Predictive accuracy of the Southwest Thames Obstetric Research Collaborative (STORK) chorionicity-specific twin growth charts for stillbirth: a validation study

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ABSTRACT

Objective: Twin pregnancy is associated with 2-3 fold increased risk of stillbirth compared to singletons. Despite the fact that the growth pattern has been shown to differ in twins compared to singletons, it is controversial whether twin-specific growth charts should be routinely used. A major goal of prenatal ultrasound is to identify fetuses suffering from growth restriction at risk of stillbirth. The main aim of this study was to compare the performance of chorionicity-specific twin charts with singleton charts, both customized and non-customized, in the antenatal prediction of small-for-gestational age (SGA) stillborn and liveborn fetuses.

Methods: This was a multicenter cohort study analyzing data from the Southwest Thames Obstetric Research Collaborative (STORK) multiple pregnancy cohort (2000-2009) and a second cohort of twin pregnancies at St. George's University Hospital (SGH) (2011-2016). The former cohort was used to compare the performance of the twin and non-customized (Poon) singleton charts. The latter cohort was used to compare the performance of the twin, customized (Gestation Related Optimal Weight [GROW]) and non-customized (Poon) singleton charts. The primary outcome was the prediction of SGA cases that were stillborn and liveborn in twin pregnancies. The estimated fetal weight (EFW) available from the last scan (24 weeks' gestation and onwards) before delivery or demise was used to classify the fetuses as SGA (<10th centile, <3rd centile) or appropriate for gestational age. The proportions of SGA stillbirths and SGA livebirths predicted were calculated using the three different charts.

Results: The STORK cohort consisted of 1850 dichorionic (DC) and 300 monochorionic (MC) twin pregnancies. The SGH cohort consisted of 579 DC and 180 MC twin pregnancies. The stillbirth rate in the STORK and SGH cohorts were 1.1% and 1.3%, respectively. In those liveborn in the STORK cohort, using a 10th centile cut-off to define SGA, the non-customized singleton chart identified a significantly greater proportion as SGA compared to the twin chart, regardless of chorionicity (p<0.001). However, there was no significant difference between the twin and the non-customized singleton charts in regards to in the proportion of stillbirth cases that were SGA (p=0.479).

In the SGH cohort, the non-customized singleton chart identified 8.5% of all liveborn fetuses as SGA (<10th centile) compared to 12.8% using the customized singleton chart and 7.1% using the twin chart (p=0.005 and p<0.001, respectively). However, there was no significant difference among the three charts in the proportion of stillbirths identified as SGA, regardless of chorionicity (p=0.999). Similar results were obtained when the third centile cut-off was used to define SGA.

Conclusions: Compared to the STORK chorionicity-specific twin charts, the customized or non-customized singleton charts identified more liveborn fetuses as SGA. However, the three charts identified a similar proportion of stillbirth SGA cases. Our preliminary results suggest that these twin charts could safely reduce unnecessary medical intervention in twin pregnancies. Further research on the topic is needed before clinical recommendations can be made.

INTRODUCTION

Twin pregnancy is a known risk factor for intrauterine fetal demise and intensive antenatal fetal surveillance is associated with a lower risk of stillbirth.[1-4] Close antenatal surveillance constitutes screening for growth abnormalities including, but not limited to, inter-twin weight discordance, selective fetal growth restriction (sFGR) and small-for-gestational age (SGA). Growth restricted fetuses are at increased risk of perinatal mortality and morbidity.[5,6] The management of these at-risk pregnancies can pose a challenge to clinicians, as iatrogenic preterm delivery is often required in order to avoid the risk of stillbirth.[7] Therefore, it is important to identify those pathological pregnancies which are truly at-risk of stillbirth, and would benefit from preterm delivery. It is equally important to distinguish the pregnancies which are not at risk of stillbirth, and thereby avoiding the risk of iatrogenic prematurity.

The proportion of twins identified as at-risk depends on the growth chart used. Until now, singleton charts have been used to screen for growth disorders in twin gestations. However, it has been reported in a number of studies that twin fetuses show diminished growth rates compared to singletons in the third trimester.[8] Near term, more than one third of all dichorionic (DC) twins are classified as SGA based on a singleton growth standard. This places a significant proportion of twin gestations at risk of intervention and perinatal morbidity associated with preterm delivery.[8-9]

The use of twin specific growth charts has been suggested in order to better identify fetuses at true risk of intrauterine compromise.[10-17] However, this suggestion has been criticized on the basis that the lower growth rate in twins might be due to relative placental insufficiency, which might be missed with the use of twin-specific charts, potentially increasing morbidity and mortality rates.[18] The importance of validation of twin charts has been emphasized, in the absence of which the use of established non-customized or customized singleton charts was suggested as an alternative.[19]

The main aim of this study was to compare the performance of chorionicity-specific twin charts with singleton charts, both customized and non-customized, in the antenatal prediction of small-for-gestational age (SGA) stillborn and liveborn fetuses

METHODS

This was a multicenter cohort study analyzing data from the Southwest Thames Obstetric Research Collaborative (STORK) multiple pregnancy cohort (2000-2009) and a second cohort of twin pregnancies at St George's University Hospital (SGH) (2011-2016). The pregnancies complicated by perinatal loss in the STORK database have been cross-checked against a national register of perinatal loss. The former cohort was used to compare the performance of the twin and non-customized (Poon) singleton charts.[10,11,20] The latter cohort was used to compare the performance of the twin, customized (Gestation Related Optimal Weight [GROW]) and non-customized (Poon) singleton charts.[20,21] Information on the maternal characteristics required for the estimation of customized singleton charts were available for the SGH cohort, but not the STORK cohort. Data on pregnancy outcomes were collected from the hospital maternity records.

The gestational age was calculated using the crown–rump length of the larger twin in the first trimester.[22] Pregnancies for which the first recorded ultrasound examination was performed after 14 weeks' gestation were excluded from the analysis in order to ensure the accuracy of gestational age measurement for the included cases. Given their rarity and the very high rate of complications, monochorionic monoamniotic pregnancies were excluded from the analysis. The assignment of chorionicity was based on findings at ultrasound examination at 11–14 weeks, where available; otherwise the findings from later scans were used.[23] Pregnancies in which the chorionicity and amnionicity were uncertain or inconsistent in the recorded examinations were excluded. Furthermore, pregnancies complicated by aneuploidy, major structural abnormalities or those undergoing termination were excluded.

The estimated fetal weight (EFW) was calculated using the Hadlock formula, which takes into account the biparietal diameter, head circumference, abdominal circumference and femur length.[24] EFW available from the last scan (24 weeks' gestation and onwards) before the delivery or the diagnosis of intrauterine demise were used to classify fetuses as SGA (<10th centile, <3rd centile) or appropriate for gestational age. There was no exclusion limit for the interval between the ultrasound scan and delivery or stillbirth. In view of the different diagnostic features reported in the literature for sFGR, we included an analysis for the three most commonly reported definitions (one twin with EFW less than the 10th centile; one twin with EFW less than the 3rd centile; EFW of one twin below the 10th centile with inter-twin EFW discordance of 25% or more).[7] Pre-specified cut-offs were also in accordance with internationally accepted definitions of SGA and FGR.[25]

Great care was taken to match the prenatal EFWs to the outcome of each individual fetus. As the main aim of the study was to investigate the performance of the charts in the antenatal detection of stillbirth and livebirth SGA fetuses, the matching of the antenatal EFW and birth outcomes was less problematic compared to if we were investigating the entire cohort. Intrauterine death (IUD) was diagnosed antenatally in almost all the cases in our cohort, and therefore it was possible to match the EFW for these pregnancies. In the twin pregnancies with two liveborn fetuses, the smaller twin was invariably identified prenatally as these pregnancies have frequent ultrasound scans. Another tool to match the EFW with the outcome at birth was the fetal sex, which is often described as per the policy of labeling twins throughout the gestation at each antenatal visit and matching this information with delivery information/outcomes.

The primary outcome was the stillborn and liveborn SGA cases which were detected as SGA according to the estimated fetal weight in twin pregnancies. The secondary outcomes were the detection of preterm birth and stillbirth cases using the three commonly used diagnosis criteria for sFGR. The results were reported separately for SGA less than the 10th centile and SGA less than the 3rd centile. The results were also reported separately for DC and monochorionic (MC) twin pregnancies. The Poon chart was used as a representative of non-customized singleton charts, as it was constructed using a population similar to ours. [20]

The STORK chorionicity-specific twin growth charts were developed as part of a study funded by the Twin and Multiple Birth Association (TAMBA) (UK Charity No: 1076478).

Statistical Analysis

Regression equations provided in individual studies were used to obtain the EFW centiles. The customized fetal weight centiles were calculated using the GROW software (v.6.7.8.1, The Perinatal Institute).[21] The proportion of all livebirths and stillbirths that were SGA, stratified according to chorionicity, were calculated. After constructing data matrices, group comparisons were made using the Fisher's exact test or McNemar's test, as appropriate. The accuracy values of each chart were calculated using the validation cohort. The p values less than 0.05 were considered statistically significant. The analysis was performed using R for Windows (Version 3.4.2, The R Foundation for Statistical Computing).[26]

RESULTS

The STORK cohort consisted of 1850 DC and 300 MC twin pregnancies. The SGH cohort consisted of 579 DC and 180 MC twin pregnancies. The overall stillbirth rate in the STORK and SGH cohorts were 1.1% (48 out of 4300 fetuses) and 1.3% (19 out of 1518 fetuses), respectively. Table 1 outlines the proportion of all liveborn and stillborn fetuses with EFW less than the 10^{th} and less than the 3^{rd} centile for gestational age in the STORK cohort. This analysis was performed on a per fetus basis. The non-customized singleton chart identified a significantly greater proportion of the liveborn fetuses as SGA (<10^{th} centile) compared to the twin charts (p<0.001). The observed differences between the non-customized singleton and twin charts were less for DC than MC twin pregnancies (EFW <10^{th} centile: 13.9% vs 11.9% in DC and 16.5% vs 9.9% in MC twin pregnancies, respectively) (Table 1). There was no significant difference in the proportion of stillbirth cases below the 10^{th} centile (54.8% vs 48.4%, p=0.479 in DC and 35.3% vs 35.3%, p=0.999 in MC twin pregnancies, respectively) (Table 1). Similar results were demonstrated for EFW less than the 3^{rd} centile (Table 1). The area under the curve (AUC) of estimated fetal weight for the prediction of stillbirth in the STORK cohort were 0.64 (95% CI: 0.54-0.74) and 0.68 (95% CI: 0.59-0.78) for singleton and chorionicity-specific twin charts, respectively. There was no statistically significant difference between charts (P=0.10, DeLong's test).

The incidence of stillbirth and preterm birth applying different sFGR definitions using singleton and twin charts in the STORK cohort can be seen in Table 2. This analysis was performed on a per pregnancy basis. Using the EFW <10^{th} centile of one twin definition of sFGR, there was no significant difference between the twin charts and the non-customized singleton chart in the incidence of IUD (13.0% twins vs 8.1% singleton chart, p=0.523) or preterm delivery <34 weeks' gestation (34.8% twins vs 25.8% singleton chart, p=0.394) in MC twin pregnancies (Table 2). However, in DC twins the twin charts performed better in predicting preterm delivery below 34 weeks (18.5% twins vs 11.8% singleton charts, p=0.032) (Table 2).

The twin[11], non-customized[20] and customized singleton charts[21] were compared in the SGH cohort (Table 3). There were significant differences among the three charts in the proportion of livebirths identified as SGA (defined as EFW <10^{th} centile) (Table 3). The non-customized singleton chart identified 8.5% of all liveborn fetuses as SGA compared to 12.8% using the customized singleton chart and 7.1% using the twin chart (p<0.001 and p=0.005, respectively). A similar pattern was noted when analyzing MC twins separately (10.6% vs 15.8% and 8.0%, p<0.001 and p=0.026, respectively). The difference between the charts was less marked for an EFW cut-off <3rd centile (3.9% vs 5.5% vs 3.4%, respectively) (p=0.004 for the comparison between the non-customized and customized singleton charts and p<0.001 for the comparison between the customized singleton and twin charts) (Table 3). However, despite markedly increased rates of SGA identified using the customized singleton chart, there were no significant differences in the proportion of stillbirths identified as SGA using the three charts, regardless of the cut-off value used for SGA or the chorionicity (Table 3). The accuracy of twin, non-customized and customized singleton charts for the prediction of stillbirth using 10th centile cut-off for SGA were 0.91 (0.87-0.94), 0.88 (95% CI: 0.85-0.91), 0.84 (0.79-0.87), respectively for MC twins and 0.93 (0.91-0.94), 0.92 (0.90-0.93), 0.87 (0.86-0.90) for DC twins. The AUC of estimated fetal weight for the prediction of stillbirth in the SGH cohort were 0.71 (95% CI: 0.57-0.84), 0.68 (95% CI: 0.53-0.83), 0.70 (95% CI: 0.57-0.84) for customized singleton, singleton and chorionicity-specific twin charts, respectively. There were no statistically significant differences between AUC values between charts (P>0.05 for all, DeLong's test).

The exact number of fetuses defined as SGA (whether stillborn or liveborn) was plotted as Venn diagrams (supplementary material).

DISCUSSION

Summary of main findings

The twin charts identified a smaller proportion of livebirths as SGA than either the non-customized or customized singleton charts. However, the three charts identified a similar proportion of stillbirths with SGA. Compared to the twin-specific charts, the customized singleton chart did not improve the detection of stillborn fetuses with SGA.

Clinical and research implications

Intensive surveillance is recommended for twin pregnancies due to their high risk nature.[7,27,28] However, twin pregnancies show a diminished growth rate starting from 30 weeks' gestation, and near term a third of all fetuses are classified as SGA using singleton charts.[8] The rationale behind the use of twin-specific charts is to tailor the growth charts to recognise this different growth rate in twins, so that fewer fetuses will be identified as SGA, thereby reducing unnecessary intervention. Concern has been expressed that this approach might classify a pathological growth trajectory as normal, whereas a singleton chart would not.[19] However, the notion of customizing growth charts according to pregnancy specific variables is not new.[21] In fact, empirical evidence suggests that customized charts offer a better means of monitoring compared to one size fits all approach.[29] On this basis, adjusting for major pregnancy specific variables (twin pregnancy, chorionicity) should in theory offer a similar benefit as adjusting for maternal height or ethnicity.[30] Our study suggests that twin-specific growth charts identify a significantly lower proportion of livebirths as SGA without any significant reduction in the detection of stillbirth. The antenatal labeling of SGA or sFGR in a twin pregnancy increases the risk of iatrogenic preterm birth, with its associated risk of disability secondary to prematurity. This suggests that these twin charts could safely reduce unnecessary medical intervention in twin pregnancies.

The management of twin pregnancies near term is controversial as most studies now show an increased risk of IUD with each additional week of prolonged gestation starting from 36-37 weeks' gestation.[31,32] Furthermore, twins show a reduction in weight gain trajectory starting from 30-32 weeks' gestation. However, avoiding unnecessary interventions is particularly important for twin pregnancies which are already at high risk of preterm delivery, both spontaneous and iatrogenic, which carries an increased burden not only of morbidity, but also financial.[33,34] Our study provides preliminary evidence supporting the safety of twin-specific growth charts and provides the basis for future large prospective multicenter trials.

Despite the proposed benefit of using customized singleton charts,[29] we found no benefit of customized or non-customized singleton charts over twin-specific charts in twin pregnancies. Despite a marked increase in pregnancies labeled as SGA using the customized charts, there were no significant differences among the three investigated growth charts in the detection of stillbirth SGA cases. This observation might be due to greater influence of the twin gestation and chorionicity on growth rate compared to the maternal factors.

Study strengths and limitations

The strengths of our study include the use of a large cohort of twin pregnancies and the use of contemporary growth charts. The selected charts were not in active clinical use in our population, thus reducing the possibility of intervention bias. The singleton chart used in our study is derived from a large cohort of singleton pregnancies followed up at a tertiary care center in the United Kingdom, which is similar to our population.

However, the number of stillbirth SGA cases was small, so the analysis for the prediction of stillbirth is likely to be underpowered. STORK charts were originally derived from the STORK cohort so the results we observed in this cohort are likely to overestimate the performance of these twin charts. However, this does not apply to the more recent SGH cohort included in our analysis. It should be also noted that the Poon and GROW charts were derived from birthweights whereas the STORK charts were derived from EFW.[11,20,21] We could not incorporate some of the most recent customized twin charts in our study[12,13] as some of the variables used in their customized models were not routinely recorded in the SGH cohort, so validation was not possible. Neither was it possible to test customized singleton growth charts in the STORK cohort as some of the required maternal variables were not available.

Doppler studies are important for the differentiation of pathological FGR from constitutional smallness (SGA).[25] Therefore, Doppler studies have been recommended as an important tool for the risk assessment of twin pregnancies, as outlined in the ISUOG guideline and a recent consensus article focusing on the management of sFGR.[7,35] We did not incorporate the Doppler variables in this study, as the main aim was to assess the performance of the STORK twin charts, and to compare them with other commonly used growth charts. Nevertheless, it is important to acknowledge that the difference in the performance among the various growth charts may be less obvious when the Doppler studies are included in the clinical assessment of these pregnancies.

Finally, we did not apply any restrictions on the time interval between the ultrasound scans and delivery, which is likely to reduce the predictive performance of the EFW, but this should apply equally to all the growth charts investigated.

Conclusion

Compared to the STORK chorionicity-specific twin charts, the customized or non-customized singleton charts identified more liveborn fetuses as SGA. However, the three charts identified a similar proportion of stillbirth SGA cases. This suggests that these twin charts could safely reduce unnecessary medical intervention in twin pregnancies. A large multicentre prospective cohort study is needed in order to compare the twin-specific, customized twin-specific, singleton and customized singleton charts.

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Supplementary Figures

Supplementary Figure 1. Venn diagram of liveborn small for gestational age (SGA; estimated fetal weight below the 10th centile) fetuses from either dichorionic or monochorionic twin pregnancies according to the growth charts by Poon (non-customized singleton), Stirrup (Twins) and GROW (customized singleton). Poon, Stirrup and GROW charts detected additional 23 (1.5%), 2 (0.1%) and 81 (5.4%) fetuses as SGA despite these fetuses being identified as approriate-for-gestational age by the other two charts.

Supplementary Figure 2. Venn diagram of liveborn small for gestational age (SGA; estimated fetal weight below the 10th centile) fetuses from monochorionic twin pregnancies according to the growth charts by Poon (non-customized singleton), Stirrup (Twins) and GROW (customized singleton). Poon, Stirrup and GROW charts detected additional 3 (0.9%), 0 (0.0%) and 20 (5.7%) fetuses as SGA despite these fetuses being identified as approriate-for-gestational age by the other two charts.

Supplementary Figure 3. Venn diagram of liveborn small for gestational age (SGA; estimated fetal weight below the 10th centile) fetuses from dichorionic twin pregnancies according to the growth charts by Poon (non-customized singleton), Stirrup (Twins) and GROW (customized singleton). Poon, Stirrup and GROW charts detected additional 20 (1.7%), 2 (0.2%) and 61 (5.3%) fetuses as SGA despite these fetuses being identified as approriate-for-gestational age by the other two charts.

Supplementary Figure 4. Venn diagram of liveborn small for gestational age (SGA; estimated fetal weight below the 3rd centile) fetuses from either dichorionic or monochorionic twin pregnancies according to the growth charts by Poon (non-customized singleton), Stirrup (Twins) and GROW (customized singleton). Poon, Stirrup and GROW charts detected additional 18 (1.2%), 2 (0.1%) and 32 (2.1%) fetuses as SGA despite these fetuses being identified as approriate-for-gestational age by the other two charts.

Supplementary Figure 5. Venn diagram of liveborn small for gestational age (SGA; estimated fetal weight below the 3rd centile) fetuses from dichorionic twin pregnancies according to the growth charts by Poon (non-customized singleton), Stirrup (Twins) and GROW (customized singleton). Poon, Stirrup and GROW charts detected additional 15 (1.3%), 1 (<0.1%) and 21 (1.8%) fetuses as SGA despite these fetuses being identified as approriate-for-gestational age by the other two charts.

Supplementary Figure 6. Venn diagram of liveborn small for gestational age (SGA; estimated fetal weight below the 3rd centile) fetuses from monochorionic twin pregnancies according to the growth charts by Poon (non-customized singleton), Stirrup (Twins) and GROW (customized singleton). Poon, Stirrup and GROW charts detected additional 3 (0.9%), 1 (0.3%) and 11 (3.2%) fetuses as SGA despite these fetuses being identified as approriate-for-gestational age by the other two charts.

Supplementary Figure 7. Venn diagram of stillborn small for gestational age (SGA; estimated fetal weight below the 10th centile) fetuses from either dichorionic or monochorionic twin pregnancies according to the growth charts by Poon (non-customized singleton), Stirrup (Twins) and GROW (customized singleton). All three charts identified most of the stillborn fetuses (n=8, 42.1%) as SGA.

Supplementary Figure 8. Venn diagram of stillborn small for gestational age (SGA; estimated fetal weight below the 3rd centile) fetuses from either dichorionic or monochorionic twin pregnancies according to the growth charts by Poon (non-customized singleton), Stirrup (Twins) and GROW (customized singleton). All three charts identified some of the stillborn fetuses (n=4, 21.1%) as SGA.

The Poon circles denote the number of fetuses identified as SGA by the non-customized singleton chart. The Stirrup circles denote the number of fetuses identified as SGA by the twin charts. The GROW circles denote the number of fetuses identified as SGA by the customized singleton chart. The numbers inside the diagrams denote the number of SGA fetuses in that group and the intersection of Venn diagrams show the number of SGA fetuses jointly identified by the intersecting growth charts.

Table 1. The proportion of liveborn and stillborn fetuses with estimated fetal weight less than the 10th and less than 3rd centile for gestational age in the Southwest Thames Obstetric Research Collaborative (STORK) cohort using different charts stratified according to chorionicity. The analyses were performed on per fetus basis.

	Livebirths (n=4252)			
	Total	**Non-customized singleton chart (Poon)[20]**	**Chorionicity-specific twin charts (Stirrup)[11]**	**P value***
<10th centile				
- All twins, n (%)	4252	605 (14.2)	494 (11.6)	<0.001
- Monochorionic twins, n (%)	583	96 (16.5)	58 (9.9)	<0.001
- Dichorionic twins, n (%)	3669	509 (13.9)	436 (11.9)	<0.001
<3rd centile				
- All twins, n (%)	4252	286 (6.7)	270 (6.3)	0.201
- Monochorionic twins, n (%)	583	41 (7.0)	23 (3.9)	<0.001
- Dichorionic twins, n (%)	3669	245 (6.7)	247 (6.7)	0.924
	Stillbirths (n=48)			
	Total	**Non-customized singleton chart (Poon)[20]**	**Chorionicity-specific twin charts (Stirrup)[11]**	**P value***
<10th centile				
- All twins, n (%)	48	23 (47.9)	21 (43.8)	0.479
- Monochorionic twins, n (%)	17	6 (35.3)	6 (35.3)	0.999
- Dichorionic twins, n (%)	31	17 (54.8)	15 (48.4)	0.479
<3rd centile				
- All twins, n (%)	48	18 (37.5)	17 (35.4)	0.999
- Monochorionic twins, n (%)	17	5 (29.4)	4 (23.5)	0.999
- Dichorionic twins, n (%)	31	13 (41.9)	13 (41.9)	0.999

The comparison between the two charts was performed using the McNemar's test

Table 2. The incidence of intrauterine death (IUD) and preterm birth in twin pregnancies with selective fetal growth restriction (sFGR), using three different definitions: (1) estimated fetal weight (EFW) of one twin less than the 10th centile, (2) EFW of one twin less than 3rd centile and (3) EFW less than the 10th centile with inter-twin EFW discordance more than 25%, in the Southwest Thames Obstetric Research Collaborative (STORK) cohort. The analyses were performed on a per pregnancy basis.

Monochorionic twin pregnancies (n=300)			
	One fetus with EFW <10th centile		
	Non-customized singleton chart (Poon)[20] (n=62)	**Chorionicity-specific twin charts (Stirrup)[11] (n=46)**	**P value**
Pregnancies complicated with IUD, n (%)	5 (8.1)	6 (13.0)	0.523
Preterm delivery (<32 weeks), n (%)	7 (11.3)	6 (13.0)	0.774
Preterm delivery (<34 weeks) n (%)	16 (25.8)	16 (34.8)	0.394
	One fetus with EFW <3rd centile		
	Non-customized singleton chart (Poon)[20] (n=38)	**Chorionicity-specific twin charts (Stirrup)[11] (n=25)**	**P value**
Pregnancies complicated with IUD, n (%)	5 (13.2)	4 (16.0)	0.999
Preterm delivery (<32 weeks), n (%)	6 (15.8)	5 (20.0)	0.927
Preterm delivery (< 34 weeks) n (%)	9 (23.7)	10 (40.0)	0.261
	One fetus with EFW <10th centile and EFW discordance >25%		
	Non-customized singleton chart (Poon)[20] (n=23)	**Chorionicity-specific twin charts (Stirrup)[11] (n=21)**	**P value**
Pregnancies complicated with IUD, n (%)	4 (17.4)	4 (19.0)	0.999
Preterm delivery (<32 weeks), n (%)	5 (21.7)	6 (28.6)	0.732
Preterm delivery (< 34 weeks) n (%)	8 (34.8)	9 (42.9)	0.757
Dichorionic twin pregnancies (n=1850)			
	One fetus with EFW <10th centile		
	Non-customized singleton chart (Poon)[20] (n=280)	**Chorionicity-specific twin charts (Stirrup)[11] (n=271)**	**P value**
Pregnancies complicated with IUD, n (%)	14 (5.0)	13 (4.8)	0.999
Preterm delivery (<32 weeks), n (%)	15 (5.4)	23 (8.5)	0.178
Preterm delivery (<34 weeks) n (%)	33 (11.8)	50 (18.5)	0.032
	One fetus with EFW< 3rd centile		
	Non-customized singleton	**Chorionicity-specific twin**	**P**

	chart (Poon)[20] (n=156)	charts (Stirrup)[11] (n=182)	value
Pregnancies complicated with IUD, n (%)	10 (6.4)	11 (6.0)	0.999
Preterm delivery (<32 weeks), n (%)	8 (5.1)	19 (10.4)	0.106
Preterm delivery (<34 weeks) n (%)	16 (10.3)	37 (20.3)	0.015
	One fetus with EFW <10th centile and EFW discordance >25%		
	Non-customized singleton chart (Poon)[20] (n=114)	**Chorionicity-specific twin charts (Stirrup)[11] (n=123)**	**P value**
Pregnancies complicated with IUD, n (%)	11 (9.6)	10 (8.1)	0.819
Preterm delivery (<32 weeks), n (%)	14 (12.3)	16 (13.0)	0.999
Preterm delivery (<34 weeks) n (%)	26 (22.8)	29 (23.6)	0.999

The comparison between the two charts was performed using the Fisher's exact test

Table 3. The proportion of all livebirths and stillbirths with estimated fetal weight (EFW) less than the 10th and less than 3rd centile in the St George's Hospital (SGH) cohort using different charts stratified according to chorionicity. The analyses were performed on a per fetus basis.

	Livebirths (n=1499)						
	Total	**Non-customized singleton chart (Poon)[20]**	**Chorionicity-specific twin charts (Stirrup)[11]**	**Customized singleton chart (GROW)[21]**	**P value***	**P value†**	**P value‡**
EFW <10th centile							
- All twins, n (%)	1499	127 (8.5)	106 (7.1)	192 (12.8)	0.005	<0.001	<0.001
- Monochorionic twins, n (%)	349	37 (10.6)	28 (8.0)	55 (15.8)	0.026	<0.001	<0.001
- Dichorionic twins, n (%)	1150	90 (7.8)	78 (6.8)	137 (11.9)	0.074	<0.001	<0.001
EFW <3rd centile							
- All twins, n (%)	1499	59 (3.9)	51 (3.4)	83 (5.5)	0.243	0.004	<0.001
- Monochorionic twins, n (%)	349	19 (5.4)	16 (4.6)	29 (8.3)	0.505	0.024	0.001
- Dichorionic twins, n (%)	1150	40 (3.5)	35 (3.0)	54 (4.7)	0.441	0.060	<0.001
	Stillbirths (n=19)						
	Total	**Non-customized singleton chart (Poon)[20]**	**Chorionicity-specific twin charts (Stirrup)[11]**	**Customized singleton chart (GROW)[21]**	**P value***	**P value†**	**P value‡**
EFW <10th centile							
- All twins, n (%)	19	9 (47.4)	9 (47.4)	10 (52.6)	0.999	0.999	0.999
- Monochorionic twins, n (%)	11	6 (54.5)	6 (54.5)	7 (63.6)	0.999	0.999	0.999
- Dichorionic twins, n (%)	8	3 (37.5)	3 (37.5)	3 (37.5)	0.999	0.999	0.999
EFW <3rd centile							
- All twins, n (%)	19	5 (26.3)	6 (31.6)	7 (36.8)	0.999	0.617	0.999
- Monochorionic twins, n (%)	11	3 (27.3)	4 (36.4)	5 (45.5)	0.999	0.479	0.999
- Dichorionic twins, n (%)	8	2 (25.0)	2 (25.0)	2 (25.0)	0.999	0.999	0.999

*McNemar's test comparing Non-customized singleton chart (Poon) with chorionicity-specific twin charts (Stirrup)

†McNemar's test comparing Non-customized singleton chart (Poon) with customized singleton chart (GROW)

‡McNemar's test comparing Chorionicity-specific twin charts (Stirrup) with customized singleton chart (GROW)