



# Fetal Medicine Foundation fetal and neonatal population weight charts

K. H. NICOLAIDES<sup>1</sup>, D. WRIGHT<sup>2</sup>, A. SYNGELAKI<sup>1</sup> , A. WRIGHT<sup>2</sup> and R. AKOLEKAR<sup>3</sup> 

<sup>1</sup>Kings College Hospital, London, UK; <sup>2</sup>University of Exeter, Exeter, UK; <sup>3</sup>Medway Maritime Hospital, Gillingham, UK

**KEYWORDS:** birth weight; estimated fetal weight; fetal biometry; reference range; small-for-gestational age

## ABSTRACT

**Objective** To develop fetal and neonatal population weight charts. The rationale was that, while reference ranges of estimated fetal weight (EFW) are representative of the whole population, the traditional approach of deriving birth-weight (BW) charts is misleading, because a large proportion of babies born preterm arise from pathological pregnancy. We propose that the reference population for BW charts, as in the case of EFW charts, should comprise all babies at a given gestational age, including those still in utero.

**Methods** Two sources of data were used for this study. For both, the inclusion criteria were singleton pregnancy, dating by fetal crown–rump length at 11 + 0 to 13 + 6 weeks' gestation, availability of ultrasonographic measurements of fetal head circumference (HC), abdominal circumference (AC) and femur length (FL) and live birth of phenotypically normal neonate. Dataset 1 comprised a sample of 5163 paired measurements of EFW and BW; ultrasound examinations were carried out at 22–43 weeks' gestation and birth occurred within 2 days of the ultrasound examination. EFW was derived from the HC, AC and FL measurements using the formula reported by Hadlock et al. in 1985. Dataset 2 comprised a sample of 95 579 pregnancies with EFW obtained by routine ultrasonographic fetal biometry at 20 + 0 to 23 + 6 weeks' gestation (n = 45 034), 31 + 0 to 33 + 6 weeks (n = 19 224) or 35 + 0 to 36 + 6 weeks (n = 31 321); for the purpose of this study we included data for only one of the three visits per pregnancy. In the development of reference ranges of EFW and BW according to gestational age, the following assumptions were made: first, that EFW and BW have a common median, dependent on gestational age; and second, that deviations from the median occur in both EFW and BW and these deviations are correlated with different levels of spread for EFW and BW, dependent on gestational age. We adopted

a Bayesian approach to inference, combining information from the two datasets using Markov Chain Monte-Carlo sampling. The fitted model assumed that the mean log transformed measurements of EFW and BW are related to gestational age according to a cubic equation and that deviations about the mean follow a bivariate Gaussian distribution.

**Results** In the case of EFW in Dataset 2, there was a good distribution of values < 3<sup>rd</sup>, < 5<sup>th</sup>, < 10<sup>th</sup>, > 90<sup>th</sup>, > 95<sup>th</sup> and > 97<sup>th</sup> percentiles of the reference range of EFW according to gestational age throughout the gestational age range of 20 + 0 to 36 + 6 weeks. In the case of BW, there was a good distribution of values only for the cases delivered > 39 weeks' gestation. For preterm births, particularly at 27–36 weeks, BW was below the 3<sup>rd</sup>, 5<sup>th</sup> and 10<sup>th</sup> percentiles in a very high proportion of cases, particularly in cases of iatrogenic birth. The incidence of small-for-gestational-age fetuses and neonates in the respective EFW and BW charts was higher in women of black than those of white racial origin.

**Conclusion** We established a BW chart for all babies at a given gestational age, including those still in utero, thereby overcoming the problem of underestimation of growth restriction in preterm birth. BW and EFW charts have a common median but differ in the levels of spread from the median. Copyright © 2018 ISUOG. Published by John Wiley & Sons Ltd.

## INTRODUCTION

There is an apparent contradiction in the relationship between the ultrasonographic estimation of fetal weight (EFW) and birth weight (BW). Although the EFW recorded within a few days before birth correlates strongly with BW and, for a given gestational age, these two measurements have essentially the same median<sup>1</sup>, in reported reference ranges, the median

Correspondence to: Prof. K. H. Nicolaides, Fetal Medicine Research Institute, King's College Hospital, 16–20 Windsor Walk, Denmark Hill, London SE5 8BB, UK (e-mail: kypros@fetalmedicine.com)

Accepted: 23 April 2018

BW according to gestational age for babies born preterm is substantially lower than the median EFW<sup>2-5</sup>. This difference is likely to be the consequence of pathological fetal growth in a high proportion of preterm births. Reference ranges of EFW are representative of the whole population, whereas in reference ranges of BW, particularly for gestational ages <37 weeks, there is overrepresentation of pathological pregnancies. One-third of preterm births are iatrogenic, due mainly to hypertensive disorders and/or suspected fetal growth restriction; there is also evidence of impaired placentation in a substantial proportion of spontaneous preterm births<sup>6-10</sup>.

In this study, we propose that the reference population for BW charts, as in the case of EFW charts, should comprise all babies at a given gestational age, including those still *in utero*. Development of these charts was based on the assumptions that, first, for a given gestational age, the median BW is the same as the median EFW in the reference population, and, second, deviations from the median occur in both BW and EFW and these deviations follow a bivariate Gaussian distribution, with different levels of spread for BW and EFW, dependent on gestational age. These assumptions enable data on EFW derived from routine scans early in gestation to be combined with BW at term to produce reference charts for BW and EFW for gestational ages from 20+0 to 42+6 weeks.

## METHODS

### Study population

Two sources of data were used for this study, based on the same inclusion criteria: singleton pregnancy, dating by fetal crown-rump length at 11+0 to 13+6 weeks' gestation, availability of ultrasonographic measurements of fetal head circumference (HC), abdominal circumference (AC) and femur length (FL), and live birth of phenotypically normal neonate. The pregnancies were examined at King's College Hospital, London and Medway Maritime Hospital, Kent, UK, between January 2006 and December 2017. The ultrasound scans were carried out by sonographers who had received The Fetal Medicine Foundation (FMF) Certificate of Competence in ultrasound examination.

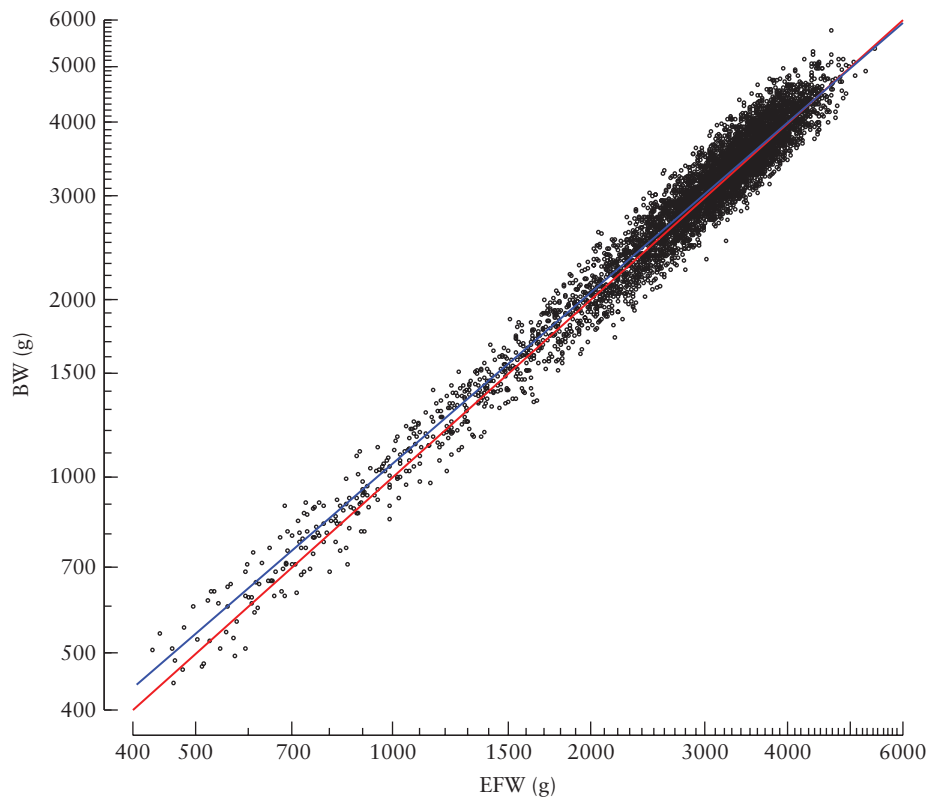
Dataset 1 comprised a sample of 5163 paired measurements of EFW and BW. The ultrasound examinations were carried out at 22-43 weeks' gestation and birth occurred within 2 days of the scan<sup>1</sup>. This dataset, in which pathological pregnancies were inevitably overrepresented, was used to examine the relationship between EFW and BW; it was not used to establish the reference ranges. EFW was derived from the HC, AC and FL measurements using the formula of Hadlock *et al.*<sup>11</sup>. The selection of this formula was based on a previous systematic review of the literature<sup>1</sup>, in which we identified all models for EFW and found that the formula of Hadlock *et al.*<sup>11</sup> was the most accurate among 70 published models for the

prediction of BW, having the lowest Euclidean distance and highest proportion of pregnancies with an absolute mean error of <10.

Dataset 2, from which the reference ranges were established, comprised a sample of 95 579 pregnancies (not included in Dataset 1) with EFW obtained by routine ultrasonographic fetal biometry at 20+0 to 23+6 weeks' gestation ( $n=45\,034$ ), 31+0 to 33+6 weeks ( $n=19\,224$ ) or 35+0 to 36+6 weeks ( $n=31\,321$ ). In the participating hospitals, all women with singleton pregnancy are offered routine ultrasound examinations at 11+0 to 13+6 and 20+0 to 23+6 weeks' gestation. During the period 2011 to 2014, an additional scan was offered at 31+0 to 33+6 weeks, and subsequently (between 2014 and 2017) this was offered at 35+0 to 36+6 weeks. For the purpose of this study, we included data for only one of the second- or third-trimester visits; we used all data obtained at 31+0 to 33+6 or 35+0 to 36+6 weeks and used the data of the visit at 20+0 to 23+6 weeks only for pregnancies that did not have a third-trimester scan. In the selection of patients, care was taken to include routine scans and not follow-up scans for maternal medical conditions or a suspected problem in fetal growth. Since the objective of the study was to establish reference ranges, rather than normal ranges, we included all pregnancies undergoing these routine ultrasound examinations. In the case of BW, we restricted data to pregnancies delivering at 39+0 to 41+6 weeks because deliveries at earlier gestations constitute a fraction of the total and many of these arise from pathological pregnancies; consequently, they are not representative of the whole population, including those still *in utero*.

### Statistical analysis

Measurements of EFW and BW were log transformed to make the deviations from median close to Gaussian in distribution and the variation about the median more stable across the range of gestational ages. A Bayesian approach to inference was adopted, combining information from Datasets 1 and 2 using Markov Chain Monte-Carlo sampling. The fitted model assumed that the mean log-transformed measurements of EFW and BW were related to gestational age according to a cubic equation and that deviations about the mean followed a bivariate Gaussian distribution. Gross outliers were identified from an initial model and observations with standardized residuals beyond  $\pm 3.89$  (the 0.00005<sup>th</sup> percentile of the Gaussian distribution) were excluded from the final model. A range of model diagnostics was produced to assess the goodness-of-fit of the model. This included summary statistics and Gaussian probability plots of  $z$ -scores for data on EFW and BW. Non-parametric quantile regression was used for direct estimation of percentiles of the EFW and BW data for comparison with the parametric model. Details of the analysis and model diagnostics are given in Appendix S1.



**Figure 1** Association between estimated fetal weight (EFW), derived from model of Hadlock *et al.* using measurements of head circumference, abdominal circumference and femur length<sup>11</sup>, and birth weight (BW) in Dataset 1. Regression line is blue and line EFW = BW is red.

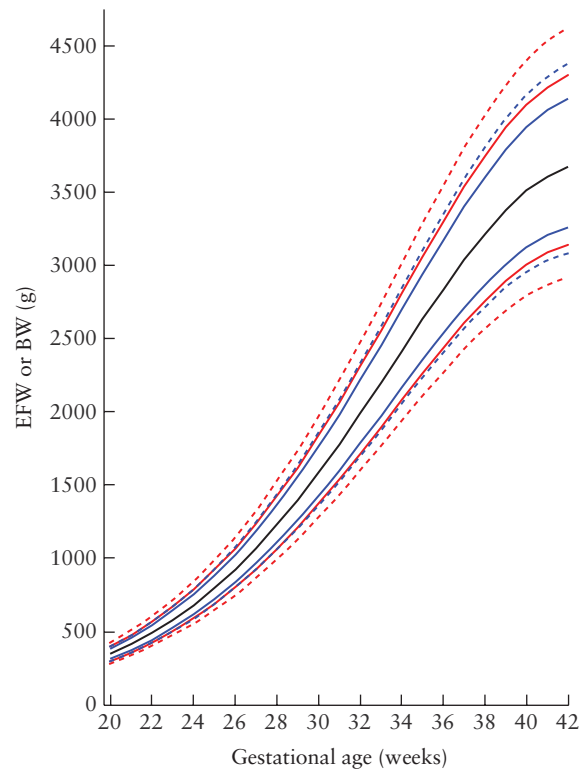
Statistical software package R was used for data analyses<sup>12</sup>. The R packages *mvtnorm*<sup>13</sup> and *quantreg*<sup>14</sup> were used for multivariate Gaussian statistics and quantile regression.

**RESULTS**

Pregnancy characteristics of the two datasets are summarized in supplementary Tables S1 and S2. The association between EFW and BW in the 5163 pregnancies of Dataset 1, in which birth occurred within 2 days of the ultrasound examination, is shown in Figure 1. For a given gestational age, the median EFW is essentially the same as the median BW. Further evidence to support the assumption of equivalence in means of EFW and BW is provided in Appendix S1.

The median, 3<sup>rd</sup>, 10<sup>th</sup>, 90<sup>th</sup> and 97<sup>th</sup> percentiles of EFW and BW according to gestational age are shown in Figure 2 and the median, 3<sup>rd</sup>, 5<sup>th</sup>, 10<sup>th</sup>, 25<sup>th</sup>, 75<sup>th</sup>, 90<sup>th</sup>, 95<sup>th</sup> and 97<sup>th</sup> percentiles of EFW and BW for each gestational week between 20 + 3 and 41 + 3 weeks are shown in Table 1. The standard deviation and percentiles of EFW and BW for each gestational day between 20 + 0 and 42 + 6 weeks are shown in Table S3.

The distribution of EFW according to gestational age in our chart is compared with those of the World Health Organization (WHO)<sup>5</sup> and INTERGROWTH-21<sup>st</sup><sup>4</sup> charts in Figure 3 and Table S4. The median and 10<sup>th</sup> percentiles of the WHO chart<sup>5</sup>, and more so those of



**Figure 2** Median for both estimated fetal weight (EFW) and birth weight (BW) according to gestational age (solid black line), and 10<sup>th</sup> and 90<sup>th</sup> percentiles (solid colored lines) and 3<sup>rd</sup> and 97<sup>th</sup> percentiles (dashed lines) for EFW (blue) and BW (red).

**Table 1** Median, 3<sup>rd</sup>, 5<sup>th</sup>, 10<sup>th</sup>, 25<sup>th</sup>, 75<sup>th</sup>, 90<sup>th</sup>, 95<sup>th</sup> and 97<sup>th</sup> percentiles of estimated fetal weight (EFW) and birth weight (BW) in second half of gestation

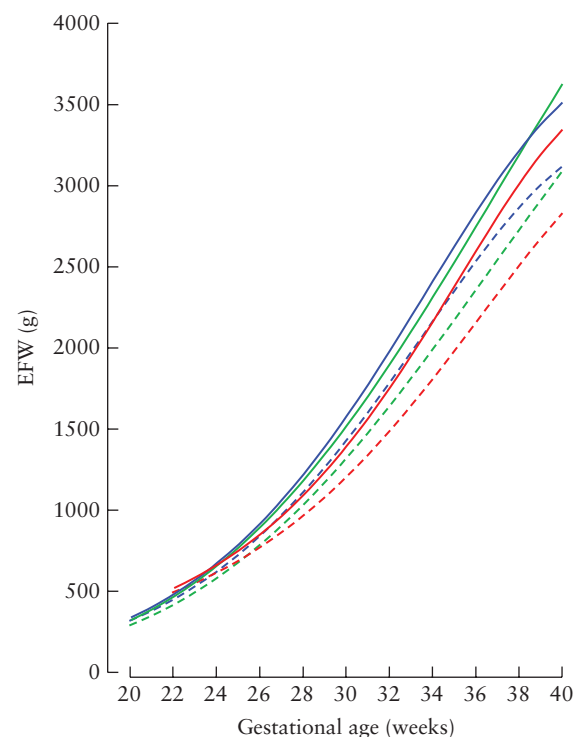
Gestational age		Percentile																	
		3 <sup>rd</sup>		5 <sup>th</sup>		10 <sup>th</sup>		25 <sup>th</sup>		Median	75 <sup>th</sup>		90 <sup>th</sup>		95 <sup>th</sup>		97 <sup>th</sup>		
Weeks	Days	EFW	BW	EFW	BW	EFW	BW	EFW	BW		EFW	BW	EFW	BW	EFW	BW	EFW	BW	EFW
20	143	300	283	306	290	314	301	329	322	346	364	372	381	398	392	414	399	424	
21	150	358	337	364	345	375	359	392	384	413	435	445	455	475	468	494	477	507	
22	157	424	399	432	410	444	427	466	456	491	517	528	542	564	557	587	567	603	
23	164	501	472	510	484	525	504	550	538	580	611	624	641	668	659	695	671	713	
24	171	588	554	599	568	616	592	646	633	682	719	734	754	785	776	818	791	839	
25	178	686	646	699	664	719	691	755	739	797	841	859	883	919	909	957	926	982	
26	185	796	750	811	771	835	803	877	859	926	978	999	1027	1069	1058	1113	1078	1143	
27	192	918	866	936	889	964	926	1013	992	1070	1131	1154	1188	1236	1224	1288	1248	1322	
28	199	1052	993	1072	1020	1105	1062	1162	1138	1228	1299	1326	1365	1420	1407	1480	1435	1520	
29	206	1197	1130	1221	1161	1258	1210	1324	1297	1400	1481	1512	1558	1620	1606	1689	1638	1735	
30	213	1353	1278	1380	1313	1423	1369	1498	1468	1586	1678	1713	1767	1836	1822	1914	1858	1967	
31	220	1518	1435	1549	1475	1598	1538	1683	1649	1782	1888	1926	1988	2066	2051	2154	2092	2213	
32	227	1691	1599	1725	1643	1780	1714	1876	1839	1988	2107	2150	2221	2307	2291	2406	2338	2472	
33	234	1868	1768	1907	1817	1968	1895	2075	2034	2201	2334	2381	2461	2555	2540	2666	2593	2740	
34	241	2048	1938	2091	1993	2159	2079	2277	2233	2416	2564	2615	2705	2808	2793	2930	2851	3012	
35	248	2226	2108	2273	2167	2347	2262	2478	2430	2631	2793	2849	2948	3060	3045	3194	3110	3284	
36	255	2398	2272	2449	2336	2531	2439	2672	2621	2839	3017	3076	3186	3306	3292	3451	3362	3549	
37	262	2561	2427	2616	2496	2704	2607	2857	2802	3037	3229	3292	3412	3539	3526	3696	3602	3801	
38	269	2709	2568	2768	2642	2862	2760	3026	2968	3219	3424	3490	3620	3754	3742	3921	3824	4034	
39	276	2839	2692	2901	2770	3001	2894	3174	3114	3379	3596	3665	3804	3944	3934	4120	4021	4239	
40	283	2945	2795	3011	2876	3115	3006	3297	3236	3512	3740	3811	3959	4103	4095	4288	4187	4412	
41	290	3025	2872	3094	2956	3201	3090	3390	3328	3613	3851	3923	4078	4225	4220	4417	4315	4546	

Both EFW and BW are given in g. It was assumed that EFW and BW have a common median, dependent on gestational age.

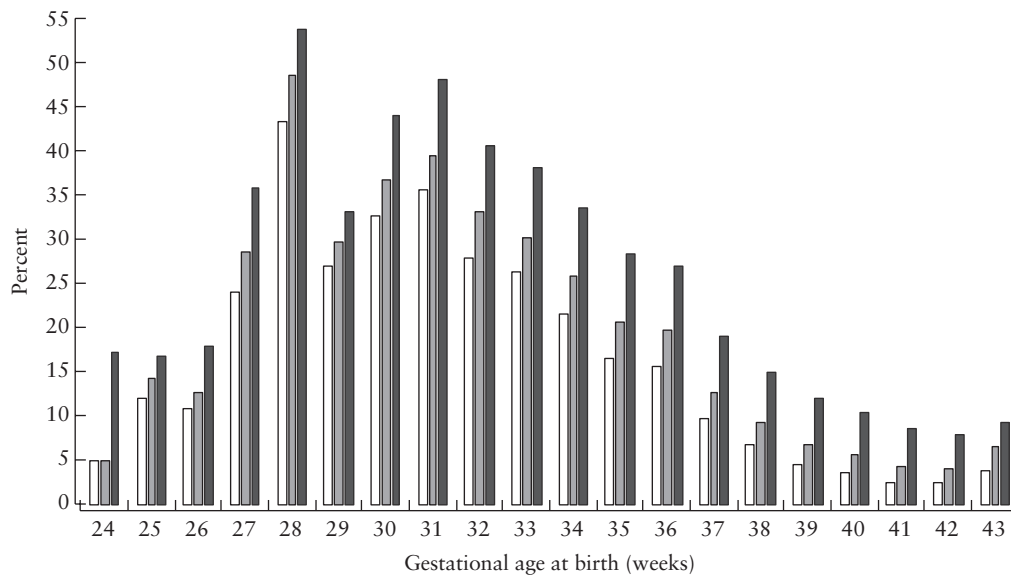
the INTERGROWTH-21<sup>st</sup> chart<sup>4</sup>, are substantially lower than the respective ones in our FMF chart between 24 and 38 weeks of gestation.

The proportion of cases in Dataset 2 with EFW and BW < 3<sup>rd</sup>, < 5<sup>th</sup>, < 10<sup>th</sup>, > 90<sup>th</sup>, > 95<sup>th</sup> and > 97<sup>th</sup> percentiles of the appropriate reference range according to gestational age is shown in Table S5. The distribution of EFW values was well balanced throughout the gestational-age range of 20 + 0 to 36 + 6 weeks, whereas a good distribution of BW values was observed only in cases delivered > 39 weeks' gestation. For preterm births, particularly at 27–36 weeks, BW was below the 3<sup>rd</sup>, 5<sup>th</sup> and 10<sup>th</sup> percentiles in a very high proportion of cases (Figure 4, Table S6). This was particularly marked in cases delivered preterm due to iatrogenic causes (40.3%, 45.1% and 52.5% for BW < 3<sup>rd</sup>, < 5<sup>th</sup> and < 10<sup>th</sup> percentile, respectively); this is not surprising because, in 1200 (67.0%) of the 1790 cases of iatrogenic preterm birth, the indication for delivery was hypertensive disease and/or fetal growth restriction. However, a high proportion of small-for-gestational-age (SGA) neonates was also observed among spontaneous preterm births; the proportion of spontaneous preterm births with BW below the 3<sup>rd</sup>, 5<sup>th</sup> and 10<sup>th</sup> percentiles was 8.6%, 12.4% and 19.8%, respectively (Table S6).

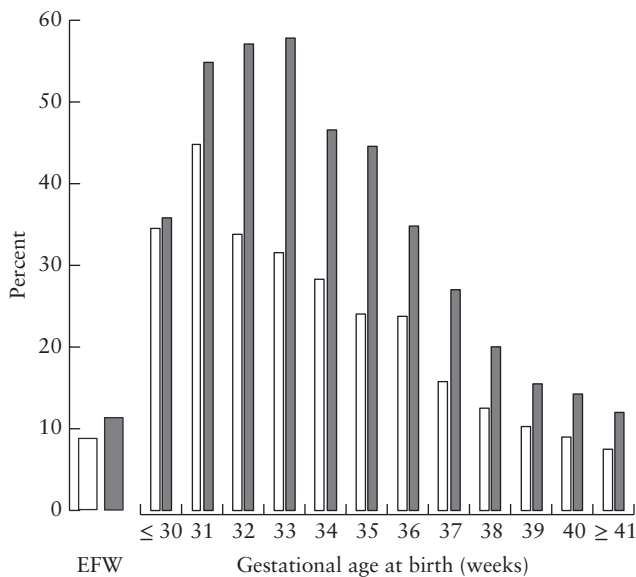
The proportion of pregnancies in women of white and black racial origin in Dataset 2 with EFW and BW < 3<sup>rd</sup>, < 5<sup>th</sup> and < 10<sup>th</sup> percentiles of the appropriate reference range according to gestational age is shown in



**Figure 3** Comparison of 50<sup>th</sup> (solid lines) and 10<sup>th</sup> (dashed lines) percentiles of estimated fetal weight (EFW) according to gestational age, between World Health Organization (green)<sup>5</sup>, INTERGROWTH-21<sup>st</sup> (red)<sup>4</sup> and our Fetal Medicine Foundation (blue) charts.



**Figure 4** Percentage of cases in Dataset 2 with birth weight below 3<sup>rd</sup> (□), 5<sup>th</sup> (■) and 10<sup>th</sup> (■) percentiles of reference range of birth weight according to gestational age.



**Figure 5** Percentage of pregnancies of white women (□) and black women (■) in Dataset 2 with estimated fetal weight (EFW) (left) or birth weight (right) below 10<sup>th</sup> percentile of appropriate reference range.

Table S7 and the proportions of cases with EFW and BW < 10<sup>th</sup> percentiles are illustrated in Figure 5. The data demonstrate that the incidence of SGA fetuses and neonates in the respective EFW and BW charts was higher in women of black than in women of white racial origin.

**DISCUSSION**

**Principal findings of the study**

In this study we have established reference ranges according to gestational age for BW and EFW. These two charts have a common median but they differ in

the levels of spread from the median. The BW charts rely on the principle that, at a given gestational age, especially < 37 weeks, the reference population should include not only those babies that have been born, but all also, because preterm births are inherently pathological, babies still *in utero*.

The study has demonstrated that a very high proportion of preterm births are SGA; this should not be surprising because, in many such cases, there is iatrogenic birth for hypertensive disease and/or fetal growth restriction. A high proportion of SGA neonates is also observed among spontaneous preterm births, providing further support to histological and uterine artery Doppler findings suggesting that in many such births there is impaired placentation<sup>6-10</sup>. Consequently, to varying degrees, all preterm births arise from pathological pregnancy and it is misleading to use data from such pregnancies to establish reference ranges of BW according to gestational age.

In our heterogeneous unselected population, arising from two maternity hospitals in England, about 20% of the women were of black racial origin and in these women the incidence of SGA fetuses and neonates was higher than in white women. This finding is compatible with the results of a previous study which reported that fetal growth is affected by several maternal characteristics: BW increased with maternal weight, height and parity and, after adjustment for these variables, BW was lower in black than in white women<sup>15</sup>. It could therefore be assumed that it is physiological for black women to produce smaller babies than white women and that different reference ranges for these racial groups should be provided<sup>16</sup>. An alternative view is that, in black women living in England, the delivery of smaller babies is a consequence of pathological influences that would be masked by customized BW percentiles. We have reported that, in black women, after adjustment for other demographic and pregnancy characteristics, there

is increased risk for several adverse pregnancy outcomes, including miscarriage, stillbirth, pre-eclampsia, fetal growth restriction and both iatrogenic and spontaneous preterm birth; it is uncertain whether such increased risks are a consequence of genetic predisposition, socioeconomic deprivation or both<sup>17</sup>. We have also shown that BW according to gestational age is reduced in antepartum stillbirths and there is no significant difference in the proportion of antepartum stillbirths that are SGA when BW is corrected for maternal characteristics<sup>15</sup>.

### Strengths and limitations of the study

The main strength of our study is the production of BW reference charts for all babies at a specific gestational age, including those still *in utero*. This avoids bias and underestimation of SGA in the assessment of BW in babies born preterm. Additional strengths include the large study population of women undergoing routine ultrasound examination in pregnancy for Database 2 and use of their data only once to avoid the potential correlation of measurements from different visits, the close proximity of the ultrasound examination to birth for Database 1, the dating of pregnancies based on fetal crown–rump length, the fact that trained sonographers carried out fetal biometry according to a standardized protocol and the utilization for calculation of EFW of a widely used model<sup>11</sup> which has been shown to be the most accurate of 70 previously reported models<sup>1</sup>. In the establishment of reference ranges, we included all pregnancies undergoing routine ultrasound examination and did not attempt to select only uncomplicated pregnancies in women thought to be healthy and well-nourished.

A potential limitation of this study is our assumption that, for a given gestational age, EFW and BW have the same median. This was based on the findings from Dataset 1, but was not possible to investigate further for the whole population. Another limitation is the extent of extrapolation and interpolation resulting for use of EFW and BW data. We wanted to include data on EFW arising from routine screening of the whole population and this inevitably restricted the data to the three narrow gestational age ranges of 20+0 to 23+6, 31+0 to 33+6 and 35+0 to 36+6 weeks. In the case of BW, we restricted data to pregnancies delivering at term to avoid bias from inclusion of preterm births, many of which arise from pathological pregnancies. Despite the extensive extrapolation and interpolation of data, the model diagnostics demonstrated a satisfactory fit of the model.

### Comparison with previous studies

Salomon *et al.*<sup>3</sup> used the Hadlock formula<sup>11</sup> to construct EFW charts from biometric data obtained during routine ultrasound examination at 20–36 weeks' gestation in 18 959 normal fetuses. The authors compared the EFW to BW charts obtained during the same study period and in the same single health authority and noted that, for

preterm births, the EFW was substantially higher than the BW; they recommended that the EFW of preterm fetuses should not be compared with the distribution of BW, because fetal growth restriction is over-represented in preterm births, but rather they should be compared with EFW charts. In our study, we have taken this observation further, highlighting that there is an inherent problem in the traditional construction of BW charts, especially for preterm births, and recommend that they should be revised based on data from all babies at a given gestational age, including those still *in utero*.

Marsál *et al.*<sup>2</sup> recognized that BW charts do not represent the intrauterine population and proposed that it would be preferable to use EFW charts to assess the growth of both fetuses and neonates. They performed a longitudinal study of ultrasonographic fetal biometry at 10–41 weeks' gestation in 86 uncomplicated pregnancies that delivered at term; they then combined the data from 759 EFWs and 86 BWs to derive an intrauterine growth chart using a fourth-degree polynomial equation. We agree with Marsál *et al.*<sup>2</sup> on the need to revise BW charts and have demonstrated that EFW and BW charts have a common median, but they differ in the levels of spread from the median.

Two international multicenter studies have recently reported the construction of charts of EFW according to gestational age<sup>4,5</sup>. In the INTERGROWTH-21<sup>st</sup> project, data were derived from 2404 live babies without congenital abnormality, who were born within 14 days of an ultrasound scan; women were recruited from urban areas in several countries (Brazil, China, England, India, Italy, Kenya, Oman, Pakistan, South Africa, Thailand and USA) and had serial ultrasound scans and fetal biometry throughout pregnancy<sup>4</sup>. Two cohorts of women were examined; one was unselected and the other was selected to include healthy, well-nourished, pregnant women who were at low risk of adverse maternal and perinatal outcomes. The authors reported that the data from different centers were similar and they therefore pooled all data and used fractional polynomial models to construct an international optimal fetal growth chart that would be appropriate for healthy pregnancies in all countries of the world<sup>4</sup>.

In the WHO study, data were derived from 1387 healthy women with low-risk pregnancies and unrestricted nutritional and social background who had serial ultrasound scans throughout pregnancy; women were recruited from 10 countries (Argentina, Brazil, Democratic Republic of the Congo, Denmark, Egypt, France, Germany, India, Norway and Thailand) and a total of 7924 sets of ultrasound measurements were analyzed by quantile regression to establish longitudinal reference intervals for EFW<sup>5</sup>. The authors reported that there were significant differences in fetal growth between countries.

In our study, in comparison with the INTERGROWTH-21<sup>st</sup> and WHO studies, the population was unselected and considerably larger, the data were derived from two centers in the same country and the scans were

carried out by sonographers with extensive training in ultrasound examination in pregnancy. Our approach, like the one of INTERGROWTH-21st, used a parametric model. This differs from the approach of the WHO study, which used non-parametric quantile regression. A benefit of the parametric models is that they can be used easily to obtain *z*-scores and percentiles for individual measurements. A drawback is the imposition of a specific parametric relationship. We used a cubic polynomial to represent the relationship between median level of log-transformed weight assuming the same median for both EFW and BW. Our model assumed that deviations around the median for BW and EFW followed a bivariate Gaussian distribution.

The 10<sup>th</sup> percentile of our EFW chart was considerably higher than those of the INTERGROWTH-21<sup>st</sup> and WHO charts<sup>4,5</sup>. For example, at 36 weeks' gestation, the 10<sup>th</sup> percentile according to our chart was 2531 g, whereas the respective values in the WHO and INTERGROWTH-21<sup>st</sup> charts are 2352 g and 2144 g. Such differences are likely to be a consequence of underlying differences in the study populations and demonstrate that the desire for a single international standard for all countries is not appropriate; a single standard would underestimate growth restriction in countries with normal big babies, such as Norway, and overestimate growth restriction in countries with normal small babies, such as India.

## Conclusions

This study has highlighted the necessity for construction of BW charts to be based on all babies at a particular gestational age, including those still *in utero*. Within a given country there are variations in BW that depend on maternal characteristics, such as racial origin, but adjustment for such characteristics may be inappropriate because such adjustments could result in underestimation of the increased perinatal risk of a disadvantaged group. The value of adjustment for maternal weight, height and parity remains controversial.

If our charts are to be used in different countries it would be necessary to ensure that the distribution of values is appropriate, otherwise adjustments would be necessary either to tailor the charts for a specific setting or to change the cut-offs for defining SGA or large-for-gestational age. In the latter case, these charts could be considered as a benchmark rather than a reference chart.

## ACKNOWLEDGMENT

This study was supported by a grant from The Fetal Medicine Foundation (Charity No: 1037116).

## REFERENCES

- Hammami A, Zumaeta AM, Syngelaki A, Akolekar R, Nicolaides KH. Ultrasonographic estimation of fetal weight: development of new model and assessment of performance of previous models. *Ultrasound Obstet Gynecol* 2018. <https://doi.org/10.1002/uog.19066> [Epub ahead of print].
- Marsál K, Persson PH, Larsen T, Lilja H, Selbing A, Sultan B. Intrauterine growth curves based on ultrasonically estimated foetal weights. *Acta Paediatr* 1996; 85: 843–848.
- Salomon LJ, Bernard JP, Ville Y. Estimation of fetal weight: reference range at 20–36 weeks' gestation and comparison with actual birth-weight reference range. *Ultrasound Obstet Gynecol* 2007; 29: 550–555.
- Stirnemann J, Villar J, Salomon LJ, Ohuma E, Ruyan P, Altman DG, Nosten F, Craik R, Munim S, Cheikh Ismail L, Barros FC, Lambert A, Norris S, Carvalho M, Jaffer YA, Noble JA, Bertino E, Gravett MG, Purwar M, Victora CG, Uauy R, Bhutta Z, Kennedy S, Papageorghiou AT, for The International Fetal and Newborn Growth Consortium for The 21st Century (INTERGROWTH-21st). International estimated fetal weight standards of the Intergrowth-21st project. *Ultrasound Obstet Gynecol* 2017; 49: 478–486.
- Kiserud T, Piaggio G, Carroli G, Widmer M, Carvalho J, Neerup Jensen L, Giordano D, Cecatti JG, Abdel Aleem H, Talegawkar SA, Benachi A, Diemert A, Tshetu Kitoto A, Thinkhamrop J, Lumbiganon P, Tabor A, Kriplani A, Gonzalez Perez R, Hecher K, Hanson MA, Gülmezoglu AM, Platt LD. The World Health Organization fetal growth charts: a multinational longitudinal study of ultrasound biometric measurements and estimated fetal weight. *PLoS Med* 2017; 14: e1002220.
- Arias F, Rodriguez L, Rayne SC, Kraus FT. Maternal placental vasculopathy and infection: two distinct subgroups among patients with preterm labor and preterm ruptured membranes. *Am J Obstet Gynecol* 1993; 168: 585–591.
- Arias F, Rodriguez L, Victoria A, Cho K, Kraus F. Placental histology and clinical characteristics of patients with preterm premature rupture of membranes. *Obstet Gynecol* 1997; 89: 265–271.
- Kim YM, Chaiworapongsa T, Gomez R, Bujold E, Yoon BH, Rotmensch S, Thaler HT, Romero R. Failure of physiologic transformation of the spiral arteries in the placental bed in preterm premature rupture of membranes. *Am J Obstet Gynecol* 2002; 187: 1137–1142.
- Kim YM, Bujold E, Chaiworapongsa T, Gomez R, Yoon BH, Thaler HT, Rotmensch S, Romero R. Failure of physiologic transformation of the spiral arteries in patients with preterm labor and intact membranes. *Am J Obstet Gynecol* 2003; 189: 1063–1069.
- Fonseca E, Yu CK, Singh M, Papageorghiou AT, Nicolaides KH. Relationship between second-trimester uterine artery Doppler and spontaneous early preterm delivery. *Ultrasound Obstet Gynecol* 2006; 27: 301–305.
- Hadlock FP, Harrist RB, Sharman RS, Deter RL, Park SK. Estimation of fetal weight with the use of head, body, and femur measurements—a prospective study. *Am J Obstet Gynecol* 1985; 151: 333–337.
- R Development Core Team. R. A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. 2011; ISBN 3-900051-07-0, URL <http://www.R-project.org/>
- Genz A, Bretz F, Miwa T, Mi X, Leisch F, Scheipl F, Hothorn T. mvtnorm: Multivariate Normal and t Distributions. *R package 2016; version 1.0-5*. <http://CRAN.R-project.org/package=mvtnorm>.
- Koenker R. quantreg: Quantile Regression. R package 2016; version 5.29. <https://CRAN.R-project.org/package=quantreg>.
- Poon LC, Volpe N, Muto B, Syngelaki A, Nicolaides KH. Birthweight with gestation and maternal characteristics in live births and stillbirths. *Fetal Diagn Ther* 2012; 32: 156–165.
- Buck Louis G, Grewal J, Albert P, Sciscione A, Wing DA, Grobman WA, Newman RB, Wapner R, D'Alton ME, Skupski D, Nageotte MP, Ranzini AC, Owen J, Chien EK, Craigo S, Hediger ML, Kim S, Zhang C, Grantz KL. Racial/ethnic standards for fetal growth: the NICHD Fetal Growth Studies. *Am J Obstet Gynecol* 2015; 213: 449.e1–41.
- Khalil A, Rezende J, Akolekar R, Syngelaki A, Nicolaides KH. Maternal racial origin and adverse pregnancy outcome: a cohort study. *Ultrasound Obstet Gynecol* 2013; 41: 278–285.

## SUPPORTING INFORMATION ON THE INTERNET

The following supporting information may be found in the online version of this article:

 **Appendix S1** Statistical analysis and justification

**Table S1** Characteristics of study population of 5163 pregnancies with paired measurements of estimated fetal weight and birth weight separated by a maximum of 2 days (Dataset 1)

**Table S2** Characteristics of study population of 95 579 pregnancies in Dataset 2

**Table S3** Median, 3<sup>rd</sup>, 5<sup>th</sup>, 10<sup>th</sup>, 25<sup>th</sup>, 75<sup>th</sup>, 90<sup>th</sup>, 95<sup>th</sup> and 97<sup>th</sup> percentiles of estimated fetal weight (EFW) and birth weight (BW) (in g) for each gestational age (GA) day between 20 and 42 weeks

**Table S4** Comparison of 10<sup>th</sup>, 50<sup>th</sup> and 90<sup>th</sup> percentiles of estimated fetal weight (in g) according to gestational age (GA) between our FMF chart and WHO<sup>5</sup> and INTERGROWTH-21<sup>st</sup> 4 charts

**Table S5** Number and percentage of cases in Dataset 2 with estimated fetal weight (EFW) < 3<sup>rd</sup>, < 5<sup>th</sup> < 10<sup>th</sup>, > 90<sup>th</sup>, > 95<sup>th</sup> and > 97<sup>th</sup> percentiles of reference range of EFW, according to gestational age (GA), and respective values for birth weight (BW)

**Table S6** Number and percentage of cases in Dataset 2 with birth weight below 3<sup>rd</sup>, 5<sup>th</sup> and 10<sup>th</sup> percentiles of reference range of birth weight according to gestational age (GA), for iatrogenic and spontaneous births

**Table S7** Number and percentage of pregnancies of white and black women in Dataset 2 with estimated fetal weight (EFW) and birth weight (BW) below 3<sup>rd</sup>, 5<sup>th</sup> and 10<sup>th</sup> percentiles of the appropriate reference range according to gestational age (GA)