OBSTETRICS

From population reference to national standard: new and improved birthweight charts

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BACKGROUND: Antenatal detection of intrauterine growth restriction remains a major obstetrical challenge, with the majority of cases not detected before birth. In these infants with undetected intrauterine growth restriction, the diagnosis must be made after birth. Clinicians use birthweight charts to identify infants as small-for-gestational-age if their birthweights are below a predefined threshold for gestational age. The choice of birthweight chart strongly affects the classification of small-for-gestational-age infants and has an impact on both research findings and clinical practice. Despite extensive literature on pathological risk factors associated with small-for-gestational-age, controversy exists regarding the exclusion of affected infants from a reference population.

OBJECTIVE: This study aims to identify pathological risk factors for abnormal fetal growth, to quantify their effects, and to use these findings to calculate prescriptive birthweight charts for the Dutch population.

MATERIALS AND METHODS: We performed a retrospective cross-sectional study, using routinely collected data of 2,712,301 infants born in The Netherlands between 2000 and 2014. Risk factors for abnormal fetal growth were identified and categorized in 7 groups: multiple gestation, hypertensive disorders, diabetes, other pre-existing maternal medical conditions, maternal substance (ab)use, medical conditions related to the pregnancy, and congenital malformations. The effects of these risk factors on mean birthweight were assessed using linear regression. Prescriptive birthweight charts were derived from live-born singleton infants, born to ostensibly healthy mothers after uncomplicated pregnancies and spontaneous onset of labor. The Box-Cox-*t* distribution was used to model birthweight and to calculate sex-specific percentiles. The new charts were compared to various existing birthweight and fetal-weight charts.

RESULTS: We excluded 111,621 infants because of missing data on birthweight, gestational age or sex, stillbirth, or a gestational age not between 23 and 42 weeks. Of the 2,599,640 potentially eligible infants, 969,552 (37.3%) had 1 or more risk factors for abnormal fetal growth and were subsequently excluded. Large absolute differences were observed between the mean birthweights of infants with and without these risk factors, with different patterns for term and preterm infants. The final low-risk population consisted of 1,629,776 live-born singleton infants (50.9% male), from which sex-specific percentiles were calculated. Median and 10th percentiles closely approximated fetal-weight charts but consistently exceeded existing birthweight charts.

CONCLUSION: Excluding risk factors that cause lower birthweights results in prescriptive birthweight charts that are more akin to fetal-weight charts, enabling proper discrimination between normal and abnormal birthweight. This proof of concept can be applied to other populations.

Key Words: birthweight, fetal growth, intrauterine growth restriction, reference charts, risk factors, small-for-gestational-age

Birthweight charts are easy-to-use tools that can help determine whether birthweight is appropriate for the corresponding gestational age. Care providers are especially interested to know whether a child is small-for-gestational-age (SGA) because of the associated higher risks of neonatal mortality and morbidity.[1,2] The classification serves as a proxy measure for intrauterine growth restriction (IUGR), which is a pregnancy condition in which the fetus does not reach its biological growth potential. Although the terms SGA and IUGR are often used interchangeably, conceptually they are different. SGA refers to a statistical definition that denotes a fetus or infant whose anthropometric measurements (ie, birthweight) are below a predefined threshold for gestational age. SGA infants may be small but healthy, whereas in IUGR, growth pathology is implicit. Antenatal detection of SGA, and especially IUGR, is a major obstetric challenge, with the majority of cases not detected before birth.[3,4] In these infants, the diagnosis must be made after birth.[4]

In 2008, The Netherlands Perinatal Registry (PRN, now Perined) presented new Dutch reference charts for birthweight by gestational age.[5] These charts were based on virtually all birthweight data from 2001. Hence, they were distinctly descriptive in nature, representing the actual birthweight distribution of Dutch infants.[5] After the charts were introduced, the proportion of infants classified as SGA decreased. Infants born after provider-initiated delivery due to suspected SGA tended to have birthweights well above the SGA threshold, leading to major discrepancies between the antenatal classification of SGA and the subsequent neonatal classification.[6]

In contrast to descriptive population references, prescriptive birthweight charts are derived from populations without risk factors for SGA and constitute a standard representing optimal birthweight for gestational age. Previous studies have shown that compared to descriptive birthweight charts, prescriptive birthweight charts can improve the identification of SGA infants at risk of adverse outcomes.[6,7] Moreover, they can approximate fetal-weight charts and decrease the discrepancy between the antenatal and neonatal classification of

Cite this article as: Hoftiezer L, Hof MHP, Dijs-Elsinga J, et al. From population reference to national standard: new and improved birthweight charts. Am J Obstet Gynecol 2019;220:383.e1-17.

0002-9378/$36.00

https://doi.org/10.1016/j.ajog.2018.12.023

Related editorial, page 293.

AJOG at a Glance

Why was the study conducted?

The choice of birthweight chart influences the classification of small-for-gestational-age infants and impacts both research findings and clinical practice. Population-based birthweight references underestimate the incidence of low birthweight.

Key findings

The presence of risk factors for abnormal fetal growth results in substantially lower birthweights, which significantly impacts birthweight charts. Prescriptive birthweight charts can approximate fetal-weight charts and facilitate discrimination between normal and abnormal birthweight.

What does this add to what is known?

This study adds evidence to support the development of alternative, prescriptive birthweight charts.

(suspected) SGA.[8,9] Despite extensive literature on the associations between risk factors and SGA, the actual effects of supposed risk factors on birthweight are not often quantified.[10]

In 2014, a multidisciplinary working group was established with representatives of Perined, the Dutch Society of Obstetrics and Gynaecology (NVOG), the Royal Dutch Organisation of Midwives (KNOV), and the Dutch Association of Pediatrics (NVK). One of the principal goals of this working group was to ensure national uniformity on the choice of birthweight charts, and, by extension, the definition of SGA. The consensus was to update the Dutch birthweight charts, using a low-risk subpopulation as proposed by Hoftiezer et al.[6] The aim of this study was to quantify the effects of well-known risk factors for SGA on mean birthweight, and to use these findings to calculate new and improved birthweight charts for the Dutch population. This national standard will replace the former Dutch population reference[5] and will facilitate discrimination between normal and abnormal birthweight.

Materials and Methods

Procedures

Data were extracted from the Dutch perinatal database, which is a linked database of medical registries from the 4 professional organizations that provide perinatal care in The Netherlands: the NVOG, KNOV, NVK and the National Association of General Practitioners (LHV).[11] Registration of obstetric data starts at the first antenatal visit; the neonatal registry contains data only on neonates who were hospitalized following delivery.[12] In over 95% of pregnancies, gestational age is certain, either confirmed by or based on an early ultrasound. The registry contains detailed anonymized population-based information on pregnancies, deliveries and neonatal (re)admissions.[11] Items are recorded as diagnostic codes (ie, congenital malformations), categorical variables (ie, delivery onset method), or continuous variables (ie, highest diastolic blood pressure). Overall, the Perined database contains data from over 97% of all pregnancies in The Netherlands and is considered to be an unbiased representation of the Dutch population.[6,11,12]

For the present analysis, we used data on births between January 1, 2000, and December 31, 2014. Stillbirths and records with missing birthweight, gestational age, or sex were excluded. Risk factors for SGA and excessive fetal growth were identified through an extensive literature search and expert consultation, and were regarded as exclusion criteria if also present in the database. We identified 7 categories: multiple gestation, hypertensive disorders, diabetes, other pre-existing maternal medical conditions, maternal substance (ab)use, medical conditions related to the pregnancy, and congenital malformations. More details are provided in Supplementary Table 1. Infants who were born after provider-initiated birth (ie, elective induction of labor or pre-labor cesarean delivery) were also considered high-risk, because of anticipated overrepresentation of growth-restricted infants.[13] Obvious outliers that likely resulted from data errors were removed from the data.

The final low-risk study population consisted of live-born singleton infants, born to ostensibly healthy mothers after uncomplicated pregnancies and spontaneous onset of labor. Percentiles were fitted from 23 weeks of gestational age onward, and for male and female infants separately.

Statistical analysis

Statistical analyses were performed with SAS 9.4 software (SAS Institute, Cary, NC) and R 3.3.1 (R Core Team [2016], R Foundation for Statistical Computing, Vienna, Austria).

Baseline characteristics were analyzed using descriptive statistics. Linear regression was used to model the relationship between birthweight and each individual risk category. To account for the effect of gestational age, the analyses were stratified by gestational age in completed weeks.

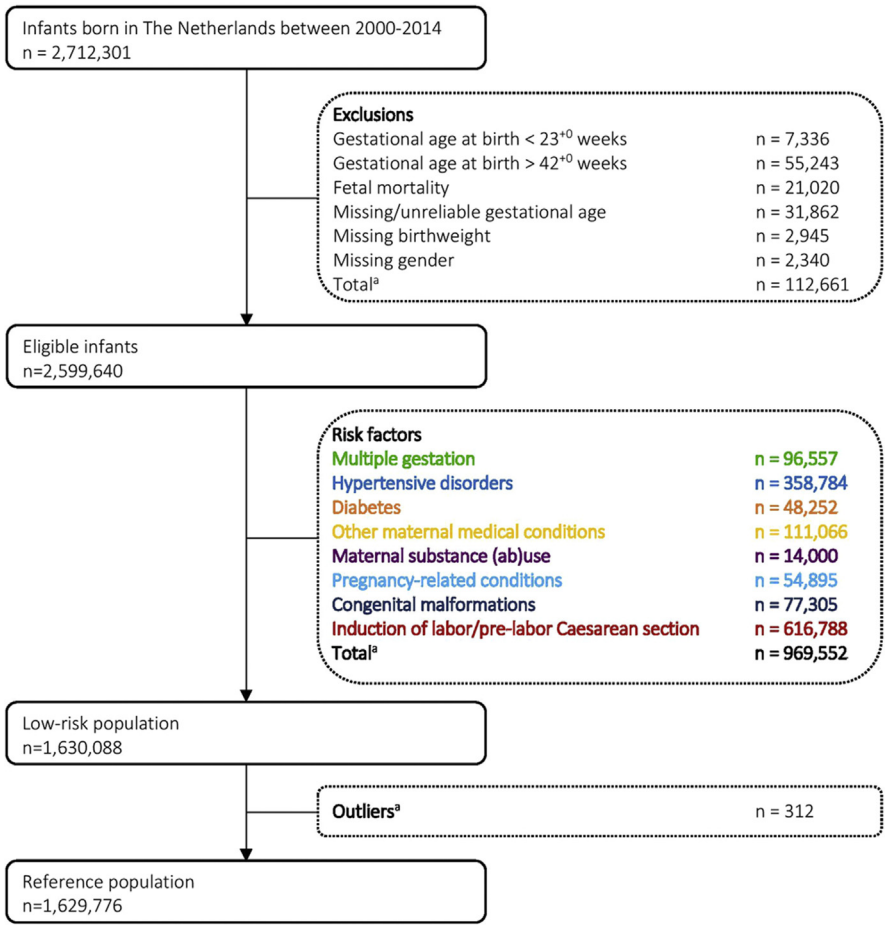
After excluding all high-risk pregnancies, sex-specific birthweight percentiles were generated with the lambda-mu-sigma-tau method. This method assumes that data can be transformed with a Box-Cox power transformation to fit a desired distribution.[14] In particular, we used the Box-Cox-t power formula to transform the data to fit a t-distribution. First, the Box-Cox-t power formula transforms birthweight $Y(t)$ at gestational age t into a new variable, $Z(t)$, by using the following formula

$$Z(t) = \begin{cases} \frac{1}{\sigma(t)\nu(t)}\left(\left[\frac{Y(t)}{\mu(t)}\right]^{\nu(t)} - 1\right) & \text{if } \nu(t) \neq 0, \\ \frac{1}{\sigma(t)} log\left[\frac{Y(t)}{\mu(t)}\right] & \text{if } \nu(t) = 0, \end{cases}$$

where $\nu(t)$ is the power parameter (L), $\mu(t)$ the location parameter (M), and $\sigma(t)$ the scale parameter (S). Second, it is assumed that the transformed variable $Z(t)$ follows a Student's t distribution with $\tau(t)$ degrees of freedom (T). By using the inverse of the Box-Cox-t power formula, values can be transformed to fit the original birthweight data.

To fit the lambda-mu-sigma-tau method with the Box-Cox-t power transformation to the data, we used the GAMLSS package for R statistical software.[15] All 4 parameters of the Box-Cox-t power formula were modeled as smooth functions of gestational age using P-splines.[16] The penalty parameters of the P-splines were estimated using local maximum likelihood. Model selection was based on the generalized Akaike Information Criterion (AIC); the models with the smallest generalized Akaike Information Criterion were selected. Model fit was assessed by visual inspection of the smoothed centiles superimposed on observed empirical centiles and by comparing the predicted vs observed frequency below selected percentiles. The resulting percentiles were compared with the previous Dutch birthweight charts[5] and Hadlock's fetal-weight chart,[17] which, at the time of this study, was recommended by the NVOG for monitoring fetal growth. We also compared our charts to 2 existing and widely adopted international birthweight charts.[18–20]

FIGURE 1
Flow diagram of the study population



[a]More than 1 criterion may apply to the same infant/pregnancy.

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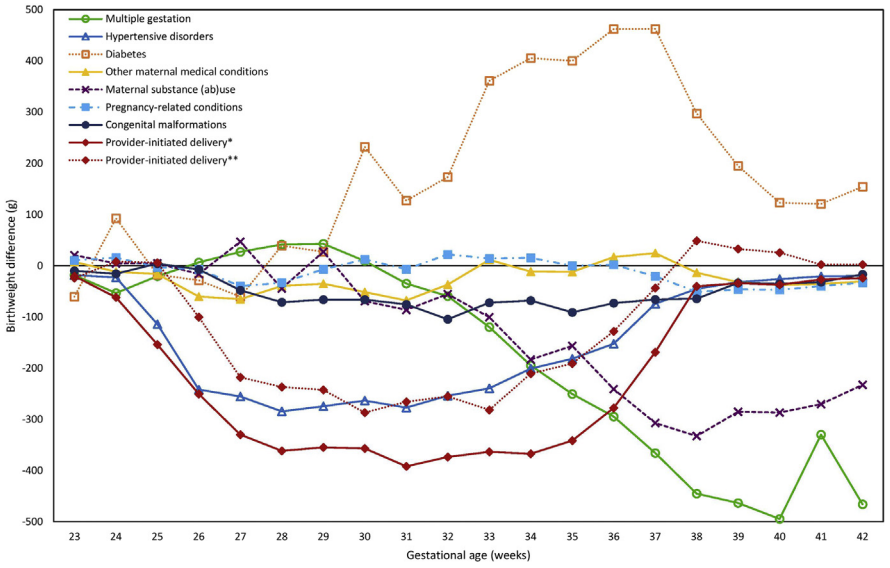
Results

Between 2000 and 2014, a total of 2.7 million infants were born in The Netherlands. We excluded 112,661 infants (4.2%) because of missing data, fetal death, or gestational age not between 23 and 42 weeks (Figure 1). To obtain a low-risk population, another 969,552 infants (37.3%) were excluded because of the presence of 1 or more risk factors.

Figure 2 shows the differences in mean birthweight between infants with risk factors vs infants without. From 31 weeks' gestation onward, twins and higher-order multiple births had lower birthweights than singleton infants. Infants with congenital malformations weighed slightly less than infants without malformations. Mean birthweights of (preterm) infants born to hypertensive mothers were considerably lower than birthweights of infants born to normotensive mothers. The maximum difference was 285 g around 28 weeks' gestation, corresponding to approximately 25% of the mean birthweight at this age. The negative effect of maternal substance (ab)use on birthweight increased with increasing gestational age. Maternal diabetes resulted in higher birthweights; this effect was more pronounced in mothers who had pregestational diabetes as opposed to gestational diabetes (data not shown). The effects of other maternal medical conditions and pregnancy-related conditions appeared to be relatively small and variable, most likely because of the heterogeneity of the included conditions.

The principal cause of exclusion was provider-initiated delivery (63.6%), followed by hypertensive disorders (37.0%) (Figure 1). Over 83% of provider-initiated preterm births had additional risk factors for SGA. In term infants, the proportion of infants without additional risk factors for SGA ranged from 31.6% to 79.9% for infants born at 37 and 42 weeks' gestation, respectively (Supplementary Table 2). Figure 2 shows that preterm infants without additional risk factors for SGA still had considerably lower birthweights than infants who were born after spontaneous onset of labor. From 38 weeks' gestation onwards, mean

FIGURE 2
Quantified effects[a] of risk factors on mean birthweight



[a]Each risk factor has its own reference population, namely, the population without that particular risk factor. *Provider-initiated delivery with risk factors for abnormal fetal growth. **Provider-initiated delivery without risk factors for abnormal fetal growth.

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birthweights were similar regardless of how labor was initiated.

In general, the exclusion rate decreased with increasing gestational age (Supplementary Table 2). The relatively high proportion of exclusions at 23 weeks' gestation may be explained by late termination of pregnancy (and subsequent provider-initiated delivery) because of severe congenital malformations. The high rate of exclusions at 41 and 42 weeks' gestation resulted from a relatively high proportion of provider-initiated deliveries, most likely because of (impending) post-term pregnancy.

After visually inspecting the scatterplot of the remaining birthweights and corresponding gestational ages, 312 records were identified as outliers and were excluded from the dataset. The neonatal mortality rate among these outliers was more than 50 times higher than among the study population (ie, 64.1 vs 1.3 per 1000 live births), suggesting that at least some outliers may have been extreme but realistic birthweights. Because these extreme birthweights likely resulted from either extreme IUGR or excessive fetal growth, exclusion was considered justified.

The remaining 1,629,776 infants (60.1%) served as the reference population for the new birthweight charts. Table 1 shows the baseline characteristics of the reference population. Among the excluded records were relatively more preterm births, low birthweights, and hospital deliveries. Other differences were considered not to be clinically relevant, although statistically significant because of extremely large sample sizes.

Details on the new birthweight charts are given in Supplementary Tables 3 and 4. Comparison of the smoothed percentiles superimposed on the empirical percentiles in Figure 3 indicates a good fit. Supplementary Table 5 shows that the new percentiles performed well, with similar proportions of infants classified below each percentile as expected. When applied to high-risk infants only (n = 969,552), 14.8% of term and 33.6% of preterm infants had birthweights below the 10th percentile (Supplementary Figure 1), as opposed to ±10% of low-risk infants (Supplementary Figure 1 and Supplementary Table 5).

In Figure 4, the new percentiles for male infants are superimposed on existing birthweight and fetal-weight charts. The fetal-weight chart[17] agrees almost perfectly with our percentiles; the differences between the existing and new birthweight charts tend to decrease with increasing gestational age and with increasing birthweight. Similar results were found for female infants, except that the non–sex-specific fetal-weight charts[17] slightly but consistently overestimated the generally lower birthweights of female infants (supplementary Figure A2). The maximum differences between the 10th percentiles of the former Dutch population reference[5] and the new, prescriptive birthweight chart were found at 31 weeks' gestation, that is, 380 g (+35.9%) and 333 g (+30.1%) for male infants born to nulliparous and multiparous mothers, respectively. The 10th percentile of another, widely adopted population reference, also ran consistently below our 10th percentile.[18] Finally, the percentiles of the prescriptive INTERGROWTH-21st birthweight chart were much lower than our prescriptive percentiles, and in contrast to the other charts, the differences did not converge with increasing gestational age (Figure 4).[19,20]

Comment

This article describes the development of prescriptive birthweight charts, derived from a large population of Dutch infants without risk factors for SGA or excessive fetal growth.

Numerous authors in many countries have put a great deal of thought into the desired properties of birthweight charts. Despite extensive literature on the subject, there is little evidence to support a particular approach. Sources of controversy include the choice of infants who should be included in a population and whether to evaluate specific groups of infants with certain charts.[21] In 2 previous studies, we found that prescriptive birthweight charts are the most effective in identifying clinically important adverse outcomes in SGA infants.[6,9] These results provided

the rationale for the development of prescriptive birthweight charts, to serve as a standard for the Dutch population.

Interpretation

The new birthweight charts differ from the former Dutch birthweight charts[5] in several respects, such as their prescriptive nature and the starting point at 23 weeks' instead of 25 weeks' gestation. Our decision to exclude all infants with risk factors for SGA or excessive fetal growth primarily affected the lower percentiles for preterm infants. This reflects the relatively high prevalence of risk factors for SGA among preterm infants and, consequently, the higher number of exclusions; it also reflects the relatively few exclusions based on risk factors for excessive fetal growth. Another important distinction is that the new birthweight charts are no longer stratified by parity and ethnicity.[5] Stratification by parity or ethnicity implies that the lower birthweights associated with these characteristics are considered normal. However, several studies have shown that the effects of both parity and ethnicity on fetal growth may not be purely physiological.[22–25] Maternal ethnicity, for example, is inextricably linked with low socio-economic status, which, in turn, has been shown to be associated with adverse outcomes.[12,26] To avoid the possibility that the risks associated with the lower birthweights of certain groups of infants are underestimated, the new charts were stratified only by sex.

Our birthweight chart paralleled the Hadlock fetal-weight chart from 23 to 40 weeks.[17] These results demonstrate that the bias caused by the inclusion of preterm infants affected by IUGR can be eliminated by the use of a prescriptive rather than a descriptive sample. In addition to making antenatal and neonatal results more comparable, it demonstrates that if the proper prescriptive birthweight chart is available, there is no need for an estimated fetal-weight chart. Because estimated weights are subject to many sources of error that do not affect birthweights,[27] use of the latter is preferred.

TABLE 1
Baseline characteristics of the study population

	Reference population		Excluded records	
	n	%	n	%
	1,629,776	100.0	1,082,525	100.0
Ethnic origin				
Dutch	1,287,800	79.0	860,006	79.4
Mediterranean	126,078	7.7	77,117	7.1
Other European	56,187	3.4	34,706	3.2
Creole	37,750	2.3	29,483	2.7
Hindustani	17,582	1.1	13,053	1.2
Asian	36,905	2.3	19,105	1.8
Other	56,186	3.4	44,175	4.1
Missing	11,288	0.7	4880	0.5
Sex				
Male	830,348	50.9	560,428	51.8
Female	799,428	49.1	519,757	48.0
Missing	0	0.0	2340	0.2
Parity				
Nulliparous	727,978	44.7	518,713	47.9
Multiparous	901,683	55.3	563,691	52.1
Missing	115	0.0	121	0.0
Socioeconomic status				
Very low	428,544	26.3	292,599	27.0
Low	297,946	18.3	203,499	18.8
Average	278,634	17.1	184,557	17.0
High	273,969	16.8	175,739	16.2
Very high	332,111	20.4	212,212	19.6
Missing	18,572	1.1	13,919	1.3
Maternal age, y				
<18	6156	0.4	3560	0.3
18–35	1,403,960	86.1	888,428	82.1
≥35	219,440	13.5	190,152	17.6
Missing	220	0.0	385	0.0

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When this study was initiated, there were many alternative birthweight charts available, including charts specifically designed for universal application.[18–20] The concept of an international standard is highly appealing, because it would facilitate comparison between countries. In 2014, researchers of the INTERGROWTH-21st Consortium proposed international birthweight standards based on a subpopulation of low-risk infants.[19] The generalizability of these charts was supported by the finding that fetal and neonatal length follow similar growth patterns among different populations around the globe, provided that all other circumstances are optimal/equal.[28] Both the INTERGROWTH-21st[19,20] and our prescriptive birthweight charts were based on a

TABLE 1
Baseline characteristics of the study population *(continued)*

	Reference population		Excluded records	
	n	%	n	%
	1,629,776	100.0	1,082,525	100.0
Gestational age, wk				
<28	2572	0.2	18,749	1.7
28 to <32	4454	0.3	17,772	1.6
32 to <37	66,387	4.1	104,237	9.6
≥37	1,556,363	95.5	909,905	84.1
Missing	0	0.0	31,862	2.9
Birthweight, g				
<1000	2007	0.1	21,635	2.0
1000 to <2000	9791	0.6	45,783	4.2
2000 to <3000	228,828	14.0	253,659	23.4
3000 to <4000	1,139,347	69.9	609,763	56.3
≥4000	249,803	15.3	148,740	13.7
Missing	0	0.0	2945	0.3
Place of delivery[a]				
Home delivery	504,731	31.0	34,237	3.2
Midwife-led in-hospital delivery	287,281	17.6	42,243	3.9
Hospital delivery	826,567	50.7	994,390	91.9
Missing	11,197	0.7	11,655	1.1
Perinatal mortality				
Fetal death	0	0.0	21,020	1.9
Death <24 h	1279	0.1	5424	0.5
Death <2 to 7 days	527	0.0	2037	0.2
Death <8 to 28 days	234	0.0	1002	0.1

[a] The role division between midwives and obstetricians has been established in the so-called List of Obstetric Indications (LOI), which is considered an instrument for risk identification and a guideline for determining who will be the most appropriate care provider for each individual pregnant woman, depending on her specific situation. Around 80% of all pregnant women start their antenatal health care in the primary level of care. If pregnancy, childbirth, and the postpartum period are uncomplicated, the woman remains under the care of the primary midwife. She can make the choice of a home or short-stay in-hospital delivery, both supervised by their own midwife. Women with initial pathology and women in whom pathology occurs (or threatens to occur) during pregnancy, labor, or postpartum are referred to the obstetrician who will take over the care for as long as deemed necessary.[12]

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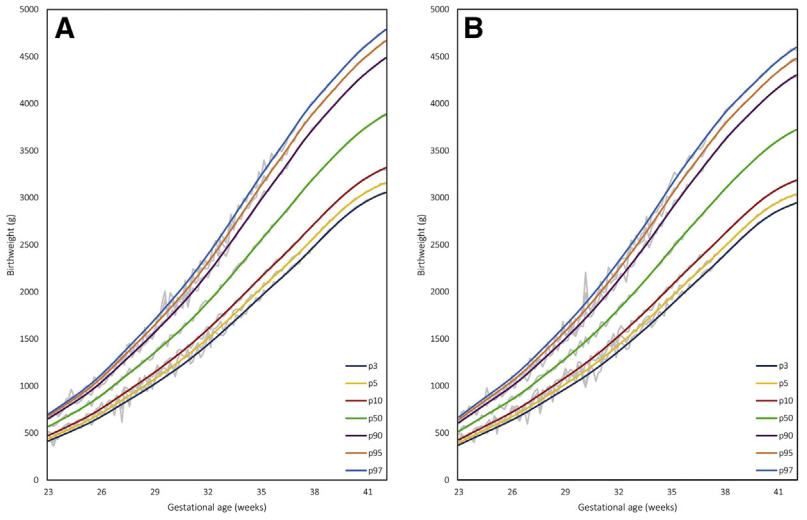
low-risk population. Assuming that growth patterns are indeed similar between populations, we expected our new birthweight charts to agree with the INTERGROWTH-21st charts.[19,20] However, it is noteworthy that the values on our birthweight charts, and in particular for the lower percentiles, were considerably higher than those on the INTERGROWTH-21st charts.[19,20] There may be several explanations for this discrepancy. First, it is possible that the conclusions regarding similarity of growth patterns cannot be generalized for the Dutch population, who are among the tallest people on the planet. Alternatively, the actual similarity of the growth patterns might be questioned. In 2017, Kiserud et al reported similarly large differences between growth patterns of different populations, and concluded that growth patterns were not equal between populations.[29] Finally, although there may be similar growth patterns for fetal and neonatal length between different populations, this may just not apply to birthweight. Differences in birthweight between populations may be caused by differences in body composition (for example, because of different eating habits). Perhaps the solution is to declare a universal standard and to adopt different centile cut-offs for 2 different populations after outcome-based validation. For now, it is evident that the INTERGROWTH-21st birthweight charts[19,20] underestimate (normal) birthweights of Dutch infants and are therefore not recommended for use in The Netherlands.

Strengths and limitations

One of the principal strengths of our study was the use of a large sample, allowing for stable estimates of percentiles even at the extremes of birthweight and gestational age. We identified many potential risk factors for abnormal fetal growth, and by quantifying the actual effects of these risk factors on mean birthweight, we were able to strengthen the rationale behind our choice of exclusion criteria. To the best of our knowledge, this approach has not been taken before. We expect that it will help readers to increase their understanding of the differences between descriptive and prescriptive birthweight charts, and the consequences of applying either to an individual patient or research population. Some of the effects were different from what we expected. For example, prior to 30 weeks' gestation, twins and higher-order multiples were heavier than singleton infants. We hypothesized that this resulted from a different distribution of the other risk factors. In this study, we focused on quantifying the effects of different risk factors on mean birthweight. However, different centiles of birthweight might be affected by different amounts,[10,29] and we intend to investigate this in more detail in a subsequent study.

We recognize that our study has some limitations, including the retrospective design, which poses a higher risk of bias.[30] Because we used an existing database, our sample may have lacked the accuracy and degree of clinical detail

FIGURE 3
New Dutch birthweight charts for male (A) and female (B) infants superimposed on empirical percentiles



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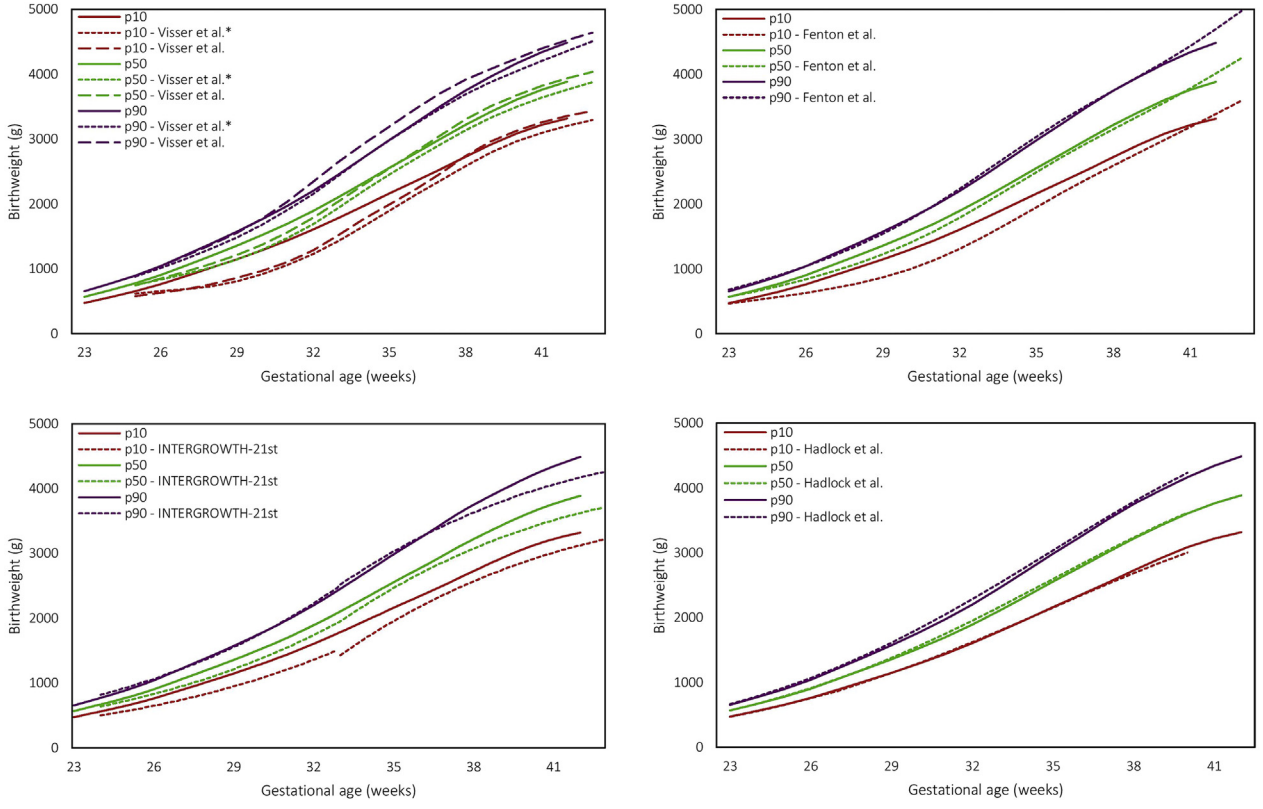
necessary to identify, in retrospect, all pregnancies with risk factors for abnormal fetal growth. Information on some of the risk factors that we identified was either limited (eg, smoking) or not available at all (eg, body mass index[10]). Misclassification of some "high-risk" births as "low-risk" births could theoretically cause a slight downward shift in the lower percentiles. To resolve the issue of underreporting of risk factors, we excluded all provider-initiated deliveries as a proxy for high-risk pregnancies. In concordance with the results of Joseph et al,[13] infants born after provider-initiated deliveries indeed had lower birthweights than infants born after spontaneous onset of labor. Although most iatrogenic preterm births had additional risk factors for abnormal fetal growth, we identified a subgroup of more than 10.000 cases with no known risk factors but significantly lower

FIGURE 4
New Dutch birthweight charts[a] vs alternative weight charts for male infants



[a]Solid lines represent the new Dutch birthweight charts. *Nulliparous mothers.

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birthweights, suggesting the absence or underreporting of well-known risk factors or the presence of yet-unknown risk factors that were not part of the registration/database. The exclusion of all provider-initiated deliveries resulted in the exclusion of a fairly large number of term infants who were likely normally grown. However, birthweight distributions are much more likely influenced by the inappropriate inclusion of abnormally grown infants than by the inadvertent exclusion of healthy infants.

Another disadvantage of our prescriptive charts, although not so much of our study, was the lack of reference values for head circumference and length. Unfortunately, both measures are not routinely collected in The Netherlands. When we compared 2 alternative head circumference and length charts, we found that the exclusion of risk factors for abnormal fetal growth also affects the reference values for birth length and head circumference, with consistently higher 10th percentiles for the prescriptive chart[31] compared to the population reference.[18] Clearly, methodological differences between the studies complicate the interpretation of these findings. Nevertheless, it appears that defining normal head circumference and birth length is not straightforward. Hopefully future data collection in The Netherlands will allow us to investigate this subject in more detail.

Worldwide, birthweight charts are updated every now and then, and, despite major methodological differences, the thresholds to define abnormal birthweight are seldom questioned. Although we have shown the benefits of prescriptive birthweight charts in 2 previous studies,[6,9] the performance of the new birthweight charts should be evaluated to determine the optimal cut-offs for risk stratification.

The prescriptive birthweight standard described in this study will be implemented nationally and replace the former, descriptive Dutch birthweight population reference. These new birthweight charts can improve identification of SGA infants at risk for clinically important adverse outcomes and can decrease the discrepancy between the in utero and neonatal classification of (suspected) SGA, which will facilitate communication between health care providers among each other and between health care providers and (expectant) parents. If used in conjunction with physical examination, history taking, and other sources of information, they should allow more timely intervention and, where possible, prevention—the ultimate goal being improvement of both neonatal and long-term outcomes. ■

Acknowledgments

This research was supported by the Isala Science and Innovation Fund and Nutricia Early Life Nutrition. The sponsors had no role in the design and conduct of the study, collection, management, analysis, and interpretation of the data, or in the preparation, review, approval of the manuscript, or decision to submit the manuscript for publication.

We thank our collaborators from the Working Group Reference Charts who provided insight and expertise that greatly assisted the research:

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Received July 27, 2018; revised Nov. 11, 2018; accepted Dec. 12, 2018.

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The authors report no conflict of interest.

This work was supported by unrestricted research grants from Nutricia Early Life Nutrition and the Isala Innovation and Science Fund.

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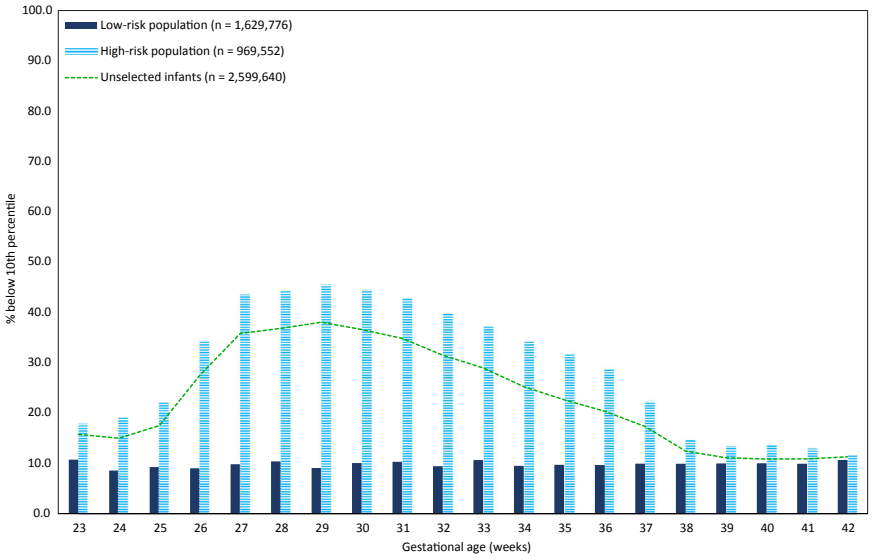
SUPPLEMENTARY FIGURE 1
Percentage of infants with birtweights below the 10th percentile



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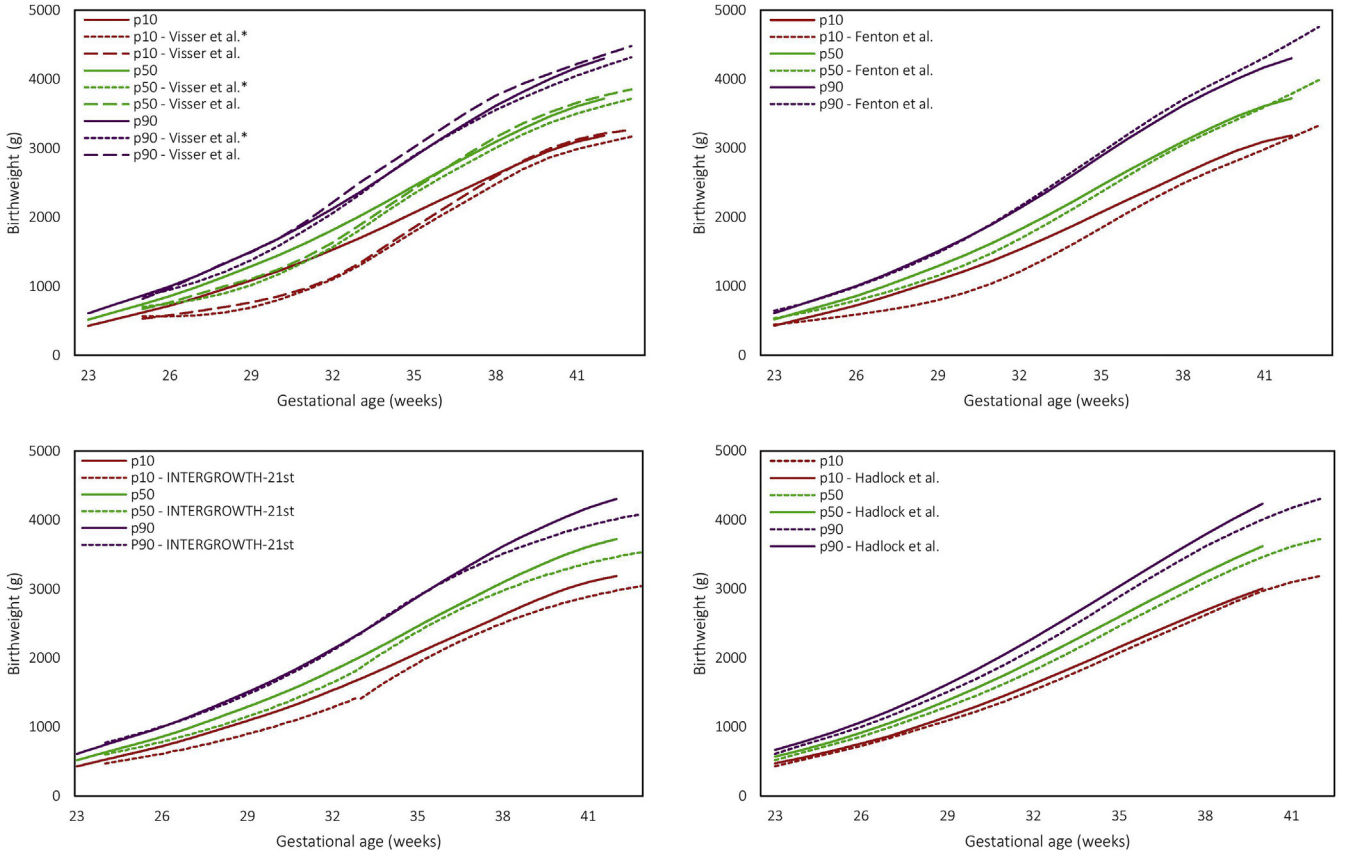
SUPPLEMENTARY FIGURE 2
New Dutch birthweight charts[a] vs alternative weight charts for female infants



[a]Solid lines represent the new Dutch birthweight charts. *Nulliparous mothers.

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SUPPLEMENTARY TABLE 1
Risk factors for abnormal fetal growth[a]

Hypertensive disorders
Diastolic blood pressure >90 mm Hg
Pre-existing hypertension
Pregnancy-induced hypertension
(Pre-)eclampsia
Hemolysis, elevated liver enzymes and low platelets syndrome
Diabetes
Pre-existing diabetes (type 1 or 2)
Gestational diabetes
Pre-existing maternal medical conditions
Respiratory disorders
Congenital heart defects
Thromboembolic disorders
Cardiovascular disease
Anemia
Hemoglobinopathy
Systemic disease
(Recurrent) urinary tract infections
Epilepsy requiring anticonvulsant therapy
Uterine malformation
Obesity
HIV/AIDS
Use of medicines
Other maternal medical conditions (not otherwise specified)
Maternal substance (ab)use
Alcohol consumption
Smoking
Drug (ab)use
Medical conditions related to the pregnancy
TORCH syndrome
Vaginal bleeding
Abnormal placental attachment
Polyhydramnios
Other maternal medical conditions related to the pregnancy (not otherwise specified)

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SUPPLEMENTARY TABLE 1
Risk factors for abnormal fetal growth[a] *(continued)*

Congenital malformation of:
Central nervous system
Sensory organs
Cardiovascular system
Gastrointestinal tract
Respiratory system
Genitourinary system
Skin
Abdominal wall
Musculoskeletal system
Other (not otherwise specified)
Chromosomal abnormalities/syndromes
Endocrine disorders/inborn errors of metabolism
Congenital malignancies
Provider-initiated delivery
Induction of labor
Pre-labor cesarean delivery

TORCH, toxoplasmosis, rubella, cytomegalovirus, herpes simplex, and syphilis.

[a] Neonatal deaths per se were not excluded because this would result in a disproportionately large number of exclusions among preterm infants, which would compromise estimation of percentiles. Preliminary analyses showed significantly lower mean birthweights of term neonatal deaths vs survivors, yet no effect on the empirical percentiles if these deaths were excluded.

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SUPPLEMENTARY TABLE 2
Age-specific risk factor frequencies

Gestational age, completed wk	Population 2000–2014	Eligible infants (denominator)	Reference population	Excluded records[a]								
				Multiple gestation	Hypertensive disorders	Diabetes	Other maternal medical disorders	Maternal substance (ab)use	Pregnancy-related conditions	Congenital malformations	Provider-initiated deliveries	Provider-initiated deliveries without risk factors
	n	n	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (*%*)[b]
23	3484	1336	418 (31.3)	288 (21.6)	62 (4.6)	2 (0.1)	48 (3.6)	6 (0.4)	116 (8.7)	371 (27.8)	484 (36.2)	113 (23.3)
24	2098	1186	490 (41.3)	380 (32.0)	72 (6.1)	6 (0.5)	42 (3.5)	11 (0.9)	161 (13.6)	111 (9.4)	95 (8.0)	26 (27.4)
25	2,234	1442	518 (35.9)	465 (32.2)	158 (11.0)	9 (0.6)	78 (5.4)	13 (0.9)	221 (15.3)	201 (13.9)	182 (12.6)	41 (22.5)
26	2844	2128	555 (26.1)	640 (30.1)	408 (19.2)	31 (1.5)	167 (7.8)	15 (0.7)	343 (16.1)	358 (16.8)	614 (28.9)	92 (15.0)
27	3325	2695	591 (21.9)	767 (28.5)	774 (28.7)	22 (0.8)	249 (9.2)	27 (1.0)	454 (16.8)	486 (18.0)	1010 (37.5)	137 (13.6)
28	3900	3308	693 (20.9)	965 (29.2)	936 (28.3)	50 (1.5)	340 (10.3)	32 (1.0)	537 (16.2)	551 (16.7)	1330 (40.2)	168 (12.6)
29	4649	4069	825 (20.3)	1261 (31.0)	1252 (30.8)	70 (1.7)	404 (9.9)	40 (1.0)	661 (16.2)	568 (14.0)	1681 (41.3)	226 (13.4)
30	5977	5415	1212 (22.4)	1601 (29.6)	1668 (30.8)	89 (1.6)	539 (10.0)	77 (1.4)	874 (16.1)	717 (13.2)	2196 (40.6)	245 (11.2)
31	7700	7173	1724 (24.0)	2162 (30.1)	2132 (29.7)	113 (1.6)	658 (9.2)	80 (1.1)	989 (13.8)	856 (11.9)	2812 (39.2)	303 (10.8)
32	11,020	10,441	2810 (26.9)	3303 (31.6)	3122 (29.9)	212 (2.0)	820 (7.9)	94 (0.9)	1147 (11.0)	910 (8.7)	3799 (36.4)	469 (12.3)
33	16,448	15,860	4891 (30.8)	4898 (30.9)	4472 (28.2)	354 (2.2)	1050 (6.6)	165 (1.0)	1503 (9.5)	1164 (7.3)	5158 (32.5)	675 (13.1)
34	26,806	26,137	9414 (36.0)	7322 (28.0)	7190 (27.5)	605 (2.3)	1563 (6.0)	256 (1.0)	2007 (7.7)	1710 (6.5)	7763 (29.7)	1096 (14.1)
35	40,658	39,951	16,615 (41.6)	9395 (23.5)	10,401 (26.0)	1023 (2.6)	2244 (5.6)	386 (1.0)	2398 (6.0)	2227 (5.6)	10,978 (27.5)	1861 (17.0)
36	75,692	74,882	32,657 (43.6)	14,871 (19.9)	19,070 (25.5)	2215 (3.0)	4049 (5.4)	650 (0.9)	3532 (4.7)	3527 (4.7)	23,580 (31.5)	4953 (21.0)
37	180,910	179,776	72,876 (40.5)	24,283 (13.5)	44,555 (24.8)	6701 (3.7)	10,392 (5.8)	1278 (0.7)	5851 (3.3)	7113 (4.0)	78,570 (43.7)	24,867 (31.6)
38	392,554	391,116	184,522 (47.2)	15,837 (4.0)	67,261 (17.2)	16,817 (4.3)	20,643 (5.3)	2440 (0.6)	8719 (2.2)	12,496 (3.2)	160,311 (41.0)	82,234 (51.3)
39	618,911	617,208	415,118 (67.3)	5760 (0.9)	72,527 (11.8)	10,150 (1.6)	25,622 (4.2)	3311 (0.5)	9949 (1.6)	15,736 (2.5)	126,211 (20.4)	73,415 (58.3)
40	714,494	712,634	550,598 (77.3)	1944 (0.3)	70,559 (9.9)	7030 (1.0)	25,572 (3.6)	3176 (0.4)	9323 (1.3)	16,145 (2.3)	72,911 (10.2)	39,618 (54.3)
41	459,008	457,818	317,363 (69.3)	384 (0.1)	46,929 (10.3)	2561 (0.6)	15,198 (3.3)	1801 (0.4)	5556 (1.2)	10,894 (2.4)	90,709 (19.8)	63,480 (70.0)
42	45,142	45,065	15,886 (35.3)	31 (0.1)	5236 (11.6)	192 (0.4)	1388 (3.1)	142 (0.3)	554 (1.2)	1164 (2.6)	26,394 (58.6)	21,101 (79.9)
Total	2,617,854	2,599,640	1,629,776 (62.7)	96,557 (3.7)	258,784 (10.0)	48,252 (1.9)	111,066 (4.3)	14,000 (0.5)	54,895 (2.1)	77,305 (3.0)	616,788 (23.7)	315,120 (51.1)

[a] More than 1 criterion may apply to the same infant/pregnancy; [b] Row percentage of this column indicates the proportion of infants without risk factors (numerator) within provider-iniated deliveries (denominator).

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SUPPLEMENTARY TABLE 3
Birthweight chart for male infants[a]

Gestational age, exact wk	μ	σ	ν	τ	p3	p5	p10	p50	p90	p95	p97
23	567.51	0.11	1.55	7.61	415	440	473	568	654	681	700
24	669.40	0.11	1.41	7.27	495	523	561	669	771	804	827
25	776.82	0.11	1.27	6.92	579	611	654	777	895	934	962
26	904.08	0.11	1.14	6.55	677	713	763	904	1,042	1,089	1,123
27	1051.54	0.11	1.02	6.19	789	831	888	1052	1215	1271	1313
28	1202.02	0.11	0.90	5.88	904	951	1016	1202	1391	1458	1508
29	1356.43	0.11	0.79	5.66	1022	1075	1147	1356	1572	1650	1709
30	1520.88	0.11	0.69	5.57	1150	1208	1288	1521	1765	1854	1922
31	1697.33	0.11	0.61	5.62	1288	1352	1439	1697	1972	2073	2149
32	1892.79	0.11	0.53	5.90	1442	1510	1606	1893	2202	2315	2401
33	2105.18	0.11	0.48	6.46	1607	1681	1785	2105	2453	2580	2674
34	2328.30	0.11	0.45	7.34	1780	1858	1971	2328	2719	2857	2959
35	2555.22	0.12	0.45	8.63	1956	2040	2161	2555	2986	3135	3242
36	2773.85	0.12	0.50	10.49	2126	2214	2344	2774	3241	3397	3508
37	2999.81	0.12	0.54	13.26	2300	2393	2531	3000	3504	3668	3783
38	3220.54	0.12	0.56	17.65	2490	2584	2727	3221	3750	3917	4032
39	3421.87	0.12	0.54	24.19	2679	2773	2917	3422	3964	4132	4247
40	3607.76	0.11	0.53	32.84	2845	2940	3086	3608	4167	4339	4455
41	3762.48	0.11	0.56	43.76	2971	3069	3220	3762	4342	4517	4635
42	3886.04	0.12	0.62	57.86	3058	3160	3318	3886	4488	4668	4788

[a] The extent of deviation from the normal distribution is given by the ν and τ parameters; if ν is 0 and τ reaches infinity, the data are approximately normally distributed. Because none of our transformed birthweight data were normally distributed, the variation in birthweight was expressed in percentiles. To determine the exact percentile corresponding to an observed weight at a given gestational age, use the following formula: $Z = \frac{1}{\sigma * \nu} * \left(\left[\frac{Y}{\mu} \right]^{\nu} - 1 \right)$. Y corresponds to the infant's birthweight, and Z follows a t-distribution with τ degrees of freedom. Values for each exact gestational age day as well as additional percentiles are available upon request.

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SUPPLEMENTARY TABLE 4
Birthweight chart for female infants[a]

Gestational age, exact wk	μ	σ	ν	τ	p3	p5	p10	p50	p90	p95	p97
23	517.50	0.12	0.85	5.06	373	396	428	518	609	643	669
24	631.16	0.12	0.83	5.20	461	488	526	631	740	780	810
25	742.33	0.11	0.80	5.30	548	580	622	742	867	913	947
26	857.42	0.11	0.77	5.32	638	673	721	857	999	1051	1091
27	991.42	0.11	0.74	5.30	741	781	835	991	1154	1214	1260
28	1139.24	0.11	0.70	5.32	854	899	961	1139	1326	1395	1448
29	1290.09	0.11	0.66	5.39	968	1019	1088	1290	1503	1582	1642
30	1449.40	0.11	0.62	5.48	1087	1144	1221	1449	1692	1782	1850
31	1624.97	0.11	0.58	5.71	1220	1282	1368	1625	1900	2001	2078
32	1816.72	0.11	0.53	6.12	1368	1436	1530	1817	2126	2239	2324
33	2018.57	0.12	0.49	6.69	1526	1598	1700	2019	2365	2489	2582
34	2233.24	0.12	0.46	7.34	1692	1770	1881	2233	2619	2756	2857
35	2457.87	0.12	0.43	8.22	1867	1950	2070	2458	2885	3034	3143
36	2675.97	0.12	0.41	9.67	2044	2130	2256	2676	3139	3297	3411
37	2886.25	0.12	0.40	11.99	2217	2305	2437	2886	3382	3548	3665
38	3094.54	0.12	0.39	16.42	2398	2487	2622	3095	3616	3785	3903
39	3286.68	0.12	0.38	24.63	2580	2668	2803	3287	3818	3986	4101
40	3462.84	0.11	0.40	35.59	2743	2831	2968	3463	4005	4173	4286
41	3611.05	0.11	0.43	46.90	2863	2954	3096	3611	4172	4343	4459
42	3722.45	0.12	0.48	59.13	2943	3038	3185	3722	4303	4479	4597

[a] The extent of deviation from the normal distribution is given by the ν and τ parameters; if ν is 0 and τ reaches infinity, the data are approximately normally distributed. Because none of our transformed birthweight data were normally distributed, the variation in birthweight was expressed in percentiles. To determine the exact percentile corresponding to an observed weight at a given gestational age, use the following formula: $Z = \frac{1}{\sigma * \nu} * \left(\left[\frac{Y}{\mu}\right]^{\nu} - 1\right)$. Y corresponds to the infant's birthweight, and Z follows a t-distribution with τ degrees of freedom. Values for each exact gestational age day as well as additional percentiles are available upon request.

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SUPPLEMENTARY TABLE 5
Observed frequency below selected percentiles

	n	p3		p5		p10		p50		p90		p95		p97	
Male infants		n	%	n	%	n	%	n	%	n	%	n	%	n	%
<28 wk	1445	40	2.8	62	4.3	142	9.8	731	50.6	1302	90.1	1367	94.6	1396	96.6
28–31 wk	2724	86	3.2	143	5.2	276	10.1	1341	49.2	2456	90.2	2604	95.6	2648	97.2
32–36 wk	37,555	1074	2.9	1822	4.9	3693	9.8	18,813	50.1	33,923	90.3	35,761	95.2	36,486	97.2
≥37 wk	788,624	23,197	2.9	38,985	4.9	78,657	10.0	395,688	50.2	709,550	90.0	748,968	95.0	764,931	97.0
Total	830,348	24,397	2.9	41,012	4.9	82,768	10.0	416,573	50.2	747,231	90.0	788,700	95.0	805,461	97.0
Female infants															
<28 wk	1127	32	2.8	57	5.1	101	9.0	567	50.3	1010	89.6	1083	96.1	1100	97.6
28–31 wk	1730	51	2.9	76	4.4	171	9.9	874	50.5	1570	90.8	1656	95.7	1683	97.3
32–36 wk	28,832	821	2.8	1392	4.8	2762	9.6	14,452	50.1	25,936	90.0	27,419	95.1	28,017	97.2
≥37 wk	767,739	22,798	3.0	37,878	4.9	76,753	10.0	384,578	50.1	690,557	89.9	729,122	95.0	744,700	97.0
Total	799,428	23,702	3.0	39,403	4.9	79,787	10.0	400,471	50.1	719,073	89.9	759,280	95.0	775,500	97.0

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