Prediction of large for gestational age neonates by routine third trimester ultrasound

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What does the study add to what is already known

First, the predictive performance for LGA neonates by routine ultrasonography during the third trimester is higher if the scan is carried out at 35^{+0}-36^{+6} weeks than at 31^{+0}-33^{+6} weeks, the method of screening is EFW than fetal AC, the outcome measure is birthweight >97^{th} than >90^{th} percentile and if delivery occurs within 10 days than at any stage after assessment. Second, prediction of >80% of LGA neonates necessitates use of EFW >70^{th} percentile.

What are the clinical implications of the study

ABSTRACT

Objectives: First, to evaluate and compare the performance of routine ultrasonographic estimated fetal weight (EFW) and fetal abdominal circumference (AC) at 31^{+0} - 33^{+6} and 35^{+0} - 36^{+6} weeks' gestation in the prediction of large for gestational age (LGA) neonates born at ≥37 weeks' gestation. Second, to assess the additive value of fetal growth velocity between 32 and 36 weeks' gestation on the performance of EFW at 35^{+0} - 36^{+6} weeks' gestation for prediction of LGA neonates. Third, to define the predictive performance for LGA neonates of different EFW cut-offs at routine ultrasound examination at 35^{+0} - 36^{+6} weeks' gestation. Fourth, to propose a two-stage strategy for identifying pregnancies with LGA fetuses that may benefit from iatrogenic delivery during the 38^{th} gestational week.

Methods: First, data from 21,989 singleton pregnancies that had undergone routine ultrasound examination at 31^{+0} - 33^{+6} weeks' gestation and 45,847 that had undergone routine ultrasound examination at 35^{+0} - 36^{+6} weeks were used to compare the predictive performance of EFW and AC for LGA neonates with birthweight >90^{th} and >97^{th} percentiles born at ≥37 weeks' gestation. Second, data from 14,497 singleton pregnancies that had undergone routine ultrasound examination at 35^{+0} - 36^{+6} weeks' gestation and had a previous scan at 30^{+0} – 34^{+6} weeks were used to determine, through multivariable logistic regression analysis, whether addition of growth velocity, defined by a difference in EFW and AC Z-scores between the early and late third trimester scans divided by the time interval between them, improved the performance of EFW at 35^{+0} - 36^{+6} weeks in the prediction of delivery of LGA neonates born at ≥37 weeks' gestation. Third, in the database of the 45,847 pregnancies that had undergone routine ultrasound examination at 35^{+0} - 36^{+6} weeks' gestation the screen positive and detection rate of LGA neonates born at ≥37 weeks' gestation and at ≤10 days from the initial scan were calculated for different EFW percentile cut-offs between the 50^{th} and 90^{th} percentile.

Results: First, the areas under the receiver operating characteristic curves (AUROC) of screening for LGA neonates were significantly higher with EFW Z-score than AC Z-score and at 35^{+0} - 36^{+6} than at 31^{+0} - 33^{+6} weeks' gestation ($p<0.001$). Second, the performance of screening for LGA neonates achieved by EFW Z-score at 35^{+0} - 36^{+6} weeks was not significantly improved by addition of EFW or AC growth velocity. Third, in screening by EFW >90^{th} percentile at 35^{+0} - 36^{+6} weeks' gestation the predictive performance for LGA neonates born at ≥37 weeks' gestation was modest (65% and 46% for neonates with birthweight >97^{th} and >90^{th} percentiles, respectively, at screen positive rate of 10%), but the performance was better for prediction of LGA neonates born at ≤10 days from the scan (84% and 71% for neonates with birthweight >97^{th} and >90^{th} percentiles, respectively, at screen positive rate of 11%). Fourth, screening by EFW >70^{th} percentile at 35^{+0} - 36^{+6} weeks' gestation predicted 91% and 82% of LGA neonates with birthweight >97^{th} and >90^{th} percentiles born at ≥37 weeks' gestation, at screen positive rate of 32%, and the respective values of screening by EFW >85^{th} percentile for prediction of LGA neonates born at ≤10 days from the scan were 88%, 81% and 15%. On the basis of these results it was proposed that routine fetal biometry at 36 weeks' gestation is a screening rather than diagnostic test for fetal macrosomia and that EFW >70^{th} percentile should be used to identify pregnancies in need for another scan at 38 weeks and in the latter those with EFW >85^{th} percentile should be considered for iatrogenic delivery during the 38^{th} week.

Conclusions: First, the predictive performance for LGA neonates by routine ultrasonographic examination during the third trimester is higher if the scan is carried out at 36 than at 32 weeks, the method of screening is EFW than fetal AC, the outcome measure is birthweight >97^{th} than >90^{th} percentile and if delivery occurs within 10 days than at any stage after assessment. Second, prediction of LGA neonates by EFW >90^{th} percentile is modest and the study presents a two-stage strategy for maximizing the prenatal prediction of LGA neonates.

INTRODUCTION

Large for gestational age (LGA) neonates with birthweight >90th percentile are at increased risk of perinatal death, birth injury and adverse neonatal outcome.[1-5] Such risks could potentially be reduced by elective cesarean section or early induction of labor to reduce the inevitable increase in fetal size with advancing gestational age.[6-8] However, there is uncertainty as to the best approach for identifying such LGA fetuses, because of first, the existence of a wide range of charts for fetal size and birthweight, second, the controversy of universal versus selective ultrasound examination based on maternal risk factors and the results of abdominal palpation or serial measurements of symphysial-fundal height, third, lack of consistent data on the performance of EFW versus AC for prediction of LGA neonates, fourth, limited data on the best time for a universal third trimester scan at 32 versus 36 weeks' gestation, and fifth, the performance of sonographic fetal biometry in the prediction of LGA neonates.

First, we have addressed the issue of inconsistency between fetal and neonatal growth charts by developing EFW and birthweight reference ranges with a common median.[9] Second, there is some evidence that the predictive performance for LGA neonates is higher by universal sonographic fetal biometry during the third trimester than the traditional method of selective ultrasonography based on maternal risk factors and the results of measurements of symphysial-fundal height.[10] Third, a systematic review of 36 articles reported that there was no difference in accuracy between ultrasonographic EFW and AC in the prediction of a macrosomic baby at birth.[11] However, a study of 5,163 singleton pregnancies with fetal biometry at 22-43 weeks' gestation and livebirth of phenotypically normal neonates within two days of the ultrasound examination reported that the most accurate formula for prediction of birthweight, among 70 models identified by systematic review of 45 studies, was that of Hadlock et al.,[12] which incorporated measurements of head circumference (HC), AC and femur length (FL).[13] Fourth, on the issue of timing of the third trimester scan there is some evidence that the predictive performance of a scan for LGA neonates at 36 weeks' gestation may be superior to that at 32 weeks.[14,15] Fifth, there is uncertainty as to the additive value for prediction of LGA neonates of fetal growth velocity on the performance of EFW during the late third trimester.[16-18]

The objectives of this study are first, to evaluate and compare the performance of routine ultrasonographic estimated fetal weight (EFW) and fetal abdominal circumference (AC) at 31^{+0} - 33^{+6} and 35^{+0} - 36^{+6} weeks' gestation in the prediction of LGA neonates born at ≥37 weeks' gestation; second, to assess the additive value of fetal growth velocity between 32 and 36 weeks' gestation on the performance of EFW at 35^{+0} - 36^{+6} weeks' gestation for prediction of LGA neonates; third, to define the predictive performance for LGA neonates of different EFW cut-offs at routine ultrasound examination at 35^{+0} - 36^{+6} weeks' gestation; and fourth, to propose a two-stage strategy for identifying pregnancies with LGA fetuses that may benefit from iatrogenic delivery during the 38th gestational week.

METHODS

There are three parts to this study. First, data from 21,989 singleton pregnancies that had undergone routine ultrasound examination at 31^{+0} - 33^{+6} weeks' gestation and 45,847 that had undergone routine ultrasound examination at 35^{+0} - 36^{+6} weeks were used to compare the predictive performance for LGA neonates with birthweight >90th and >97th percentiles of EFW and AC. The patients were examined at King's College Hospital, London or Medway Maritime Hospital, Gillingham, UK. In the participating hospitals all women with singleton pregnancies are offered routine ultrasound examinations at 11^{+0} - 13^{+6} and at 19^{+0} to 23^{+6} weeks' gestation. During a period (May 2011 to March 2014) an additional scan was offered at 31^{+0} to 33^{+6} weeks, but

subsequently (March 2014 and September 2018) this was changed to 35^{+0} to 36^{+6} weeks. In the selection of patients care was taken to include routine scans and not follow-up scans for maternal medical conditions or a suspected problem in fetal growth. In the first or second trimester visit we recorded maternal demographic characteristics and medical history and in the third trimester visits we carried out an ultrasound examination for fetal anatomy and measurement of fetal HC, AC and FL for calculation of EFW using the formula by Hadlock et al.[12] Gestational age was determined by the measurement of fetal crown-rump length at 11-14 weeks or the fetal head circumference at 19-24 weeks.[19,20] The ultrasound examinations were carried out by examiners who had obtained the Fetal Medicine Foundation certificate of competence in ultrasound examination for fetal abnormalities. Data from the patients included in this study were the subject of previous publications.[4,15,21-27]

Second, data from 14,497 singleton pregnancies that had undergone routine ultrasound examination at 35^{+0} - 36^{+6} weeks' gestation and had a previous scan at least two weeks earlier at 30^{+0} - 34^{+6} weeks were used to determine whether addition of growth velocity between the early and late third trimester scans improved the performance of EFW at 35^{+0} - 36^{+6} weeks in the prediction of delivery of LGA neonates.

Third, the database of the 45,847 pregnancies that had undergone routine ultrasound examination at 35^{+0} - 36^{+6} weeks' gestation was used to define the predictive performance of different EFW cut-offs for LGA neonates.

The women gave written informed consent to participate in the studies, which was approved by the NHS Research Ethics Committee. The inclusion criteria for this study were singleton pregnancies delivering a non-malformed live birth or stillbirth. We excluded pregnancies with aneuploidies and major fetal abnormalities.

Patient characteristics

Patient characteristics recorded included maternal age, racial origin (White, Black, South Asian, East Asian and mixed), method of conception (natural, *in vitro* fertilization or use of ovulation induction drugs), cigarette smoking during pregnancy, medical history of chronic hypertension and diabetes mellitus, obstetric history including parity (parous or nulliparous if no previous pregnancies at $\geq$ 24 weeks' gestation), and previous pregnancy with SGA. The maternal weight and height were measured.

Outcome measures

Data on pregnancy outcome were collected from the hospital maternity records or the general medical practitioners of the women. The outcome measures of the study were birth of a neonate with birthweight >90^{th} and >97^{th} born at ≥37 weeks' gestation based on the Fetal Medicine Foundation fetal and neonatal population weight charts.[24]

Statistical analysis

Data were expressed as median and interquartile range (IQR) for continuous variables and n (%) for categorical variables. Mann-Whitney U-test and χ^2-square test or Fisher's exact test, were used for comparing outcome groups for continuous and categorical data, respectively. Significance was assumed at 5%.

Study 1: The observed measurements of EFW and birthweight were converted to Z-scores and

percentiles adjusted for gestational age according to the Fetal Medicine Foundation fetal and neonatal population weight charts.[3] Similarly, AC was converted to Z-scores and percentiles adjusted for gestational age according to the reference ranges of Snijders and Nicolaides.[12] Logistic regression analysis was undertaken to determine the significance of contribution of AC and EFW Z-score in prediction of delivery of LGA neonates with birthweight >90th and >97th percentile born at ≥37 weeks' gestation. The performance of screening was determined by receiver operating characteristic (ROC) curves and the areas under the ROC curves (AUROC) of screening at 31^{+0} - 33^{+6} and 35^{+0} - 36^{+6} weeks' gestation in the prediction of LGA neonates were compared.[18]

Study 2: In the dataset of 14,497 singleton pregnancies with paired measurements of fetal biometry at 30^{+0} - 34^{+6} and 35^{+0} - 36^{+6} weeks' gestation, the observed measurements of AC and EFW were expressed as Z-scores for gestational age.[25,26] Fetal growth velocity was defined as the difference in AC Z-scores and EFW Z-scores between the two ultrasound scans divided by the time interval in days between them. Multivariable regression analysis was carried out to determine whether the addition of AC and EFW growth velocity to the EFW Z-score at 35^{+0} - 36^{+6} weeks' gestation improved the performance of screening for LGA neonates with birthweight >90th and >97th percentiles born at ≥37 weeks' gestation. The performance of screening was determined by ROC curves.

Study 3: The screen positive and detection rate of LGA neonates with birthweight >90th and >97th percentiles born at ≥37 weeks' gestation and at ≤10 days from the initial scan, at different EFW percentile cut-offs between the 50th and 90th percentile were estimated.

The statistical software package SPSS 24.0 (IBM SPSS Statistics for Windows, Version 24.0, Armonk, NY: IBM Corp; 2016) and Medcalc (Medcalc Software, Mariakerke, Belgium) were used for data analyses.

RESULTS

Patient characteristics

The characteristics of the study population are shown in Table 1. The characteristics of those with a scan at 31^{+0} - 33^{+6} weeks' gestation were similar to those with a scan at 35^{+0} - 36^{+6} weeks. In both study periods in the group of neonates with birthweight >90th percentile, compared to those with birthweight ≤90th percentile, the median maternal age, weight and height, EFW Z-score, AC Z-score and birthweight Z-score were higher, fewer women were of non-White racial origin, were smokers and more women had pre-existing diabetes mellitus and were parous with previous pregnancy with an LGA neonate.

Delivery at ≥37 weeks' gestation occurred in 20,901 (95.1%) of the 21,989 pregnancies examined at 31^{+0} - 33^{+6} weeks' gestation and in 44,918 (98.0%) of the 45,847 examined at 35^{+0} - 36^{+6} weeks' gestation.

Performance of screening for LGA neonates

Screening at 35^{+0} - 36^{+6} versus 31^{+0} - 33^{+6} weeks' gestation and by EFW versus fetal AC

The AUROCs of screening for LGA neonates born at ≥37 weeks' gestation were significantly higher if first, the scan was carried out at 35^{+0} - 36^{+6} weeks' gestation than at 31^{+0} - 33^{+6} weeks, second, the method of assessment was EFW Z-score than AC Z-score, and third, the outcome

measure was birthweight >97th than >90th percentile (Table 2, Figure 1).

Effect of growth velocity on prediction of LGA neonates

In the dataset with paired measurements of fetal biometry at 30^{+0} - 34^{+6} and 35^{+0} - 36^{+6} weeks' gestation, multivariable logistic regression analysis demonstrated that in the prediction of LGA neonates with birthweight >90th percentile born at ≥37 weeks' gestation, there was no significant improvement in performance of screening by addition of either AC growth velocity or EFW growth velocity to the EFW Z-score at 35^{+0} - 36^{+6} weeks' gestation (AUROC 0.891, 95% CI 0.883-0.899 vs. 0.887, 95% CI 0.879-0.896 and 0.892, 95% CI 0.884-0.900 vs. 0.887, 95% CI 0.879-0.896; the detection rates, at 10% false positive rate, were 66%, 66%, 65%, respectively. Similarly, in the prediction of LGA neonates with birthweight >97th percentile born at ≥37 weeks' gestation, there was no significant improvement in performance of screening by addition of either AC growth velocity or EFW growth velocity to the EFW Z-score at 35^{+0} - 36^{+6} weeks' gestation (AUROC 0.921, 95% CI 0.909-0.933 vs. 0.919, 95% CI 0.906-0.931 and 0.922, 95% CI 0.910-0.934 vs. 0.919, 95% CI 0.906-0.931; the detection rates, at 10% false positive rate, were75%, 76%, 75%, respectively.

Screening at different EFW percentile cut-offs for births at ≥37 weeks' gestation

The predictive performance for LGA neonates with birthweight >90th and >97th percentile after birth at ≥37 weeks' gestation in screening by EFW at a series of cut-offs between the 50th and 90th percentile at 35^{+0} to 36^{+6} weeks' gestation is shown in Table 3. Screening by EFW >90th percentile predicted 65% of neonates with birthweight >97th percentile and 46% of those with birthweight >90th percentile with respective positive predictive values of 17% and 43%. The respective values in screening by EFW >70th percentile were 91% and 82% and 7% and 24%. In the population of 44,918 pregnancies delivering at ≥37 weeks' gestation the median interval between the scan and delivery was 3.9 (range 0.1-7.6) weeks.

Screening at different EFW percentile cut-offs for births at ≤10 days from the scan

The predictive performance for LGA neonates with birthweight >90th and >97th percentile after birth within 10 days of the scan at 35^{+0} to 36^{+6} weeks' gestation in screening by EFW at a series of cut-offs between the 50th and 90th percentile is shown in Table 3 and the ROC curves of such screening are shown in Figure 2. Screening by EFW >90th percentile predicted 84% of neonates with birthweight >97th percentile and 71% of those with birthweight >90th percentile with respective positive predictive values of 28% and 51%. The respective values in screening by EFW >85th percentile were 88% and 81% and 22% and 43%.

Proposed strategy for management of LGA fetuses

On the assumption that in pregnancies with suspected fetal macrosomia iatrogenic delivery by induction of labor or elective cesarean section during the 38th gestational week, compared to expectant management, would reduce the risk of associated perinatal death, birth injury and adverse neonatal outcome, we propose a two-stage strategy for identifying pregnancies that could potentially benefit from such intervention. The first- stage is routine ultrasound examination at 35^{+0} to 36^{+6} weeks' gestation to identify pregnancies with EFW >70th percentile. In the second stage, these pregnancies with EFW >70th percentile are offered a second ultrasound examination at the beginning of 38 weeks and those with EFW >85th percentile are offered iatrogenic delivery.

On the basis of the results in Table 3 it is anticipated that about 30% of pregnancies, those with

EFW >70th percentile, will be offered another scan at 38 weeks, and about 15% of the total would undergo iatrogenic delivery during the 38th week. However, in our study population 21.6% (9,885 / 45,847) of pregnancies delivered <39 weeks' gestation, including 20.9% (3,050 / 14,626) of those with EFW >70th percentile at the 35^{+0} - 36^{+6} weeks scan. Future implementation studies are necessary to define the exact proportion of the population stratified into the different management groups.

DISCUSSION

Main findings of the study

The findings of this study demonstrate that the predictive performance for LGA neonates by routine ultrasonographic examination during the third trimester is higher if first, the scan is carried out at 35^{+0} - 36^{+6} weeks' gestation than at 31^{+0} - 33^{+6} weeks; second, the method of screening is EFW than fetal AC; third, the outcome measure is birthweight >97th than >90th percentile; and fourth, if delivery occurs within 10 days than at any stage after assessment. The predictive performance for LGA neonates by EFW at 35^{+0} - 36^{+6} weeks is not improved by the addition of fetal growth velocity.

We found that screening by EFW >90th percentile at 35^{+0} - 36^{+6} weeks' gestation predicted 65% of neonates with birthweight >97th percentile born at ≥37 weeks' gestation and 46% of those with birthweight >90th percentile with respective positive predictive values of 17% and 43%. The respective values in screening by EFW >70th percentile were 91% and 82% and 7% and 24%.

Comparison with findings from previous studies

We found that the predictive performance for LGA neonates of EFW is superior to that of fetal AC. This finding is consistent with the results of a study that investigated the ability of ultrasonographic fetal biometry to predict birthweight in neonates born within two days of the ultrasound examination and reported that models incorporating measurements of fetal HC, AC and FL were superior to those using AC alone or AC and FL.[13]

Our findings that the predictive performance for LGA neonates by fetal biometry at 35^{+0} - 36^{+6} weeks' gestation is superior to that at 31^{+0} - 33^{+6} weeks is consistent with the results of a previous study comparing the performance of ultrasonographic fetal biometry in 3,690 pregnancies at 30^{+0} - 33^{+6} weeks' gestation and 2,288 at 34^{+0} - 37^{+0} weeks[14] and another study comparing the fetal biometry in 25,727 pregnancies at 30^{0} - 34^{+6} weeks' gestation and 6,181 at 34^{+0} - 37^{+6} weeks.[15]

Our finding that growth velocity between 32 and 36 weeks' gestation did not improve the prediction of LGA neonates provided by EFW at 36 weeks is consistent with the results of a study that examined 3,440 pregnancies and reported that serial fetal biometry did not improve the prediction of LGA neonates provided by the last EFW before delivery alone,[17] and of another study that examined 2,696 pregnancies and reported that the growth velocity in AC between 22 and 32 weeks did not improve the prediction of LGA neonates provided by AC at 32 weeks.[18] Similarly, in previous studies we reported that growth velocity between 22 and 36 weeks and between 32 and 36 weeks did not improve the predictive performance for SGA neonates provided by EFW at 36 weeks.[23,24] Solomon et al., examined 356 pregnancies at 11-14, 20-24 and 30-34 weeks' gestation and on the basis of fetal biometry and growth velocity between ultrasound examinations developed models that provided modest prediction of SGA and LGA neonates.[16]

Implications for clinical practice

All pregnant women should be offered a routine third trimester scan because such policy is more effective in identifying both LGA and SGA fetuses than selective ultrasonography based on maternal risk factors and the results of measurements of symphysial-fundal height. As shown in this study the best time of performing such a scan is about 36 weeks' gestation. However, the scan should be considered to be a screening rather than diagnostic test for LGA neonates. Selection of EFW >90th percentile as the cut-off necessary to identify the high-risk group in need of further assessment and / or iatrogenic delivery during the 38th gestational week, with the aim of reducing the risk of associated perinatal death, birth injury and adverse neonatal outcome, is inadequate because the majority of affected fetuses would be missed.

This study provides the framework for stratification of risk for LGA neonates and management of pregnancies undergoing routine fetal biometry at 36 weeks' gestation. We propose a two-stage strategy for identifying pregnancies that could potentially benefit from iatrogenic delivery during the 38th gestational week. In the first-stage at 36 weeks' gestation an EFW cut-off is selected to include the majority of expected LGA neonates at an acceptably low screen positive rate; in the second-stage the screen positive group from first-stage screening have a second scan at the beginning of the 38th week and those with EFW above a certain cut-off are offered iatrogenic delivery. We propose a pragmatic approach of selecting the EFW cut-off of the 70th percentile for the first-stage and the 85th percentile for the second-stage. However, the EFW cut-offs and protocols for management of the screen positive groups will inevitably vary according to findings of implementation studies, local preferences and health economic considerations. Future studies will examine whether the implementation of such protocols could improve perinatal outcome.

Strengths and limitations of the study

The strengths of this screening study for LGA neonates are first, examination of a large population of pregnant women attending for routine assessment of fetal growth and wellbeing at either 31^{+0} - 33^{+6} or 35^{+0} - 36^{+6} weeks' gestation, second, trained sonographers that carried out fetal biometry according to a standardized protocol,[8] third, use of the Fetal Medicine Foundation fetal and neonatal references ranges which have a common median,[3] fourth, direct comparison of the predictive performance of EFW and fetal AC, and fifth, presentation of a strategy for prenatal prediction of LGA neonates and the management of affected pregnancies.

A limitation of the study, in relation to the comparison of predictive performance for SGA neonates of the scan at 31^{+0} - 33^{+6} vs. that at 35^{+0} - 36^{+6} weeks' gestation, is that this was not a randomized study. However, the findings are valid because during the two consecutive periods of study the characteristics of the population were similar, the two hospitals were the same and the ultrasonographers carrying out the scans had received the same training and followed the same protocol for conducting the scan.

Conclusions

The predictive performance for LGA neonates by routine ultrasonographic examination during the third trimester is higher if the scan is carried out at 35^{+0} - 36^{+6} weeks' gestation than at 31^{+0} - 33^{+6} weeks, but prediction of LGA neonates by EFW >90th percentile is modest. The study presents a two-stage approach for stratifying the pregnancies undergoing routine ultrasound examination at 36 weeks' gestation into management groups based on findings of EFW. This approach is likely to have a higher predictive performance for LGA neonates than screening by EFW >90th percentile. Future implementation studies will define the impact of the proposed approach in prenatal prediction of LGA neonates and reduction of adverse perinatal outcome.

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FIGURE LEGENDS

Figure 1. Receiver operating characteristics curves of estimated fetal weight (red curve) and abdominal circumference (black curve) at 35^{+0} - 36^{+6} weeks' gestation (solid lines) and at 31^{+0} - 33^{+6} weeks (interrupted lines), in the prediction of large for gestational age neonates with birthweight >90^{th} (left) and 97^{th} (right) percentile delivering at ≥37 weeks' gestation.

Figure 2. Receiver operating characteristics curves of prediction of large for gestational age neonates with birthweight >90^{th} (blach curves) and 97^{th} (red curves) percentile delivering at ≥37 weeks' gestation (interrupted lines) and delivering within 10 days of assessment (solid lines).

Table 1. Maternal and pregnancy characteristics of the study populations.

Characteristic	Screening at 31^{+0} - 33^{+6} weeks		Screening at 35^{+0} - 36^{+6} weeks	
	BW ≤90th percentile (n=20,124)	BW >90th percentile (n=1,865)	BW ≤90th percentile (n=41,618)	BW >90th percentile (n=4,229)
Maternal age in years, median (IQR)	30.5 (25.9-34.4)	31.3 (26.9-35.1)***	31.5 (27.2-35.3)	32.2 (28.3-35.8)***
Maternal weight in Kg, median (IQR)	76.0 (68.0-86.2)	85.0 (76.0-96.0)***	78.2 (70.0-89.0)	88.0 (78.5-100.0)***
Maternal height in cm, median (IQR)	164 (160-168)	167 (163-171)***	165 (160-169)	167 (163-171)***
Racial origin				
White, n (%)	13,927 (69.2)	1,497 (80.3)***	30,677 (73.7)	3,483 (82.4)***
Black, n (%)	4,393 (21.8)	270 (14.5)***	6,708 (16.1)	488 (11.5)***
South Asian, n (%)	908 (4.5)	36 (1.9)***	2,085 (5.0)	100 (2.4)**
East Asian, n (%)	427 (2.1)	27 (1.4)	882 (2.1)	57 (1.3)**
Mixed, n (%)	469 (2.3)	35 (1.9)	1,266 (3.0)	101 (2.4)*
Cigarette smoker, n (%)	2,269 (11.3)	118 (6.3)***	3,565 (8.6)	158 (3.7)***
Conception				
Natural, n (%)	19,550 (97.1)	1,812 (97.2)	40,205 (96.6)	4,065 (96.1)
Ovulation drugs, n (%)	171 (0.8)	15 (0.8)	228 (0.5)	29 (0.7)
In vitro fertilization, n (%)	403 (2.0)	38 (2.0)	1,185 (2.8)	135 (3.2)
Medical conditions				
Chronic hypertension, n (%)	279 (1.4)	27 (1.4)	530 (1.3)	50 (1.2)
Diabetes mellitus type 1, n (%)	65 (0.3)	17 (0.9)***	118 (0.3)	49 (1.2)***
Diabetes mellitus type 2, n (%)	123 (0.6)	12 (0.6)	169 (0.4)	39 (0.9)***
Past obstetric history				
Nulliparous, n (%)	9,945 (49.4)	635 (34.0)	19,456 (46.7)	1,404 (33.2)
Parous with prior LGA, n (%)	950 (4.7)	439 (23.5)***	1,825 (4.4)	956 (22.6)***
Parous without prior LGA, n (%)	9,229 (45.9)	791 (42.4)**	20,337 (48.9)	1,869 (44.2)***
GA at screening, median (IQR)	32.2 (32.0-32.6)	32.3 (32.0-32.6)*	36.1 (35.9-36.4)	36.1 (35.9-36.4)
EFW Z-score, median (IQR)	-0.09 (-0.75-0.57)	1.04 (0.51-1.59)***	-0.03 (-0.66-0.57)	1.21 (0.71-1.75)***
AC Z-score, median (IQR)	-0.19 (-0.62-0.28)	0.56 (0.14-0.96)***	-0.09 (-0.59-0.40)	0.86 (0.40-1.33)***
GA at delivery in weeks, median (IQR)	40.0 (39.0-40.9)	40.0 (39.0-40.9)	39.9 (39.0-40.8)	40.0 (39.1-40.9)***
Birthweight Z-score, median (IQR)	-0.17 (-0.85-0.43)	1.63 (1.43-1.95)***	-0.13 (-0.79-0.45)	1.63 (1.44-1.93)***
Birthweight in grams, median (IQR)	3343 (3038-3630)	4245 (4054-4420)***	3365 (3070-3645)	4240 (4065-4400)***

GA = gestational age; EFW = estimated fetal weight; AC = abdominal circumference; IQR = interquartile range; LGA = large for gestational age.
* p<0.05; ** p<0.01; *** p<0.001

Table 2. Comparisons of areas under the curve (95% confidence interval) in screening for LGA neonates by estimated fetal weight and fetal abdominal circumference.

Outcome measure	Delivery at ≥37 weeks' gestation		
	Estimated fetal weight	Abdominal circumference	P value
35^{+0} - 36^{+6} weeks			
BW >10^{th} percentile	0.861 (0.856-0.867)	0.837 (0.831-0.843)	P<0.001
BW >97^{th} percentile	0.902 (0.894-0.910)	0.882 (0.872-0.891)	P<0.001
31^{+0} - 33^{+6} weeks			
BW >10^{th} percentile	0.815 (0.806-0.825)	0.790 (0.780-0.800)	P<0.001
BW >97^{th} percentile	0.853 (0.838-0.868)	0.828 (0.812-0.845)	P<0.001

Table 3. Predictive performance for large for gestational age neonates by estimated fetal weight above specific percentile cut-offs at 35^{+0} to 36^{+6} weeks' gestation.

Estimated fetal weight	Screen positive rate	Birthweight >90th percentile		Birthweight >97th percentile	
		Detection rate	Positive predictive value	Detection rate	Positive predictive value
Birth at ≥37 weeks	**n/45,847 (%; 95% CI)**	**n/4,229 (%; 95% CI)**	**% (95% CI)**	**n/1,190 (%; 95% CI)**	**% (95% CI)**
>90th percentile	4,503 (9.8; 8.9-10.7)	1,944 (46; 44-48)	43 (42-44)	775 (65; 62-68)	17 (16-18)
>85th percentile	7,096 (15.5; 14.7-16.3)	2,535 (60; 58-62)	36 (35-37)	916 (77; 74-80)	13 (12-14)
>80th percentile	9,630 (21.0; 20.1-21.8))	2,927 (69; 67-71)	30 (29-31)	992 (83; 80-86)	10 (9-11)
>75th percentile	12,131 (26.5; 25.4-27.2)	3,238 (77; 75-79)	27 (26-28)	1,050 (88; 85-91)	9 (8-10)
>70th percentile	14,626 (31.9; 30.8-32.3)	3,455 (82; 80-84)	24 (23-25)	1,085 (91; 88-94)	7 (6-8)
>65th percentile	17,070 (37.2; 36.8-38.5)	3,653 (86; 84-88)	21 (20-22)	1,121 (94; 91-97)	7 (6-8)
>60th percentile	19,498 (42.5; 41.3-42.7)	3,800 (90; 88-92)	20 (19-21)	1,142 (96; 93-99)	6 (5-7)
>55th percentile	21,931 (47.8; 47.1-48.5)	3,912 (93; 91-95)	18 (17-19)	1,150 (97; 94-100)	5 (4-6)
>50th percentile	24,269 (52.9; 52.2-53.6)	3,992 (94; 92-96)	16 (15-17)	1,156 (97; 94-100)	5 (4-6)
Birth at ≤10 days	**n/2,901 (%; 95% CI)**	**n/236 (%; 95% CI)**	**% (95% CI)**	**n/110 (%; 95% CI)**	**% (95% CI)**
>90th percentile	325 (11.2; 10.1-12.4)	167 (71; 65-77)	51 (46-56)	92 (84;77-91)	28 (23-33)
>85th percentile	445 (15.3; 14.0-16.6)	190 (81; (76-86)	43 (38-48)	97 (88; 82-94)	22 (17-27)
>80th percentile	564 (19.4; 18.0-20.8)	204 (86; 82-90)	36 (32-40)	99 (90; 84-96)	18 (15-21)
>75th percentile	665 (22.9; 21.4-24.4)	217 (92; 89-95)	33 (29-37)	101 (92; 87-97)	15 (12-18)
>70th percentile	795 (27.4; 25.8-29.0)	222 (94; 91-97)	28 (25-31)	103 (94; 90-98)	13 (11-15)
>65th percentile	925 (31.9; 30.2-33.6)	228 (97; 95-99)	25 (22-28)	106 (96; 92-100)	11 (9-13)
>60th percentile	1,039 (35.8; 34.1-38.5)	229 (97; 95-99)	22 (20-24)	107 (97; 94-100)	10 (8-12)
>55th percentile	1,162 (40.0; 38.2-41.8)	231 (98; 96-100)	20 (18-22)	107 (97; 94-100)	9 (7-11)
>50th percentile	1,271 (43.8; 42.0-45.6)	231 (98; (96-100)	18 (16-20)	107 (97; 94-100)	8 (7-9)

CI = confidence interval; EFW = estimated fetal weight.