

## OBSTETRICS

# Customized growth charts for twin vs singleton pregnancies and their ability to identify small for gestational age-associated risk of adverse perinatal outcome

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**BACKGROUND:** Twin fetuses are born earlier and have slower growth than singletons. It is uncertain as to what degree this is pathological or a physiological adaptation.

**OBJECTIVE:** We set out to develop a customized chart for twin pregnancy and compare it with the corresponding singleton chart in its ability to assess risk of adverse perinatal outcomes.

**STUDY DESIGN:** The cohort consisted of 8457 twin pregnancies (16,914 fetuses) without information on chorionicity, recorded during routine care in 127 UK hospitals. We performed a mixed-effects linear regression analysis to calculate customized coefficients for maternal height, weight, parity, and ethnic origin and to determine pregnancy-specific optimal weights at 37 weeks. This weight was linked to a proportionality curve derived from serial scans of twin pregnancies with normal outcomes. We compared the new customized standard for twins with that for singletons by calculating rate of small for gestational age (<10th centile)—associated risk of stillbirth and a set of adverse neonatal outcomes (need for resuscitation, Apgar score <7 at 5 minutes, admission to neonatal intensive care unit, or neonatal death), using generalized estimating equations and odds ratios and 95% confidence intervals. The effect of customization on small for gestational age and large for gestational age rates in different ethnic groups was compared with 3 uncus-

**RESULTS:** The same maternal physiological characteristics (maternal height, early pregnancy weight, parity, and ethnic origin) were found to affect the twin weight standard as singletons, and high body mass index had similarly a significantly negative effect on weight at birth. The average optimal weight at 37+0 weeks for the same maternal characteristics was 389 g less for a twin compared to a singleton fetus.

Customized twin and singleton standards designated as small for gestational age 13.4% and 44.2% of twins, respectively. Small for gestational age by customized twin standard had a higher risk of stillbirth (odds ratio, 7.2; confidence interval, 4.8–10.9) than small for gestational age by singleton standard (2.8; 1.9–4.1), and small for gestational age by singleton but not by twin standard (68.9% of all singleton standard small for gestational age cases) had no increase in stillbirth risk. Neonates small for gestational age by customized twin standard had an increased need for resuscitation (odds ratio, 1.3; confidence interval, 1.1–1.7), lower Apgar score (<7) at 5 minutes (odds ratio, 1.8; confidence interval, 1.2–2.6), higher admission rate to neonatal intensive care unit (odds ratio, 1.3; confidence interval, 1.0–1.6), and increased risk of neonatal death (odds ratio, 5.4; confidence interval, 1.3–23.5), while neither of these risks were increased with singleton standard. Small for gestational age rates by population-based twin standards were higher than by the customized twin standard, but the additional cases were not or only weakly associated with stillbirth risk.

**CONCLUSION:** Use of a singleton standard for twins results in a 3 times higher small for gestational age rate, without detecting additional cases at risk of stillbirth or adverse neonatal outcomes. The results suggest that the use of a twin-specific chart to monitor twin pregnancies is safe in recognizing small for gestational age—associated risk of adverse outcomes and is likely to result in fewer unnecessary investigations, interventions, and maternal anxiety.

**Key words:** birthweight, customized charts, fetal growth, fetal weight, neonatal death, stillbirth, twin pregnancy

## Introduction

Fetal growth restriction has long been known to be strongly associated with adverse outcomes in singleton as well as

twin pregnancies.<sup>1,2</sup> Growth in twins follows a lower trajectory, and it is debated as to what degree this is due to an inherently pathological process or a form of physiological adaptation.<sup>3,4</sup>

While small for gestational age (SGA) estimated fetal weight (EFW) can be an early indicator of growth problems in twin pregnancies, there is no consensus on whether the definition of SGA should be based on twin-specific or singleton charts.<sup>5–8</sup> Use of a singleton chart for twins will result in a higher SGA rate, and hence a more diluted, weaker association of SGA cases with adverse outcomes.<sup>6,9–14</sup> Yet

this raises the question of whether the lower trajectory of a twin-specific standard fails to identify all cases at risk.<sup>15</sup> There is also debate about whether twin charts apply similarly to dichorionic (DC) and monochorionic (MC) pregnancies.<sup>16–18</sup> Finally, it has been suggested that, as is the case with singletons,<sup>19,20</sup> maternal constitutional characteristics also affect normal growth in twins.<sup>21–23</sup>


We set out to investigate these questions through analysis of the routinely collected dataset of the Growth Assessment Protocol (GAP),<sup>24</sup> a program for standardized surveillance of fetal

**Cite this article as:** Gardosi J, Hugh O, Mytton J, et al. Customized growth charts for twin vs singleton pregnancies and their ability to identify small for gestational age-associated risk of adverse perinatal outcome. *Am J Obstet Gynecol* 2025;XXX:XX–XX.

0002-9378

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## AJOG at a Glance

**Why was this study conducted?**

There is ongoing debate whether the slower growth of twin fetuses is a pathological or physiological adaptation. We wanted to examine whether a twin-specific chart, customized for maternal constitutional characteristics, improves the identification of twin pregnancies at risk of adverse perinatal outcomes.

**Key findings**

The optimal 37-week twin weight is 389 g less than the equivalent singleton standard. As a result, 44.2% of twins are being classified as small for gestational age (SGA) according to the singleton standard, compared to 13.4% by the twin-specific standard. The additional cases designated SGA by the singleton standard do not represent an increased risk of adverse outcomes, suggesting that it is safe to use the twin-specific chart.

**What does this add to what is known?**

Adjustment for maternal characteristics improves performance compared to population-based standards for growth in twins and reduces false positive assessment of SGA in heterogeneous populations.

growth adopted by the majority of maternity hospitals in the United Kingdom's National Health Service (NHS).

**Materials and methods****Data origin**

The cohort consisted of all 8457 twin pregnancies (16,914 fetuses) born from January 2015 to February 2025 in 127 NHS hospitals in the UK GAP program which represented approximately two-thirds of all NHS units. Routine recording of core data items relevant to care was mandatory and included constitutional maternal characteristics such as height, weight at first visit, parity and ethnic origin, and pathological variables such as hypertension and diabetes. Expected date of delivery was based on a routine dating scan in the first trimester. EFW measurements were usually based on Hadlock's 3 parameter formula.<sup>25</sup> Outcome data included gestational age at delivery, birthweight, sex, live birth, and stillbirth, defined as delivery with no sign of life from 24+0 weeks of gestation. An additional set of neonatal outcomes (need for resuscitation, Apgar score <7 at 5 minutes, admission to a neonatal intensive care unit [NICU], and neonatal death [up to 28 days]) were able to be recorded from 2022, when a linkup was established with a maternity

information system in use in several participating hospitals.

Ethics committee approval was not required as all data were recorded prospectively as part of routine care and fully anonymized before release for analysis.

**Customized twin chart**

We created a customized chart for twins along previously described methods for singleton charts,<sup>26</sup> developing coefficients by mixed-effects multivariable regression analysis to derive term optimal weight (TOW) and a proportionality fetal weight curve to outline the trajectory by which this weight is expected to be reached.

**Term optimal weight**

We included all liveborn twin pregnancies delivered between 34+0 and 37+6 weeks. Stepwise mixed-effects linear regression with a random intercept was used to account for interdependence which allowed both twins in each pregnancy to be included. Variables were maternal height, weight at first pregnancy visit, parity, ethnic origin, and gestational age and weight at birth. The regression analysis used a significance level of 0.05%. The resultant constant was centered on gestational age of 37+0 weeks (259 days) and a 'standard mother' with average characteristics, as listed in [Tables 1 and 2](#).

The TOW for each pregnancy was calculated using this constant and the significant coefficients of the non-pathological variables in the analysis.

As chorionicity was not recorded routinely, a subgroup analysis was performed on pregnancies with mixed-sex twins to assess difference in TOW between DC pregnancies and the overall cohort.

**Proportionality curve**

To derive formulas for a twin-specific proportionality curve, we selected a subgroup of pregnancies with 3 or more third trimester scans and live births between 34+0 and 37+6 weeks, after excluding pregnancies with low (<18.5) and high ( $\geq 30.0$ ) body mass index (BMI) and >25% twin-twin discordance of birthweight. We created a model of mixed-effect linear regression using a nested random effect to account for scans by fetus within the pregnancy. The best model fit was assessed using root mean square error and Bayesian information criterion.

The resultant fetal weight curve was converted into the previously described proportionality curve<sup>26</sup> where weight values at all gestational ages from 24 weeks were expressed as a fraction of the term value, here set at 37+0 weeks and made equivalent to 100%. The distribution of TOWs determined the coefficient of variation (CV) of the model, with  $TOW \times CV \pm 1.28$  marking the points through which the 90th and 10th centile lines, respectively, of the proportionality curve pass at 37+0 weeks.

**Comparison of weight standards**

SGA rates were calculated for the cohort of 8457 twin pregnancies using the customized twin standard (GROW-T) and compared with the customized singleton standard (GROW-S), derived from the same population and based on the current GROW application (v 2.0.6.3) for fetal weight and birthweight.<sup>27</sup> A generalized estimating equation model was used to calculate SGA-related odds ratios (ORs) of outcomes with 95% confidence intervals, using a logistic regression framework with an exchangeable correlation

**TABLE 1**  
**Characteristics of study cohort (N=8457 twin pregnancies)**

| Characteristic                       | n (%), unless otherwise stated |
|--------------------------------------|--------------------------------|
| Maternal height (cm)                 |                                |
| Mean (SD)                            | 165.1 (6.7)                    |
| Median (IQR)                         | 165 (161–170)                  |
| Maternal weight (kg)                 |                                |
| Mean (SD)                            | 75.5 (18.8)                    |
| Median (IQR)                         | 71 (62–85)                     |
| Body mass index (kg/m <sup>2</sup> ) |                                |
| Mean (SD)                            | 27.6 (6.5)                     |
| Median (IQR)                         | 26.3 (23.0–30.9)               |
| <18.5                                | 180 (2.1)                      |
| ≥30                                  | 2481 (29.3)                    |
| ≥35                                  | 1086 (12.8)                    |
| Parity                               |                                |
| 0                                    | 3696 (43.7)                    |
| 1                                    | 2905 (34.4)                    |
| 2                                    | 1091 (12.9)                    |
| 3+                                   | 765 (9.0)                      |
| Ethnicity                            |                                |
| British European                     | 5734 (67.8)                    |
| South Asian                          | 745 (8.8)                      |
| East European                        | 557 (6.6)                      |
| Other                                | 1240 (14.6)                    |

IQR, interquartile range; SD, standard deviation.

structure to account for the nonindependence of outcomes within twin pairs. The model incorporated twin pair identifiers as clustering variables to ensure appropriate adjustment for the intrapair correlation.

We calculated the SGA and large for gestational age (LGA) rates at birth for our 3 main ethnic groups (British European, South Asian, and East European) according to 3 population-based twin-specific standards: (1) South Thames Obstetric Research Collaborative (STORK)<sup>5</sup>; (2) National Institute of Child Health and Human Development (NICHD)<sup>6</sup>; and (3) Fetal Medicine Foundation (FMF).<sup>28</sup> We compared this with SGA and LGA rates in the same groups according to GROW-T, customized for ethnicity as well as average maternal height, weight, and

parity, and assessed the respective still-birth risk in each SGA group. We also calculated diagnostic characteristics (sensitivity, false positive rate, positive predictive value, negative predictive value, positive likelihood ratio, and diagnostic OR) for each standard for detecting the different outcomes.

### Statistical tools

Analyses were performed using Excel (2024; Microsoft, Redmond, WA), R (version 4.4.1; R Foundation for Statistical Computing, Vienna, Austria), and SAS (version 9.4; SAS institute, Cary, NC).

## Results

### Variables affecting twin weight

Table 1 presents the characteristics of the 8457 twin pregnancies in the study cohort. Mean maternal weight in early

pregnancy was 75.5 kg, with a BMI ≥30 rate of 29.3. The results of the regression analysis are shown in Table 2, with the significant physiological variables determining optimal weight at birth. High BMI had a negative effect on birthweight, with deficit increasing with higher BMI. The constant gives the average TOW of 2667 g at 37+0 weeks for an average British-European mother in her second pregnancy, with height 166 cm, early pregnancy weight 73 kg, and baby's sex not specified (Table 2). In Supplemental Table 2, the coefficients for these variables are compared with the corresponding values derived from singleton term pregnancies centered at 40 weeks and adjusted by the proportionality equation to the same 37-week gestational age at which the twin coefficients were calculated. The twin constant of 2667 g is 389 g less than the 3055 g TOW of a singleton pregnancy with the same characteristics at 37 weeks, according to GROW-S<sup>29</sup> (Supplemental Table 2).

Subgroup analysis of TOW for DC twins, by selecting pregnancies with mixed sex twins (n=2855, 33.8% of all pregnancies) showed an average TOW of 2675 g, only 8 g more than the above mentioned TOW of 2667 g in the mixed cohort of DC and MC pregnancies.

### Customized growth chart for twins

The fetal weight curve was derived from a subcohort of 1022 normal outcome pregnancies with a record of 3 or more scans from 24+0 to 37+6 weeks (average 4.8 per pregnancy), BMI 18.5 <30, birthweight discordance <25%, and both fetuses liveborn.

The fetal weight formula for the derived curve is:

$$pEFW = \exp(0.5587224 + 0.04748862 \times gest - 0.0000739 \times gest^2)$$

(Gest represents gestational age at scan, in days).

This fetal weight curve was transformed into a proportionality curve with the calculated TOW at 37 weeks representing

**TABLE 2**  
**Twin birthweight coefficients (N = 13,512 fetuses)**

| Variable             | Coefficient | SE   | 95% CI         |
|----------------------|-------------|------|----------------|
| Constant             | 2666.9      | 6.4  |                |
| Gestation (d)        |             |      |                |
| Linear               | 33.9        | 0.9  | 32.1–35.7      |
| Quadratic            | 0.13        | 0.06 | 0.02–0.25      |
| Ethnicity            |             |      |                |
| South Asian          | –80.9       | 11.1 | –103.2 to 59.6 |
| East European        | 23.4        | 12.1 | 1.1–48.4       |
| Multiparity          | –58.2       | 6.1  | –70.1 to 46.2  |
| Maternal height (cm) |             |      |                |
| Linear               | 5.4         | 0.6  | 4.3–6.5        |
| Maternal weight (kg) |             |      |                |
| Linear               | 3.9         | 0.4  | 3.1–4.7        |
| Quadratic            | –0.02       | 0.01 | –0.03 to 0.01  |
| Body mass index      |             |      |                |
| <18.5                | –60.1       | 23.7 | –106.5 to 13.8 |
| 30<35                | –24.0       | 11.4 | –46.4 to 1.6   |
| ≥35                  | –43.0       | 17.5 | –77.2 to 8.8   |
| Sex                  |             |      |                |
| Male                 | 48.0        | 2.7  | 42.8–53.2      |
| Female               | –48.0       | 2.7  | –53.2 to 42.8  |

Twin SD: 307.9; CV: 12.3%.

Centered on British European mother with height 166 cm, weight 73 kg, second pregnancy, and 37+0 weeks of gestation.

CI, confidence interval; SE, standard error.

100%, and each gestational age point displaying the corresponding predicted weight according to the formula:

$$TOW(gest) = \frac{pEFW(gest)}{pEFW(37 \text{ weeks})} \times TOW(37 \text{ weeks})$$

The p10 and p90 lines of the chart can also be delineated with the same proportionality formula, after applying the following equation for the p10 and p90 points:

$$P10/P90 = TOW \pm TOW \times 1.28 \times 0.123$$

where 1.28 represents the Z score for the 10th/90th centile limits and 0.123 represents the CV of the model.

### Small for gestational age by twin specific vs singleton chart and adverse outcome

By pregnancy (ie, where at least one fetus was SGA), the SGA rate (<10th centile) by GROW-T was 24.6% compared to 64.9% by GROW-S (Table 3). Pregnancies with SGA according to GROW-T were delivered on average 1 week earlier (35+4 weeks), while those with SGA by GROW-S only were delivered at 36+5 weeks, similar to those without an SGA fetus (36+5). Analyzed by individual fetuses, the overall SGA rate was 13.8% by GROW-T and 44.4% according to GROW-S (Table 4).

In Figure 1, birthweights of the 16,790 live-born twins are plotted with the new twin centile lines (90th, 50th, and 10th), customized for the average maternal

characteristics of the cohort (Table 2). The 10th centile of the singleton GROW nomogram,<sup>27,29</sup> customized to the same characteristics, is shown running close to the 50th centile line of the twin-specific standard.

The association of SGA with pregnancy outcome is shown in Table 4. Cases designated as SGA had an increased risk of stillbirth, but the risk was much higher with SGA according to GROW-T (OR, 7.2) than with GROW-S (OR, 2.8). All cases that were SGA by GROW-T were also SGA by GROW-S, but 5170/7507 (68.9%) of cases were SGA by the singleton standard only, and these did not have an increased risk of stillbirth.

Neonatal outcomes (need for resuscitation, Apgar <7, admission to NICU, and neonatal death) showed significant risk when SGA is according to the twin-specific standard only, and again, the majority of cases that were SGA by GROW-S were not SGA by GROW-T (962/1351, 71.2%; Table 4). Because of the smaller cohort containing information on these variables, we performed a sensitivity analysis which showed no difference between cohorts in a series of pregnancy characteristics (Supplemental Table 1).

### Customized vs population-based twin standards

Table 5 lists average LGA (>90) and SGA (<10) rates overall and for the 3 largest ethnic groups in our population (British European, South Asian, and East European), by each twin-specific standard. SGA rates for the 3 ethnic groups varied widely according to each uncustomized standard (STORK 16.5%–33.5%; NICHD 15.4%–31.9%; FMF 30.6%–50.0%). They varied less (12.4%–15.4%) and were overall lower with the customized GROW-T standard. Table 5 also shows stillbirths associated with fetuses designated as SGA. GROW-T had consistently the highest stillbirth rates and identified most SGA stillbirths despite having the lowest SGA rate.

Supplemental Table 3 shows that the additional cases that were SGA by the uncustomized standards but not by

TABLE 3

**Characteristics of pregnancies with at least one fetus SGA according to twin-specific (GROW-T) and singleton (GROW-S) standards**

| Characteristic           | Summary statistic | SGA by GROW-T    | SGA by GROW-S    | SGA by GROW-S only | Neither fetus SGA by either standard |
|--------------------------|-------------------|------------------|------------------|--------------------|--------------------------------------|
| Pregnancies              | n (%)             | 2079 (24.6)      | 5491 (64.9)      | 3412 (40.3)        | 2966 (35.1)                          |
| Both fetuses SGA         | n (%)             | 258 (12.4)       | 2016 (36.7)      | 953 (27.9)         | -                                    |
| Gestational age at birth | Median (IQR)      | 250 (236–257)    | 254 (244–260)    | 257 (249–261)      | 257 (248–261)                        |
| <37 weeks                | n (%)             | 1656 (79.6)      | 3613 (65.8)      | 1958 (57.4)        | 1644 (55.4)                          |
| <34 weeks                | n (%)             | 551 (26.5)       | 909 (16.6)       | 358 (10.5)         | 416 (14.0)                           |
| Birthweight              | Median (IQR)      | 2018 (1693–2265) | 2300 (1975–2535) | 2440 (2220–2625)   | 2710 (2440–2928)                     |
| Birthweight discordance  | Median (IQR)      | 19.0 (11.5–26.4) | 12.4 (6.5–19.6)  | 9.6 (5.1–15.1)     | 5.9 (2.7–10.2)                       |
| >20%                     | n (%)             | 961 (46.2)       | 1330 (24.2)      | 369 (10.8)         | 84 (2.8)                             |
| >25%                     | n (%)             | 614 (29.5)       | 725 (13.2)       | 111 (3.3)          | 24 (0.8)                             |

GROW-T, twin-specific standard; GROW-S, singleton standard; IQR, interquartile range; SGA, small for gestational age.

GROW-T (STORK: 1165/3394=34.4%; NICHD: 917/3110=29.5%; FMF: 3316/5653=58.7%) had either no (FMF) or only borderline (STORK, NICHD) stillbirth risk, with lower CI=1. In [Supplemental Table 4](#), the diagnostic characteristics are shown for perinatal

outcomes by SGA rates of each population standard as well as GROW-T and GROW-S. Sensitivities and false positive rates varied with screen positive rates (ie, the proportion of cases defined as SGA), with GROW-T tending to have the best diagnostic OR.

## Discussion

### Summary of findings

Our main findings are that (1) normal growth in a standard pregnancy proceeds with a lower trajectory in twins than in singletons, resulting in an average 389 g lower birthweight at 37

TABLE 4

**SGA rates according to twin-specific vs singleton standards and associations with adverse perinatal outcomes**

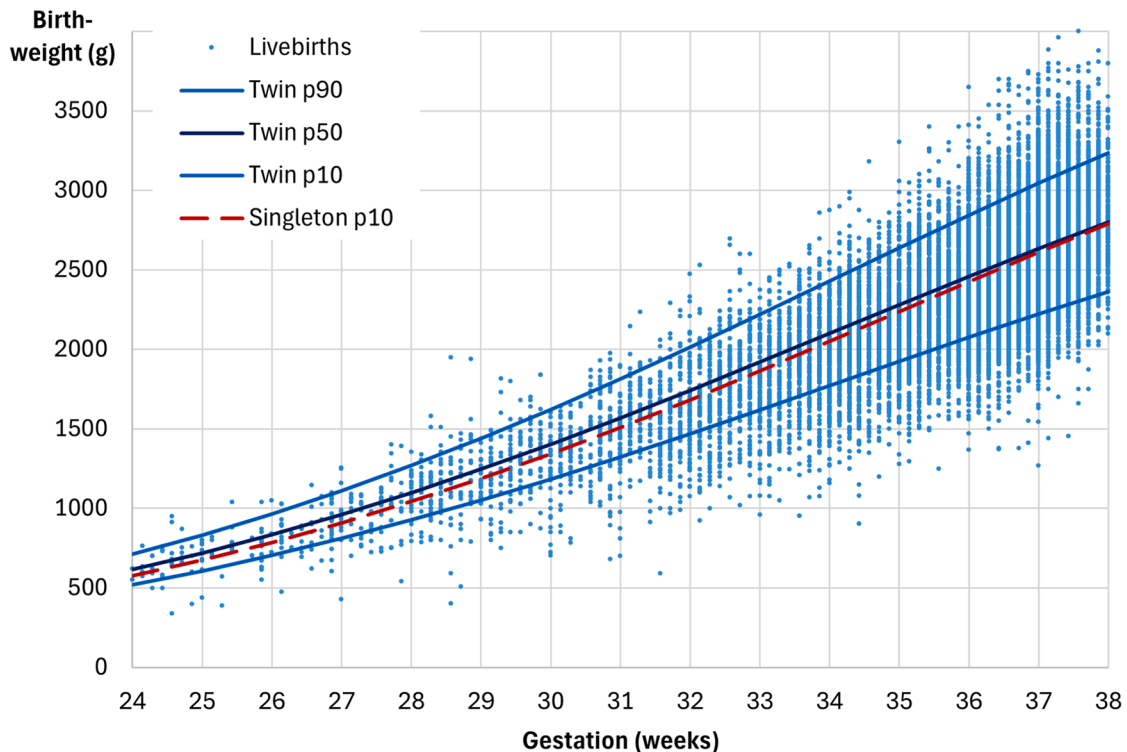
| Outcome                       | Total       | SGA by twin    | SGA by singleton | SGA by singleton only | Not SGA by either standard |
|-------------------------------|-------------|----------------|------------------|-----------------------|----------------------------|
| Stillbirth (n, %)             | 16,914      | 2337 (13.8)    | 7507 (44.4)      | 5170 (30.6)           | 9407 (55.6)                |
| (n/1000)                      | 124 (7.3)   | 73 (31.2)      | 85 (11.3)        | 12 (2.3)              | 39 (4.1)                   |
| Odds ratio (95% CI)           |             | 7.2 (4.8–10.8) | 2.8 (1.9–4.1)    | 0.6 (0.4–1.1)         | -                          |
| Live birth data cohort (n, %) | 3174        | 389 (12.3)     | 1351 (42.6)      | 962 (30.3)            | 1823 (57.4)                |
| Resuscitation                 |             |                |                  |                       |                            |
| (n, %)                        | 1031 (32.5) | 163 (41.9)     | 443 (32.8)       | 280 (29.1)            | 588 (32.3)                 |
| Odds ratio (95% CI)           |             | 1.3 (1.1–1.7)  | 1.0 (0.9–1.2)    | 0.9 (0.8–1.1)         | -                          |
| Apgar 5 score <7              |             |                |                  |                       |                            |
| (n, %)                        | 193 (6.1)   | 41 (10.5)      | 85 (6.3)         | 44 (4.6)              | 108 (5.9)                  |
| Odds ratio (95% CI)           |             | 1.8 (1.2–2.6)  | 1.1 (0.8–1.4)    | 0.8 (0.6–1.1)         | -                          |
| NICU admission                |             |                |                  |                       |                            |
| (n, %)                        | 842 (26.5)  | 165 (42.4)     | 386 (28.6)       | 221 (23.0)            | 456 (25.0)                 |
| Odds ratio (95% CI)           |             | 1.3 (1.0–1.6)  | 1.0 (0.9–1.1)    | 0.9 (0.8–1.1)         | -                          |
| Neonatal death                |             |                |                  |                       |                            |
| (n/1000)                      | 11 (3.7)    | 6 (15.4)       | 7 (5.2)          | 1 (1.0)               | 4 (2.2)                    |
| Odds ratio (95% CI)           |             | 5.4 (1.3–23.5) | 1.6 (0.4–6.9)    | 0.5 (0.1–4.2)         | -                          |

CI, confidence interval; NICU, neonatal intensive care unit; SGA, small for gestational age.



**FIGURE 1**

**Birthweight of 16,790 liveborn twins, with 90th, 50th, and 10th centile lines of the new twin standard (GROW-T), and 10th centile line of singleton standard (GROW-S<sup>27</sup>), both adjusted to average maternal characteristics**



Term optimal weight (TOW; p50) for twins at 37+0 weeks=2667 g; corresponding singleton (GROW-S) weight at 37 weeks: p50=3055 g; p10=2610 g.

weeks; (2) twin chart-defined SGA has a higher stillbirth risk than twins that were SGA according to the corresponding singleton chart; (3) SGA rate according to the singleton chart is 3 times higher but the additional cases are not at an increased stillbirth risk; (4) SGA according to twin but not singleton standard is associated with adverse neonatal outcomes; and (5) the same maternal constitutional variables affect fetal growth in twins as in singleton pregnancies; standards which do not customize for these variables have widely varying and overall higher SGA rates, with little or no identification of additional stillbirth risk.

### Interpretation of study findings and comparison with published literature

Our study confirms previous reports that customized<sup>21,23,30</sup> as well as uncustomized<sup>6,9,10,12,13</sup> twin fetal

biometry and weight standards are better predictors of adverse outcomes than various singleton charts. The same constitutional variables (maternal height, weight, parity, and ethnic origin) have a significant effect on the predicted birthweight as they do for singleton charts.<sup>26</sup> The magnitude of this variation however appears to be attenuated, when compared to the same variables in singletons (Supplemental Table 2) suggesting that maternal constitutional factors have a lesser effect on normal growth in twins. The over-riding impression is that twin babies are smaller due to genetic adjustment or intrauterine constraint. Both of these could have a role: physiological adaptation could result in a lower growth trajectory, and limited uterine capacity could initiate earlier labor.

We also observed that higher maternal BMI categories have an increasingly negative effect on birthweight (Table 2),

as demonstrated in singleton pregnancies,<sup>31</sup> and result in higher SGA rates with increasing BMI when the standard is customized.<sup>32</sup>

Shorter gestation and lower growth trajectory in twin pregnancies is generally agreed.<sup>3,5,6,12</sup> While a previous study<sup>21</sup> modeled customized coefficients for twins at 40 weeks, no twin pregnancies reached 40 weeks in our cohort. The UK National Institute of Health and Care Excellence advises delivery in uncomplicated MC and DC twin pregnancies at 36 and 37 weeks, respectively.<sup>33</sup> Such guidelines are likely to have contributed to an increase in twin deliveries between 34 and 37 weeks without a significant increase in NICU admissions, as well as a reduction in stillbirths.<sup>34</sup>

The slower twin growth trajectories translate to a much higher SGA rate when using a singleton vs twin nomogram. By designating more fetuses as

TABLE 5

**Average SGA and LGA rates at birth in main ethnic categories according to customized (GROW-T) and population charts for twins (STORK,<sup>5</sup> NICHD,<sup>6</sup> FMF<sup>28</sup>)**

| Ethnic categories                              | STORK <sup>5</sup> | NICHD <sup>6</sup> | FMF <sup>28</sup> | GROW-T      |
|--|--------------------|--------------------|-------------------|-------------|
| Total (n=16,914)<br>SB, n=124 (7.33)           |                    |                    |                   |             |
| LGA  |                    |                    |                   |             |
| n (%)  | 600 (3.5)          | 263 (1.6)          | 1001 (5.9)        | 1306 (7.7)  |
| SGA  |                    |                    |                   |             |
| n (%)  | 3394 (20.1)        | 3110 (18.4)        | 5653 (33.4)       | 2337 (13.8) |
| SGA SB   |                    |                    |                   |             |
| n (%)  | 82 (2.4)           | 81 (2.6)           | 87 (1.5)          | 73 (3.1)    |
| British European (n=11,468)<br>SB, n=92 (8.02) |                    |                    |                   |             |
| LGA  |                    |                    |                   |             |
| n (%)  | 447 (3.9)          | 186 (1.6)          | 742 (6.5)         | 884 (7.7)   |
| SGA  |                    |                    |                   |             |
| n (%)  | 2125 (18.5)        | 1921 (16.8)        | 3557 (31.0)       | 1573 (13.7) |
| SGA SB   |                    |                    |                   |             |
| n (%)  | 55 (2.6)           | 54 (2.8)           | 59 (1.7)          | 49 (3.1)    |
| South Asian (n=1490)<br>SB, n=11 (7.38)        |                    |                    |                   |             |
| LGA  |                    |                    |                   |             |
| n (%)  | 22 (1.5)           | 9 (0.6)            | 36 (2.4)          | 119 (8.0)   |
| SGA  |                    |                    |                   |             |
| n (%)  | 499 (33.5)         | 476 (31.9)         | 745 (50.0)        | 230 (15.4)  |
| SGA SB   |                    |                    |                   |             |
| n (%)  | 11 (2.2)           | 11 (2.3)           | 11 (1.5)          | 10 (4.3)    |
| East European (n=1114)<br>SB, n=4 (3.59)       |                    |                    |                   |             |
| LGA  |                    |                    |                   |             |
| n (%)  | 44 (3.9)           | 24 (2.2)           | 75 (6.7)          | 95 (8.5)    |
| SGA  |                    |                    |                   |             |
| n (%)  | 184 (16.5)         | 171 (15.4)         | 341 (30.6)        | 138 (12.4)  |
| SGA SB   |                    |                    |                   |             |
| n (%)  | 1 (0.5)            | 1 (0.6)            | 1 (0.3)           | 1 (0.7)     |

GROW-T adjusted for ethnic origin-specific average characteristics in early pregnancy:

British European: maternal height 166 cm, weight 73 kg, and parity 1.0.

South Asian: maternal height 160 cm, weight 65 kg, and parity 0.8.

East European: maternal height 166 cm, weight 67 kg, and parity 0.9.

FMF, Fetal Medicine Foundation; GROW-T, twin-specific customized standard; LGA, large for gestational age; NICHD, National Institute of Child Health and Human Development; SB, stillbirth; SGA, small for gestational age; STORK, South Thames Obstetric Research Collaborative.

SGA, the singleton standard's association with adverse outcomes weakens. In contrast, twin chart SGA—being more specific—has a stronger association with

adverse outcome, as shown in Table 4 and observed elsewhere.<sup>6,9–13</sup> Our study furthermore indicates that cases designated SGA by singleton standard

only have similar risks of stillbirth, neonatal death, and indicators of neonatal morbidity as cases not SGA by either standard (Table 4).

### Clinical implications

The high SGA rate of singleton charts applied in twin pregnancies, without identifying additional risk, could result in uncertainty, maternal anxiety, and unnecessary investigations and interventions. It is reassuring that there was no difference in gestational age at birth between 'singleton SGA only' and 'non-SGA' groups (Table 3). It may be that in practice, only the lowest centile singleton chart-defined SGA pregnancies are delivered earlier. Indeed the GROW-T SGA group showed lower birthweight and higher discordance rates, and were delivered earlier than GROW-S SGA and non-SGA groups (Table 3). The excess cases that are SGA by singleton standard only may lead to SGA being 'normalized' and not taken seriously, or to additional, unnecessary investigations once an EFW is documented as SGA. In our cohort, more than two-thirds of fetuses SGA by the singleton (44.4%) were not SGA by the twin standard (13.8%) and had no increased risk in any of a range of adverse perinatal outcomes (Table 4).

Comparison of the 4 twin-specific standards (Table 5) reveals a large variation in SGA rates, ranging from 13.8% (GROW-T) to 18.4% (NICHD<sup>6</sup>), 20.1% (STORK<sup>5</sup>), and 33.4% (FMF<sup>28</sup>). This variation could be due to differences in methodology used to develop the standards. Scan error may be a reason for the discrepancy in 10th centile limits for DC twins between STORK<sup>16</sup> and FMF,<sup>28</sup> as acknowledged recently.<sup>14</sup> GROW-T does not rely on EFWs but is instead derived from an optimized birthweight model which is combined with a longitudinal scan-based proportionality curve to outline the normal twin growth trajectory and associated centile limits. The additional SGA cases defined by the population-average standards compared to GROW-T have no or only weak stillbirth risk with borderline significance (Supplemental Table 3) and would add substantially to false positive assessments when applied in clinical practice.

### Research implications

Our results add to the increasing evidence for adoption of twin-specific charts. Although still controversial, their use is already considered 'reasonable' in International Society of Ultrasound in Obstetrics and Gynecology,<sup>35</sup> International Federation of Gynecology and Obstetrics,<sup>36</sup> and Society of Obstetricians and Gynecologists of Canada<sup>37</sup> guidelines. In addition to outcome-based analyses such as the present study, observations of normal small placentas<sup>38</sup> and reduced fat tissue<sup>39</sup> early in twin pregnancy support the notion that small fetal size in uncomplicated DC pregnancy is not due to growth restriction but represents physiological adaptation.

It has nevertheless been argued that prospective randomized trials are needed to confirm safety.<sup>4</sup> However, such trials might be challenging if observational evidence has become strong enough to reduce clinical equipoise. It could also be argued that the twin standard is safer because it results in a reduction of false positives and improves the recognition and management of fetal growth restriction when it does occur. While adoption of twin-specific charts is timely, implementation ought to be accompanied by evaluation in practice to monitor safety in different health service environments.

### Strengths and limitations

The size of our cohort, to our knowledge the largest to date, allowed comparison between SGA by twin-specific and singleton standards and relatively rare outcomes such as stillbirth. The routine recording of pregnancy characteristics also enabled the development of co-efficients for customization, which showed that SGA rates are much more consistent between groups in our multiethnic population than when population-based standards are applied. Customized standards for singleton pregnancies are not universally accepted and therefore a new version of GROW-S ('GROW Lite'<sup>40</sup>) has been released for users who wish to decide which maternal characteristics—all, any, or none—to

adjust for. Without adjustment, this then results in an optimized average chart representing the local population rather than each individual pregnancy. Similarly, GROW-T will be able to be used without individual customization.

Records of serial scans allowed us to assess growth trajectories in normal pregnancies and develop an EFW-based proportionality curve for twin pregnancy which combines with the birthweight-based TOW to derive a twin GROW chart customized for each pregnancy. As with singleton GROW, this method results in a 'perinatal' chart—a contiguous standard for fetal weight and birthweight.

Our use of a birthweight database to calculate TOW has the advantage of avoiding reliance on ultrasound estimation of fetal weight which is known to be subject to systematic overestimation in twin pregnancies.<sup>17,41</sup> Such overestimation of fetal weight in twins could be a likely explanation for the smaller singleton-vs-twin differences in fetal weight medians at 37.0 weeks for the 2 fetal weight-based standards for which such information was available: FMF singleton<sup>42</sup>: 2954 g minus twin<sup>28</sup>: 2712 g=242 g; NICHD singleton<sup>43</sup> (weighted average of 4 ethnic groups): 2997 g minus twin average<sup>6</sup>: 2766 g=231 g. This compared with a 37.0-week birthweight-based median difference between GROW-S and GROW-T of 389 g (Supplemental Table 2).

Chorionicity was not recorded in our cohort; however, the difference between growth curves of MC and DC twins is considered too small to be clinically relevant.<sup>4</sup> We tested this assumption in a DC-only subgroup identified by pregnancies with mixed sex twins, which found the TOW to be only 8 g above that of the overall cohort. Further evidence recently presented from a longitudinally scanned cohort of MC and DC pregnancies shows their growth trajectories to be similar when pathological factors are excluded.<sup>44</sup>

### Conclusion

Twin-specific nomograms increase the association between SGA-related risk of



stillbirth and a range of adverse perinatal outcomes. Singleton charts add a large proportion of SGA cases which do not identify additional risk, and our findings strengthen the argument that it is time to switch to twin-specific charts.<sup>14,45</sup> The same maternal constitutional factors affect normal growth in twins as they do in singletons, and a customized standard can further reduce excessive designations of SGA by population-based standards. ■

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Received April 25, 2025; revised July 18, 2025; accepted July 26, 2025.

All authors are employed by the Perinatal Institute, Birmingham, UK, a not-for-profit social enterprise that provides training and software tools including customized GROW charts used in this study.

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**SUPPLEMENTAL TABLE 1****Descriptives of cohorts that were available for assessment of neonatal outcomes**

| Characteristics         |              | Overall cohort   | Neonatal outcomes cohort |
|-------------------------|--------------|------------------|--------------------------|
| Pregnancies             | N            | 8457             | 1578                     |
| Maternal height         | Median (IQR) | 165 (161–170)    | 165 (160–170)            |
| Maternal weight         | Median (IQR) | 71 (62–85)       | 73 (63–87)               |
| First pregnancy         | n (%)        | 3696 (43.7)      | 700 (44.3)               |
| British ethnicity       | n (%)        | 5734 (67.8)      | 1006 (63.7)              |
| Gestational age         | Median (IQR) | 255 (245–260)    | 254 (245–260)            |
| Birthweight             | Median (IQR) | 2425 (2085–2698) | 2425 (2105–2691)         |
| Birthweight discordance | Median (IQR) | 9.6 (4.6–16.3)   | 9.5 (4.5–16.2)           |

IQR, interquartile range.

**SUPPLEMENTAL TABLE 2****Comparison of coefficients for twin (GROW-T) and singleton (GROW-S) standards**

| Characteristics             | Twin        |               | Singleton <sup>a</sup> |               |
|-----------------------------|-------------|---------------|------------------------|---------------|
|                             | Coefficient | % of constant | Coefficient            | % of constant |
| Constant <sup>b</sup>       | 2666.9      |               | 3055.4                 |               |
| Ethnicity                   |             |               |                        |               |
| South Asian                 | −80.9       | −3.1          | −128.1                 | −4.4          |
| East European               | 23.4        | 0.9           | 7.4                    | 0.2           |
| Sub-Saharan African         | −45.5       | −1.7          | −117.3                 | −4.0          |
| Maternal height (per 10 cm) | 54.0        | 2.0           | 69.6                   | 2.2           |
| Maternal weight (per 10 kg) | 37.0        | 1.4           | 48.8                   | 1.6           |
| Nulliparity                 | −58.2       | −2.2          | −109.4                 | −3.7          |
| Sex                         |             |               |                        |               |
| Male                        | 48.0        | 1.8           | 54.2                   | 1.8           |
| Female                      | −48.0       | −1.8          | −54.2                  | −1.8          |

<sup>a</sup> Regression centered on 40-week gestation; proportionalized to 37 weeks; <sup>b</sup> Centered on a British European mother of 166 cm height, 73 kg weight, and second pregnancy.

## SUPPLEMENTAL TABLE 3

Stillbirth risk associated with SGA defined by STORK,<sup>5</sup> NICHD,<sup>6</sup> and FMF<sup>28</sup> twin standards, compared with the customized twin-specific standard (GROW-T) (N = 16,914)

| SGA according to           | All (n) | Stillbirth (n) | OR   | 95% CI     |
|----------------------------|---------|----------------|------|------------|
| STORK only                 | 1165    | 9              | 2.05 | 1.02–4.17  |
| STORK                      | 3394    | 82             | 6.68 | 4.60–9.71  |
| Overlap (STORK and GROW-T) | 2229    | 73             | 9.46 | 6.46–13.84 |
| GROW-T                     | 2337    | 73             | 9.06 | 6.20–13.23 |
| GROW-T only                | 108     | 0              | -    |            |
| NICHD only                 | 917     | 8              | 2.17 | 1.01–4.65  |
| NICHD                      | 3110    | 81             | 7.18 | 4.94–10.44 |
| Overlap (NICHD and GROW-T) | 2193    | 73             | 9.65 | 6.61–14.09 |
| GROW-T                     | 2337    | 73             | 9.11 | 6.26–13.27 |
| GROW-T only                | 144     | 0              | -    |            |
| FMF only                   | 3316    | 14             | 1.22 | 0.69–2.18  |
| FMF                        | 5653    | 87             | 4.40 | 2.98–6.50  |
| Overlap (FMF and GROW-T)   | 2337    | 73             | 8.74 | 5.79–13.19 |
| GROW-T                     | 2337    | 73             | 8.74 | 5.79–13.19 |
| GROW-T only                | 0       | 0              | -    |            |

CI, confidence interval; FMF, Fetal Medicine Foundation; GROW-T, twin-specific customized standard; NICHD, National Institute of Child Health and Human Development; OR, odds ratio; SGA, small for gestational age; STORK, South Thames Obstetric Research Collaborative.

## SUPPLEMENTAL TABLE 4

**Diagnostic characteristics to detect adverse outcomes for small for gestational age defined by STORK,<sup>5</sup> NICHD,<sup>6</sup> FMF,<sup>28</sup> and customized twin-specific (GROW-T) and singleton (GROW-S) standards**

| Outcome by standard         | Sens | FPR  | PPV  | NPV  | LR+ | dOR  |
|-----------------------------|------|------|------|------|-----|------|
| <b>STORK</b>                |      |      |      |      |     |      |
| SPR: 20.1%                  |      |      |      |      |     |      |
| Stillbirth                  | 66.1 | 19.7 | 2.4  | 99.7 | 3.4 | 7.95 |
| Resuscitation needed        | 22.7 | 16.4 | 39.9 | 69.2 | 1.4 | 1.49 |
| Apgar score <7 at 5 minutes | 27.5 | 17.9 | 9.0  | 94.6 | 1.5 | 1.74 |
| NICU admission              | 29.6 | 14.5 | 42.5 | 77.1 | 2.0 | 2.49 |
| Neonatal death              | 63.6 | 18.3 | 1.2  | 99.8 | 3.5 | 7.81 |
| <b>NICHD</b>                |      |      |      |      |     |      |
| SPR: 18.4%                  |      |      |      |      |     |      |
| Stillbirth                  | 65.3 | 18.0 | 2.6  | 99.7 | 3.6 | 8.56 |
| Resuscitation needed        | 20.9 | 15.2 | 39.7 | 69.0 | 1.4 | 1.47 |
| Apgar score <7 at 5 minutes | 25.9 | 16.5 | 9.2  | 94.6 | 1.6 | 1.77 |
| NICU admission              | 26.4 | 13.7 | 41.0 | 76.5 | 1.9 | 2.26 |
| Neonatal death              | 63.6 | 16.9 | 1.3  | 99.8 | 3.8 | 8.62 |
| <b>FMF</b>                  |      |      |      |      |     |      |
| SPR: 33.4%                  |      |      |      |      |     |      |
| Stillbirth                  | 70.2 | 31.3 | 1.5  | 99.7 | 2.2 | 5.16 |
| Resuscitation needed        | 35.5 | 30.3 | 36.1 | 69.2 | 1.2 | 1.27 |
| Apgar score <7 at 5 minutes | 38.3 | 31.6 | 7.3  | 94.5 | 1.2 | 1.35 |
| NICU admission              | 41.7 | 28.5 | 34.6 | 77.3 | 1.5 | 1.80 |
| Neonatal death              | 63.6 | 31.9 | 0.7  | 99.8 | 2.0 | 3.74 |
| <b>GROW-T</b>               |      |      |      |      |     |      |
| SPR: 13.8%                  |      |      |      |      |     |      |
| Stillbirth                  | 58.9 | 13.5 | 3.1  | 99.7 | 4.4 | 9.18 |
| Resuscitation needed        | 15.8 | 10.5 | 41.9 | 68.8 | 1.5 | 1.59 |
| Apgar score <7 at 5 minutes | 21.2 | 11.7 | 10.5 | 94.5 | 1.8 | 2.04 |
| NICU admission              | 19.6 | 9.6  | 42.4 | 75.7 | 2.0 | 2.29 |
| Neonatal death              | 54.5 | 12.1 | 1.5  | 99.8 | 4.5 | 8.71 |
| <b>GROW-S</b>               |      |      |      |      |     |      |
| SPR: 44.4%                  |      |      |      |      |     |      |
| Stillbirth                  | 68.5 | 44.2 | 1.1  | 99.6 | 1.6 | 2.75 |
| Resuscitation needed        | 43.0 | 42.4 | 32.8 | 67.7 | 1.0 | 1.02 |
| Apgar score <7 at 5 minutes | 44.0 | 42.5 | 6.3  | 94.1 | 1.0 | 1.07 |
| NICU admission              | 45.8 | 41.4 | 28.6 | 75.0 | 1.1 | 1.20 |
| Neonatal death              | 63.6 | 42.5 | 0.5  | 99.8 | 1.5 | 2.37 |

dOR, diagnostic odds ratio; FMF, Fetal Medicine Foundation; FPR, false positive rate; GROW-T, twin-specific customized standard; GROW-S, singleton standard; LR+, positive likelihood ratio; NICHD, National Institute of Child Health and Human Development; NICU, neonatal intensive care unit; NPV, negative predictive value; PPV, positive predictive value; Sens, sensitivity; SPR, screen positive (=SGA) rate; STORK, South Thames Obstetric Research Collaborative.