

Original Investigation

Comparison of US Birth Weight References and the International Fetal and Newborn Growth Consortium for the 21st Century Standard

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IMPORTANCE This study introduces how the International Fetal and Newborn Growth Consortium for the 21st Century (INTERGROWTH-21st) international birth weight standards alter our previous understanding and interpretations of fetal growth restriction as represented by small for gestational age (SGA) status.

OBJECTIVES To compare the birth weight distributions of the INTERGROWTH-21st international standard to commonly used US references and examine the differences in the prevalence and neonatal mortality risk of SGA status (below the 10th percentile of a population reference).

DESIGN, SETTING, AND PARTICIPANTS We analyzed data from 16 prospective cohorts of newborns on gestational age, birth weight, and systematic mortality follow-up through 28 days from 10 low- and middle-income countries. The studies included were conducted between 1983 and 2008. The analysis was conducted in 2014. Infants were categorized as SGA using the 1991 US birth weight reference, the 1999-2000 US birth weight reference, and the new INTERGROWTH-21st standard. For each study, we compared the SGA prevalence and the risk ratio between SGA status and neonatal mortality, calculated using Poisson regression with robust error variance.

MAIN OUTCOMES AND MEASURES We examine neonatal mortality (death within the first 28 days after birth) as the main outcome measure.

RESULTS The pooled SGA prevalence was 23.7% (95% CI, 16.5%-31.0%) using the INTERGROWTH-21st standard compared with 36.0% (95% CI, 27.0%-45.0%) with the US 2000 reference. The relative decrease in prevalence was larger among infants born at 33 to less than 37 weeks' gestation compared with term infants. The pooled neonatal mortality risk did not differ significantly; the adjusted risk ratios were 2.13 (95% CI, 1.78-2.54; $P < .001$) for the INTERGROWTH-21st standard and 2.12 (95% CI, 1.81-2.48; $P < .001$) for the US 2000 reference.

CONCLUSIONS AND RELEVANCE To our knowledge, INTERGROWTH-21st is the first international newborn standard for size for gestational age for healthy fetal growth. We observed a greater-than-one-quarter reduction in SGA prevalence and no significant change in the associated neonatal mortality risk, resulting in a decrease in the percentage of neonatal death attributable to SGA. Our study sheds light on how previously published studies on SGA status may be reinterpreted with the introduction of this new birth weight standard.

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Small for gestational age (SGA) is defined as weight below the 10th percentile of a sex- and gestational age-specific birth weight reference. Often, SGA status is used as a proxy for intrauterine growth restriction, particularly in contexts in which sonographic assessment of intrauterine growth is not readily accessible. In low-resource settings with high SGA prevalence, maternal undernutrition is considered to be a large contributor to SGA births. An estimated 32.4 million newborns are born SGA annually in low- and middle-income countries (LMICs).¹ In addition, SGA status has been linked to major adverse health outcomes, such as neonatal and infant mortality,² childhood stunting,³ and chronic disease in adulthood.⁴

The definition of SGA has long been debated vis-à-vis reference populations applied in estimating the prevalence of the condition; more than 26 birth weight references with a published 10th percentile value have been identified.⁵ In addition, birth weight references include newborns with adverse exposures.^{6,7} These references were produced for the objective of comparing newborns against the general population, but they do not serve as a prescriptive *standard* that represents how newborns should be growing under optimal pregnancy conditions.

The International Fetal and Newborn Growth Consortium for the 21st Century (INTERGROWTH-21st) Study Group undertook the task of developing a new international newborn weight standard.⁸ Unlike previous birth weight references that simply described the birth weights among the general population, INTERGROWTH-21st attempted to define an international birth weight standard in the context of optimal maternal health and fetal growth. In our analysis, we first compare the sex- and gestational age-specific birth weight distributions and the 10th percentile values of the new INTERGROWTH-21st standard and 2 commonly cited US references.^{6,7} More important, with the advent of the new standard, there is an urgent need to examine how the burden of SGA status, which exists largely in LMICs, and its association with adverse health outcomes differ from previous estimates that have applied US references.^{1,2} We focus our attention on neonatal mortality as a consequence and use 16 prospective cohort data sets from 10 LMICs to explore the change in the prevalence of SGA status and its associated neonatal mortality risk after applying the new standard. Studying this change will shed light on how large an effect interventions that target SGA status may have in reducing the 2.76 million neonatal deaths that occur worldwide each year.⁹

Methods

Comparison of References

The 1991 US birth weight reference, as reported by Alexander et al⁶ (n=3 808 689, US 1991 reference), and the 1999-2000 US birth weight reference published by Oken et al⁷ (n=6 690 717, US 2000 reference) were used for our analyses. The studies included were conducted between 1983 and 2008. The analysis was conducted in 2014. The US 1991 reference is the most commonly cited among US birth weight references beyond the year

At a Glance

- We compare the birth weight distributions of the International Fetal and Newborn Growth Consortium for the 21st Century (INTERGROWTH-21st) international standard to commonly used US references and examine the differences in the prevalence and neonatal mortality risk of small for gestational age (SGA) status.
- The pooled SGA prevalence was 23.7% (95% CI, 16.5%-31.0%) using the INTERGROWTH-21st standard compared with 36.0% (95% CI, 27.0%-45.0%) with the US 2000 reference.
- The pooled neonatal mortality risk did not differ significantly; the adjusted risk ratios were 2.12 (95% CI, 1.81-2.48) for the US 2000 reference and 2.13 (95% CI, 1.78-2.54) for the INTERGROWTH-21st standard.
- We observed a greater-than-one-quarter reduction in SGA prevalence and no significant change in the associated neonatal mortality risk, resulting in a decrease in the percentage of neonatal death attributable to SGA status.

1990, and the US 1999-2000 reference is the most recently published US birth weight reference.⁵ The 2 studies^{6,7} were intended to create a population-representative fetal growth curve for use as a reference; the former described key birth weight cut-offs (5th, 10th, 50th, 90th, and 95th percentiles) for each gestational age, whereas the latter presented birth weight data for every percentile. They obtained birth certificate data from national data sources, such as the National Center for Health Statistics. The gestational age data were all derived from the date of last menstrual period. Alexander et al⁶ established criteria to remove implausible birth weight-gestational age combinations, and Oken et al⁷ applied the same criteria. No additional quality control of birth weight or last menstrual period was conducted because the data were collected by whatever protocols were used at the facilities in which the births occurred.

In contrast, the objective of the INTERGROWTH-21st Study Group was to create an international prescriptive standard of optimal growth against which fetal growth can be compared.⁸ The birth weight standard constructed (INTERGROWTH-21st standard) describes the birthweight curve among infants of pregnant women with minimal adverse exposures for fetal growth. The INTERGROWTH-21st included pregnant women from 8 countries (Brazil, Italy, Oman, United Kingdom, United States, China, India, and Kenya) who met a rigorous set of criteria that put them at a low risk of fetal growth impairment; only 35% of the screened population was eligible, for a final sample of 20 486 live births. Women with a reliable ultrasonography-based gestational age measurement were enrolled from less than 14 weeks' gestation, and newborn anthropometric measurements were taken within 12 hours of birth. **Table 1** provides a summary of the study characteristics.

Small for gestational age was defined as weight below the 10th percentile of a sex- and gestational age-specific birth weight curve. The 10th percentile values of these 3 birth weight references/standard were plotted against each other, and the difference in cutoff weight at each gestational age was calculated. The same comparison was done for the third percentile to examine differences with more severe growth restriction for the INTERGROWTH-21st standard and the US 2000 refer-

Table 1. Study Characteristics of the US 1991 Birth Weight Reference, US 2000 Birth Weight Reference, and the INTERGROWTH-21st Birth Weight Standard

| Reference | Objective | Live Births, No. | Pregnancy Dating | Population Selection | Quality Control | Data Sources |
|--|---|------------------|--|---|---|---|
| US 1991 reference ⁶ | Develop national fetal growth curve to be used as a reference point | 3 134 879 | LMP, limited to 20-44 weeks, GA imputed for cases missing only the day of last normal menses | US general population | Removal of implausible birth weight-GA combinations (details in Alexander et al ⁶) | 1991 US Live Birth File created by the National Center for Health Statistics |
| US 2000 reference ⁷ | Develop continuous national fetal growth curve as a reference point | 7 609 221 | LMP | US general population | Limited to 22-40 weeks, used same implausibility criteria as Alexander et al ⁶ | National Center for Health Statistics 1999 and 2000 natality data sets (all information from birth certificates from all live births in 1999 and 2000 in the United States) |
| INTERGROWTH-21st standard ⁸ | Create an international prescriptive standard for fetal growth | 20 486 | Ultrasonography before 14 weeks' gestation | Pregnant women from Brazil, Italy, Oman, United Kingdom, United States, China, India, and Kenya meeting strict inclusion criteria, selected from facilities with strict inclusion criteria ⁹ | Newborn measurements taken within 12 hours of birth, measurement protocol standardized across sites | Multisite collection (8 countries) |

Abbreviations: GA, gestational age; INTERGROWTH-21st, International Fetal and Newborn Growth Consortium for the 21st Century; LMP, last menstrual period.

^a Detailed criteria can be found in Villar et al.¹⁰

ence. The US 1991 reference does not provide sex-specific birth weight data on the third percentile.

We also plotted the birth weight distributions at each completed gestational week, comparing the INTERGROWTH-21st standard and the US 2000 reference. Only the 3rd, 10th, 50th, 90th, and 97th percentiles were available for the INTERGROWTH-21st standard at the time of publication.

Difference in the Prevalence of SGA and Neonatal Mortality Risk Associated With SGA Status

The Child Health Epidemiology Reference Group has previously published estimates on the burden of SGA in LMICs and the association between SGA or preterm birth and neonatal and infant mortality.^{1,2} For those analyses, prospective study cohorts from LMICs with gestational age, birth weight (with most measured within 72 hours of birth), and systematic mortality follow-up through 28 days were identified. Of the 20 cohorts included in those analyses, we were able to reanalyze 16: 7 from South Asia,¹¹⁻¹⁶ 6 from Sub-Saharan Africa,¹⁷⁻²¹ and 3 from Latin America.²²⁻²⁴ The included studies reported a total of 102 287 live births. Only weights that were measured within 72 hours of birth were used for our analysis to minimize bias. There were 83 128 live births included in the prevalence analysis and 83 042 live births included in the mortality analysis. See eTable 1 in the [Supplement](#) for the description of included studies.

For each cohort, the prevalence of SGA less than 10% (INTERGROWTH-21st, US 1991, and US 2000) and the prevalence of SGA less than 3% (INTERGROWTH-21st and US 2000) were calculated. We also cross-tabulated the SGA status of the infants as categorized by the INTERGROWTH-21st standard vs the US 1991 and 2000 references. We then calculated neonatal mortality adjusted risk ratios (aRRs) of SGA less than 10% (reference, $\geq 10\%$) and less than 3% (reference, $\geq 3\%$), using the INTERGROWTH-21st standard and the US 1991 and 2000 ref-

erences. Poisson regression with robust error variance was used to estimate neonatal mortality aRR of SGA to avoid convergence issues when adjusting for confounders²⁵ (control variables for each study are listed in eTable 2 in the [Supplement](#)). We also explored the mortality risk of exposure categories that combined SGA less than 10% and preterm: term-SGA, preterm-appropriate for gestational age (AGA), and preterm-SGA, with term-AGA as the comparison group. The INTERGROWTH-21st study had too few mothers who met the inclusion criteria and gave birth to infants at less than 33 weeks' or 42 weeks' or later gestation to create standards for those gestational ages. Hence, only gestational ages of 33 to 42 completed weeks were included in this analysis, and only infants born at 33 to less than 37 completed gestational weeks were categorized as preterm. The results were pooled using the metan command in Stata statistical software, with random effects.^{26,27} The statistical significance of the difference between the US reference aRRs and the INTERGROWTH-21st aRR was tested using the statistical approach described by Altman and Bland.²⁸ Prevalences were also pooled using the metan command in Stata statistical software, with random effects.^{26,27}

The individual studies obtained ethical approval from their respective institutions. The data that were shared with the primary author for analysis did not contain personal identifiers and thus were exempt from the Johns Hopkins Bloomberg School of Public Health Institutional Review Board.

Stata statistical software, version 13 (StataCorp), was used for this analysis.

Results

Comparing the INTERGROWTH-21st standard and both US reference 10th percentiles, we found that the difference in the 10th

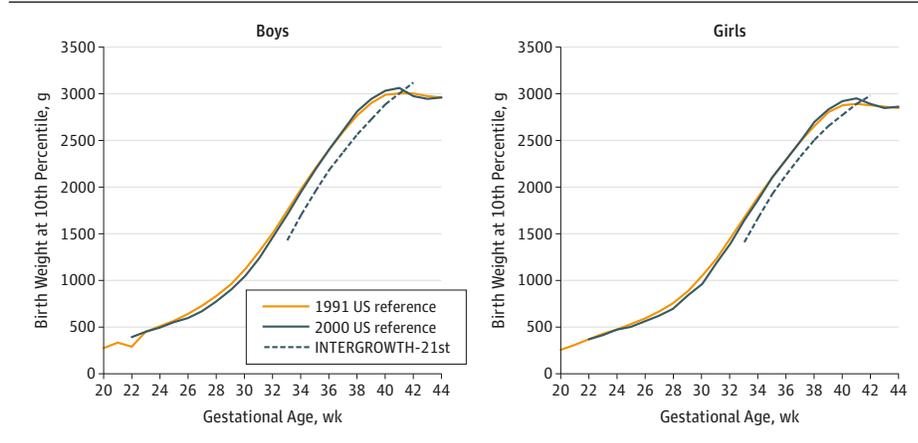
Table 2. The 10th Percentile Birth Weight Values by Gestational Age and Sex Comparing the US 2000 Reference to the INTERGROWTH-21st Standard

| Gestational Age, wk | Boys | | | | | Girls | | | | |
|---------------------|-------------------------|-----------|----------------------------------|-----------|---------------|-------------------------|-----------|----------------------------------|-----------|---------------|
| | US 2000 10th Percentile | | INTERGROWTH-21st 10th Percentile | | | US 2000 10th Percentile | | INTERGROWTH-21st 10th Percentile | | |
| | No. ^a | Weight, g | No. ^a | Weight, g | Difference, g | No. ^a | Weight, g | No. ^a | Weight, g | Difference, g |
| 22 | 13 | 393 | ... | ... | ... | 12 | 362 | ... | ... | ... |
| 23 | 18 | 453 | ... | ... | ... | 16 | 416 | ... | ... | ... |
| 24 | 23 | 498 | ... | ... | ... | 19 | 470 | ... | ... | ... |
| 25 | 27 | 554 | ... | ... | ... | 23 | 504 | ... | ... | ... |
| 26 | 31 | 594 | ... | ... | ... | 27 | 556 | ... | ... | ... |
| 27 | 35 | 674 | ... | ... | ... | 31 | 622 | ... | ... | ... |
| 28 | 42 | 766 | ... | ... | ... | 37 | 693 | ... | ... | ... |
| 29 | 53 | 906 | ... | ... | ... | 46 | 845 | ... | ... | ... |
| 30 | 72 | 1044 | ... | ... | ... | 64 | 965 | ... | ... | ... |
| 31 | 103 | 1241 | ... | ... | ... | 88 | 1180 | ... | ... | ... |
| 32 | 157 | 1475 | ... | ... | ... | 134 | 1390 | ... | ... | ... |
| 33 | 250 | 1712 | 34 | 1430 | 282 | 213 | 1638 | 17 | 1410 | 228 |
| 34 | 443 | 1957 | 48 | 1710 | 247 | 378 | 1872 | 65 | 1680 | 192 |
| 35 | 770 | 2192 | 128 | 1950 | 242 | 656 | 2099 | 114 | 1920 | 179 |
| 36 | 1418 | 2410 | 323 | 2180 | 230 | 1207 | 2299 | 293 | 2140 | 159 |
| 37 | 2889 | 2609 | 857 | 2380 | 229 | 2479 | 2495 | 803 | 2330 | 165 |
| 38 | 5939 | 2807 | 2045 | 2570 | 237 | 5330 | 2694 | 1802 | 2500 | 194 |
| 39 | 8547 | 2947 | 3009 | 2730 | 217 | 8226 | 2834 | 2869 | 2650 | 184 |
| 40 | 7348 | 3029 | 2568 | 2880 | 149 | 7445 | 2919 | 2573 | 2780 | 139 |
| 41 | 3842 | 3063 | 1179 | 3010 | 53 | 3966 | 2949 | 1195 | 2890 | 59 |
| 42 | 1268 | 2979 | 206 | 3120 | -141 | 1315 | 2893 | 224 | 2980 | -87 |
| 43 | 617 | 2949 | ... | ... | ... | 632 | 2849 | ... | ... | ... |
| 44 | 327 | 2954 | ... | ... | ... | 334 | 2863 | ... | ... | ... |

Abbreviations: ellipses, data not applicable; INTERGROWTH-21st, International Fetal and Newborn Growth Consortium for the 21st Century.

^a Number of of infants contributing birth weight data to the specified gestational week.

Figure 1. The 10th Percentile Values for the 1991 and 2000 US References and the International Fetal and Newborn Growth Consortium for the 21st Century (INTERGROWTH-21st) Standard by Gestational Age for Boys and Girls



percentile birth weight value decreased with increasing gestational age, reaching near equality at 41 completed weeks' with the US value being lower at 42 completed weeks (see Table 2 for the US 2000 reference and eTable 3 in the Supplement for the US 1991 reference; Figure 1). We observed similar trends for the third percentile values using the US2000 reference, but

the magnitude of the difference between the standard and the US reference did not decrease in the same linear fashion as for the 10th percentile values. The INTERGROWTH-21st third percentile value was lower at 33 completed gestational weeks and greater at 42 completed gestational weeks (eTable 4, eFigure 1, and eFigure 2 in the Supplement).

Figure 2. Birth Weight at 37 Completed Gestational Weeks Comparing the US 1991 (Sample Size Not Available) and 2000 References (n=2889) and the International Fetal and Newborn Growth Consortium for the 21st Century (INTERGROWTH-21st) Standard (n=849) in Boys and Girls

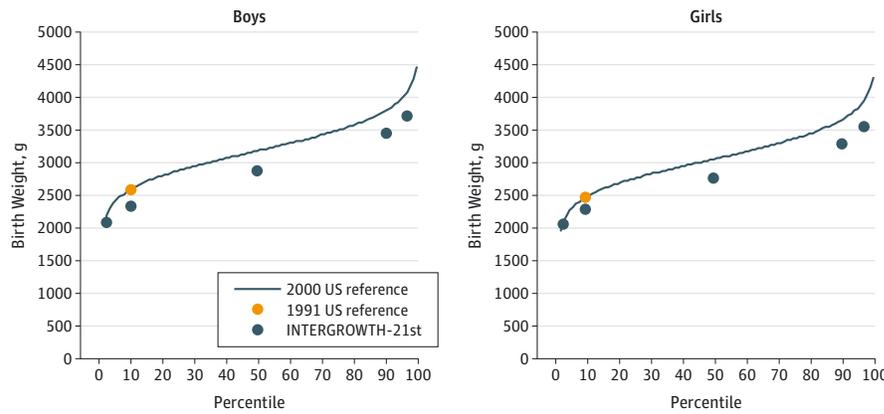
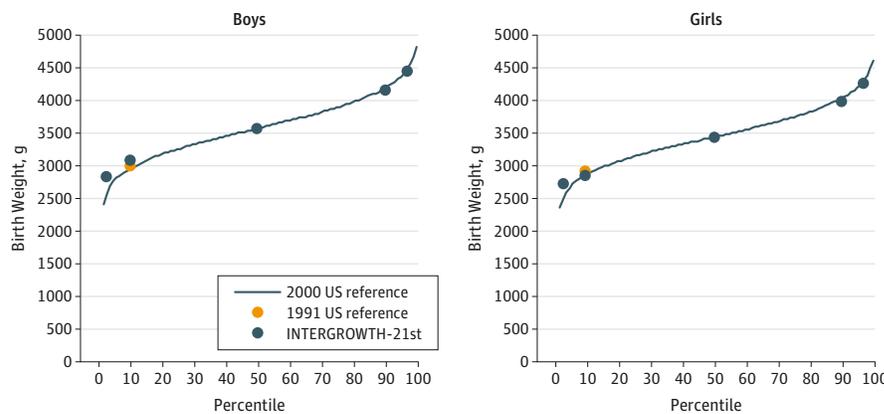


Figure 3. Birth Weight at 42 Completed Gestational Weeks Comparing the US 1991 (Sample Size Not Available) and 2000 References (n=1268) and the International Fetal and Newborn Growth Consortium for the 21st Century (INTERGROWTH-21st) Standard (n=202) in Boys and Girls



For the US 2000 reference and the INTERGROWTH-21st standard, the pattern of divergence of the 2 distributions differed by gestational age (Figure 2A and B for 37 gestational weeks and Figure 3A and B for 42 gestational weeks). At every gestational week up to 42 weeks, the US 2000 reference was higher at all available percentiles, with the absolute birth weight difference becoming more similar at each percentile. Finally, at 42 weeks, the INTERGROWTH-21st standard was higher at the lower tail but eventually converged between the 50th and 90th percentiles and then became lower than the US 2000 reference. Fewer than 100 infants of each sex contributed data for INTERGROWTH-21st from 33 to 34 completed gestational weeks (eg, n=34 for boys and n=17 for girls at 33 weeks).

The pooled SGA prevalence (using <10th percentile) was 23.7% (95% CI, 16.5-31.0%; $P < .001$) using the INTERGROWTH-21st standard, compared with 32.8% (95% CI, 24.1-41.5%; $P < .001$) with the US 1991 reference and 36.0% (95% CI, 27.0-45.0%; $P < .001$) with the US 2000 reference. The prevalence under the INTERGROWTH-21st standard was absolute 9.1% and 12.3% lower and relative 27.7% and 34.2% lower compared with the

1991 and 2000 US references, respectively (eTable 5 in the Supplement). The US 1991 reference had a pooled prevalence of 32.8% (95% CI, 24.1%-41.5%), and prevalence estimates were similar for the use of the US 2000 reference. In contrast, with the use of the INTERGROWTH-21st standard, the pooled prevalence was 23.7% (95% CI, 16.5%-31.0%). The relative change in SGA prevalence between the US references and the INTERGROWTH-21st standard was larger among those who were born at 33 to less than 37 weeks' gestation compared with term infants. The pooled SGA prevalence among neonates born at 33 to less than 37 weeks' gestation decreased from 25.1% (95% CI, 18.2%-31.9%) for the US 1991 reference to 13.3% (95% CI, 8.7%-17.8%) for the INTERGROWTH-21st standard, a 47% relative reduction. In contrast, the pooled estimate of SGA prevalence among term neonates decreased from 34.7% (95% CI, 24.8%-44.6%) for the US 1991 reference to 25.9% (95% CI, 17.4%-34.3%) for the INTERGROWTH-21st standard, a 25% relative reduction, but with overlapping CIs. Similar patterns were seen for severe SGA (using less than the third percentile) (eTable 6 in the Supplement). In each study, 1% or less of the infants were

US 1991 AGA and recategorized as INTERGROWTH-21st SGA. Approximately 12% of the infants in each study were US 1991 SGA and recategorized as INTERGROWTH-21st AGA (see eTable 7 in the Supplement for study-specific tabulations). Similar results were seen with the US 2000 reference (eTable 6 in the Supplement).

Despite the differences in SGA prevalence, the pooled neonatal mortality risk for SGA did not statistically significantly differ between the US references and the INTERGROWTH-21st standard (eTable 8 in the Supplement). The pooled aRR was 2.13 (95% CI, 1.78-2.54) for the INTERGROWTH-21st standard, 2.28 (95% CI, 1.85-2.81) for the US 1991 reference, and 2.12 (95% CI, 1.81-2.48) for the US 2000 reference (difference between INTERGROWTH-21st and US 1991, $P = .63$; difference between INTERGROWTH-21st and US 2000, $P = .97$). The association between severe SGA (<3%) and neonatal mortality was almost identical for the INTERGROWTH-21st standard and US 2000 reference (aRR, 2.71; 95% CI, 2.22-3.31; and aRR, 2.56; 95% CI, 2.14-3.05; respectively). For term-SGA, preterm-AGA, and preterm-SGA (comparison: term-AGA), the magnitude of the associations were slightly larger for INTERGROWTH-21st, but as with the other associations, they were not statistically significantly different (P values for difference between INTERGROWTH-21st and U.S. 1991: term-SGA, $P = .52$; preterm-AGA, $P = .89$; preterm-SGA, $P = .14$; between INTERGROWTH-21st and U.S. 2000: term-SGA, $P = .43$; preterm-AGA, $P = .51$; preterm-SGA, $P = .16$). For term-SGA, the pooled aRRs were 2.32 (95% CI, 1.84-2.91; $P < .001$) for the INTERGROWTH-21st standard, 2.09 (95% CI, 1.67-2.62; $P < .001$) for the US 1991 reference, and 2.05 (95% CI, 1.67-2.52; $P < .001$) for the US 2000 reference. For preterm-AGA, the pooled aRRs were 2.61 (95% CI, 2.03-3.36; $P < .001$) for the INTERGROWTH-21st standard, 2.70 (95% CI, 1.76-4.14; $P < .001$) for the US 1991 reference, and 2.30 (95% CI, 1.74-3.05; $P < .001$) for the US 2000 reference. For preterm-SGA, the pooled aRRs were 11.96 (95% CI, 9.37-15.28; $P < .001$) for the INTERGROWTH-21st standard, 8.97 (95% CI, 6.68-12.05; $P < .001$) for the US 1991 reference, and 9.05 (95% CI, 6.67-12.27; $P < .001$) for the US 2000 reference (eTable 9 in the Supplement).

Discussion

Applying the new INTERGROWTH-21st birth weight standard, we observed a roughly 30% relative reduction in the prevalence of SGA among the cohorts. We did not witness a statistically significant change in the association between SGA and neonatal mortality. This finding may be due to larger SGA infants with lower mortality risk being recategorized from SGA under the US reference to AGA under the new standard. Approximately one-tenth of the infants in each cohort were categorized as SGA by the US 1991 reference but AGA by the INTERGROWTH-21st standard, whereas a negligible number shifted in the opposite direction. The SGA-less-than-10% cut-offs using US-based references may have been too inclusive in identifying neonates at risk due to fetal growth restriction. It is also unclear as to the extent to which miscategorization of gestational age due to the use of last menstrual period in the US references may have affected these findings.

The analysis only included infants of 33 to 42 weeks' gestation because birth weight distributions were only available for those gestational weeks in the INTERGROWTH-21st standard. Although the prevalence of SGA was higher among term infants, the relative reduction in prevalence when applying the INTERGROWTH-21st standard was greater among infants born at 33 to less than 37 weeks' gestation compared with term infants. This difference in the relative change may have occurred because pathologic preterm births are overrepresented in US references. Consequently, we saw a larger relative reduction in the percentage of neonatal mortality attributable to SGA among the infants born at 33 to less than 37 weeks' gestation.

The INTERGROWTH-21st sex- and gestational age-specific birth weight standard is intended to serve as a global standard for optimal intrauterine growth. Minimal disparities in birth weight distributions were observed across the 8 populations that met INTERGROWTH-21st inclusion criteria despite contextual differences.²⁹ The INTERGROWTH-21st study used early pregnancy ultrasonography dating, unlike the US references that relied on last menstrual period.³⁰ The inclusion and exclusion criteria used to enroll women attempted to exclude individuals with barriers to optimal fetal growth. This exclusion makes this standard different from the US birth weight references that include all-singleton births during a specified period, including those with conditions and risk factors associated with fetal growth restriction and preterm birth. Because of this exclusion, the INTERGROWTH-21st study had few early-preterm or postterm infants, and few infants contributed data to the lower gestational weeks. Such data imply that we have the potential to greatly reduce preterm rates, in both developing and developed countries, if we can address known maternal risk factors.

In contrast to the highly selected INTERGROWTH-21st population, the general US population is expected to have exposures, such as lifestyle factors and elective cesarean sections, that are contributing preterm births to the birth weight references. The overall preterm rate in the INTERGROWTH-21st cohort was 5.6%. In comparison, the US preterm rate is approximately 14%,³¹ and rates in the studies included in our analysis ranged from 5% to 22%. Because infants who are born both preterm and SGA have the highest neonatal and infant mortality risk,² it is critical to identify them for secondary and tertiary prevention of disability and mortality.

The pattern of divergence between the INTERGROWTH-21st standard and the US 2000 reference differed by gestational age. For example, among preterm births (33 to <37 weeks' gestation), the INTERGROWTH-21st birth weights were lower than the US 2000 curve, but the difference between the 2 curves widened in the higher percentiles. We speculate that this divergence at the higher tail may occur because of risk factors, such as gestational diabetes and overweight and obesity, that are linked to higher birth weight and preterm birth³²⁻³⁴ and are more prevalent in a US population but excluded from the INTERGROWTH-21st study. The prevalence of gestational diabetes may be as high as 9% in the United States,³⁵ and the prevalence of obesity among adult women was 29.3% and 39.6% in the United States (taken from National Health and Nutrition

Examination Surveys for 1991 and 2000, respectively, the years from which the US birth weight references were taken).³⁶ The mothers contributing births to the lower tail of the distribution may be more similar in risk profile between the INTERGROWTH-21st standard and the US references; for example, they may comprise women who are genetically predisposed to having smaller children. At 37 weeks' gestation, there was a similar pattern of greater divergence at the higher tail of the distribution, but the disparity in weight was smaller than at earlier gestations. Finally, at 42 weeks, the INTERGROWTH-21st infants were slightly bigger in the lower tail, with the curves converging between the 50th and 90th percentiles. Similar to our hypothesis of the divergence in the weight distributions for those born at earlier gestations, the minimal divergence of the birth weight curves in later gestation may suggest that women who remain pregnant up to term tend to be healthier and at lower risk and thus have a similar risk profile to those enrolled in the INTERGROWTH-21st study. The fact that the INTERGROWTH-21st standard was consistently lower in birth weight than the US reference, except at 42 completed

weeks of gestation, may be related to various pregnancy morbidities that were excluded for INTERGROWTH-21st study but represented in the US reference.

Conclusions

We present a comparison of SGA prevalence and associated neonatal mortality risk between the new standard on optimal fetal growth and existing birth weight references. We observed lower rates of SGA prevalence without a significant change in neonatal mortality risk using the new standard; we noted a subsequent decrease in the percentage of neonatal death attributable to SGA among preterm births. The INTERGROWTH-21st standard will likely become the comparison of choice for future studies. The US references will remain useful in understanding the growth status of a newborn in relation to the general US population. Our study sheds light on how previously published studies on SGA and fetal growth restriction may be reinterpreted with the introduction of this new birth weight standard.

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