Published in final edited form as:

Am J Obstet Gynecol. 2020 February ; 222(2): 174.e1–174.e10. doi:10.1016/j.ajog.2019.08.027.

Intrauterine growth discordance across gestation and birthweight discordance in dichorionic twins

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Abstract

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Conflicts of Interest: The authors report no conflict of interest.

Clinical Trial Registration:

Date of registration: June 9, 2011

Date of initial participant enrollment: May 29, 2011

Clinical trial identification number: NCT01369940

URL of registration site: [Clinicaltrials.gov](https://clinicaltrials.gov)

Presented at: Society for Pediatric and Perinatal Epidemiologic Research 31st Annual Meeting, June 18–19, 2018, Baltimore, MD; Eunice Kennedy Shriver National Institute of Child Health and Human Development 14th Annual Fellows Retreat, April 20, 2018, Washington, DC.

Disclaimer: M.M.A., P.S.A., A.M.B., S.N.H. and K.L.G. are US federal government investigators/fellows.

Condensation:

Dichorionic inter-twin estimated weight differences increase across gestation, with an enlarging percentage of pregnancies exceeding a fixed percent discordance cut-off as gestation advances.

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Background: Though inter-twin size difference is an important measure of fetal growth, the appropriate cut-point to define discordance is unclear. Few studies have assessed inter-twin differences in estimated fetal weight longitudinally or in relation to size differences at birth.

Objectives: To estimate the magnitude of percent differences in estimated fetal weight across gestation in dichorionic twins in relation to a fixed discordance cut-point and compare classification of aberrant fetal growth by different measures (estimated fetal weight differences, birthweight discordance, small for gestational age).

Study Design: Women age 18–45 years from 8 US centers with dichorionic twin pregnancies at 8 weeks 0 days (8w0d)–13w–6d gestation planning to deliver in participating hospitals were recruited into the NICHD Fetal Growth Studies--Dichorionic Twins study and followed through delivery (n=140; 2012–2013). Ultrasounds were conducted at 6 targeted study visits to obtain fetal biometrics and calculate estimated fetal weight. Percent estimated fetal weight and birthweight differences were calculated: $(\text{Weight}_{\text{larger}} - \text{Weight}_{\text{smaller}}) / \text{Weight}_{\text{larger}} * 100$; discordance was defined as $\geq 18\%$ for illustration. Birth sizes for gestational age (both, one, or neither small for gestational age) were determined; twins were categorized into combined birthweight+small for gestational age groups: birthweight discordance $\geq 18\%$ (yes, no) with both, one, or neither small for gestational age. Linear mixed models estimated percentiles of estimated fetal weight percent differences across gestation and compared estimated fetal weight differences between combined birthweight discordance and small for gestational age groups. Fishers' exact test compared birthweight discordance and small for gestational age classifications.

Results: Median estimated fetal weight percent difference increased across gestation (5.9% at 15.0, 8.4% at 38.0 weeks), with greater disparities at higher percentiles (e.g., 90th percentile: 15.6% at 15.0, 26.3% at 38.0 weeks). As gestation advanced, an increasing percentage of pregnancies were classified as discordant using a fixed cut-point: 10% at 27.0, 15% at 34.0, and 20% at 38.0 weeks. Birthweight discordance and small for gestational age classifications differed ($P=0.002$); for birthweight discordance $\geq 18\%$ versus $< 18\%$: 44% versus 71% had neither small for gestational age; 56% versus 18% had one small for gestational age; no cases (0%) versus 11% had both small for gestational age, respectively. Estimated fetal weight percent difference varied across gestation by birthweight discordance+small for gestational age classification ($P=0.040$). Estimated fetal weight percent difference increased with birthweight discordance $\geq 18\%$ (neither small for gestational age: 0.46%/week [95% CI 0.08, 0.84]; one small for gestational age: 0.57%/week [95% CI 0.25, 0.90]), but less so without birthweight discordance (neither small for gestational age: 0.17%/week [95% CI 0.06, 0.28]; one small for gestational age: 0.03%/week [95% CI -0.17, 0.24]); both small for gestational age: 0.10%/week [95% CI -0.15, 0.36]).

Conclusion: The percentage of dichorionic pregnancies exceeding a fixed discordance cut-point increased over gestation. A fixed cut-point for defining twin discordance would identify an increasing percentage of twins as discordant as gestation advances. Small for gestational age and percent weight differences assess distinct aspects of dichorionic twin growth. A percentile cut-point may be more clinically useful for defining discordance, although further study is required to assess whether any specific percentile cut-point correlates to adverse outcomes.

Keywords

dichorionic; estimated fetal weight; fetal growth; small for gestational age; twin

Introduction

Fetal growth is an important determinant of perinatal and lifelong health.¹ Twins, representing 3.3% of U.S. births,² have a greater risk of aberrant fetal growth compared to singletons.^{2–4} In addition to traditional growth measures, inter-twin size difference, expressed as percent difference in weight (measured or estimated), is a unique aspect of twin growth associated with adverse outcomes (e.g., preterm delivery, perinatal morbidity/mortality).^{5,6} Most evidence suggests the larger twin's fetal growth curve follows that of concordant twins or singletons while the smaller twin's weight becomes increasingly growth restricted.^{7,8}

The appropriate percent cut-point for defining clinically significant inter-twin differences, i.e. discordance, is unknown.^{9,10} Lesser inter-twin weight differences (~10%) may reflect normal physiologic differences in genetic potential for dizygotic twins^{5,11,12} or epigenetic modifications.¹³ Additionally, relationships between inter-twin differences in growth measures and their associations with adverse outcomes varies among prior studies. For example, a retrospective cohort study of appropriately grown dichorionic twin pregnancies found no increased risk of adverse outcomes including preterm birth, stillbirth, or neonatal intensive care unit admission with birthweight discordance ≥20%.¹⁴ However, a prospective cohort study in unselected dichorionic twin pregnancies found birthweight discordance exceeding 18% was associated with increased risks of perinatal morbidity (composite outcome including mortality, respiratory distress syndrome, hypoxic–ischemic encephalopathy, periventricular leukomalacia, necrotizing enterocolitis, or sepsis), though having one twin small-for-gestational age (SGA), defined as birthweight < 5th percentile, was not associated with increased risk of perinatal morbidity.⁵ These findings highlight the potential varying influences of different measures of twin fetal growth, discordance in fetal growth and fetal growth restriction of one or both twins using SGA at birth as a proxy, in relation to neonatal outcomes. In addition to uncertainties regarding the relationship between these distinct measures and their ability to identify abnormal growth differences associated with adverse outcomes, it is important to note that prior discordance research largely focused on birthweight differences, while few studies assessed longitudinal estimated fetal weight discordance alone or in comparison to birthweight discordance or size for gestational age. One retrospective study presented chorionicity-specific curves of percent differences in estimated fetal weight across pregnancy,¹⁵ though its homogeneous European population limits generalizability. Therefore, in a contemporary U.S. cohort, we estimated fetal weight differences across gestation, evaluated how applying a single, fixed percentile cut-point to define discordance would classify dichorionic twin growth as being discordant or not, and explored the relationships among estimated fetal weight differences, birthweight discordance, and birth size for gestational age.

Materials and Methods

This study is a secondary analysis of a prospective cohort study of dichorionic twin pregnancies. From February 2012–January 2013, 171 women age 18–45 years from 8 centers across the U.S. with dichorionic twin pregnancies at 8 weeks 0 days (8w0d)–13w6d gestation planning to deliver in participating hospitals were recruited into the NICHD Fetal

Growth Studies--Dichorionic Twins study cohort.^{3,16} Dichorionicity was confirmed by presence of two gestational sacs with twin peak or thick intervening membrane. Gestational age was confirmed by ultrasound dating matching last menstrual period-based gestational age (for the larger twin) or determined by embryo age and date of transfer for in vitro fertilization conceptions, as described previously.³ Exclusion criteria were: planned fetal reduction, nuchal translucency ≥ 3.5 mm in either twin, sonogram detected structural or chromosomal congenital anomalies, or crown-rump length discordance $>10\%$. For this secondary analysis, additional exclusion criteria were: voluntary reduction/termination after enrollment, unknown birth outcome for both twins, congenital anomaly detected after enrollment, and percent difference in estimated fetal weight unavailable for at least one visit.

At enrollment, experienced, credentialed sonographers performed an ultrasound per standardized protocol to confirm gestational age and chorionicity and obtain baseline fetal biometric measures. At enrollment, women were interviewed with respect to sociodemographic characteristics, pre-pregnancy weight, and medical, obstetrical, and reproductive history.

Following enrollment, participants returned to undergo up to six study visits to measure fetal biometrics (measured in triplicate with the average used for analysis). Using a Hadlock regression formula,¹⁷ estimated fetal weight of each twin was calculated using head circumference, abdominal circumference, and femur length. Percent difference in estimated fetal weight (%) at each study visit was defined (Equation 1):

$$\text{Percent difference} = \frac{(\text{Estimated fetal weight [larger twin, g]} - \text{Estimated fetal weight [smaller twin, g]})}{\text{Estimated fetal weight (larger twin, g)}} * 100$$

Ultrasounds were performed using Voluson E8 machines (standard operating procedures specified; GE Healthcare, Milwaukee, WI), with an endo-vaginal multifrequency volume transducer (real-time intracavity 6–12 MHz) and transabdominal curved multifrequency volume transducer (real-time abdominal 4–8 MHz). Study data was collected into a ViewPoint clinical system (GE Healthcare) customized application. Measurements were manually entered into an online data collection system.

After delivery, relevant data, including birthweight, gestational age at delivery, and twin pair sex (same-sex male, same-sex female, unlike-sex; per ultrasound data if unavailable in delivery records [$n=5$]), were abstracted from medical charts. Percent difference in birthweight for twin pairs was calculated (analogous to Equation 1), then twin pairs were categorized as either birthweight discordant ($\geq 18\%$ difference in birthweight) or concordant ($<18\%$ difference in birthweight). We selected 18% difference in weight as the cut-point for illustration based on findings from a prospective study that found birthweight differences exceeding 18% to be associated with an increased risk of perinatal morbidity.⁵ Birth size for gestational age of each twin was determined as SGA (birthweight $<10^{\text{th}}$ percentile), large for gestational age (LGA; birthweight $>90^{\text{th}}$ percentile), or AGA (birthweight $10^{\text{th}}\text{--}90^{\text{th}}$ percentile) based on gestational age at delivery and neonatal sex specific percentiles of live-born singleton deliveries;¹⁸ twin pairs were classified as both SGA, one twin SGA, or

neither twin SGA. Finally, each twin pair was categorized into one of 6 possible combined birthweight discordance+SGA groups, i.e. birthweight discordant and both SGA, 1 SGA, or neither SGA or birthweight concordant and both SGA, 1 SGA, or neither SGA.

Additional information regarding study procedures, data collected, and quality control (sonographer training and credentialing) and assurance (random scan re-measurement) was previously reported.^{3,16,19} All women provided written informed consent and institutional review board approval was obtained for each participating site, the data coordinating center, and the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (11-CH-N178; 6/13/2011).

Statistical Methods

Percent difference in estimated fetal weight by gestational age was modeled using linear mixed models with fixed and random intercepts (centered at 15.0 weeks, the earliest week with relevant ultrasound data) and slopes. After performing diagnostic tests to verify model assumptions were met, percent difference in estimated fetal weight was modeled on the original scale since (i) data appeared normally distributed, (ii) variation appeared constant across gestational age, and (iii) changes across time appeared linear on this scale.

Using models described above, reference charts of percentiles (10th, 25th, 50th, 75th, 90th) of differences in estimated fetal weight (%) by week of gestation (15.0–38.0) were generated. To provide insight into the impact of using a single cut-point of percent difference to define “significant” inter-twin growth deviation (i.e., discordance), the 80th and 85th percentiles were also calculated and all calculated percentiles by gestational age were plotted in relation to a fixed 18% cut-point. Potential differences by twin pair sex (same-sex male, same-sex female, unlike-sex) in percent differences in estimated fetal weight percentiles across gestation were also assessed. Bootstrapping analysis was conducted (1000 simulations with random sampling from data set, with replacement) to compute 95% confidence intervals around percentiles to assess estimate uncertainty.

Categorization of aberrant growth based on either birth size for gestational age or birthweight discordance was compared using Fisher’s exact test to determine whether these measures identified the same pregnancies as having aberrant fetal growth, i.e., both or 1 twin SGA or birthweight discordant (≥ 18% difference in birthweight). To relate estimated fetal weight differences with birthweight measures, a linear mixed model was fit to evaluate differences in estimated fetal weight between combined birthweight discordance+birth size for gestational age groups at 15 weeks and then across gestation. If statistically significant differences between the combined groups were found at 15 weeks or across gestation, to determine which groups differed, pairwise comparisons (reference group: neither SGA +birthweight concordant) were performed using t-tests. A figure was generated using model-based beta estimates to graphically present estimated fetal weight differences across pregnancy within each combined category.

Percentiles of percent estimated fetal weight differences were estimated, percentiles by twin pair sex were compared, and bootstrapping analysis was conducted using R (version 3.4.4).

All other analyses were conducted using SAS software (version 9.4; SAS Institute, Inc, Cary, NC). Statistical significance was determined using 2-tailed tests ($p < 0.05$).

Results

171 women with dichorionic twin pregnancies were enrolled; 4 subsequently underwent voluntary reduction/termination, 5 deactivated, 17 had a fetal anomaly detected following enrollment, 1 miscarried before first study ultrasound, 1 was lost-to-follow-up without birth data, and 3 had no further ultrasounds. Thus, 140 women were included in this analysis (Figure 1). Women had a mean age of 31.4 (SD 6.0) years with a self-reported pre-pregnancy BMI of 27.2 kg/m² (SD 6.6) and were generally of high socio-economic status (75% having private health insurance; 54% having household income \$100,000). At birth, 13% were birthweight discordant ($> 18\%$ difference; $n=137$ pregnancies: 2 delivered at non-participating hospitals with partial delivery data available, 1 no delivery data). Based on birth size for gestational age classification ($n=132$ pregnancies: 5 missing SGA due to GA at delivery < 24 weeks [outside validated range for determining birth size for gestational age]; 3 pregnancies missing birthweight; Table 1), in most pregnancies neither twin was SGA (66%; includes $n=2$ 1 LGA/1AGA and $n=87$ both AGA), while fewer instances of both twins SGA (10%) or 1 twin SGA (23%) were observed.

The percent difference in estimated fetal weight for the 10th, 25th, 50th, 75th and 90th percentiles over gestation are presented in Table 2 and Figure 2. Median percent estimated fetal weight differences increased across pregnancy, from 5.9% at 15.0 to 8.4% at 38.0 weeks. Lesser increases were noted at the 10th percentile (from 2.3% at 15.0 to 2.7% at 38.0 weeks) and the 25th percentile (from 3.6% at 15.0 to 4.6% at 38.0 weeks). Conversely, greater increases were observed in the 75th percentile (from 9.9% at 15.0 to 15.3% at 38.0 weeks) and the 90th percentile (from 15.6% at 15.0 to 26.3% at 38.0 weeks). No differences in percent estimated fetal weight percentiles across gestation were found by twin pair sex (same-sex male, same-sex female, unlike sex; $P=0.243$). Variability of the 90th percentile from the bootstrapping analysis was generally low: 18.0 weeks (95% CI 15.2, 18.6), 24.0 weeks (95% CI 15.2, 17.1), and 30.0 weeks (95% CI 18.2, 21.0) except for at the end of pregnancy, where greater variability was observed (34 weeks: 95% CI 22.0, 27.9; 38 weeks: 95% CI 27.7, 39.1).

We evaluated the use of a single, fixed 18% cut-point to define significant estimated fetal weight discordance across pregnancy (Figure 2). Prior to 26.0 weeks gestation, less than 10% of dichorionic twin pregnancies were classified as discordant (Figure 2). This percentage increased as gestation progressed, with 15% crossing this threshold by 34.0 and nearly 20% at 38.0 weeks.

At birth, aberrant growth was categorized differently depending upon whether it was assessed by birth size for gestational age or birthweight discordance ($P=0.002$; Table 3). Among birthweight discordant pregnancies ($> 18\%$ difference in birthweight), though most (56%) had 1 twin SGA, in 44%, neither twin was SGA and in none were both SGA. Conversely, among birthweight concordant pregnancies ($< 18\%$ difference), though most (71%) had neither twin SGA, in 18% 1 twin was SGA and in 11% both twins were SGA.

Comparison of percent differences in estimated fetal weight across gestation by combined birth size for gestational age and birthweight discordance categories are presented in Figure 3. Though similar at 15 weeks of gestation ($P=0.897$), changes in percent differences in estimated fetal weight across gestation differed between the groups ($P=0.040$). In birthweight discordant pregnancies, percent difference in estimated fetal weight increased across gestation regardless of whether either twin was SGA (neither twin SGA: 0.46% per week, 95% CI 0.075, 0.84; 1 twin SGA: 0.57% per week, 95% CI 0.25, 0.90). In contrast, in birthweight concordant pregnancies, regardless of whether either twin was SGA, lesser increases in percent difference in estimated fetal weight across gestation were observed (neither twin SGA: 0.17% per week, 95% CI 0.056, 0.28; 1 twin SGA: 0.033% per week, 95% CI -0.17, 0.24; both twins SGA: 0.10% per week, 95% CI -0.15, 0.36). Compared to the birthweight concordant and neither SGA group, statistically significant differences in the change in percent difference in estimated fetal weight across gestation were only found for the birthweight discordant and at least 1 twin SGA group ($P=0.020$).

Comment

Principal Findings

In dichorionic twins, median percent estimated fetal weight difference between dichorionic twins increased linearly across gestation, with greater increases in the 75th and 90th percentiles. A fixed cut-point for defining twin discordance (e.g. 18%)⁵ would result in an increasing percentage of pregnancies classified as having clinically significant discordance as gestation advances. Birth size for gestational age and birthweight discordance (18% difference) provided distinct classifications of aberrant fetal growth; when comparing these birthweight measures in relation to percent differences in estimated fetal weight, sharper increases in differences in estimated fetal weight across gestation were found for pregnancies ultimately birthweight discordant.

Results

The overall pattern of increasing inter-twin estimated fetal weight differences with advancing gestation was similar to a 2017 retrospective study from England that was based on clinical ultrasounds. However, that study only presented percentiles similar to our Table 2 through 33 weeks of gestation due to differences in their fitted/model-based and observed/quintile regression predicted estimated fetal weight differences, limiting clinical use after this gestational age.¹⁵ Furthermore our study included a more racially/ethnically diverse cohort in which data was collected prospectively from extensively trained and credentialed sonographers following a standardized protocol. Findings from both differ from an older 1987 prospective longitudinal study of 35 healthy U.S. twin pregnancies that found “fairly constant” differences over gestation, though exact estimates at different timepoints were not reported.²⁰ Lack of consistency between the contemporary and older studies may be due to differences in study populations (a non-contemporary cohort of “normal pregnancies” not limited to dichorionic twins in the older study), formula used to calculate estimated fetal weight (Shepard²¹ in the older study versus Hadlock¹⁷), or improvements in ultrasound technologies resulting in more accurate fetal biometric measures.²²

Research and clinical implications

No consensus exists regarding what cut-point should be used to define clinically relevant estimated fetal weight or birthweight discordance. In addition to a recent prospective study suggesting a cut-point of 18% for birthweight discordance (based on a doubling of perinatal morbidity and mortality risk above that threshold),⁵ additional studies found mortality/morbidity increases with cut-points ranging from 10%,²³ 20%,^{23–26} 25%,²⁷ 30%,²⁸ to as high as 40%.²⁹ Given the disparate findings regarding the threshold of weight differences at which morbidity/mortality increases, no single optimal cut-point has emerged to define discordance, with suggested cut-points ranging from a 15% to a 30% difference in estimated fetal weight or birthweight.^{8–10,23,30–32} Regardless of the specific cut-point used, a fixed cut-point would identify an increasing percentage of pregnancies as “at-risk” as pregnancy advances. Therefore, a percentile-based definition of discordance may be more clinically useful, though further research is necessary to determine whether any specific percentile cut-point is related to adverse outcomes.

Distinguishing independent risks of discordance, SGA, and fetal (intrauterine) growth restriction, which frequently occur concomitantly,^{6,12,14,25,33,34} and pathologic and physiologic (i.e., normal differences due to genetic potential,^{5,11,12,35} epigenetic modifications,¹³ or differences in fertilization days³⁶) differences in growth patterns in twin gestations is challenging.^{3,10,31,37} Though numerous studies found discordance is an independent risk factor for adverse perinatal outcomes,^{5,6,31,38–41} potentially including risks in the larger twin,^{5,24,42,43} findings were not consistent across all studies.¹⁴ As would be expected, we found that having one twin SGA/one twin AGA was associated with birthweight discordance. Nonetheless, these measures did not correlate perfectly. As shown by our results and prior studies, birthweight discordance alone to classify aberrant fetal growth could miss instances where both twins are SGA, twin pairs may exhibit discordancy despite neither being SGA,^{14,33} or both twins may be SGA although they are birthweight concordant (<18% difference). Given these discrepancies in the classification of inter-twin growth, birthweight discordance and SGA appear to reflect different aspects of abnormal twin growth. Future studies are needed to determine the independent contribution of these different measures in relation to short and long-term morbidity of the twins.

Strengths and Limitations

Our study had a relatively small sample size, with more variability in estimated percentiles with advancing gestational age as sample size decreased due to delivery earlier in gestation. As noted, the appropriate cut-point to define discordancy remains unknown/controversial. Nonetheless, though uncertainty increased in late gestation and our choice to use 18% based on empirical evidence was only for illustration and may not reflect the optimal cut-point, our overall findings demonstrate that any fixed cut-point chosen to define discordance would classify increasing percentages of pregnancies as having clinically significant discordance as gestation progresses. Strengths include the longitudinal prospective design with standardized scanning protocol and stringent quality assurance/control,⁴⁴ allowing us to examine estimated fetal weight in relation to birthweight discordance and SGA using high quality data. Additional strengths include recruitment of a contemporary cohort of dichorionic twins, high retention, and low levels of missing data. Although certain findings may be

intuitive to some, demonstrating and quantifying these relationships is important, as intuition is not always confirmed.

Conclusions

In our sample of dichorionic twins, percent difference in estimated fetal weight increased across gestation, providing evidence that a fixed cut-point for defining twin discordance would identify increasing percentages of pregnancies as being at-risk as gestation advances. Our data suggest using a percentile cut-point may be more clinically useful, although further studies are required to determine whether gestational age-specific percentile cut-points better identify adverse outcomes than a set percentile defining twin discordance. Birthweight discordance and birth size for gestational age provide distinct measures for assessing fetal growth. Given the complexities of differentiating pathologic versus physiologic trajectories of inter-twin intrauterine estimated fetal weight differences, further research evaluating longitudinal measures of percent difference in estimated fetal weight across gestation in relation to adverse neonatal and childhood outcomes is necessary to define appropriate cut-points.

Acknowledgements

Authors acknowledge research teams at participating clinical centers for the NICHD Fetal Growth Studies--Dichorionic Twins (Christina Care Health Systems, Columbia University, Long Beach Memorial Medical Center, Northwestern University, University of Alabama at Birmingham, University of California, Irvine, Medical University of South Carolina, Women and Infants Hospital of Rhode Island) and C-TASC and Emmes in providing data and imaging support for this multi-site study.

Sources of Funding: This research was supported by the Intramural Research Program of the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development, National Institutes of Health (Contract Numbers: HHSN275200800013C; HHSN275200800002I; HHSN27500006; HHSN275200800003IC; HHSN275200800014C; HHSN275200800012C; HHSN275200800028C; HHSN275201000009C). The funding source was not involved in the study design, data collection and analysis, or manuscript drafting or submission.

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AJOG at a Glance**A. Why was this study conducted?**

- Though inter-twin size difference is an important growth measure, the appropriate cut-point for defining discordance is unclear.
- Few studies assessed differences in estimated fetal weight longitudinally or compared fetal growth classifications (percent weight difference, small for gestational age).

B. What are the key findings?

- The percentage of dichorionic pregnancies exceeding a fixed discordance cut-point increased over gestation.
- SGA and percent difference in birthweight assess distinct aspects of fetal growth.

C. What does this study add to what is already known?

- A fixed cut-point for defining twin discordance would identify increasing percentages of pregnancies as being at-risk as gestation advances.
- Further research is needed to evaluate whether gestational age-specific percentile cut-points better identify adverse outcomes than a set percentile defining twin discordance.

Figure 1:
Participant flow diagram (N=140; NICHD Fetal Growth Studies--Dichorionic Twins, USA, 2012–13)

Retention of women in this secondary analysis of NICHD Fetal Growth Studies--Dichorionic Twins. Participants were followed until occurrence of an event (e.g., delivery, deactivation). Delivery data from chart abstraction was available for n=137 women (n=1 with no delivery data; n=2 with partial delivery data due to delivery at a non-participating

hospital). Following visit 6, n=2 live births 20 weeks one twin, fetal deaths 20 weeks one twin occurred.

Numbers in parentheses represent women missing data for that visit

‡Mean gestational age (range) for women with percent difference in estimated fetal weight for that visit

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Figure 2:

Distribution of inter-twin percent differences in estimated fetal weight across gestation among dichorionic twin pregnancies (N=140; NICHD Fetal Growth Studies--Dichorionic Twins, USA, 2012–13)

Estimated 10th, 25th, 50th, 75th, 80th, 85th, 90th percentiles of inter-twin percent differences in estimated fetal weight among dichorionic twins, as estimated by linear mixed models with random slopes and intercepts, centered at 15 weeks. Percentiles plotted in relation to an 18%

cut-point to define clinically significant discordance (horizontal black line) to demonstrate impact of using a fixed cut-point across gestation to define discordance.

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Figure 3:

Percent difference in EFW* by combined birth size at gestational age†+birthweight discordance‡ group (NICHD Fetal Growth Studies--Dichorionic Twins, USA, 2012–13)

Abbreviations: BW, birthweight; EFW, estimated fetal weight; GA, gestational age; SGA, small for GA

Percent difference in EFW across gestation differed by combined birth size at GA+BW discordance group ($p=0.040$), but not at 15 weeks gestation. A statistically significant pairwise difference in percent difference in EFW across gestation was found between the BW concordant+neither SGA group (reference group; 0.17% per week, 95% CI 0.056, 0.28) and the BW discordant+1 twin SGA group (0.57% per week, 95% CI 0.25, 0.90; $p=0.020$). Estimates used to create figure derived from an unadjusted linear mixed model with random slopes and intercepts (centered at 15 weeks).

*Percent difference in weight (EFW or BW; %)= $\frac{(\text{Weight}_{\text{larger twin}} - \text{Weight}_{\text{smaller twin}})}{\text{Weight}_{\text{larger twin}}}$ *100

†Birth size for GA of each twin was determined based on GA at delivery and neonatal sex specific percentiles¹⁸ ($n=132$; missing $n=8$ [$n=5$ GA<24 weeks, $n=3$ no BW])

‡BW discordance: categorized as concordant (<18% difference in BW) or discordant (≥18% difference in BW) based on a prospective study which found BW differences exceeding 18% may be pathologic⁵

Table 1:

Maternal and neonatal characteristics at enrollment and selected birth outcomes (N=140; NICHD Fetal Growth Studies—Dichorionic Twins, USA, 2012–13)

Participant characteristics	n (%) or mean±SD
Maternal characteristics	
Race/ethnicity	
White/non-Hispanic [*]	79 (56)
Black/non-Hispanic	30 (21)
Hispanic	25 (18)
Asian	6 (4)
Age (years)	31.4±6.0
Height (cm)	165.1±6.5
Pre-pregnancy weight (kg) [†]	74.0±18.8
Pre-pregnancy BMI (kg/m ²) [†]	27.2±6.6
Marital status	
Not married	32 (23)
Married/living with partner	108 (77)
Education	
<High school	9 (6)
High school/GED	18 (13)
Some college	23 (16)
College undergraduate	58 (41)
Postgraduate college	32 (23)
Family income [‡]	
\$29,999	29 (23)
\$30,000-\$49,999	5 (4)
\$50,000-\$74,999	12 (9)
\$75,000-\$99,999	13 (10)
\$100,000	69 (54)
Health insurance [‡]	
Medicaid/self-pay/other	35 (25.2)
Private/managed care	104 (74.8)
Current job or full-time student	
No	30 (21)
Yes	110 (79)
Parity	
0	79 (56)
1	61 (44)

Participant characteristics	n (%) or mean±SD
Fertility treatment/method of conception	
IVF without donor eggs or embryos	36 (26)
IUI	8 (6)
Medications without IVF or IUI	10 (7)
Donor eggs, embryos	11 (8)
None of the above	75 (54)
Cigarettes smoked per day during pregnancy	
0	136 (97)
1	4 (3)
Site	500
Columbia University	29 (21)
Christiana	31 (22)
MUSC	14 (10)
Northwestern University	26 (19)
UC Irvine	8 (6)
Long Beach	13 (9)
University of Alabama	18 (13)
WIHRI	1 (1)
Neonatal/birth characteristics	
Neonatal sex [§]	
Like-sex male	36 (26)
Like-sex female	39 (28)
Unlike-sex	65 (46)
GA at delivery ^{//}	35.2±4.2
Birth size for GA ^{‡,¶}	
Both SGA	13 (10)
1 twin SGA	30 (23)
Neither SGA	89 (67)
Percent difference in BW (%) ^{‡,¶}	10.3±8.2
<18% difference (concordant)	119 (87)
18–24.9% difference	9 (7)
25% difference	9 (7)

SD, standard deviation; BMI, body mass index; GED, General Education Development; IVF, in vitro fertilization; IUI, intrauterine insemination; GA, gestational age; BW, birthweight; SGA, small for GA; AGA, appropriate for GA; LGA, large for GA
Percentages not summing to 100% are due to rounding.

* n=1 multi-racial (non-Hispanic white, American Indian/Alaskan Native)

[‡]Where self-reported pre-pregnancy weight missing, first visit weight used (n=2); BMI calculated using reported or measured weight and maternal height at enrollment

[‡]Missing not included: family income (n=12), health insurance (n=1), percent BW difference/discordance (n=3 missing chart abstraction data [n=2: delivered at non-participating hospital with only partial delivery data available; n=1 no delivery data]); BW for GA (n=8 pregnancies [n=5 outside range validated for determining size for GA, i.e. GA<24 weeks; n=3 missing chart abstraction data])

[§]n=5 based on ultrasound (2 same-sex female; 3 unlike-sex [classified dizygotic])

//Where GA at delivery differed between twins, earliest delivery date used (n=1)

[¶]Birth size for GA of each twin was determined based on GA at delivery and neonatal sex specific percentiles;¹⁸ neither SGA includes both twins AGA (n=87) and 1 twin AGA/1 twin LGA (n=2)

[#]Percent difference in BW (%)=(|BWlarger twin-BWsmaller twin|/BWlarger twin)*100; categorized as concordant (<18%) or discordant (≥ 18%) based on a prospective study which found BW differences exceeding 18% may be pathologic⁵

Table 2:

Percent difference in EFW (%)^{*} percentiles for dichorionic twin pregnancies by gestational age (N=140; NICHD Fetal Growth Studies--Dichorionic Twins, USA, 2012–13)

Gestational age (weeks) [†]	Percentile				
	10 th	25 th	50 th	75 th	90 th
15.0	2.3	3.6	5.9	9.9	15.6
16.0	2.3	3.7	6.0	9.9	15.6
17.0	2.4	3.7	6.1	10.0	15.7
18.0	2.4	3.8	6.2	10.1	15.7
19.0	2.5	3.9	6.3	10.2	15.8
20.0	2.6	3.9	6.4	10.4	16.0
21.0	2.6	4.0	6.5	10.5	16.2
22.0	2.7	4.1	6.6	10.6	16.4
23.0	2.7	4.1	6.7	10.8	16.6
24.0	2.7	4.2	6.8	11.0	16.9
25.0	2.8	4.2	6.9	11.2	17.3
26.0	2.8	4.3	7.0	11.4	17.6
27.0	2.8	4.3	7.1	11.6	18.1
28.0	2.8	4.4	7.2	11.8	18.5
29.0	2.8	4.4	7.3	12.1	19.0
30.0	2.8	4.4	7.4	12.4	19.6
31.0	2.8	4.5	7.5	12.7	20.2
32.0	2.8	4.5	7.6	13.0	20.9
33.0	2.8	4.5	7.8	13.3	21.7
34.0	2.8	4.5	7.9	13.7	22.5
35.0	2.7	4.5	8.0	14.0	23.3
36.0	2.7	4.6	8.1	14.4	24.2
37.0	2.7	4.6	8.2	14.8	25.2
38.0	2.7	4.6	8.4	15.3	26.3

EFW, estimated fetal weight

^{*} Percent difference in EFW (%) = $\frac{(\text{EFW}_{\text{larger twin}} - \text{EFW}_{\text{smaller twin}})}{\text{EFW}_{\text{larger twin}}} \times 100$

[†] Gestational age corresponds to exact week (i.e., 16.0 weeks).

Table 3:

Comparative analysis^{*} of categorization of fetal growth within dichorionic twin pregnancies based on BW discordance[†] or birth size for GA[‡] (NICHD Fetal Growth Studies--Dichorionic Twins, USA, 2012–13)

Birth size for GA	BW discordant n (%)	BW concordant n (%)
Both twins SGA	0 (0)	13 (11)
1 twin SGA	10 (56)	20 (18)
Neither twin SGA [§]	8 (44)	81 (71)

BW, birthweight; GA, gestational age; SGA, small for GA; AGA, appropriate for GA; LGA, large for GA

^{*}p=0.002 (Fisher's exact test) for difference between BW discordance and size for GA classifications

[†]Percent difference in BW (%)=(|BWlarger twin-BWsmaller twin|/BWlarger twin)*100; categorized as concordant (<18%) or discordant (≥18%) based on a prospective study which found BW differences exceeding 18% may be pathologic⁵

[‡]Birth size for GA of each twin was determined based on GA at delivery and neonatal sex specific percentiles¹⁸

[§]Neither SGA includes n=2 1 LGA/1 AGA (both BW concordant), n=87 both AGA