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Implication of third-trimester screening accuracy for small-for-gestational age and additive value of third-trimester growth-trajectory indicators in predicting severe adverse perinatal outcome in low-risk population: pragmatic secondary analysis of IRIS study

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KEYWORDS: centile crossing; estimated fetal weight; fetal growth restriction; growth velocity; severe adverse perinatal outcome; SGA; small-for-gestational age; third-trimester screening

CONTRIBUTION

What are the novel findings of this work?
This study showed that false-positive small-for-gestational-age screening findings do not necessarily lead to increased obstetric intervention. We found no evidence that using the third-trimester growth-trajectory measurements abdominal circumference crossing > 20 or > 50 centiles or estimated fetal weight crossing > 20 centiles is of additive value in identifying fetuses at risk of severe adverse perinatal outcome in a low-risk population. In addition, we found no convincing evidence that abdominal circumference growth velocity < 10% is of additive value in identifying fetuses at risk of severe adverse perinatal outcome.

What is the clinical implications of this work?
Obstetric-care professionals should be aware that using third-trimester growth-trajectory measurements for identification of abnormal fetal growth is not beneficial in populations remaining at low risk throughout pregnancy.

ABSTRACT

Objectives *To examine the implications of third-trimester small-for-gestational-age (SGA) screening accuracy on severe adverse perinatal outcome (SAPO) and obstetric intervention in a low-risk population. Furthermore, we aimed to explore the additive value of third-trimester sonographic growth-trajectory measurements in predicting SAPO and obstetric intervention.*

Methods *This was a secondary analysis of a Dutch national multicenter stepped-wedge-cluster randomized trial among 11 820 low-risk pregnant women. Using multilevel multivariable logistic regression analysis, we compared SAPO and obstetric interventions in SGA neonates with and without SGA suspected prenatally (true positives and false negatives) and non-SGA neonates with and without SGA suspected prenatally (false positives and true negatives). In a subsample (*n = *7989), we analyzed the associations of abdominal circumference (AC) and estimated fetal weight (EFW) < 10th centile (p10) and third-trimester growth-trajectory indicators AC and EFW crossing > 20 and AC crossing > 50 centiles and the lowest decile of AC growth-velocity Z-scores (ACGV < 10%) with SAPO and obstetric interventions.*

Results *SGA infants, i.e. the true-positive and false-negative cases, had an increased risk of SAPO (adjusted odds ratio (aOR), 4.46 (95% CI, 2.28–8.75) and aOR 2.61 (95% CI, 1.74–3.89), respectively), and obstetric intervention (aOR for: induction of labor, 2.99 (95% CI, 2.15–4.17) and 1.38 (95% CI, 1.14–1.66); Cesarean section, 1.82 (95% CI, 1.25–2.66) and 1.27 (95% CI, 1.05–1.54); medically indicated preterm delivery, 2.67 (95% CI, 1.97–3.62) and 1.20 (95% CI, 1.03–1.40)). The false-positive cases did not differ from the true negatives for all outcomes, including obstetric intervention. Of the third-trimester growth-trajectory indicators, only*

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ACGV < 10% was associated moderately with SAPO (aOR, 2.15 (95% CI, 1.17–3.97)), while AC and EFW crossing > 20 and AC crossing > 50 centiles were not. Both EFW < p10 alone (aOR, 1.95 (95% CI, 1.13–3.38)) and EFW < p10 combined with ACGV < 10% (aOR, 4.69 (95% CI, 1.99–11.07)) were associated with SAPO, and they performed equally well in predicting SAPO (area under the receiver-operating-characteristics curve, 0.71 (95% CI, 0.65–0.76) vs *0.72 (95% CI, 0.67–0.77)*, P = *0.51).*

Conclusion *Neonates who had been suspected falsely of being SGA during pregnancy had no higher rates of obstetric intervention than did those without suspicion of SGA prenatally. Our results do not support that third-trimester low fetal growth velocity (ACGV < 10%) may be of additive value for the identification of fetuses at risk of SAPO in populations remaining at low risk throughout pregnancy. AC and EFW crossing > 20 and AC crossing > 50 centiles performed poorly in identifying abnormal fetal growth.* © *2023 The Authors. Ultrasound in Obstetrics & Gynecology published by John Wiley & Sons Ltd on behalf of International Society of Ultrasound in Obstetrics and Gynecology.*

INTRODUCTION

Fetal growth restriction (FGR) is a condition in which the fetus does not achieve its appropriate genetic growth potential[1]. It increases the risk for perinatal morbidity, mortality and adverse health consequences in adulthood[2]. Screening for abnormal fetal growth is a prerequisite for its timely detection, and enables intensified surveillance (e.g. Doppler studies) for fetal distress and optimization of timing of delivery[3–5]. To classify fetuses at risk, small-for-gestational-age (SGA) is often used as a proxy for FGR[1,6]. Fetal SGA is defined by the discrepancy of estimated fetal weight (EFW) or abdominal circumference (AC) with respect to a reference curve using a predefined threshold, usually the 10th centile (p10)[7]. However, this proxy is imprecise[8,9]. Although risk of morbidity and mortality is inversely related to fetal size and stillbirths are observed mainly among undetected SGA fetuses, it has been estimated that 70% of SGA fetuses are constitutionally small and healthy[9]. In addition, false-positive screening findings can lead to unnecessary intervention, including Cesarean section, and iatrogenic (preterm) birth[10–13]. Furthermore, FGR among appropriately sized fetuses is underrecognized[9,14]. To better balance overuse and underuse of obstetric intervention, there is a need for strategies to better distinguish pathological growth patterns from normal variation.

Recently, alongside measures of SGA, in Delphi studies[15–17] it has been proposed to use sonographic assessment of trajectories of slowing growth, for example AC and/or EFW crossing more than 20–50 centiles over time. Alternatively, *Z*-score-based AC growth velocity (ACGV) has been proposed, but in a British study[9] this only had additive value when combined with EFW < p10. Whether these parameters can better identify fetuses undergoing pathological growth and at risk for severe adverse perinatal outcome (SAPO) is uncertain. Further research to gain insight into the implications of misclassified screening results and the additional value of sonographic growth-trajectory measurements is important.

Applying a pragmatic screening setting in a low-risk population receiving primary midwife-led care, using data from the large-scale Dutch intrauterine growth restriction (IUGR) Risk Selection (IRIS) trial[19], we aimed to evaluate the association of correct or incorrect prenatal prediction of SGA birth weight with perinatal outcome and obstetric intervention. Furthermore, in a subanalysis, we aimed to examine the additive value of third-trimester sonographic indicators of fetal size and growth in predicting SAPO and obstetric intervention.

METHODS

Study design, population and setting

This study is a secondary analysis using data derived from the IRIS study, a pragmatic nationwide stepped-wedge-cluster randomized trial evaluating the effectiveness of routine third-trimester ultrasound screening in reducing SAPO among low-risk pregnant women in the Netherlands[19,20]. In the Netherlands, low-risk perinatal care is led by primary-care midwives[21]. In case of (suspected) risks or complications, women are referred to secondary obstetrician-led care[3]. The intervention strategy, routine third-trimester ultrasound screening at around 28–30 weeks and 34–36 weeks, combined with care as usual (symphysis–fundus height (SFH) measurement, with ultrasound examination on clinical indication), was compared with usual care alone (control strategy)[19,20]. Between 1 February 2015 and 29 February 2016, a total of 13 520 low-risk pregnant women with a non-anomalous singleton pregnancy and a reliable estimated delivery date were included, at a mean gestational age (GA) of 22.8 (SD, 2.4) weeks, in 60 primary-care midwife-led practices. Within the IRIS study trial, detection and clinical management of suspected FGR was carried out using a multidisciplinary consensus-based protocol[17].

For the current study, two analytical samples were used. First, the complete IRIS study sample ('total sample') was used to examine associations between antenatal suspicion of SGA according to birth-weight classification and perinatal and obstetric outcome. Second, in order to include as much ultrasound data as possible, for the ultrasound subanalysis, we created a subsample which comprised women in the intervention strategy arm (who received two routine ultrasound examinations in the third trimester, one at 28–30 and one at 34–36 weeks' gestation) and women in the control strategy arm who had received at least one clinically indicated third-trimester ultrasound examination in primary care. For the growth-trajectory measurements, we included women in the intervention strategy arm and women in the control strategy arm who had received at least two third-trimester

ultrasound examinations in primary care and for whom referral to secondary/tertiary obstetrician-led care had not (yet) been indicated (Figure 1). We explored the associations of third-trimester sonographic indicators of fetal size with SAPO, SGA birth weight combined with SAPO, and obstetric intervention. Moreover, among women with at least two third-trimester ultrasound examinations, we explored the associations of fetal growth-trajectory indicators with these outcomes.

The IRIS study was approved by the Institutional Review Board of VU Medical Center (reference number, 2013.409). Written informed consent to participate was obtained from all participants. The design of the IRIS study has been described previously[20].

Antenatal SGA status, fetal-size measurements and postnatal SGA status

Based on the study protocol of the IRIS study, classification of prenatally suspected SGA was defined as AC < p10 based on any of the third-trimester ultrasound examinations[20]. In the total sample, a case was classified as having no SGA during pregnancy if all fetal third-trimester AC measurements were ≥ p10 or if no fetal third-trimester ultrasound measurements had been made due to reassuring SFH measurements. In the ultrasound subanalysis, we excluded participants with SFH data only. In addition to AC < p10 (yes/no), we included measures of EFW < p10 (yes/no) and EFW < p3 (yes/no)[3,22,23]. In this

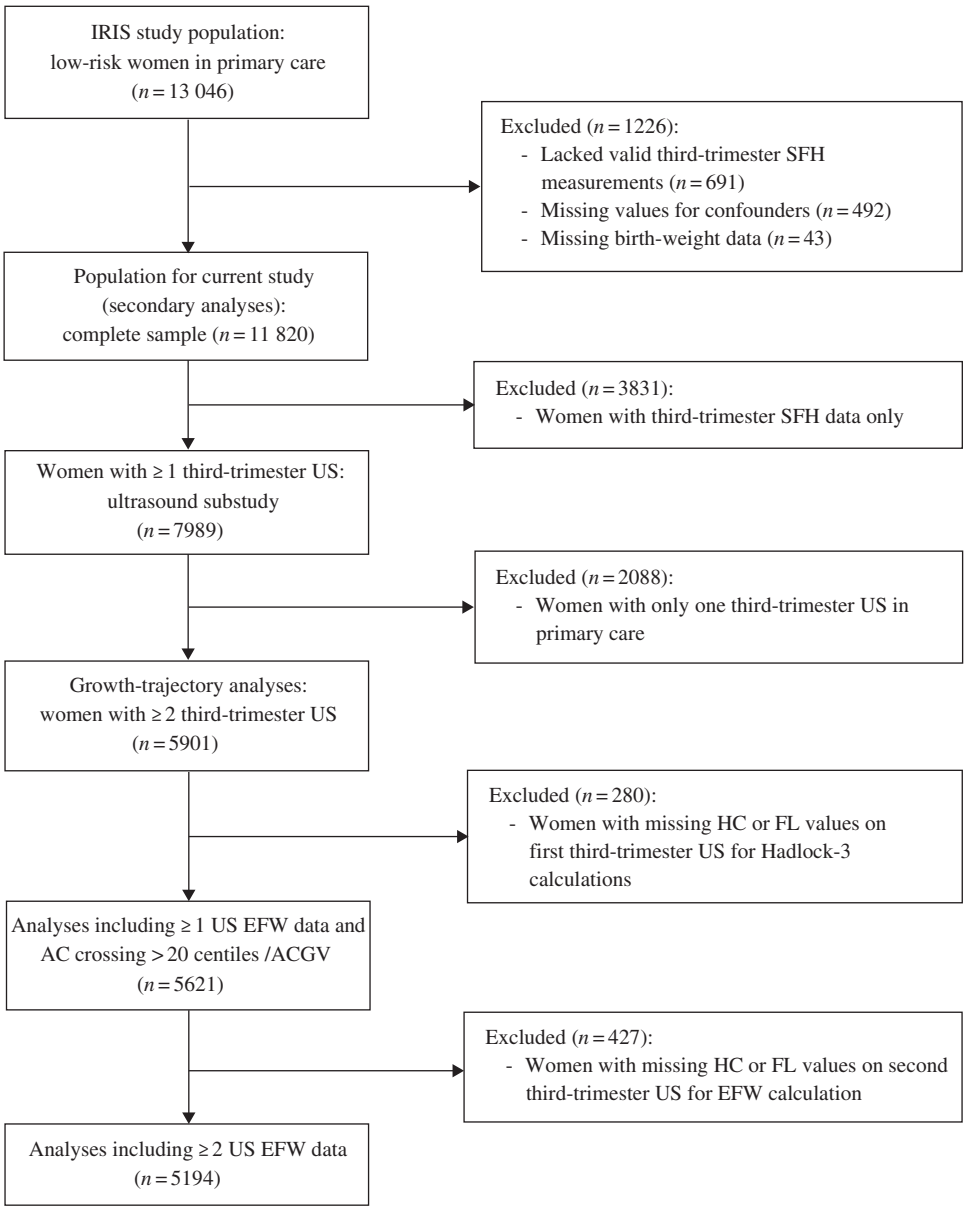

Figure 1 Flowchart of low-risk women included in our study, including total sample and women eligible for ultrasound subanalysis. For growth-trajectory measurements, women were included who received at least two third-trimester ultrasound examinations in primary care and for whom referral to secondary/tertiary obstetrician-led care had not (yet) been indicated. AC, abdominal circumference; ACGV, abdominal circumference growth velocity; EFW, estimated fetal weight; FL, femur length; HC, head circumference; SFH, symphysis–fundus height; US, ultrasound examination.

subanalysis, classification of prenatally suspected SGA was defined as AC < p10, EFW < p10 or EFW < p3 based on any of the third-trimester ultrasound examinations.

AC centiles were derived from the Verburg gestational-age specific fetal-growth chart[24]. EFW centiles were calculated using the Hadlock-3 formula and reference standard[3,22,23]. Postnatal SGA was defined as birth weight < p10, based on the Dutch sex- and gestational-age specific prescriptive Hoftiezer birth-weight chart[25], while normal birth weight (no SGA at birth) was defined as a birth weight ≥ p10.

Growth-trajectory measurements

In the ultrasound subanalysis, third-trimester slowing of growth was defined, for fetuses of any size centile, using two different kinds of growth-trajectory measurement. First, it was defined as AC or EFW crossing > 20 or > 50 centiles; i.e. a decline of > 20 centiles or a decline of > 50 centiles between the 28–30-week (T1) and the 34–36-week (T2) ultrasound assessments (AC crossing > 20 centiles, EFW crossing > 20 centiles, AC crossing > 50 centiles, EFW crossing > 50 centiles)[15,17]. Second, ACGV, based on the change in the gestational-age-adjusted *Z*-score, was calculated as follows. Difference scores were calculated as: (AC (in mm) of T2 minus AC (in mm) of T1) divided by (GA (in days) of T2 minus GA (in days) of T1). *Z*-scores were then calculated. Slow ACGV was defined by the lowest decile of the difference scores from the *Z*-score distribution (ACGV < 10%)[9]. In addition to calculating growth-trajectory measurements for fetuses of all size centiles, we also combined AC crossing > 20 centiles and ACGV < 10% with SGA fetus with EFW < p10 (i.e. EFW < p10 and AC crossing > 20 centiles; EFW < p10 and ACGV < 10%).

Outcomes

SAPO was defined as a dichotomous composite measure of 12 adverse perinatal outcomes occurring up to 7 days after birth: perinatal death, between 28 weeks' gestation and 7 days after birth; 5-min Apgar score < 4; asphyxia; impaired consciousness (decreased response to pain, stupor or coma); neonatal seizures; assisted ventilation > 24 h; septicemia; meningitis; bronchopulmonary dysplasia; intraventricular hemorrhage; cystic periventricular leukomalacia; and/or necrotizing enterocolitis[17]. Additionally, asphyxia, defined as cord-blood arterial base excess of < −12, was used as a separate outcome, as it is specifically associated with FGR[26]. Secondary outcomes comprised peripartum obstetric interventions, including induction of labor (IOL), Cesarean section and medically indicated preterm delivery (i.e. IOL or prelabor Cesarean section before onset of labor, before 37 weeks' gestation).

Covariates

Potential confounders were selected *a priori*, based on previous studies describing the association between these factors and both SGA and perinatal and peripartum outcomes[1,27], and included maternal age, parity, educational level, ethnicity, relationship status (committed relationship), employment status (paid job), prepregnancy body mass index (BMI), smoking in pregnancy and fetal sex[20]. Information on these potential confounders was collected at enrolment using questionnaires filled out by the women's midwives[20]. Maternal prepregnancy BMI was calculated as maternal weight (in kg)/maternal height (in m^2). Ethnicity was categorized into Dutch, other Western and non-Western, according to the classification of the Dutch Central Bureau of Statistics at the time of the IRIS study[28]. Relationship status and employment status were dichotomized into yes/no. Smoking in pregnancy was defined as smoking at any time from conception until inclusion in the study (including if the woman had stopped smoking in the first trimester) and dichotomized into yes/no[29].

Analyses

For the analyses of the total sample, the study population was divided into four groups, based on antenatal suspicion of SGA if AC < p10 at any of the third-trimester ultrasound examinations (based on the Verburg gestational-age specific fetal-growth chart[24]), or no suspicion if AC ≥ p10 at every third-trimester ultrasound examination or all SFH measurements were normal, and postnatal SGA defined as birth weight < p10 (based on the Dutch sex- and gestational-age specific Hoftiezer birth-weight chart[25]) or no SGA if birth weight ≥ p10. These four groups comprised: SGA neonates with SGA suspected prenatally (true positives), SGA neonates without SGA suspected prenatally (false negatives), non-SGA neonates with SGA suspected prenatally (false positives) and non-SGA neonates without suspected SGA (true negatives; reference group). Neonatal descriptive statistics were calculated for all groups (means, SDs, percentages). Differences in neonatal characteristics were compared using multilevel multivariable logistic regression (or Fisher's exact test in case of small numbers or empty cells) for categorical variables and multilevel multivariable linear regression for continuous variables. *Post-hoc* pairwise comparisons using Bonferroni correction were applied if the overall group variable was significant. Multilevel multivariable logistic regression analyses (or Fisher's exact test in case of small numbers) were used to compare perinatal and obstetric outcomes between the four groups. The analyses were corrected for the potential confounders described above. All models included a fixed effect for fetal SGA according to birth-weight SGA category and a random effect for midwifery practice to account for clustering of women within the 60 midwifery practices. In spite of our large sample size, the numbers of individual components of SAPO were too low to be compared between the four categories.

Based on the ultrasound subanalysis, associations between sonographic indicators of suspected fetal SGA (AC < p10; EFW < p10) and fetal slowing-growth-trajectory indicators (AC crossing > 20 centiles, EFW

crossing > 20 centiles, AC crossing centiles > 50 centiles, EFW crossing centiles > 50 centiles, ACGV < 10% and their combinations) and outcomes (SAPO, SGA birth weight combined with SAPO, asphyxia and obstetric intervention) were calculated using multilevel multivariable logistic regression analysis, or Fisher's exact test in case of small numbers. The analyses were corrected for the potential confounders described above. To evaluate whether combinations of sonographic indicators of suspected SGA and slowing fetal growth trajectories differed from indicators of SGA alone in predicting SAPO, we calculated areas under the receiver-operating-characteristics (ROC) curve (AUC) based on the predicted values of the respective models. Differences in AUCs were tested statistically only if the respective indicators predicted SAPO significantly. All analyses were performed using complete case analyses. A two-sided significance level of 5% was used. Sensitivity analyses were performed with data of the IRIS study intervention group only, in order to exclude women in the control group who received third-trimester ultrasound based on clinical indication alone. Analyses were conducted using the Statistical Package for Social Sciences version 26.0 for Windows (IBM SPSS Statistics for Windows, IBM Corp., Armonk, NY, USA) and Stata Statistical Software: Release 16 (StataCorp LLC, College Station, TX, USA).

RESULTS

Study population

Maternal or perinatal outcomes were available for 13 046 women. For 691 of these women, valid information on third-trimester SFH measurements was lacking, 492 had missing values for demographic or obstetric confounders and for 43 there were no data on birth weight, leaving 11 820 participants (91% of 13 046) included in one or more of our main analyses. The sample of the ultrasound subanalysis included only those low-risk women receiving either routine or clinically indicated third-trimester ultrasound examinations in primary care and for whom referral to secondary/tertiary obstetrician-led care had not (yet) been indicated. This subanalysis was based on 7989 women receiving at least one ultrasound examination and 5901 women receiving at least two (Figure 1).

Maternal characteristics of the total low-risk sample are presented in Table 1. In Table 2, neonatal characteristics are presented according to birth-weight classification. The overall incidence of SGA infant based on the Hoftiezer birth-weight chart was 8.9% (1050/11 820). On average, true positives were delivered 1 week earlier (at 38.8 weeks) in comparison to the other three groups (which had means ranging from 39.7 to 39.9 weeks). True positives also had the lowest mean birth weight (2581 g). The majority (68.1%) of neonates with birth weight ≥ p10 that were falsely suspected of being SGA during pregnancy (false positives) were female. In contrast, undetected SGA neonates (false negatives) were more likely to be male (53.6%). Perinatal deaths occurred only among infants without antenatal suspicion of SGA, i.e. in the false-negative ($n = 6$; 0.7%) and true-negative ($n = 16$; 0.2%) groups.

Association of SGA-screening classification with outcome (total sample)

Associations between antenatal suspicion of SGA by AC < p10 and SGA birth-weight classification (i.e. true positive, false negative, false positive and true negative) with the risk of SAPO and obstetric intervention are shown in Table 3. Overall, SGA infants, including both true positives (5.5%) and false negatives (3.7%), had an increased risk of SAPO compared with the true negatives (1.3%). Furthermore, compared with true negatives, mothers of SGA infants had increased rates of obstetric intervention. Neonates that were falsely suspected of SGA during pregnancy (false positives), did not differ significantly from the reference group of true negatives for all outcomes, including obstetric intervention.

Third-trimester ultrasound indicators and association with outcome (ultrasound subanalysis)

Table 4 shows the associations of third-trimester ultrasound indicators with SAPO, SGA with SAPO, asphyxia and obstetric interventions. The fetal biometry indicators AC < p10, EFW < p10 (approximately 2-fold) as well as EFW < p3 (approximately 3-fold) were moderately associated with an increased risk of SAPO. Also, the group with the lowest decile of ACGV (ACGV < 10%) had an approximately 2-fold increased risk of SAPO and was the only growth-trajectory indicator to statistically significantly predict SAPO, albeit moderately. All of these associations were stronger for the combination of SGA birth weight and SAPO. The indicator EFW < p10 combined with ACGV < 10% had the strongest associations

Table 1 Maternal characteristics of total sample ($n = 11\,820$)

Characteristic	*Value*
Nulliparous	5791 (49.0)
Maternal age (years)	30.8 ± 4.3
Ethnicity	
Dutch	8995 (76.1)
Other Western	1182 (10.0)
Non-Western	1643 (13.9)
Educational level	
Low	1135 (9.6)
Middle	4172 (35.3)
High	6513 (55.1)
Committed relationship with father	11 572 (97.9)
Employment status	
Paid job	10 019 (84.8)
Maternal prepregnancy BMI (kg/m^2)	23.8 ± 4.2
Smoking in pregnancy	1643 (13.9)
Hypertensive disease in pregnancy	934 (7.9)
Transfer to obstetric-led care in pregnancy	3050 (25.8)

Data are given as *n* (%) or mean ± SD. BMI, body mass index.

with SAPO (odds ratio (OR), 4.69 (95% CI, 1.99–11.07)) and with SGA birth weight with SAPO (OR, 29.72 (95% CI, 9.58–92.24)). However, ROC-curve analysis revealed no differences between EFW < p10 alone and the combination of EFW < p10 with ACGV < 10%, with respect to accuracy in predicting SAPO (AUC, 0.71 (95% CI, 0.65–0.76) *vs* 0.72 (95% CI, 0.67–0.77), $P = 0.51$), and the results were very similar regarding the accuracy in predicting SGA birth weight and SAPO (AUC, 0.81 (95% CI, 0.66–0.96) and 0.72 (95% CI, 0.56–0.87), respectively, $P = 0.22$). Neither AC crossing > 20 or > 50 centiles nor EFW crossing > 20 centiles was associated with SAPO or with SGA birth weight and SAPO, also when EFW < p10 was combined with AC crossing > 20 centiles. EFW crossing > 50 centiles did not occur. Repeating our analyses with asphyxia as a separate perinatal outcome revealed a similar but stronger pattern of results compared with SAPO.

Ultrasound indicators AC < p10, EFW < p10, EFW < p3, AC crossing > 20 centiles, ACGV < 10% and EFW < p10 with ACGV < 10%, were all associated with increased IOL and medically indicated preterm delivery. These associations were strongest for EFW < p3 and EFW < p10 combined with ACGV < 10%. EFW crossing > 20 centiles was associated with an almost 3-fold increased rate of medically indicated preterm delivery but was not associated with any of the other outcomes. Only EFW < p3 was associated with an increased rate of Cesarean section. AC crossing > 50 centiles was not associated with any of the obstetric interventions.

Sensitivity analyses

We repeated the analyses using data from the IRIS study intervention strategy only ($n = 6572$). When we limited the analyses of neonatal outcome according to

Table 2 Neonatal characteristics according to antenatal suspicion of small-for-gestational age (SGA)* and SGA birth-weight (BW) classification of total sample ($n = 11\,820$)

	SGA: BW < p10 (n = *1050*)		*BW ≥ p10* (n = *10 770*)		
Neonatal characteristic	*True positive: AC < p10* (n = *182*)	*False negative: SFH/AC ≥ p10* (n = *868*)	*False positive: AC < p10* (n = *182*)	*True negative: SFH/AC ≥ p10* (n = *10 588*)	P†
GA at delivery (weeks)	38.8 ± 1.9[b,c,d]	39.7 ± 1.7[a]	39.9 ± 1.2[a]	39.8 ± 1.4[a]	< 0.001
BW (g)	2581 ± 398[b,c,d]	2791 ± 320[a,c,d]	3285 ± 334[a,b,d]	3576 ± 448[a,b,c]	< 0.001
BW centile	4 ± 2.9[c,d]	5 ± 2.9[c,d]	33 ± 19.6[a,b,d]	56 ± 25.8[a,b,c]	< 0.001
Male gender	81/182 (44.5)[b,c,d]	465/868 (53.6)[a,c]	58/182 (31.9)[a,b,d]	5405/10 588 (51.0)[a,c]	< 0.001
Perinatal death	0/182 (0)[b,d]	6/868 (0.7)[a,c,d]	0/182 (0)[b,d]	16/10 588 (0.2)[a,b,c]	0.02‡

Data are given as mean ± SD or *n*/*N* (%). *Prenatal SGA based on abdominal circumference (AC) < 10th centile (p10). †Means and proportions were compared between groups with *post-hoc* pairwise comparisons using Bonferroni correction; superscript letters indicate means (or proportions in case of categorical variables) which differed significantly at ($P < 0.05$) from: [a]true positives; [b]false negatives; [c]false positives; and [d]true negatives. ‡Fisher's exact test because of zero cell counts. GA, gestational age; SFH, symphysis–fundus height.

Table 3 Severe adverse perinatal outcome (SAPO) and obstetric intervention according to antenatal suspicion of small-for-gestational age (SGA)* and SGA birth-weight (BW) classification of total sample ($n = 11\,820$)

	SGA: BW < p10 (n = *1050*)				*BW ≥ p10* (n = *10 770*)		
	True positive: AC < p10 (n = *182*)		*False negative: SFH/AC ≥ p10* (n = *868*)		*False positive: AC < p10* (n = *182*)		*True negative (ref): SFH/AC ≥ p10* (n = *10 588*)
	n/N *(%)*	*aOR (95% CI)*†	n/N *(%)*	*aOR (95% CI)*†	n/N *(%)*	*aOR (95% CI)*†	(n/N *(%)*)
Composite SAPO‡	10/182 (5.5)	4.46 (2.28–8.75)**	32/868 (3.7)	2.61 (1.74–3.89)**	1/182 (0.5)	0.45 (0.06–3.25)	138/10 588 (1.3)
Intervention							
IOL§	56/182 (30.8)	2.99 (2.15–4.17)**	157/864 (18.2)	1.38 (1.14–1.66)**	26/181 (14.4)	1.14 (0.74–1.73)	1383/10 541 (13.1)
CS	37/182 (20.3)	1.82 (1.25–2.66)**	146/868 (16.8)	1.27 (1.05–1.54)**	15/182 (8.2)	0.73 (0.43–1.25)	1251/10 588 (11.8)
PTD¶	15/164 (9.1)	2.67 (1.97–3.62)**	21/777 (2.7)	1.20 (1.03–1.40)**	0/166 (0)	0.95 (0.67–1.36)	73/9553 (0.8)

*Prenatal SGA based on abdominal circumference (AC) < 10th centile (p10). †All adjusted odds ratios (aOR) referent to true negatives; adjusted for maternal age, parity, educational level, ethnicity, committed relationship status, work status (paid job), prepregnancy body mass index, smoking in pregnancy and fetal sex. ‡SAPO was defined as a dichotomous composite measure of 12 adverse perinatal outcomes occurring up to 7 days after birth: perinatal death, between 28 weeks' gestation and 7 days after birth; 5-min Apgar score < 4; asphyxia; impaired consciousness (decreased response to pain, stupor or coma); neonatal seizures; assisted ventilation > 24 h; septicemia; meningitis; bronchopulmonary dysplasia; intraventricular hemorrhage; cystic periventricular leukomalacia; and/or necrotizing enterocolitis. §Total $n = 11\,768$ due to missing values on synthetic oxytocin or rupture of membranes. ¶Total $n = 10\,660$ due to missing values. **Statistically significant CI. CS, Cesarean section; IOL, induction of labor; ref, reference values; PTD, medically indicated preterm delivery; SFH, symphysis–fundus height.

Table 4 Associations of third-trimester ultrasound (US)-based screening indicators of suspected fetal growth restriction with severe adverse perinatal outcome (SAPO), neonatal small-for-gestational age (SGA) < 10th centile (p10) with SAPO, asphyxia and peripartum obstetric intervention

							Obstetric intervention					
	SAPO		*SGA + SAPO*		*Asphyxia*		*Induction of labor*		*Cesarean section*		*Medically indicated PTD*	
US indicator	n/N *(%)*	*OR (95% CI)*	n/N *(%)*	*OR (95% CI)*	n/N *(%)*	*OR (95% CI)*	n/N *(%)*	*OR (95% CI)*	n/N *(%)*	*OR (95% CI)*	n/N *(%)*	*OR (95% CI)*
AC < p10*	11/328 (3.4); 114/7659 (1.5)	2.30 (1.22–4.31)§	10/328 (3.0); 20/7659 (0.3)	12.01 (5.58–25.87)§	8/328 (2.4); 76/7659 (1.0)	2.89 (1.35–6.15)§	76/327 (23.2); 1120/7626 (14.7)	1.76 (1.35–2.29)§	51/328 (15.5); 1026/7659 (13.4)	1.19 (0.88–1.62)	14/296 (4.7); 63/6834 (0.9)	5.36 (2.96–9.67)§
EFW < p10*	15/525 (2.8); 110/7459 (1.5)	1.95 (1.13–3.38)§	14/528 (2.7); 16/7459 (0.2)	12.67 (6.15–26.10)§	12/528 (2.3); 72/7459 (1.0)	2.58 (1.18–5.60)§	115/525 (21.9); 1081/7428 (14.6)	1.65 (1.33–2.05)§	78/528 (14.8); 999/7459 (13.4)	1.12 (0.87–1.44)	21/480 (4.4); 56/6649 (0.8)	5.39 (3.23–8.97)§
EFW < p3†	4/78 (5.1); 121/7909 (1.5)	FE 0.03§	4/78 (5.1); 26/7909 (0.3)	FE < 0.001§	4/78 (5.1); 80/7909 (1.0)	FE 0.01§	29/78 (37.2); 1167/7875 (14.8)	3.62 (2.24–5.86)§	22/78 (28.2); 1055/7909 (13.3)	2.21 (1.33–3.69)§	8/70 (11.4); 69/7059 (1.0)	10.94 (4.81–24.90)§
AC crossing > 20 centiles*	10/661 (1.5); 58/5240 (1.1)	1.37 (0.70–2.70)	1/658 (0.2); 13/5218 (0.2)	FE 1.00	7/661 (1.1); 44/5540 (0.8)	1.10 (0.53–2.32)	118/658 (17.9); 755/7217 (14.5)	1.29 (1.04–1.60)§	89/661 (13.5); 647/5240 (12.3)	1.11 (0.87–1.40)	7/598 (1.2); 19/4707 (0.4)	2.92 (1.22–6.98)§
AC crossing > 50 centiles*	2/47 (4.3); 66/5805 (1.1)	FE 0.103	0/47 (0.0); 14/5780 (0.2)	FE 1.00	2/47 (4.3); 49/5805 (0.8)	FE 0.06	8/47 (17.0); 858/5779 (14.8)	1.41 (0.69–2.89)	11/47 (23.4); 720/5805 (12.4)	1.97 (0.99–3.93)	1/38 (2.6); 25/5223 (0.5)	FE 1.72
EFW crossing > 20 centiles*	13/840 (1.4); 53/4354 (1.2)	1.29 (0.68–2.43)	1/13 (0.1); 12/4354 (0.3)	FE 0.70	9/840 (1.1); 38/4354 (0.9)	1.10 (0.53–2.32)	127/835 (15.6); 616/4339 (14.2)	1.11 (0.90–1.36)	106/840 (12.6); 552/4354 (12.7)	0.99 (0.80–1.24)	10/758 (1.2); 19/3903 (0.5)	2.89 (1.27–6.56)§
ACGV < 10%*	13/590 (2.2); 55/5311 (1.0)	2.15 (1.17–3.97)§	5/586 (0.9); 9/5290 (0.2)	5.05 (1.69–15.12)§	11/590 (1.9); 40/5311 (0.8)	2.53 (1.27–5.03)§	114/587 (19.3); 759/5288 (14.4)	1.44 (1.16–1.79)§	71/590 (12.0); 665/5311 (12.8)	0.96 (0.74–1.24)	8/538 (1.5); 18/4767 (0.4)	3.98 (1.72–9.20)§
EFW < p10 and AC crossing > 20 centiles‡	2/99 (3.0); 64/5522 (1.2)	FE 0.33	1/98 (1.0); 12/5499 (0.2)	FE 0.21	2/99 (2.0); 47/5522 (0.9)	FE 0.63	21/99 (21.2); 806/5499 (14.7)	1.57 (0.96–2.55)	16/99 (16.2); 686/5522 (12.4)	1.36 (0.79–2.33)	4/90 (4.4); 22/4966 (0.4)	FE 0.01§
EFW < p10 and ACGV < 10%‡	6/122 (5.0); 60/5499 (1.1)	4.69 (1.99–11.07)§	5/120 (4.2); 8/5477 (0.1)	29.72 (9.58–92.24)§ FE < 0.001§	5/122 (4.2); 44/5499 (0.8)	5.43 (2.03–14.52)§ FE 0.04§	38/122 (31.1); 789/5476 (14.4)	2.68 (1.82–3.97)§	15/122 (12.3); 687/5499 (12.5)	1.02 (0.57–1.70)	5/114 (4.4); 21/4942 (0.4)	10.75 (3.98–29.03)§ FE < 0.001§

Data in *n*/*N* columns are *n* with outcome/*N* with US parameter < threshold; *n* with outcome/*N* with US parameter ≥ threshold. Population values differ for some US indicators due to missing values (see also Figure 1). SAPO was defined as a dichotomous composite measure of 12 adverse perinatal outcomes occurring up to 7 days after birth: perinatal death, between 28 weeks' gestation and 7 days after birth; 5-min Apgar score < 4; asphyxia; impaired consciousness (decreased response to pain, stupor or coma); neonatal seizures; assisted ventilation > 24 h; septicemia; meningitis; bronchopulmonary dysplasia; intraventricular hemorrhage; cystic periventricular leukomalacia; and/or necrotizing enterocolitis. For data in odds ratios (OR) columns, if 25% of expected cell counts were < 5 but *n* per cell was ≥ 5, both OR with 95% CI and *P*-value of two-sided Fisher's exact test (FE) are reported. If 25% of expected cell counts were < 5 and *n* per cell was < 5, only *P*-values of two-sided FE are reported. Centile crossing was calculated between 28–30-week and 34–36-week US assessments. Analyses with EFW crossing > 50 percentiles were not carried out, as there were zero cases. *ORs for AC < p10; EFW < p10; ACGV < 10%; AC/EFW crossing > 20 centiles and AC crossing > 50 centiles are referent to fetuses with, respectively, AC/EFW ≥ p10 or those with ACGV ≥ 10% or without AC/EFW crossing > 20 centiles, or without AC crossing > 50 centiles. †ORs for EFW < p3 are referent to fetuses with EFW ≥ p3. ‡ORs for EFW < p10 combined with AC crossing > 20 centiles or with ACGV <10% are referent to infants with EFW ≥ p10 and/or EFW < p10 without AC crossing > 20 centiles/ACGV < 10%. §Statistically significant. AC, abdominal circumference; ACGV, abdominal circumference growth-velocity *Z*-score; EFW, estimated fetal weight; p3, 3rd centile; Medically indicated PTD, preterm delivery following induction of labor or Cesarean section before onset of labor, before 37 weeks' gestation.

prenatal suspicion of SGA and SGA status at birth to the intervention group (Table S1), we found an increased percentage of SAPO (OR, 6.11 (95% CI, 2.79–13.40)) and medically indicated preterm delivery (OR, 2.68 (95% CI, 1.84–3.89)) only in the true-positive group and no longer in the false-negative group. In contrast, the incidence of CS among SGA infants (i.e. both true positives and false negatives) was no longer increased in comparison to the true negatives. All other associations were comparable. Furthermore, sensitivity analysis of the ultrasound subanalysis in the intervention strategy arm revealed overall patterns of associations between ultrasound indicators and the outcomes SAPO and obstetric interventions that were similar to those of the complete analysis (Table S2). Again, ACGV < 10% was the only growth-trajectory-based parameter to be associated with SAPO (OR, 2.25 (95% CI, 1.11–4.55) and with higher rates of SGA at birth combined with SAPO (*P*-value from Fisher's exact test (FE) = 0.01). Moreover, associations were found of EFW < p10 and ACGV < 10% with SAPO (OR, 6.79 (95% CI, 2.50–18.38)) and of SGA at birth with SAPO (FE = 0.001). However, AC crossing > 50 centiles was now associated with higher rates of asphyxia (FE = 0.048).

DISCUSSION

Main findings

SGA at birth, with or without antenatal suspicion of SGA (true positives and false negatives), was associated with a higher risk of SAPO and obstetric interventions, including IOL, Cesarean section and medically indicated preterm delivery. We did not find higher rates of obstetric intervention in neonates with birth weight ≥ p10 which had been falsely suspected of SGA during pregnancy (false positives). Furthermore, we found that the growth-trajectory measurement ACGV < 10% alone was moderately associated with an increased risk of SAPO and of neonatal SGA with SAPO. Interestingly, EFW < p10 alone and the combination of EFW < p10 and ACGV < 10% performed equally well in predicting SAPO.

Interpretation

Although all SGA infants in general had higher rates of SAPO and obstetric intervention, we found that the lowest mean GA at delivery, highest rates of obstetric intervention and strongest association with SAPO were among those which had been suspected prenatally, i.e. the true positives. Comparably, previous work showed that lower GA at the time of FGR diagnosis was strongly associated with a reduced probability of live birth or survival[30]. However, interestingly, in contrast with earlier findings, the birth-weight centiles of true positives and false negatives were comparable[13]. Presumably, growth-restricted fetuses, rather than those with SGA only, were more likely to be detected due to increased sonographic surveillance related to other risk factors, such as hypertension or decreased fetal movements, and, subsequently, interventions were performed more frequently to prevent severe outcomes such as mortality and asphyxia[31]. This is consistent with earlier research which showed that prenatally detected SGA infants display more severe outcomes than do prenatally undetected SGA infants[10]. Nevertheless, in absolute numbers, the vast majority of SAPO occurred among neonates with a birth weight ≥ p10[32].

In contrast to previous findings[13], we did not find a lower mean GA, or increased rates of IOL and/or medically indicated preterm delivery in false positives. According to the IRIS study protocol, in case of mild fetal SGA (> p5 and < p10) combined with normal Doppler umbilical artery and middle cerebral artery pulstaility indices and amniotic fluid index, the obstetric-care professional could opt for expectant management of labor and/or referral of women back to midwife-led care[17]. We speculate that these scenarios occurred more frequently among suspected SGA fetuses eventually reaching a birth weight ≥ p10 compared with those that did not. This also suggests that, in case of sonographic suspicion of SGA alone, obstetric intervention might be avoided when additional clinical parameters are taken into account. Future studies should address this, as over-medicalization can lead to iatrogenic harm and increased healthcare costs[33–37].

In line with theoretical work[15,17] and a previous population-based study by Sovio *et al.*[9], we found some evidence that the detection of FGR in low-risk populations may be improved by the use of sonographic measures of fetal-growth trajectories. More specifically, we observed that the third-trimester *Z*-score-based indicator, ACGV < 10%, which represents the proportional change in fetal growth velocity, was associated with SAPO, but AC and EFW crossing > 20 and AC crossing > 50 centiles were not. In addition, AC crossing > 20 centiles was associated with increased rates of IOL. One could speculate that AC crossing > 20 centiles helped in identifying fetuses at risk of SAPO and, consequently, SAPO was prevented by early IOL. However, in the IRIS trial, in which fetal AC crossing > 20 centiles was an indication for further diagnostic tests, enabling timely obstetric management, we did not find a reduction of SAPO in the routine ultrasound intervention strategy, in which AC crossing > 20 centiles was highly prevalent[19]. Moreover, ACGV < 10% was also associated with increased rates of IOL, but this did not lead to prevention of SAPO. One problem with using crossing centiles in comparison to ACGV < 10% is that crossing > 20 or > 50 centiles reflects a much larger relative drop in centiles among small fetuses compared with larger ones. Therefore, it is more likely that using this indicator in low-risk populations might lead to higher rates of IOL based on false-positive suspicion of FGR in fetuses ≥ p10. Another problem is that using crossing centiles excludes fetuses towards the bottom of the growth chart, because, by definition, fetuses already below p20 or p50 cannot drop > 20 or > 50 centiles, respectively. Re-evaluation is essential, as using slowing growth measurements to screen for FGR was suggested in a previous Dutch Delphi study, and is currently used in

practice[3,17]. In the sensitivity analyses, we found that AC crossing > 50 centiles was associated with higher rates of asphyxia. However, this analysis was underpowered due to small cell counts and should be replicated in clinical samples, in which this approach might be more relevant.

In contrast to the findings of Sovio *et al.*[9], ACGV < 10% alone was associated with SAPO, albeit modestly. However, we did not find evidence that adding ACGV < 10% to EFW < p10 optimizes the detection of fetuses at risk of SAPO in a low-risk population. Therefore, large-scale replication studies are needed to examine further whether the addition of (recently developed) indicators of fetal-growth trajectories can improve the differentiation between fetuses with and those without pathology[38,39].

Strengths and limitations

Our study has several strengths. We used data from a large-scale nationwide trial, with reliable and extensive prospective data collection, enabling us to adjust for multiple confounders. Additionally, the SAPO data were collected by initial selection of potential cases using the national Dutch perinatal registry data and subsequent reliable data extraction from hospital files[19]. Our study also had limitations. As we classified ethnicity into three categories, we could not adjust for different rates of certain perinatal outcomes among various ethnic groups within these categories. Also, the various components of SAPO were probably not caused solely by FGR. However, when analyzing asphyxia, which is a known consequence of FGR, separately, we observed a very similar pattern of results[40]. Nevertheless, development of more objective criteria for diagnosing FGR (e.g. histological evaluation of the placenta) and identification of outcomes that distinguish better between adverse consequences of the treatment and those of the disease are needed[26]. Lastly, for analyses of associations of ultrasound parameters with SAPO and obstetric intervention, we had to exclude women in the usual-care strategy who did not have third-trimester ultrasound examinations, due to reassuring SFH measurements. This may have led to a less healthy group of women from the control strategy arm entering the subanalysis. However, for all women in the subanalysis who had received at least two third-trimester ultrasound examinations, the selection process ensured that referral to secondary obstetrician-led care had not (yet) been indicated. More importantly, the sensitivity analyses based on the intervention strategy (routine ultrasonography) only, showed similar patterns of findings. Overall, we believe the findings may be generalized to low-risk populations.

Conclusion

Infants with birth weight ≥ p10 falsely suspected of being SGA during pregnancy (false positives) did not have higher rates of obstetric intervention, indicating no overtreatment, compared with true negatives. For the detection of abnormal growth among fetuses of all size centiles, the added value of ACGV < 10% alone is apparently limited in a low-risk population. Moreover, based on our findings, incorporating third-trimester AC or EFW crossing > 20 and AC > 50 centiles alone cannot be recommended as an indicator of abnormal fetal growth in populations remaining at low risk throughout pregnancy.

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REFERENCES

1. Royal College of Obstetricians & Gynaecologists. The investigation and management of the small-for-gestational-age fetus [Internet]. Green-top Guideline No. 31, 2014. https://www.rcog.org.uk/globalassets/documents/guidelines/gtg_31.pdf.
2. Barker DJ. Adult consequences of fetal growth restriction. *Clin Obstet Gynecol* 2006; **49**: 270–283.
3. Nederlandse Vereniging voor Obstetrie en Gynacologie. NVOG richtlijn Foetale groeirestrictie (FGR). 2017.
4. ACOG Practice Bulletin No. 204 Summary: Fetal Growth Restriction. *Obstet Gynecol* 2019; **133**: 390–392.
5. Bruin C, Damhuis S, Gordijn S, Ganzevoort W. Evaluation and Management of Suspected Fetal Growth Restriction. *Obstet Gynecol Clin North Am* 2021; **48**: 371–385.
6. Figueras F, Caradeux J, Crispi F, Eixarch E, Peguero A, Gratacos E. Diagnosis and surveillance of late-onset fetal growth restriction. *Am J Obstet Gynecol* 2018; **218**(2S): S790–S802.e1.
7. McCowan L, Horgan RP. Risk factors for small for gestational age infants. *Best Pract Res Clin Obstet Gynaecol* 2009; **23**: 779–793.
8. McIntire DD, Bloom SL, Casey BM, Leveno KJ. Birth weight in relation to morbidity and mortality among newborn infants. *N Engl J Med* 1999; **340**: 1234–1238.
9. Sovio U, White IR, Dacey A, Pasupathy D, Smith GCS. Screening for fetal growth restriction with universal third trimester ultrasonography in nulliparous women in the Pregnancy Outcome Prediction (POP) study: a prospective cohort study. *Lancet* 2015; **386**(10008): 2089–2097.
10. Andreasen LA, Tabor A, Norgaard LN, Rode L, Gerds TA, Tolsgaard MG. Detection of growth-restricted fetuses during pregnancy is associated with fewer intrauterine deaths but increased adverse childhood outcomes: an observational study. *BJOG* 2021; **128**: 77–85.
11. Gardosi J, Madurasinghe V, Williams M, Malik A, Francis A. Maternal and fetal risk factors for stillbirth: population based study. *BMJ* 2013; **346**: f108.
12. Nohuz E, Riviere O, Coste K, Vendittelli F. Prenatal identification of small-for-gestational age and risk of neonatal morbidity and stillbirth. *Ultrasound Obstet Gynecol* 2020; **55**: 621–628.
13. Monier I, Blondel B, Ego A, Kaminiski M, Goffinet F, Zeitlin J. Poor effectiveness of antenatal detection of fetal growth restriction and consequences for obstetric management and neonatal outcomes: a French national study. *BJOG* 2015; **122**: 518–527.
14. MacDonald TM, Hui L, Tong S, Robinson AJ, Dane KM, Middleton AL, Walker SP. Reduced growth velocity across the third trimester is associated with placental insufficiency in fetuses born at a normal birthweight: a prospective cohort study. *BMC Med* 2017; **15**: 164.
15. Gordijn SJ, Beune IM, Thilaganathan B, Papageorghiou A, Baschat AA, Baker PN, Silver RM, Wynia K, Ganzevoort W. Consensus definition of fetal growth restriction: a Delphi procedure. *Ultrasound Obstet Gynecol* 2016; **48**: 333–339.
16. Melamed N, Baschat A, Yinon Y, Athanasiadis A, Mecacci F, Figueras F, Berghella V, Nazareth A, Tahlak M, McIntyre HD, Da Silva Costa F, Kihara AB, Hadar E, McAuliffe F, Hanson M, Ma RC, Gooden R, Sheiner E, Kapur A, Divakar H, Ayres-de-Campos D, Hiersch L, Poon LC, Kingdom J, Romero R, Hod M. FIGO (International Federation of Gynecology and Obstetrics) initiative on fetal growth: best practice advice for screening, diagnosis, and management of fetal growth restriction. *Int J Gynaecol Obstet* 2021; **152** (Suppl 1): 3–57.

17. Verfaille V, de Jonge A, Mokkink L, Westerneng M, van der Horst H, Jellema P, Franx A, IRIS study group. Multidisciplinary consensus on screening for, diagnosis and management of fetal growth restriction in the Netherlands. *BMC Pregnancy Childbirth* 2017; **17**: 353.
18. McCowan LM, Figueras F, Anderson NH. Evidence-based national guidelines for the management of suspected fetal growth restriction: comparison, consensus, and controversy. *Am J Obstet Gynecol* 2018; **218**(2S): S855–S868.
19. Henrichs J, Verfaille V, Jellema P, Viester L, Pajkrt E, Wilschut J, van der Horst HE, Franx A, de Jonge A; IRIS study group. Effectiveness of routine third trimester ultrasonography to reduce adverse perinatal outcomes in low risk pregnancy (the IRIS study): nationwide, pragmatic, multicentre, stepped wedge cluster randomised trial. *BMJ* 2019; **367**: l5517.
20. Henrichs J, Verfaille V, Viester L, Westerneng M, Molewijk B, Franx A, van der Horst H, Bosmans JE, de Jonge A, Jellema P, IRIS study group. Effectiveness and cost-effectiveness of routine third trimester ultrasound screening for intrauterine growth restriction: study protocol of a nationwide stepped wedge cluster-randomized trial in The Netherlands (The IRIS Study). *BMC Pregnancy Childbirth* 2016; **16**: 310.
21. Mannien J, Klomp T, Wiegers T, Pereboom M, Brug J, de Jonge A, van der Meijde M, Hutton E, Schellevis F, Spelten E. Evaluation of primary care midwifery in The Netherlands: design and rationale of a dynamic cohort study (DELIVER). *BMC Health Serv Res* 2012; **12**: 69.
22. Hadlock FP, Deter RL, Harrist RB, Park SK. Computer assisted analysis of fetal age in the third trimester using multiple fetal growth parameters. *J Clin Ultrasound* 1983; **11**: 313–316.
23. Hadlock FP, Harrist RB, Shah Y, Park SK. The femur length/head circumference relation in obstetric sonography. *J Ultrasound Med* 1984; **3**: 439–442.
24. Verburg BO, Steegers EA, De Ridder M, Snijders RJ, Smith E, Hofman A, Moll HA, Jaddoe VW, Witteman JC. New charts for ultrasound dating of pregnancy and assessment of fetal growth: longitudinal data from a population-based cohort study. *Ultrasound Obstet Gynecol* 2008; **31**: 388–396.
25. Hoftiezer L, Hof MHP, Dijs-Elsinga J, Hogeveen M, Hukkelhoven C, van Lingen RA. From population reference to national standard: new and improved birthweight charts. *Am J Obstet Gynecol* 2019; **220**: 383.e1–17.
26. Gordijn SJ, Ganzevoort W. Search for the best prediction model, definition and growth charts for fetal growth restriction using a composite of adverse perinatal outcomes: a catch-22? *Ultrasound Obstet Gynecol* 2022; **60**: 305–306.
27. Sovio U, Moraitis AA, Wong HS, Smith GCS. Universal *vs* selective ultrasonography to screen for large-for-gestational-age infants and associated morbidity. *Ultrasound Obstet Gynecol* 2018; **51**: 783–791.
28. Kooijman MN, Kruithof CJ, van Duijn CM, Duijts L, Franco OH, van IMH, de Jongste JC, Klaver CC, van der Lugt A, Mackenbach JP, Moll HA, Peeters RP, Raat H, Rings EH, Rivadeneira F, van der Schroeff MP, Steegers EA, Tiemeier H, Uitterlinden AG, Verhulst FC, Wolvius E, Felix JF, Jaddoe VW. The Generation R Study: design and cohort update 2017. *Eur J Epidemiol* 2016; **31**: 1243–1264.
29. Xaverius PK, O'Reilly Z, Li A, Flick LH, Arnold LD. Smoking Cessation and Pregnancy: Timing of Cessation Reduces or Eliminates the Effect on Low Birth Weight. *Matern Child Health J* 2019; **23**: 1434–1441.
30. Monier I, Ancel PY, Ego A, Guellec I, Jarreau PH, Kaminski M, Goffinet F, Zeitlin J; EPIPAGE 2 Study Group. Gestational age at diagnosis of early-onset fetal growth restriction and impact on management and survival: a population-based cohort study. *BJOG* 2017; **124**: 1899–1906.
31. Verlijsdonk JW, Winkens B, Boers K, Scherjon S, Roumen F. Suspected versus non-suspected small-for-gestational age fetuses at term: perinatal outcomes. *J Matern Fetal Neonatal Med* 2012; **25**: 938–943.
32. Mendez-Figueroa H, Truong VT, Pedroza C, Khan AM, Chauhan SP. Small-for-gestational-age infants among uncomplicated pregnancies at term: a secondary analysis of 9 Maternal-Fetal Medicine Units Network studies. *Am J Obstet Gynecol* 2016; **215**: 628.e1–7.
33. Seijmonsbergen-Schermers AE, Scherjon S, de Jonge A. Induction of labour should be offered to all women at term: AGAINST: Induction of labour should not be offered to all women at term: first, do no harm. *BJOG* 2019; **126**: 1599.
34. Miller S, Abalos E, Chamillard M, Ciapponi A, Colaci D, Comande D, Diaz V, Geller S, Hanson C, Langer A, Manuelli V, Millar K, Morhason-Bello I, Castro CP, Pileggi VN, Robinson N, Skaer M, Souza JP, Vogel JP, Althabe F. Beyond too little, too late and too much, too soon: a pathway towards evidence-based, respectful maternity care worldwide. *Lancet* 2016; **388**: 2176–2192.
35. Bentley JP, Roberts CL, Bowen JR, Martin AJ, Morris JM, Nassar N. Planned Birth Before 39 Weeks and Child Development: A Population-Based Study. *Pediatrics* 2016; **138**: e20162002.
36. Teitler JO, Plaza R, Hegyi T, Kruse L, Reichman NE. Elective Deliveries and Neonatal Outcomes in Full-Term Pregnancies. *Am J Epidemiol* 2019; **188**: 674–683.
37. Noble KG, Fifer WP, Rauh VA, Nomura Y, Andrews HF. Academic achievement varies with gestational age among children born at term. *Pediatrics* 2012; **130**: e257–264.
38. Hugh O, Gardosi J. Fetal weight projection model to define growth velocity and validation against pregnancy outcome in a cohort of serially scanned pregnancies. *Ultrasound Obstet Gynecol* 2022; **60**: 86–95.
39. Grantz KL, Grewal J, Kim S, Grobman WA, Newman RB, Owen J, Sciscione A, Skupski D, Chien EK, Wing DA, Wapner RJ, Ranzini AC, Nageotte MP, Craigo S, Hinkle SN, D'Alton ME, He D, Tekola-Ayele F, Hediger ML, Buck Louis GM, Zhang C, Albert PS. Unified Standard for Fetal Growth Velocity: the Eunice Kennedy Shriver National Institute of Child Health and Human Development Fetal Growth Studies. *Am J Obstet Gynecol* 2022; **227**: 916–922.e1.
40. Malhotra A, Allison BJ, Castillo-Melendez M, Jenkin G, Polglase GR, Miller SL. Neonatal Morbidities of Fetal Growth Restriction: Pathophysiology and Impact. *Front Endocrinol (Lausanne)* 2019; **10**: 55.

SUPPORTING INFORMATION ON THE INTERNET

The following supporting information may be found in the online version of this article:

Table S1 Sensitivity analyses of Table 3 (intervention group only)

Table S2 Sensitivity analyses of Table 4 (intervention group only)