gestational age[13].

Figure 4. Fetal head in transverse section with biparietal diameter (BPD) from outer to inner cranial edge corresponding to 19 weeks + 0 days. Image by the author.

Which method is better?

Precision in predicting the day of delivery

Average differences between LMP-based and ultrasound-based EDD are small. On average, a fetus will be estimated as 1–3 days older according to the LMP estimate compared with the ultrasound estimates[14,15]. However, in most studies, the ultrasound pregnancy dating method is more precise in predicting the actual date of delivery than is the LMP-based period[4,7,16]. The strength of the ultrasound method is its estimation of gestational age with a narrower standard deviation and, more importantly, the ability to classify correctly a higher proportion of preterm and postterm pregnancies[8,17].

Limitations of the methods

The LMP-based method may be flawed by recall bias and irregularities in the menstrual cycle, as well as irregularities in ovulation events also in women with regular menstrual cycles[8]. Further, the precision of the LMP-based pregnancy dating method is usually not considered superior to the ultrasound method even when combined with other suggested ways to improve the precision, such as by modifying the calculation formula (Naegele's rule) according to cycle length, by adding 3 days, or by using additional information, such as a known date of ovulation or conception as these corrections would not affect the variance of the method[4,8,17].

The ultrasound method may be flawed by a misclassification bias in pregnancies that do not fit with the method's basic assumption of uniform fetal growth in the first half of pregnancy. Other limitations can be of a technical nature, for example, unfavorable fetal positioning or maternal obesity. The resulting imprecision of the ultrasound method will affect a smaller number of pregnancies than that associated with the LMP method. However, the reason for misclassification when using the ultrasound method can be factors that also imply higher perinatal risks; therefore, although there are few such cases, accurate dating of these pregnancies is important[18,19].

Discrepancy between pregnancy dating methods

Commonly, there is little or no discrepancy between LMP-based and ultrasound-based estimates, and the error is attributed mainly to imprecision of the LMP-based estimate[8,17]. However, discrepancy between LMP-based and ultrasound-based estimates is associated with maternal characteristics, fetal sex, and adverse outcomes[18–23]. These associations may be helpful for identifying pregnancies at risk for adverse perinatal outcomes[18–23].

Consequences of choice of pregnancy dating method

Assessment of gestational age by ultrasound has many benefits, such as reduction in the frequency of induction for postterm pregnancy[24–26], and improved pregnancy outcomes[24,27]. It has been argued that these beneficial effects on pregnancy outcomes when pregnancy dating is based on ultrasound reflect the corrections of large discrepancies between the LMP-based and ultrasound-based estimates, although these benefits may not be the same in subgroups, such as growth restricted fetuses at risk for misclassification by the ultrasound method[17,28].

Late preterm birth and early term birth

Birth is considered as preterm before 37 weeks + 0 days (259 days) and as term from 37 weeks + 0 days to 41 weeks + 6 days (259–293 days). The definition of late preterm birth is from 34 weeks + 0 days to 36 weeks + 6 days (238–258 days), and early term birth is from 37 weeks + 0 days to 38 weeks + 6 days (259–272 days). Although often treated as term, late preterm infants more commonly present with prematurity-related morbidity, such as hyperbilirubinemia, respiratory distress syndrome of the newborn, and transient tachypnea of the newborn, as well as require interventions to support breathing and readmission for hospital care[29]. Late preterm infants form the largest group of all preterm infants, and the increasing number in this group raises concerns about public health impact[29].

A fetus that is larger than average in early gestation, such as male compared with female fetuses, can be misclassified as older when pregnancy dating is ultrasound based[30]. This *overestimation* of gestational age by ultrasound inflates postterm birth rates[31]. Such misclassification implies that the fetus is less mature than its ultrasound-based gestational age, which could adversely affect the clinical management and neonatal outcomes during the late preterm and early term periods.

Late term birth and post-term birth

The definition of late term birth is 41 weeks + 0 days to 41 weeks + 6 days (287–293 days), and postterm birth is after 42 weeks + 0 days (294 days). Induction of labor is generally recommended for a prolonged pregnancy because of the increased risks associated with postterm birth such as intrauterine fetal death, delivery by cesarean section, and meconium aspiration[32]. It has been argued that the excess morbidity and mortality in the postterm period is mainly related to undetected growth restriction[33].

Fetuses that are smaller than average early in gestation, which happens more often in female compared with male fetuses, or in cases of early fetal growth restriction, can be more mature than their ultrasound-based gestational age estimate. This misclassification can adversely affect the clinical management and neonatal outcomes in the late term and postterm periods[18,34].

Adverse effects

The noninvasive LMP-based method is not associated with adverse effects, except for the possible influence of harmful clinical decisions based on an erroneous gestational age. Because mechanical and thermal energy is transmitted to the fetus during the ultrasound examination, the ultrasound-based method has been evaluated for possible adverse side effects, such as adverse effects on lateralization in the developing fetal brain or intrauterine growth restriction. The ultrasound method is considered to be safe, but there is consensus in the ultrasound community about the need to keep exposure as low as reasonably achievable to avoid possible side effects[35–37]. For these reasons, the benefits of routinely performed ultrasound examinations should be balanced with the possible side effects of additional exposure.

Methodological considerations in research

Many adverse neonatal outcomes are related to abnormal fetal growth, such as intrauterine fetal death or neonatal death in cases of fetal growth restriction, or delivery complications associated with macrosomia. Commonly studied outcomes are birth of an infant who is small for gestational age (SGA) or large for gestational age (LGA). These outcomes are used instead of birthweight to identify growth deviations related to adverse outcomes. However, these outcomes are complicated to study, as for other size-related perinatal outcomes, because they can be biased by early fetal size deviations if pregnancy dating is ultrasound-based. It is therefore important that the pregnancy dating method is specified when describing research studies[38–40].

Specific factors affecting the precision, limitations, and consequences of pregnancy dating methods

Intrauterine growth deviation

LMP-based estimates are not based on fetal size and are therefore unbiased by early fetal size deviations. However, the ultrasound method is often considered to be superior for all pregnancies because of the uniform fetal growth in the first part of the pregnancy[8]. However, this assumption may not be fulfilled in cases of early fetal growth deviation[18,21,23].

In a large study that compared second-trimester ultrasound biometry with known gestational age after *in vitro* fertilization, gestational age estimated with ultrasound biometry was underestimated in fetuses later diagnosed as being SGA infants at birth[41]. This finding agrees with that of the Extremely Preterm Infants in Sweden Study, which reported an elevated risk for SGA when ultrasound-based gestational age was at least 7 days less than the LMP-based gestational age[42]. These situations imply that there is a risk of *underestimating* the true gestational age using the ultrasound method.

Conversely, when the fetus is larger than expected from the LMP method at the time of ultrasound-based pregnancy dating, or when there is accelerated growth between first- and second-trimester ultrasound examinations, there is an increased risk for LGA at birth[43,44]. These situations imply that there is a risk of *overestimating* the true gestational age using the ultrasound method.

Maternal characteristics

The precision of the LMP-based method is biased by maternal characteristics such as obesity, polycystic ovary syndrome, stress, and chronic diseases that might affect menstrual cycle length and regularity. One example is maternal obesity, which may cause irregular cycles and a prolongation of the interval between the LMP and conception[45,46]. This implies that there is a risk of *overestimating* the true gestational age by the LMP-based method.

The ultrasound-based method can be biased by maternal characteristics if these are also associated with differences in fetal growth. Genetic differences, such as maternal height, can affect infant size and possibly even early fetal size[19]. Maternal obesity is associated with discrepancies between LMP-based and ultrasound-based EDD, which can be due to the association between obesity and irregular menstrual cycles[19,47,48]. However, in pregnancies induced by artificial reproduction techniques, obesity is also related to *underestimation* of ultrasound-based gestational age. This suggests a possible negative influence of obesity on early fetal growth[41].

Fetal sex

The LMP method is generally expected to be unbiased by fetal sex, and using this method for pregnancy dating results in as many female as male infants being born at term, although maternal characteristics associated with a longer menstrual cycles could also affect the more susceptible male fetuses to a higher degree[34,49].

However, fetal sex can affect the assessment of gestational age by ultrasound[30,50,51]. When gestational age is estimated using ultrasound measurements in the second trimester at around 18 gestational weeks, the mean difference (male *vs.* female) in BPD is considered to be 1 mm[51]. When pregnancy dating is based on ultrasound, more male than female infants will be born in the late term and postterm period. This imbalance seems to reflect a misclassification bias because of the smaller mean size of female fetuses and suggests that the rate of postterm female births decreases because many females are born earlier than their estimated ultrasound-based gestational age because their actual gestational age is more advanced than the estimated gestational age[34,52].

Underestimation of ultrasound-based gestational age in female fetuses can manifest as a higher risk for meconium aspiration and intrauterine fetal death in the late term and postterm period[34].

By contrast, *overestimation* of ultrasound-based gestational age in male fetuses would be expected to increase the risks for prematurity-related adverse perinatal outcomes before term birth. That is, male fetuses may be less mature than the ultrasound-based gestational age estimate because of their larger size at the time of pregnancy dating by ultrasound.

Formulae

Naegele's formula for calculating the EDD from the LMP is less precise in women with an irregular menstrual cycle. For these women, the EDD is estimated more accurately using a modified Naegele's formula[2,5].

The choice between different ultrasound formulae can affect the rates of preterm and postterm rates[51,53,54]. This is important to consider when preparing guidelines and comparing outcomes between different birth cohorts[10,11,13,51,53,54] It is also important to consider the gestational age range that the formula is validated for and the type of fetal measurements included in the formula[10,13,53].

Technical equipment and user variability

The pregnancy wheels used to calculate EDD by LMP are made of paper or plastic and have two sliding layers that must be adjusted correctly. When a pregnancy wheel is used, there is a risk that the wrong date is chosen or read, and there is no correction for leap years. Medical software programs are also used to calculate EDD by LMP, and there can be errors in the formulae, user errors, and erroneous dates may be registered in the medical software[55].

Ultrasound machines have evolved since pregnancy dating by ultrasound was first used. For example, narrower beam width shortens lateral measurements, and the reference curves first evaluated may perform suboptimally when used with newer machines[56]. In addition, when ultrasound is used for pregnancy dating, the performance can vary between different machines and probes, as well as between different examiners, and some measurements may have better reproducibility[57].

Time-points for pregnancy dating

LMP-based pregnancy dating is based on the woman's self-reporting at the first antenatal visit early in pregnancy. If the first visit occurs late in pregnancy, the late reporting (i.e., when more time has passed since the LMP date) may decrease the precision because of errors in recalling the correct date.

The ultrasound-based method is usually considered more accurate when performed in the first rather than in the second trimester. This is based on the smaller individual variance observed in early *vs.* late biometry[13,58].

Pregnancy dating based on a first-trimester ultrasound examination can reduce the risk of misclassification bias related to sex differences in fetal growth, as reflected in the normalization of the male-to-female ratio in post-term deliveries when EDD is based on first-trimester ultrasound examination or the LMP instead of a second-trimester ultrasound examination[52].

According to the recommendations of the International Society of Ultrasound in Obstetrics and Gynecology, pregnancy dating is optimally based on a first-trimester ultrasound examination at 10 weeks + 0 days to 13 weeks + 6 days[58]. There are other recommendations; for example, the American College of Obstetricians and Gynecologists guidelines advise that information from ultrasound biometry may be used for pregnancy dating only if it differs sufficiently from the LMP estimate[59].

Pregnancy dating in Sweden

Estimated date of the delivery

In Swedish clinical practice, the most common definition of gestational age at EDD is 39 weeks + 6 days. This is equivalent to 279 completed days according to the first day of pregnancy at 0 weeks + 0 days (as in zero completed days) but contrasts with the international definition of 40 weeks + 0 days (at 280 completed days)[60]. However, the Swedish definition of normal pregnancy length is aligned with the definition of the World Health Organization as from 37 weeks + 0 days to 41 weeks + 6 days (259 to 293 completed days), and with postterm pregnancy starting at 42 weeks + 0 days (294 completed days)[60].

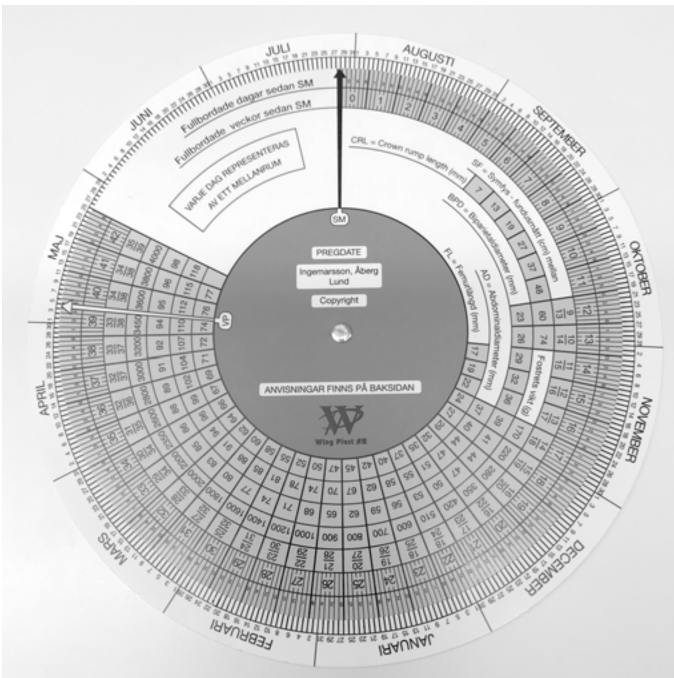

Figure 5. Pregnancy wheel (Ingemarsson, Åberg) for calculation of the estimated day of delivery based on the last menstrual period. The black arrow indicates the date of the first day of the last menstrual period. The white arrow indicates the estimated day of the delivery, corresponding to 39 weeks + 6 days. Photo by the author.

Antenatal care and pregnancy dating in clinical practice

When a pregnant woman attends her first antenatal visit, the midwife will ask her to recall the date of the first day of the LMP, and a pregnancy wheel or medical software may be used as a quick tool to calculate the LMP-based EDD (Figure 5). In Sweden, all women are offered free antenatal care, and the midwife will record medical information, such as the LMP and the corresponding EDD, in the woman's medical records. This information is later transferred to the Medical Birth Register, along with other prospectively recorded, detailed medical information.

Routine obstetric ultrasound was first introduced in Malmö in 1976 as a second-trimester ultrasound examination for pregnancy dating[6]. In Sweden, ultrasound examinations for pregnancy dating are performed predominantly in the second trimester, around gestational week 18, although a few centers have offered a first-trimester ultrasound examination for pregnancy dating since the beginning of ultrasound pregnancy dating. According to a 1996 study, when 59 clinics in Sweden provided obstetric and antenatal care, ultrasound examinations were performed at gestational weeks 16–20 in 52 clinics and at weeks 10–15 in three clinics[61].

The proportion of first-trimester pregnancy dating increased in Sweden after the introduction of first-trimester risk assessment for chromosomal abnormalities using the combination of nuchal translucency, biochemistry, and maternal age. In 2016, based on national register data for 48,131 pregnancies (40% of all births in 2016), 36% involved pregnancy dating performed in the first trimester (CRL-based in 7% and BPD-based in 29%) and 64% involved dating in the second trimester[62,63].

All pregnant women are offered a second trimester ultrasound examination during pregnancy, usually for the purposes of pregnancy dating and also to assess viability, multiple gestations, fetal malformations, position of the placenta, and amniotic fluid. This offer is accepted by more than 95% of all pregnant women[64]. The ultrasound examinations are mostly performed in specialized antenatal clinics of hospitals offering obstetric care for Sweden's relatively low population of about 10 million. In the larger cities, private antenatal clinics also perform ultrasound examinations during pregnancy.

According to the 2010 Guidelines on Fetal Biometry of the Swedish Association of Obstetricians and Gynecologists, pregnancy dating should ideally be based on an ultrasound examination in gestational weeks 11–14, if available, and otherwise on an ultrasound examination in gestational weeks 15–22[65]. The assessment of gestational age can be based on CRL if the measurement is 4–85 mm but should be based on outer-to-inner BPD measurements if these are in the range of 21–55 mm. Ultrasound measurements are used to correct the EDD regardless of the discrepancy with the LMP-based EDD, if any, with the exception of pregnancies resulting from artificial reproduction techniques, which are not dated by ultrasound[65].

There is no routine assessment, from a national perspective, of adherence to guidelines in terms of which formulae are actually used in medical software or in the ultrasound machine software to determine the EDD by LMP or by ultrasound. The difficulty in identifying the factors that can bias the information eventually registered in the Medical Birth Register may be an obstacle to research on pregnancy dating.

Aims

General and specific aims

To examine the correlates and consequences of the discrepancy between pregnancy dating by LMP and by ultrasound.

Paper I

- To assess the influence of ultrasound-based pregnancy dating on adverse prematurity-related outcomes in early term and late preterm male infants compared with their female counterparts, by comparing these outcomes between the period of years when pregnancy dating in Sweden was based mainly on the LMP (1973–1978) and when ultrasound was used (1995–2010).

Paper II

- To identify associations between maternal and fetal characteristics that were present at the time of pregnancy dating and large discrepancies between the EDD by LMP and by ultrasound in a population-based sample of Swedish pregnancies.

Paper III

- To assess associations between pregnancy dating method discrepancy (last menstrual period *vs*. ultrasound methods) and a series of adverse pregnancy, delivery, and neonatal outcomes.

Paper IV

- To describe current practice for pregnancy dating in Sweden, in relation to national guidelines, and management of discrepancy between methods for pregnancy dating.

Material and Methods

Overview of the studies and data sources

The papers included in this doctoral thesis, are based on data from the Swedish Medical Birth Register, the National Patient Register, the Cause of Death Register, and a survey distributed to all units in Sweden that perform pregnancy dating.

Table 1. Overview of the studies

Study	Design	Time period(s)	Study population (n)
I	Cohort study	1973–1978 1995–2010	1,314,602 births
II	Cross-sectional study	1995–2010	1,201,679 births
III	Cohort study	1995–2010	1,201,679 births
IV	Survey-based study	2017	38 units

Medical Birth Register

The Medical Birth Register contains information on more than 99% of all births in Sweden since 1973. The register includes data about maternal sociodemographic characteristics and prospectively collected information during pregnancy, delivery, and the neonatal period (the first 28 days)[64]. The register has been evaluated as reliable for research purposes, and has good internal validity[66].

More variables have been included, and others removed, since the start of this register in 1973. For example, information on smoking at the time of the first antenatal visit and maternal height have been included since 1982, and information on maternal weight at the first visit was included in 1992 although calculated values are available for the time period 1983–1989. Stillbirths were recorded if occurring after 27 gestational weeks + 6 days until a change in legislation on July 1, 2008, after which the cutoff was after 21 gestational weeks + 6 days[67].

National Patient Register

The National Patient register contains records from inpatient settings since 1987, with fewer than 1% of cases lacking a main diagnosis. This register also contains records from outpatient settings since 2001, with 25–30% of visits lacking a main diagnosis at the beginning but only 4% in 2016[68]. The diagnosis codes are classified according to the World Health Organization's International Classification of Diseases (ICD) and are registered by a physician when the woman and infant are discharged from the hospital, although registration may be delegated to a midwife in the obstetric setting. Different versions have been used: ICD-8 (1960–1986), ICD-9 (1987–1996), and ICD-10 (1997–present). The register has been evaluated as appropriate for population-based research and has high validity for many diagnoses[69].

Cause of Death Register

The Cause of Death Register was started in 1961 and contains information about the cause of death for all persons who die in Sweden or who are registered in Sweden but die abroad. Fetal deaths and stillborn infants are not included in this register but are instead included in the Medical Birth Register[70].

Study populations and methods

Paper I

This cohort study included data on 1,314,602 births recorded in the Medical Birth Register. We compared rates of prematurity-related adverse outcomes in male infants born at early term (gestational weeks 37–38) or late preterm (gestational weeks 35–36) in relation to birth in gestational week 39–40, with those of female infants. To assess the dating method's influence on outcomes according to fetal sex, we then compared the odds ratio (OR) for adverse outcomes among male in relation to female infants between the period of years when pregnancy dating in Sweden was based mainly on the LMP (1973–1978) and when ultrasound was used (1995–2010) (Figure 6).

A relative increase in male compared to female odds for prematurity-related outcomes was hypothesized because of a suspected bias introduced in the ultrasound-based gestational age estimate based on the size differences between male and female fetuses at the time of pregnancy dating.

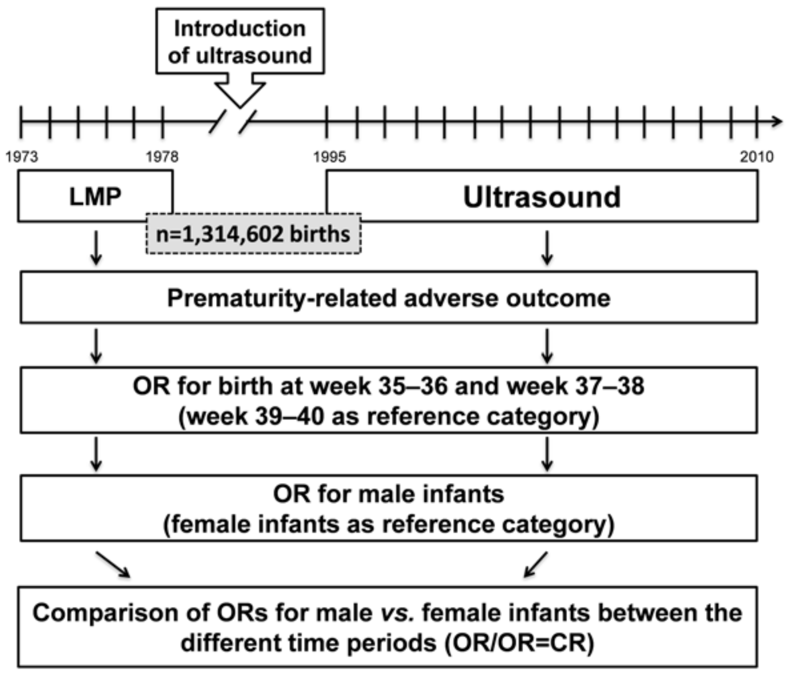

Figure 6. Study design, Paper I.

LMP, last menstrual period; OR, odds ratio.

Paper II

This cross-sectional study was based on all singleton births in Sweden from 1995 to 2010. Associations were examined between factors present at the time of the pregnancy dating ultrasound examination, i.e. fetal sex, maternal characteristics, and diagnoses that can theoretically affect early fetal growth, and a large negative or positive discrepancy between EDD by LMP and by ultrasound (Figures 7–9) [71–77].

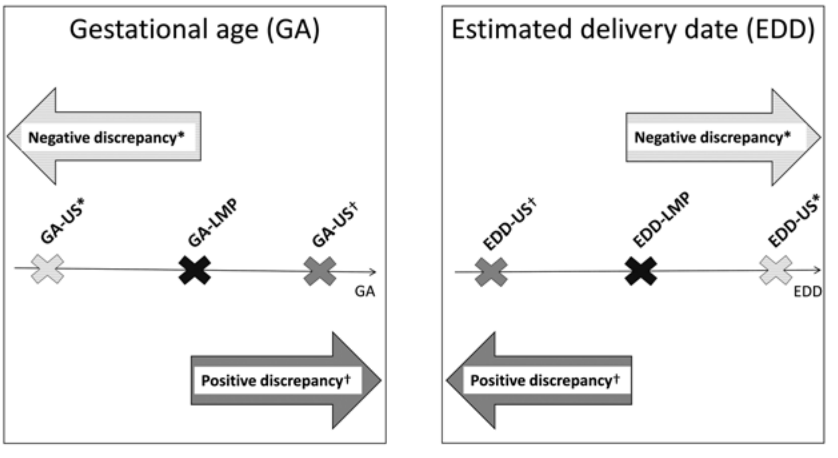

Figure 7. Discrepancy in days (EDD-LMP minus EDD-US).

EDD, estimated day of delivery; LMP, last menstrual period; US, ultrasound; OR, odds ratio

**Negative discrepancy* was defined as an EDD by LMP earlier than the EDD by US, that is a more advanced gestational age by LMP estimation than by US estimation. Hence, a fetus was *smaller (younger) than expected* when dated by US and the EDD was moved to a later date. †*Positive discrepancy* was defined as an EDD by LMP later than the EDD by US. This corresponded to a less advanced gestational age by LMP estimation than that estimated by US examination. Hence, the fetus was *larger (older) than expected* when dated by US and the EDD was moved to an earlier date.

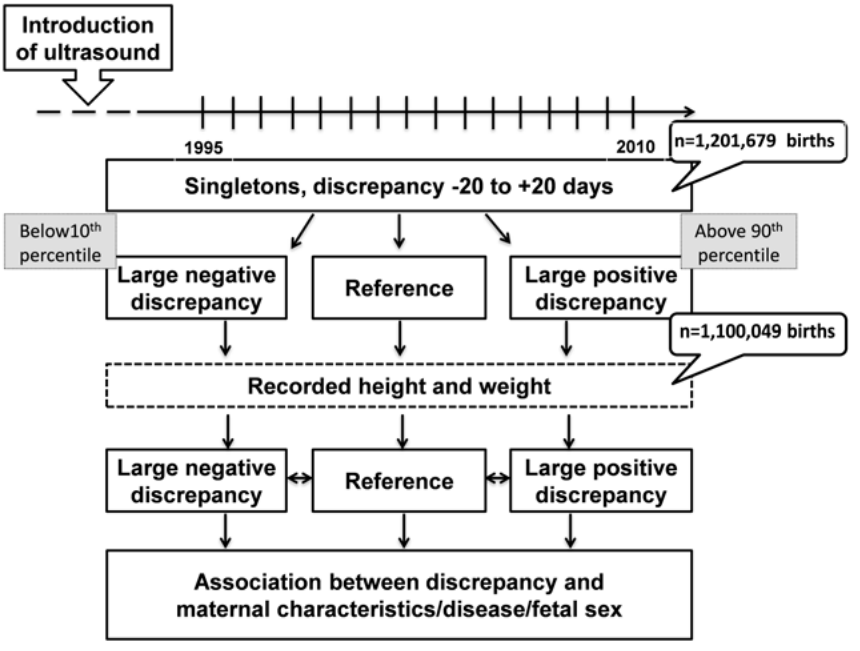

Figure 8. Study design, Paper II.

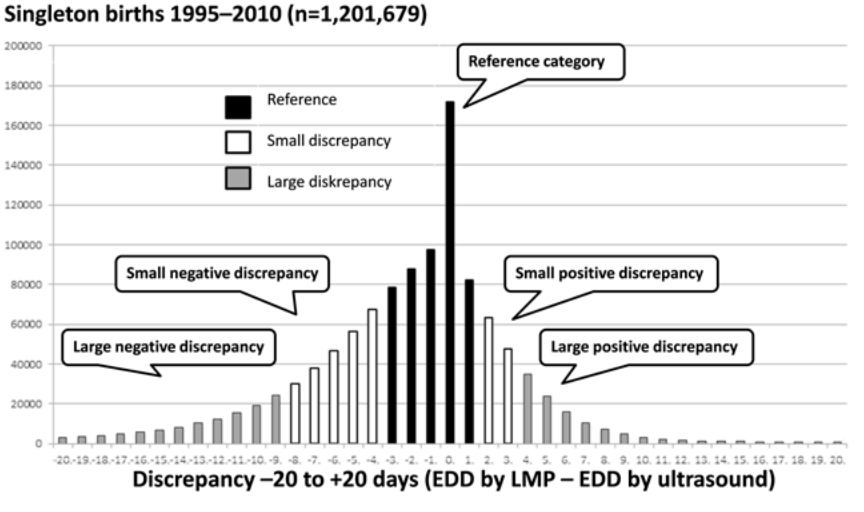

Figure 9. Histogram with discrepancy categories.
EDD, estimated day of delivery; LMP, last menstrual period

Paper III

This register-based cohort study included all singleton births, live and still-born, in Sweden from 1995 to 2010, with valid documentation of the EDD based on both the LMP and ultrasound, and a discrepancy between estimates of 20 days or less. The same data set as in Study II was divided into five discrepancy categories (Figures 9). Discrepancies between pregnancy dating methods were assessed for associations with adverse pregnancy, delivery, and neonatal outcomes that could be related to infant size.

Paper IV

This survey study was based on a questionnaire sent to all ultrasound units in Sweden that performed pregnancy dating ultrasound examinations. The aim was to map the units' pregnancy dating routines in relation to national guidelines. A qualitative aspect was also introduced by including questions on the assessment of discrepancies between pregnancy dating methods and by allowing for free comments.

Study design

Cohort studies

In cohort studies, a group of individuals are followed over time. Associations between exposure and specified outcomes, such as being diagnosed with a disease, are then compared between the exposed and unexposed individuals. In cohort studies, the investigated outcomes should not have occurred at the baseline, and both exposed and unexposed individuals should be considered at risk for these outcomes. A time-to-event approach can be applied to exposure and outcomes, but events can also be registered only in terms of occurrence or nonoccurrence. Cohort studies can be efficient when the exposure is rare and the outcomes are relatively common. The effect measurements are typically expressed as risk ratios, which are calculated from the risk in the exposed cohort compared with that in the unexposed cohort. However, logistic regression analysis is often used to allow for adjustments, and the resulting OR can be interpreted as an approximation of the risk ratio provided there is a low probability of the outcome occurring[78].

Cross-sectional studies

Cross-sectional studies describe the prevalence of selected outcomes at a given time. Such studies can provide information on the size of a problem and help to generate hypotheses. Using statistical analysis, the associations between risk factors and outcomes can also be assessed. As the study has no longitudinal component, the direction of the associations between the defined exposures and outcomes can be difficult to determine[78].

Survey studies

A survey study can be a cost-effective, feasible design that can be used for descriptive and hypothesis-generating purposes. It can be limited by low response rates, which would raise questions about the characteristics of the nonresponders. However, external validity will be satisfactory if the responders can be assumed to be representative of the study population[79].

Bias in epidemiological studies

Selection bias

Selection bias can be a problem in cohort, cross-sectional, and survey studies if associations between the exposure and the outcome differ between included and nonincluded individuals. The risk of selection bias is reduced, but not eliminated, in population-based cohorts, such as those originating from population-based registers with high coverage. For example, the few women who will not attend antenatal care can be of lower socioeconomic status and have a higher probability of developing adverse outcomes when exposed to risk than the general population[78].

Information bias

Information bias is a result of the inclusion of erroneous information in the study; for example, when information is not collected prospectively but is instead collected after time has elapsed, the participant may not recall the information accurately. Another example can be diagnosis codes that are similar and therefore systematically interchanged by mistake, or maternal weight and height being registered in the opposite fields of the medical form[78].

Confounding

Confounders are factors that affect both exposure and outcome and, therefore, the effect of the exposure is mixed with the effect of the confounder. For example, if both the exposure and the outcome are more common in cases of higher maternal age, then maternal age would be a confounder. The influence of these confounders can be reduced by identification and adjustment in the analysis. However, in an observational study without the possibility of randomization, there is always a risk of residual confounding[78].

Statistical analyses

Descriptive statistical methods

In Paper I, the rates of adverse prematurity-related outcomes were reported as the number of infants per 1000 live births.

In Paper IV, analyses were conducted using descriptive statistical methods, presenting numbers, proportions, mean and median values, and range.

Logistic regression analyses

Crude and adjusted ORs with 95% confidence intervals (95% CIs) were obtained from the logistic regression analyses and were calculated for adverse prematurity-related outcomes in Paper I, for large discrepancies between pregnancy dating methods in Paper II, and for adverse pregnancy, delivery, and neonatal outcomes in Paper III.

Cohort ratio

In Paper I, the relative changes in the ORs for adverse prematurity-related outcomes among male infants in relation to their female counterparts, were calculated as the ratio between the ORs for each time period (cohort ratio, CR).

Adjustments

Paper I

The multivariate analyses were adjusted for maternal age, parity, and level of hospital care.

Paper II

All models were adjusted for maternal age, parity, height, body mass index (BMI: weight [kg]/height^2 [m^2]), smoking in early pregnancy, and employment status, as appropriate. Analyses were also adjusted for maternal comorbidity, which was defined as one of the selected diagnoses.

Paper III

In four models, we adjusted first for BMI <18.5 kg/m^2 or >30 kg/m^2, maternal age <20 years or >30 years, smoking or snuff use, living without a partner, and not being employed, and then, secondly, fetal sex, third, diabetes mellitus or preeclampsia, and, fourth, SGA or LGA at birth were added as covariates.

Ethical considerations

In accordance with Swedish law, which seeks to regulate the use of personal information to protect personal integrity, this project was subjected to ethical vetting before the data were retrieved from the Medical Birth Register and the National Patient Register[80]. All studies were approved by the Regional Ethical Review Board in Uppsala, Sweden, reference number 2012/412, with an amendment approved November 15, 2017.

Papers I–III

Personal integrity

The risk of harm or discomfort for the included individuals was considered small because the data were pseudonymized before access by our research group and the results are presented only at the group level. Because the studies are register-based, there was no contact between the researchers and included individuals. It could be considered more intrusive to contact these individuals than to include them without a specific notice.

Informed consent

Papers I–III were register-based studies and were conducted without consent. The consent procedure was hindered by the large number of included individuals needed for the study of rare outcomes (more than 1,000,000 births with information about both the mother and child) and because some individuals may have died. Ideally, although difficult in practice, there should be the opportunity to opt out of research for those individuals who perceive that the use of their personal data is a violation of their integrity[81].

Risk *vs.* benefit

Although health data are sensitive information, the risk for personal harm or discomfort was judged as small in Studies I–III. The expected benefit was that the knowledge gained would contribute to improvements in clinical routines in ultrasound pregnancy dating that would further reduce perinatal mortality and morbidity. Therefore, the result can be argued to be in the public interest—if not directly for the included mothers, then for their children when the latter reach childbearing age, for other parents-to-be, and for children yet to be born[80].

Studies of this kind are unique to the Nordic countries because of the almost complete coverage and quality of the national health registers in these countries. It can be considered an ethical obligation to conduct research using the existing registers because this allows for studies that are time and cost effective, minimizes drop-out, and allows for many types of research questions when information from different registers can be linked together.

Ethical conduct

The results have been analyzed only at the group level to protect individuals from any possibility of identification. All data files containing health data were considered to contain sensitive information and were safely stored to avoid unauthorized access.

Paper IV

This survey study did not include any sensitive personal questions about the responders. Nevertheless, the results are presented without identifying the units or the respondents to protect the personal integrity of the respondents. The study design allowed for cost-effective and rapid access to information instead of a more resource-consuming design, such as interviews, and to use research resources in a cost-effective way is also good ethical conduct[79].

Results

Paper I

Adverse outcomes were lower for both female and male infants in the later time period, but the reduction in prematurity-related morbidity was less marked for male than for female infants. In the later period and with ultrasound as the main pregnancy dating method, in relation to female infants, male infants born in the early term period had higher odds for pneumothorax (CR 2.05; 95% CI 1.33–3.16), respiratory distress syndrome of the newborn (CR 1.99; 95% CI 1.33–2.98), low Apgar score (CR 1.26; 95% CI 1.08–1.47), and hyperbilirubinemia (CR 1.12; 95% CI 1.06–1.19) (Paper I; Table 3). A similar trend was seen for late preterm male infants (Paper I; Table 4).

Paper II

Women in obesity class III (BMI >40 kg/m^2) had the highest odds for large *positive* discrepancies (OR 2.16, 95% CI 2.01–2.33), followed by women with diabetes mellitus, young maternal age, multiparity, obesity class II (BMI 35.0–39.9 kg/m^2), obesity class I (BMI 30.0–34.9 kg/m^2), overweight (BMI 25.0–29.9 kg/m^2), underweight (BMI <18.5 kg/m^2), gestational diabetes, female fetus, shorter stature, preeclampsia, smoking, snuff use, and unemployment (Paper II; Table 2).

Large *negative* discrepancies were associated with male fetuses (OR 1.80, 95% CI 1.77–1.83), maternal age >30 years, being 3-parous or more, not living with a partner, taller stature, being unemployed, and smoking (Paper II; Table 3).

Paper III

Adverse outcomes in pregnancy, delivery, and during the neonatal period were associated with higher or lower risks according to the discrepancy category (Figures 10–13). For pregnancy outcomes, preeclampsia and diabetes mellitus, and in the neonatal period, neonatal death (OR 95% CI 1.91–2.50), the risks were higher in cases of large negative discrepancies. For delivery outcomes, except for delivery by cesarean section, the risks were higher in cases of large positive discrepancies.

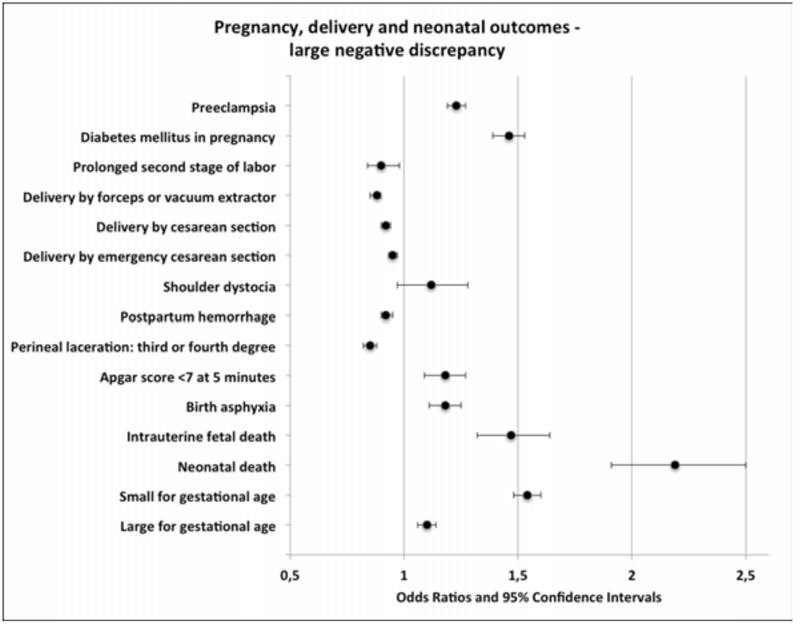

Figure 10. Large negative discrepancies and associated odds ratios (95% confidence intervals) for adverse pregnancy, delivery, and neonatal outcomes.

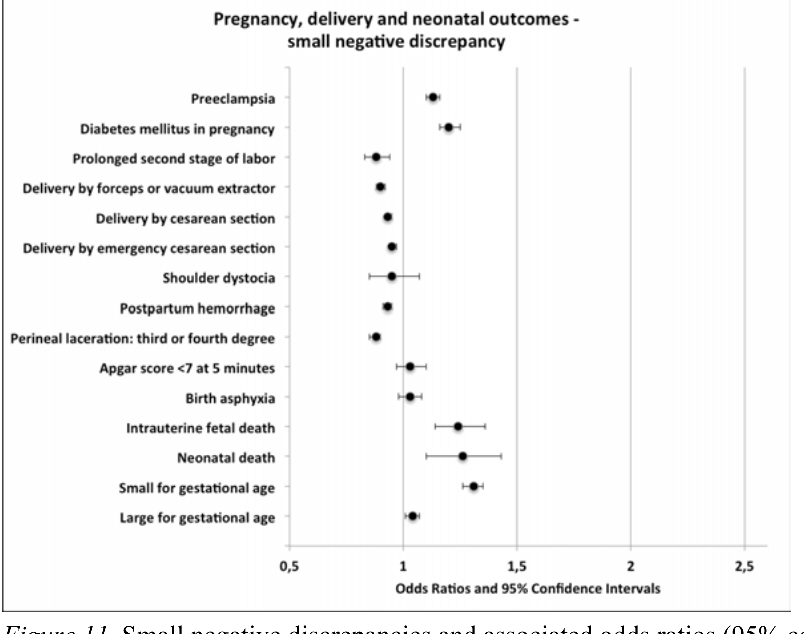

Figure 11. Small negative discrepancies and associated odds ratios (95% confidence intervals) for adverse pregnancy, delivery, and neonatal outcomes.

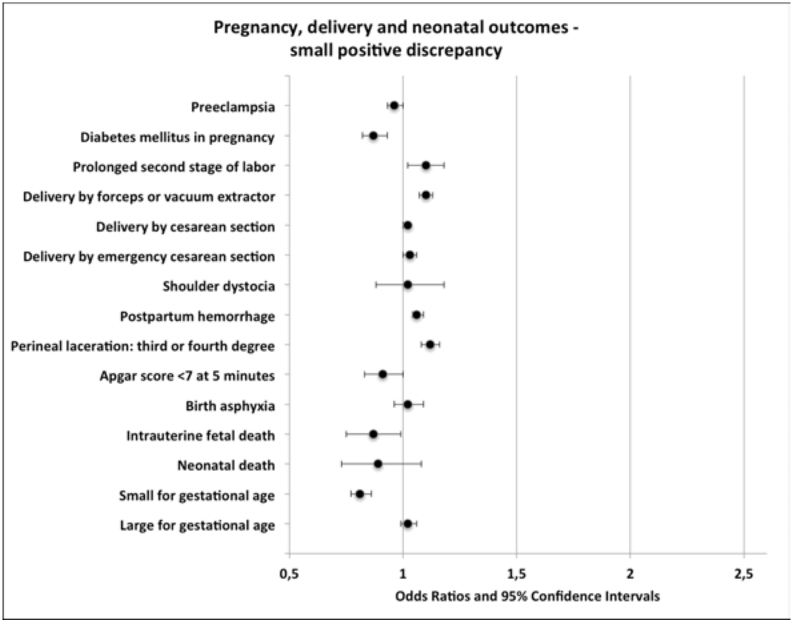

Figure 12. Small positive discrepancies and associated odds ratios (95% confidence intervals) for adverse pregnancy, delivery, and neonatal outcomes.

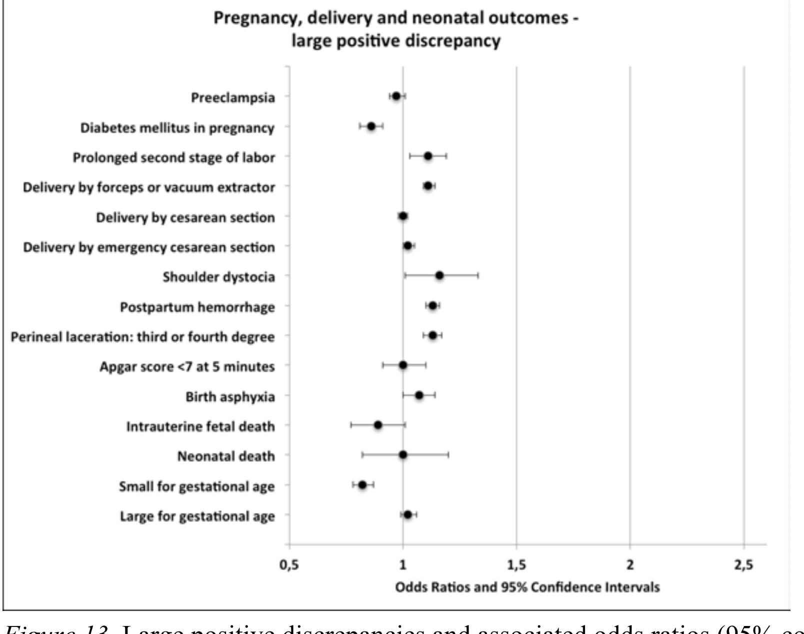

Figure 13. Large positive discrepancies and associated odds ratios (95% confidence intervals) for adverse pregnancy, delivery, and neonatal outcomes.

Paper IV

There was a high response rate (88%) and the responders indicated overall good adherence to national guidelines, except for early pregnancy dating (Figure 14–15).

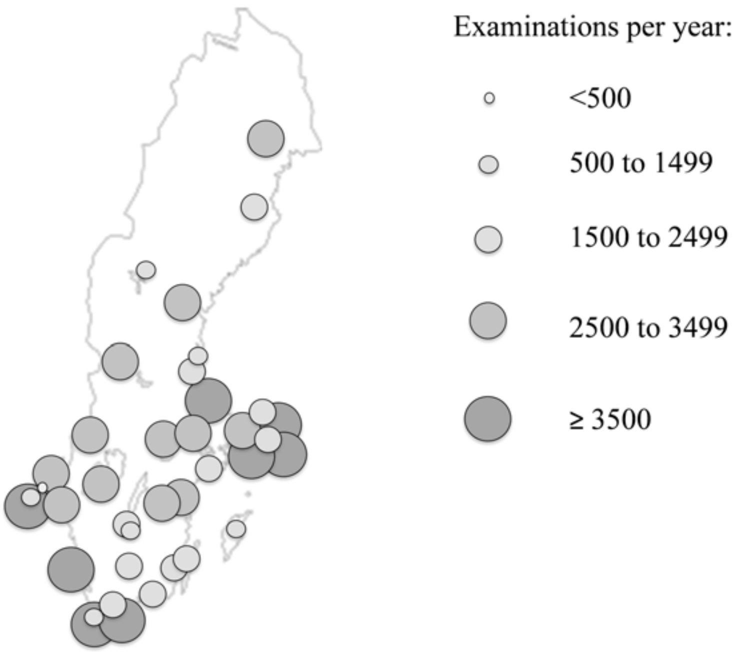

Figure 14. Responders' (n = 38) replies about the number of second-trimester routine ultrasound examinations performed per year. There were no replies from five units situated in different counties.

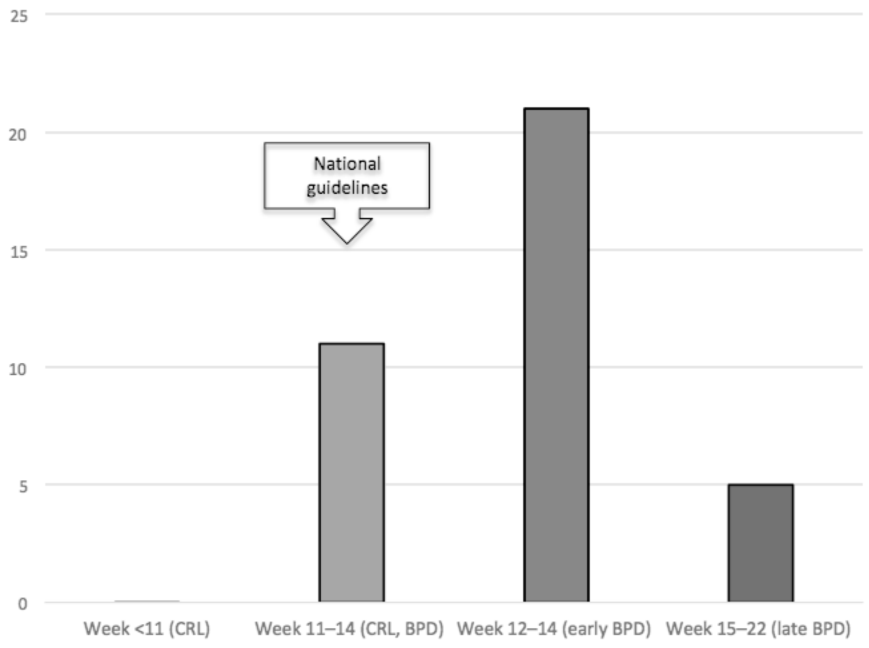

Figure 15. Choice of ultrasound examination for pregnancy dating purposes, if more than one examination was performed.

CRL, crown-rump-length; BPD, biparietal diameter.

Discussion

Principal findings

Paper I

Comparing 1973–78 with 1995–2010, male infants on the edge of prematurity did not benefit from progress in medical care as much as female infants in terms of prematurity-related outcomes. This might reflect a bias introduced by the ultrasound pregnancy dating method.

Paper II

The associations found in this large population-based study between discrepancy between EDD by last menstrual period and EDD by ultrasound, and characteristics such as fetal sex and maternal height indicated that ultrasound-based pregnancy dating may have introduced systematic errors because of the use of fetal size as a proxy for gestational age. The largest effect estimates were found for obesity in cases of large negative discrepancies.

Paper III

In this large population-based cohort study, discrepancies between EDD by LMP and by ultrasound were associated with several adverse pregnancy, delivery, and neonatal outcomes. Most importantly, a large negative discrepancy was associated with higher odds for neonatal and intrauterine fetal death, as well as SGA.

Paper IV

There was overall good compliance with the national guidelines, except for pregnancy dating from gestational week 11, based on CRL measurements, in which the common routine was to date pregnancy only when the BPD was 21 mm or above. The management of discrepancies between methods for pregnancy dating in clinical practice varied widely, probably because of the lack of national guidelines.

Methodological considerations

Paper I

The study was limited by the different versions of diagnosis coding (ICD-8, ICD-9, and ICD-10), which limited the number and precision of the diagnoses that could be compared between time periods. The study design aimed to avoid the difficulties in comparing neonatal outcomes between the different time periods. Comparing the odds for male infants in relation to female infants for prematurity-related outcomes allowed reasonable comparisons between the time periods. Using this method, any bias that could have interfered with the results would have had to have affected male and female infants differently and only in one of the time periods.

Paper II

The large register-based cohort, which could be considered population based, provided high external validity. The detailed information in the Medical Birth Register was prospectively recorded, which minimized recall bias. A limitation of the study was that no information on the regularity of menstrual cycles was included in the register. Another limitation was a possible inclusion bias because some women were excluded if the register lacked information on height and weight.

Paper III

The same methodological considerations as in Study II apply to Study III.

Paper IV

Although there was a very high response rate, this study is limited by its retrospective design and because the results were based only on one person's answers on behalf of the unit. The qualitative approach, although limited, added value to the hypothesis-generating part of the study.

Considerations regarding clinical implications

Paper I

Adverse effects of ultrasound pregnancy dating should be considered, especially in selected groups, because variation in early growth related to fetal or maternal factors can lead to misclassification of gestational age and can affect perinatal outcomes. Male infants born at the limit of preterm birth may need more support to prevent prematurity-related adverse outcomes than indicated by their ultrasound-based gestational age.

Paper II

Discrepancies between the LMP-based and ultrasound-based methods are not rare, and clinicians should be aware that one or both methods can be unreliable. Increased awareness of maternal and fetal characteristics that can bias gestational age estimates can be helpful in clinical situations, especially if large discrepancies between methods are noted. This may be especially important at the extremes of pregnancy length, when gestational age influences clinical decision-making.

Paper III

Discrepancies between the two pregnancy dating methods are associated with adverse perinatal outcomes, which may be useful knowledge for identifying pregnancies at risk of adverse outcomes. A large negative discrepancy seemed to be the most important risk indicator and, therefore, the discrepancy category most likely to benefit from further monitoring.

Paper IV

There has been a shift towards more first trimester ultrasound examinations in Sweden. However, these examinations are not optimally utilized for pregnancy dating purposes. Early pregnancy dating is preferred because of increasing growth variance with advancing gestational age. First-trimester ultrasound biometry may be useful for reducing the misclassification bias caused by sex differences in fetal growth[34,52,82]. However, first trimester pregnancy dating can also be biased by early growth restriction[83], and an additional ultrasound examination would impose additional costs and potentially adverse exposure[35–37]. It would be desirable for the national guidelines to address the management of discrepancies between methods for pregnancy dating. Such discrepancies may constitute an indication for a repeat ultrasound examination because it suggests higher odds for adverse outcomes[18–23,84].

Conclusions

Paper I

The increased risk for prematurity-related outcomes in male infants between the two time periods may reflect a bias introduced by the ultrasound-based pregnancy dating method. This suggests that a proportion of male infants might be less mature at birth than the ultrasound-based estimate suggests.

Paper II

Maternal and fetal characteristics affect the probability of large discrepancy between pregnancy dating methods based on last menstrual period and ultrasound. This information may be useful in identifying some pregnancies where ultrasound-based dating estimates may be biased due to early growth deviations.

Paper III

Discrepancies between EDD by LMP and by ultrasound were associated with adverse outcomes during pregnancy, delivery, and in the neonatal period. These associations support the hypothesis that a smaller or larger than expected fetal size from that based on the date of the LMP, when ultrasound-based pregnancy dating is performed, might in some cases reflect decelerated or accelerated early fetal growth, which could later lead to size-related adverse perinatal outcomes.

Paper IV

This study revealed that many units changed their practice according to unwritten guidelines whereas others followed written guidelines. This observation emphasized the need for regular guideline updates and efforts to improve their implementation as a part of providing high-quality care.

Summary and future perspectives

Clinicians are dependent on estimates of gestational age because there is no one method that enables counting from the very moment of conception in each pregnancy. Pregnancy dating methods need to be accurate enough for several purposes, such as correctly identifying postterm high-risk pregnancies for labor induction. To assess the reliability of the estimate, the clinician must be familiar with the situations that affect the precision of the estimation method or which could introduce bias. The available methods produce very similar mean estimates but differ in precision (standard deviation) and bias (identifying which individuals will fall outside the defined standard deviations). In the studies included in this thesis, misclassification bias associated with fetal sex, maternal height, and fetuses at risk for being SGA at birth was suspected to have been introduced with the second-trimester pregnancy dating method predominately used in Sweden.

One way to reduce bias in both first- and second-trimester ultrasound pregnancy dating may be to develop customized pregnancy dating formulae. Another more feasible way may be to introduce earlier, first-trimester routine ultrasound-based pregnancy dating and to evaluate the potential bias associated with this method. However, implementing an additional ultrasound examination would impose additional health care costs and fetal exposure to the mechanical and thermal energy during the ultrasound examination.

Ideally, before the introduction of an additional first-trimester ultrasound examination for dating purposes, a randomized controlled trial should be performed at the national level. Such a study design would permit comparison of the precision of this method and the number of adverse perinatal events associated with measurements taken during first-trimester ultrasound dating (with second-trimester malformation screening) or second-trimester ultrasound dating and malformation screening. It would also be possible to evaluate the accompanying costs and plan for long-term follow-up of adverse effects that may be related to additional ultrasound exposure.

Another approach may be to use the data from the high-coverage Swedish Pregnancy Register, which was started in 2013[85]. The register has merged with the National Quality Register for Prenatal Diagnosis, in which the date of the ultrasound examination and fetal biometry values have been registered since 2006, but with lower coverage. Cohorts exposed to either first-trimester pregnancy dating by ultrasound (including later second-trimester malformation screening) or second-trimester pregnancy dating and malformation screening, could be identified retrospectively, and the associated adverse perinatal outcomes in each cohort could be compared. Compared with a randomized controlled trial, such a register-based study would be more cost-effective and clearly feasible, but may also be hampered by, for example, selection bias.

A third approach may be to start using the Swedish Pregnancy Register to define at what gestational age those infants without adverse perinatal events were dated, and then to try retrospectively to define an optimal time point for pregnancy dating.

Although it is important to revise critically the methods and concepts that clinicians and researchers work with based on existing knowledge, I believe clinicians should continue using the ultrasound-based method for pregnancy dating as the best method for estimating gestational age and predicting the day of delivery. It is a method without many adverse effects and with generally high precision. However, the added knowledge from these and other studies on discrepancies between LMP-based and ultrasound-based methods indicates that it is important to be aware of situations in which a fetus may be smaller, especially, or larger than expected at the ultrasound pregnancy dating examination. This information may be useful as a risk indicator and to indicate the need for close monitoring.

Sammanfattning på svenska

Målet med denna avhandling var att studera situationer då graviditetsdateringen enligt ultraljud kan vara mindre tillförlitlig, t.ex. i jämförelse med datering enligt sista mens.

För att fatta rätt beslut om handläggning under graviditet och vid förlossning är det viktigt att veta hur långt gången graviditeten är. Det kan bero på en dags skillnad i skattad graviditetslängd om en graviditetskomplikation handläggs som sent missfall eller som extrem förtidsbörd. Samma sak gäller i slutet av graviditeten då det beror på en dags skillnad om förlossningen handläggs som en normal lågriskförlossning eller överburen högriskförlossning.

Vanligtvis skattas först graviditetslängden genom att räkna antal dagar som förflutit sedan den sista menstruationens första dag vilket ger beräknad partus enligt sista mens. Sedan erbjuds alla kvinnor i Sverige en ultraljudsundersökning i första halvan av graviditeten då beräknad partus enligt ultraljud skattas och detta datum används sedan för fortsatt klinisk handläggning. Denna undersökning utförs oftast i andra trimestern, omkring graviditetsvecka 18.

Ultraljudsmetoden innebär ett antagande att fosters likformiga storleksökning i början av graviditeten gör att man kan använda fostrets storlek för att skatta dess ålder. Hypotesen som låg till grund för denna avhandling var att skillnader i storlek redan i tidig graviditet, t.ex. pojkars större storlek i förhållande till flickor redan vid tiden för ultraljudsdateringen, orsakar systematiska fel i skattningen av graviditetslängd, vilket ibland leder till felbedömning av graviditetslängden och negativa konsekvenser.

I en tidigare studie, som föregick detta projekt, sågs att sedan ultraljudsdatering av graviditeter införts i Sverige föddes det fler pojkar än flickor i den period då beräknat förlossningsdatum enligt ultraljud passerats med minst en vecka. Flickorna hade dessutom, i relation till pojkar, högre risk för dödlighet och sjuklighet vid födsel i denna period – troligen till följd av underskattad graviditetslängd.

I den första studien i denna avhandling sågs en motsvarande ökad risk för sjuklighet relaterad till underburenhet hos pojkar jämfört med flickor vid födsel i graviditetsvecka 37-38 sedan ultraljudsdatering av graviditetslängd införts, vilket tolkades som en följd av överskattning av graviditetslängden med ultraljud hos pojkar jämfört med flickor.

I den andra studien var syftet att undersöka om det fanns ett samband mellan faktorer som kunde antas ha påverkat tidig fostertillväxt och skillnaden i dagar mellan datering enligt sista menstruationens första dag och enligt ultraljud. Risken för att beräknad partus justerades vid ultraljudsundersökningen var ökad vid t.ex. övervikt/fetma, diabetes, hög/låg ålder och om kvinnan fött flera barn. Det var även ökad risk för att fostret skattades som mindre/yngre enligt ultraljud om mamman var kort eller bar på ett flickfoster, medan det var ökad risk för att fostret skattades som större/äldre om mamman var lång eller bar på ett pojkfoster, vilket tolkades som under- respektive överskattning av graviditetslängd när ultraljudsmetoden användes.

I den tredje delstudien undersöktes risk för ofördelaktigt utfall under graviditet, förlossning och nyföddhetsperiod när det beräknade förlossningsdatumet enligt sista mens skiljde sig mycket från dateringen enligt ultraljud. Risken under graviditet för diabetes och havandeskapsförgiftning var större om fostret var mindre än förväntat vid ultraljudsdateringen. Risken var större för förlossningsutfall som kan relateras till stort barn om fostret var större än förväntat vid ultraljudsdateringen. Risken för intrauterin fosterdöd, neonatal död, låg Apgar-poäng och syrebrist var större om fostret var mindre än förväntat vid tiden för ultraljudsundersökningen än enligt sista mens.

I den fjärde studien beskrevs aktuella och tidigare rutiner för datering av graviditetslängd i Sverige i relation till nationella riktlinjer från 2010. En enkät utformades och distribuerades till alla enheter som utför dateringsultraljud. Svarsfrekvensen var 88%. I landet finns god följsamhet till de skriftliga riktlinjerna, med undantag för datering enligt tidig ultraljudsundersökning. Vid en majoritet av enheterna användes inte mätningar från en utförd tidig ultraljudundersökning för datering om inte fostrets biparietal-diameter (BPD) var 21 mm eller större, trots att de skriftliga riktlinjerna rekommenderar datering baserad på crown-rump-length (CRL) från graviditetsvecka 11.

Sammanfattningsvis kan ultraljudsmetodens träffsäkerhet påverkas av faktorer hos den gravida kvinnan och hos fostret. Skillnader mellan den skattade graviditetslängden enligt sista mens och enligt ultraljud kan tyda på ökade risker, främst till följd av avvikande tillväxt, och vara ett skäl för upprepad ultraljudsundersökning för bedömning av fostrets tillväxt och välmående.

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Appendix

Questionnaire – Study IV

Q1-6 Baseline information

Q1. My position is:
Q2. Name and e-mail
Q3. County Council
Q4. What unit/s are the answers valid for?
Q5. Type of unit/s
Q6. Number of second trimester ultrasound examinations – "routine ultrasound"

Q7-20 Clinical practice for pregnancy dating

Q7. When will an examination for pregnancy dating routinely be performed in your unit?
Q8. If more than one ultrasound examination is performed during pregnancy – which of them is used for pregnancy dating purposes?
Q9. What early pregnancy ultrasound examinations are pregnant women offered in your clinical unit?
Q10. If an ultrasound examination has been performed in another unit – do you use EDD according to that examination?
Q11. What method is used to calculate EDD by last menstrual period according to your unit´s practice?
Q12. What program or *formulae* are routinely used in your unit to determine EDD by US?
Q13. Have you introduced the population-based reference charts according to Eik-Nes for pregnancy dating in your unit?
Q14. What is your clinical practice for pregnancy dating by biparietal diameter (BPD)?
Q15. What is your clinical practice for pregnancy dating by crown-rump-length (CRL)?
Q16. If you stopped using CRP for pregnancy dating – what year was that?
Q17. If you stopped using CRP for pregnancy dating – what was the reason for this decision?
Q18. How is pregnancy dating performed in multiple pregnancies?
Q19. How is pregnancy dating performed after assisted reproduction?

Q20. How many weeks plus days is the pregnancy length assumed to be on the estimated day of delivery in your unit?

Q22-26 Historical changes in clinical practice concerning pregnancy dating by ultrasound

Q21. What year did ultrasound become routine for pregnancy dating in your unit instead of last menstrual period?

- Second trimester pregnancy dating became routine practice in the year of…
- First trimester pregnancy dating became routine practice in the year of…
- Commentaries (i.e. if it was a gradual change):

Q22. Has your clinical practice then changed from second to first trimester ultrasound examination for pregnancy dating?

Q23. Has clinical practice then been changed back to second trimester pregnancy dating in your unit?

Q24. If yes – why?

Q25. Please, estimate the fraction of first trimester pregnancy dating examinations relative to second trimester pregnancy dating. Mark the years when a change took place.

Q26-30 Assessment of the estimated pregnancy length

Q26. If there is discrepancy between EDD by last menstrual period and EDD by ultrasound – will a follow-up examination be planned?

Q27. After the indicated extent of discrepancy – in how many days would such a follow-up examination be planned?

Q28. If a pregnant women says that EDD by ultrasound does not cohere with a known date of confinement or an ovulation test – could this affect the unit's clinical decisions, i.e. time-point for induction of labor?

Q29. What factors could affect how valid the EDD by ultrasound is considered for clinical purposes in your unit?

Q30: Other comments

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