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# Maternal and pathological pregnancy characteristics in customised birthweight centiles and identification of at-risk small-for-gestational-age infants: a retrospective cohort study

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**Objective** To regenerate coefficients for the New Zealand customised birthweight centile calculator using an updated birth cohort, and compare the identification of at-risk small-for-gestational-age (SGA) infants between full customisation (including maternal characteristics) and an ultrasound-based fetal weight and infant gender partial customisation.

**Design** Retrospective cohort study of prospectively collected maternity data.

**Setting** National Women's Health Auckland, New Zealand.

**Population** Singleton pregnancies in the period 2006–2009; $n$ = 24 176.

**Methods** Multiple linear regression analysis was performed for full customisation (adjusted for gestation, infant gender, maternal characteristics and pathological variables) and ultrasound-and-gender customisation (adjusted for gestation and infant gender).

**Main outcome measures** Risks of SGA-related perinatal death were compared between models.

**Results** Changes occurred in some ethnicity coefficients, including Chinese (−135 g), Tongan (−101 g) and Samoan (−89 g), and ten ethnicities were added. Overall, full customisation identified SGA infants with higher odds of perinatal death (OR 5.6, 95% CI 3.6–8.7) than infants classed as SGA by ultrasound-and-gender customisation (OR 2.1, 95% CI 1.4–3.3) ($P$ = 0.02). In subgroup analyses, infants classed as SGA by full but not ultrasound-and-gender customisation ($n$ = 888, 3.4%) had an increased risk of perinatal death (RR 4.7, 95% CI 2.7–7.9); however, those identified as SGA by ultrasound-and-gender customisation alone were not at an increased risk ($n$ = 676, 2.6%, RR 1.1, 95% CI 0.4–3.6). The population attributable risk (PAR) of SGA-related perinatal death was higher for full (49.8%) than for ultrasound-and-gender (43.0%) customisation.

**Conclusions** Updating the New Zealand customised birthweight centile calculator resulted in revised coefficients that better reflect a contemporary birth cohort. Inclusion of maternal characteristics in a birthweight customisation model increases the detection of SGA infants at risk of perinatal death.

**Keywords** Birthweight, customised centiles, fetal growth restriction, intrauterine growth restriction, perinatal morbidity, perinatal mortality, small for gestational age.

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## Introduction

Small-for-gestational-age (SGA) infants are at an increased risk of perinatal morbidity and mortality.[1] Traditionally, SGA has been defined as a birthweight of less than the tenth percentile using population-based standards, and these population birthweight reference standards in Western countries are often derived from cohorts of predominantly European births that pre-date the epidemic of obesity.[2,3] Due to the association between prematurity and fetal growth restriction,[4,5] population birthweight reference standards under-diagnose SGA, compared with intrauterine fetal growth standards.[6,7] Customised birthweight centiles, which use an intrauterine fetal weight reference, and also adjust for maternal and fetal physiological factors, better identify SGA infants at risk of perinatal morbidity and

mortality compared with infants classified as SGA by population centiles alone.[1,8]

Some authors have suggested that the improved association between customised SGA and adverse perinatal outcomes predominantly stems from the use of an intrauterine fetal weight reference at preterm gestations,[6,9,10] and that after adjustment for infant gender, further customisation using maternal characteristics such as height, weight and parity confers little added benefit.[11,12] These previous studies have been performed in non-obese, predominantly European cohorts, and may therefore have underestimated the effect of maternal characteristics on birthweight.

We have previously published New Zealand coefficients for customised birthweight centiles derived from a birth cohort at National Women's Health (NWH), Auckland, in the period 1993–2000;[13] however, the subgroup of women used to generate these coefficients may not have been representative of the total birthing population. Current data collection in our hospital now includes all of the variables required for generating fully customised birthweight centile models. We are now able to update our calculator using a large contemporary birth cohort and to account for pathological factors associated with birthweight, such as smoking, hypertensive disease and diabetes.[14–16] With this large multi-ethnic cohort with high rates of overweight and obese women, we are also able to investigate whether additional benefit is gained by excluding the effects of pathological factors and adjusting for maternal physiological characteristics in a full customisation model, compared with a partial customisation model that uses the same ultrasound fetal weight reference adjusted for infant gender alone.

The primary aims of the current study were therefore to: (1) regenerate coefficients for the New Zealand customised birthweight centile calculator using a large, updated birth cohort; and (2) compare full customisation with customisation adjusted for ultrasound fetal weight reference and infant gender alone. We hypothesised that full customisation would better identify SGA infants at risk of perinatal mortality than an ultrasound-and-gender customisation model.

## Methods

The NWH clinical database of births from 2006 to 2009 was used for the present cohort study. NWH is a tertiary referral hospital in Auckland, New Zealand, with a diverse ethnic population and approximately 7500 maternities per year. The NWH database of births consists of de-identified, prospectively collected maternity data for all births occurring at 20 weeks of gestation or later, and includes demographic data, antenatal complications, and detailed delivery and newborn data. Data are routinely checked for completeness, out-of-range values and inconsistency.[17] Ethical approval for this study was gained from the Northern X Regional Ethics Committee (NTX/09/179/EXP).

Included in the study were women booked to deliver at NWH from January 2006 to December 2009 with singleton pregnancies ($n$ = 29 573). Consistent with previous methodology,[13,18] the population used to calculate birthweight customisation coefficients excluded pregnancies with major congenital abnormalities, preterm birth (<37 weeks of gestation) and stillbirth (Figure 1). The eligible study population consisted of 26 611 women. Of these, 2429 (9.1%) had incomplete or missing data on one or more variables required to generate centile coefficients: 2033 (7.6%) were missing height; 1599 (6.0%) were missing weight; and 352 (1.3%) were missing smoking status. An additional six women could not be classified into one of our ethnicity categories (recorded ethnicity as 'Other'), and so were excluded, leaving a final term study population of 24 176 women (Figure 1).

The physiological and pathological variables included in the full customisation multivariable analysis are variables that have previously been found to be associated with birthweight, and are included in previously published full customisation models:[14,18] i.e. maternal height, weight, parity, ethnicity, gestation, infant gender, cigarette smoking, diabetes, hypertensive disease and antepartum haemorrhage (APH). Maternal height and weight were recorded at the

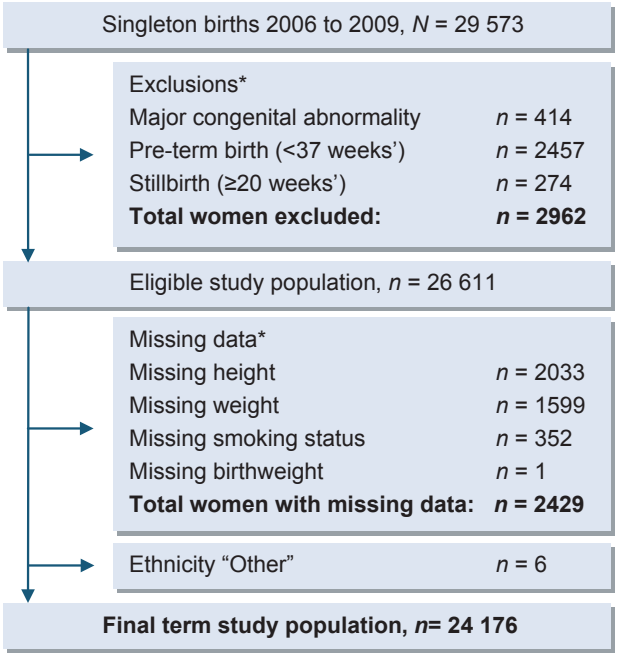


**Figure 1.** Flow of study participants. *More than one exclusion criteria or missing data variable may apply to the same pregnancy, so numbers do not total.

first antenatal booking visit, and were measured to the nearest centimetre and kilogram, respectively. Parity was defined as the number of times a woman had given birth to liveborn infant(s) of any birthweight or gestation, or to a stillborn infant after 20 weeks of gestation or where the infant weighed 400 g or more, if gestation was unknown.[19] Self-determined ethnicity was grouped and prioritised according to New Zealand Ministry of Health guidelines.[20] The ethnicities included were NZ European, Māori, Fijian, Niuean, Tongan, Cook Island Māori, Samoan, Other Pacific Peoples, South-East Asian, Indian (including Fijian Indian), Chinese, Other Asian, Latin American/Hispanic, African, Middle Eastern and Other European. South-East Asian ethnicity includes women from countries such as Vietnam, Thailand and Indonesia, and Other Asian includes women from the Indian subcontinent (excluding India), as well as Japan, Korea and others.

Gestational age was derived from the first day of the last menstrual period (LMP) if known, or by ultrasound if the LMP was unknown. Pregnancies were routinely dated during second-trimester fetal anomaly scanning, between 18 and 20 weeks of gestation. The estimated date of delivery (EDD) was only adjusted if fetal ultrasound measurements differed from the LMP gestation by more than 7 days before 20 weeks of gestation, or by >2 SD after 20 weeks of gestation, according to the Australasian Society for Ultrasound in Medicine guidelines.[21,22]

Cigarette smoking status was recorded both at booking and at delivery. If a woman was smoking at either time point she was defined as a smoker for the purposes of this study. Diabetes included either a pre-existing diagnosis of diabetes (type-1 or -2 diabetes mellitus) or gestational diabetes mellitus (GDM). GDM was diagnosed by a 75-g oral glucose tolerance test with a fasting venous plasma glucose level of ≥5.5 mmol/l, and/or at 2 hours of ≥9.0 mmol/l, adhering to the Australasian Diabetes in Pregnancy Society guidelines.[23] Hypertensive disease included all women with chronic hypertension, gestational hypertension or pre-eclampsia, as defined by the International Society for the Study of Hypertension in Pregnancy.[24] For the purposes of this study, APH was defined as vaginal bleeding from any cause at or beyond 20 weeks of gestation after excluding placenta praevia.[17] Placenta praevia was excluded from this definition as it has not been associated with clinically important reductions in birthweight.[25]

For the second aim, comparing perinatal mortality between full and ultrasound-and-gender customisation, in addition to the term population, the total study population included women with preterm birth and stillbirth, resulting in a sample of 25 976 women. Perinatal death included both stillbirths (defined as the birth of an infant with no signs of life at 20 weeks of gestation or later, or where the infant weighed 400 g or more, if gestation was unknown) and neonatal deaths (defined as death within the first 28 days of life of a liveborn infant born at 20 weeks of gestation or later, or with a birthweight of ≥400 g, if gestation was unknown).[17]

## Statistical methods

The method of full customisation used is as described by Gardosi et al.[7,18] Coefficients for predicting birthweight were created in the term study population using multiple linear regression analysis.[13,18] The full customisation model included gestational age, infant gender, maternal characteristics (ethnicity, height, weight and parity) and pathological factors (smoking, diabetes, hypertensive disease and APH). Coefficients to the third order (linear, quadratic and cubic) are required for gestation and booking weight, as the relationship between these variables and birthweight is not linear. To allow comparison with previous studies, coefficients are presented representing a 'standard mother':[14] i.e. a nulliparous European woman of height 163 cm and booking weight 64 kg, delivering at a gestational age of 280 days with the infant's gender unspecified. The ultrasound-and-gender customisation model included gestational age and infant gender alone, and is equivalent to models previously used by Gardosi et al.[26] and Hutcheon et al.[11] The $R^2$ statistic was compared between each multivariable model (full and ultrasound-and-gender) using the *F*-test.

Birthweight centiles for both full and ultrasound-and-gender models were calculated for the total study population ($n$ =25 976). To create birthweight centiles, an individual term optimal birthweight (TOW) is calculated using all the coefficients from the regression model except (in the case of full customisation) smoking, diabetes, hypertensive disease and APH. This is the equivalent of using the previously generated regression model and assuming that all the TOWs are derived from a population of non-smokers with no diabetes, hypertensive disease or APH, i.e. excluding pathological factors. Adjustment for gestation is then provided by applying a proportionality growth function derived from Hadlock's ultrasound-based fetal weight equation,[18,27] and this gives a gestation-related optimal weight (GROW). The actual birthweight is then compared with the GROW normal range, and a centile is generated.[18]

SGA was defined as a birthweight of less than the tenth centile using either the full customisation model ($SGA_{full}$) or the partial model of ultrasound-and-gender customisation ($SGA_{us}$). Separate odds ratios (ORs) of perinatal death for $SGA_{us}$ infants and $SGA_{full}$ infants were calculated through logistic regression analysis, and compared using the Wald test.

Infants were grouped into four categories relative to their SGA status: non-SGA by both criteria; SGA by ultrasound-and-gender customisation alone; SGA by full customisation alone; and SGA by both criteria. The relative risk (RR, 95%

 

CI) of perinatal death (stillbirth and neonatal death) for each group was calculated using non-SGA by both criteria as the reference group. Perinatal mortality was also compared between models by calculating the population-attributable risk (PAR) of SGA-related perinatal death.[28] PARs were calculated for full customisation and ultrasound-and-gender customisation using commonly used definitions of SGA (below the third, fifth and tenth customised centiles). All statistical tests were performed using SAS 9.2 (SAS Institute Inc., Cary, NC, USA).

## Results

In the term cohort used to derive the new customised centile coefficients ($n$ = 24 176), substantial variation in maternal characteristics, birthweight and smoking rates was seen between ethnicities (Table 1). Mean gestational age at delivery was 39.3 weeks of gestation (SD 1.2 weeks), and there was little variation in gestation between ethnic groups. Diabetes was diagnosed in 6.2% ($n$ = 1500) of pregnancies: GDM in 5.2% ($n$ = 1250), type-2 diabetes in 0.6% ($n$ = 162) and type-1 diabetes in 0.4% ($n$ = 88). Hypertensive disease was present in 8.3% ($n$ = 2011) of pregnancies; gestational hypertension 3.6% ($n$ = 880), pre-eclampsia 2.4% ($n$ = 591) and chronic hypertension 2.2% ($n$ = 540).

Multiple regression coefficients for full customisation and ultrasound-and-gender customisation are presented in Table 2. The full customisation model explained significantly more of the variability in birthweight ($R^2$ = 31%) than the ultrasound-and-gender customisation model ($R^2$ = 18%) ($P < 0.001$; Table 2). The $R^2$ values were unchanged after adjustment for the differing numbers of variables between models (adjusted $R^2$).

Ethnicity coefficients have changed from the previous New Zealand calculator:[13] for Chinese (−135 g), Tongan (−101 g), Samoan (−89 g) and Indian (−61 g) women. There was also a small change in the coefficient for Māori women (−5 g). An additional ten ethnicity coefficients that were not available in the previous New Zealand calculator are presented in Table 2, along with coefficients for the pathological variables of smoking, hypertensive disease and diabetes.

Within the total study population ($n$ = 25 976), ultrasound-and-gender customisation identified 2859 (11.0%) $SGA_{us}$ infants, whereas full customisation identified 3071 (11.8%) $SGA_{full}$ infants. Perinatal death occurred in 201 infants (seven per 1000 total births), with 86 deaths (43%) occurring in infants who were classified as non-SGA by both models (both non-SGA, 3.9 per 1000 total births; Table 3). Infants who were $SGA_{us}$ had twice the odds of perinatal death compared with non-$SGA_{us}$ infants (OR 2.1, 95% CI 1.4–3.3), whereas $SGA_{full}$ infants had a greater than five-fold increased odds of perinatal death compared with non-$SGA_{full}$ infants (OR 5.6, 95% CI 3.6–8.7). Overall, infants classed as SGA by full customisation had a greater odds of perinatal death than infants who were classed SGA by ultrasound-and-gender customisation ($P$ = 0.02).

**Table 1.** Characteristics of term study population by maternal ethnicity

| Ethnicity | *n* (%) | Smoker | Nulliparous | Maternal age (years) | Weight (kg)* | Height (cm) | Birthweight (g) |
|---|---|---|---|---|---|---|---|
| NZ European | 9792 (40.5) | 630 (6.4) | 4875 (49.8) | 33.0 (4.9) | 65 (59–74) | 166.6 (6.4) | 3541 (458) |
| Other European | 2303 (9.5) | 102 (4.4) | 1309 (56.8) | 32.9 (4.8) | 64 (58–72) | 166.3 (6.3) | 3515 (477) |
| Māori | 1720 (7.1) | 620 (36.1) | 707 (41.1) | 27.7 (6.8) | 76 (65–90) | 166.0 (6.1) | 3498 (486) |
| Samoan | 1226 (5.1) | 249 (20.3) | 439 (35.8) | 28.6 (6.4) | 88 (75–105) | 166.3 (6.1) | 3662 (492) |
| Tongan | 1108 (4.6) | 173 (15.6) | 324 (29.2) | 28.8 (6.3) | 93 (80–106) | 167.3 (5.7) | 3732 (499) |
| Chinese | 2957 (12.2) | 91 (3.1) | 1752 (59.3) | 30.9 (5.1) | 56 (51–62) | 161.5 (5.2) | 3369 (433) |
| Indian | 1678 (6.9) | 31 (1.9) | 875 (52.2) | 29.9 (4.6) | 61 (54–69) | 159.1 (6.1) | 3196 (422) |
| African | 271 (1.1) | 9 (3.3) | 83 (30.6) | 29.8 (5.9) | 67 (60–77) | 162.1 (6.9) | 3452 (488) |
| Cook Island Māori | 407 (1.7) | 141 (34.6) | 143 (35.1) | 27.0 (6.8) | 83 (71–100) | 165.6 (6.0) | 3566 (480) |
| Fijian | 192 (0.8) | 11 (5.7) | 94 (49.0) | 28.6 (5.7) | 69 (60–84) | 163.4 (7.0) | 3448 (493) |
| Latin American | 158 (0.7) | 9 (5.7) | 90 (57.0) | 32.3 (4.6) | 63 (56–70) | 162.5 (6.5) | 3493 (436) |
| Middle Eastern | 392 (1.6) | 12 (3.1) | 171 (43.6) | 29.2 (5.8) | 64 (57–73) | 161.4 (6.0) | 3419 (464) |
| Niuean | 323 (1.3) | 80 (24.8) | 117 (36.2) | 27.0 (6.5) | 85 (74–98) | 164.4 (6.0) | 3558 (495) |
| South-East Asian | 379 (1.6) | 10 (2.6) | 198 (52.2) | 31.3 (5.4) | 56 (51–63) | 158.3 (5.8) | 3333 (491) |
| Other Asian | 1160 (4.8) | 45 (3.9) | 642 (55.3) | 31.2 (5.2) | 56 (51–63) | 159.2 (6.2) | 3295 (455) |
| Other Pacific Peoples | 110 (0.5) | 21 (19.1) | 46 (41.8) | 29.3 (6.8) | 82 (70–100) | 164.4 (6.3) | 3501 (525) |
| **Total study population** | **24 176 (100)** | **2234 (9.2)** | **11 865 (49.1)** | **31.3 (5.7)** | **65 (57–76)** | **164.7 (6.8)** | **3487 (479)** |

Data are presented as *n* (%) and mean (SD), as appropriate.
*Presented as median (IQR).

**Table 2.** Multiple linear regression coefficients (g) for full customisation and ultrasound-and-gender customisation models

| | Study population *n* = 24 176 | | | | | |
|---|---|---|---|---|---|---|
| | Full customisation | | | Ultrasound-and-gender customisation | | |
| | Coefficient (g) | SE | *P* | Coefficient (g) | SE | *P* |
| **Gestation (from 280 days)** | | | | | | |
| Linear term | 21.5 | 0.56 | <0.001 | 21.9 | 3.78 | <0.001 |
| Quadratic term | −0.28 | 0.036 | <0.001 | −0.25 | 0.039 | <0.001 |
| Cubic term | −0.0009 | 0.0029 | 0.79 | −0.0007 | 0.0031 | <0.001 |
| **Gender** | | | | | | |
| Female | −60.6 | 2.56 | <0.001 | −60.0 | 2.79 | <0.001 |
| Male | 60.6 | 2.56 | <0.001 | 60.0 | 2.79 | <0.001 |
| **Maternal height (from 163 cm)** | | | | | | |
| Height | 8.6 | 0.45 | <0.001 | | | |
| **Booking weight (from 64 kg)** | | | | | | |
| Linear term | 7.33 | 0.302 | <0.001 | | | |
| Quadratic term | −0.111 | 0.0125 | <0.001 | | | |
| Cubic term | 0.0008 | 0.0001 | <0.001 | | | |
| **Ethnic group** | | | | | | |
| European | Ref | | | | | |
| Māori | −71.8 | 11.0 | <0.001 | | | |
| Samoan | −4.6 | 13.0 | 0.73 | | | |
| Tongan | 23.4 | 13.9 | 0.09 | | | |
| Chinese | −34.0 | 9.0 | <0.001 | | | |
| Indian | −210.5 | 11.0 | <0.001 | | | |
| African | −139.7 | 24.6 | <0.001 | | | |
| Cook Island Māori | −45.2 | 20.7 | 0.03 | | | |
| Fijian | −90.6 | 29.0 | 0.002 | | | |
| Latin American | 4.0 | 31.9 | 0.90 | | | |
| Middle Eastern | −90.9 | 20.6 | <0.001 | | | |
| Niuean | −76.3 | 23.0 | <0.001 | | | |
| South-East Asian | −34.8 | 21.2 | 0.10 | | | |
| Other Asian | −88.1 | 12.9 | <0.001 | | | |
| Other European | −15.2 | 9.2 | 0.10 | | | |
| Other Pacific Peoples | −55.9 | 38.3 | 0.14 | | | |
| **Parity** | | | | | | |
| Parity 1 | 120.1 | 5.8 | <0.001 | | | |
| Parity 2 | 164.9 | 8.7 | <0.001 | | | |
| Parity 3 | 140.9 | 14.3 | <0.001 | | | |
| Parity 4+ | 163.2 | 15.5 | <0.001 | | | |
| **Pathological variables** | | | | | | |
| Hypertensive disease | −77.8 | 9.5 | <0.001 | | | |
| Diabetes | 40.9 | 11.3 | <0.001 | | | |
| Smoker | −124.7 | 9.4 | <0.001 | | | |
| Antepartum haemorrhage | −61.3 | 13.5 | <0.001 | | | |
| **Model** | | | | | | |
| Constant | 3513 | | | 3553 | | |
| Standard error of model | 396.6 | | | 433.7 | | |
| $R^2$ statistic* | 0.31 | | | 0.18 | | |

**F*-test of difference between $R^2$ values; $P < 0.001$.

There were 888 (3.4%) infants that were $SGA_{full}$ alone, and 676 (2.6%) infants that were $SGA_{us}$ alone (Table 3). Infants who were $SGA_{us}$ alone had a similar rate of perinatal death as both non-SGA infants (RR 1.1, 95% CI 0.4–3.6), whereas infants who were $SGA_{full}$ alone had a greater than four-fold increased risk of stillbirth (RR 4.3, 95% CI 2.2–8.4), neonatal death (RR 5.4, 95% CI 2.2–12.9) and overall perinatal death (RR 4.7, 95% CI 2.7–7.9) compared

**Table 3.** Perinatal death by SGA classification

| | Both non-SGA $n$ = 22 229 | | $SGA_{us}$ only $n$ = 676 | | $SGA_{full}$ only $n$ = 888 | | Both SGA $n$ = 2183 | |
|---|---|---|---|---|---|---|---|---|
| Perinatal death | 86 | (0.4%) | 3 | (0.4%) | 16 | (1.8%) | 96 | (4.4%) |
| | Ref. | – | 1.1 | (0.4–3.6) | 4.7 | (2.7–7.9) | 11.4 | (8.5–15.2) |
| Stillbirth | 58 | (0.3%) | 3 | (0.4%) | 10 | (1.1%) | 79 | (3.6%) |
| | Ref. | – | 1.7 | (0.5–5.4) | 4.3 | (2.2–8.4) | 13.9 | (9.9–19.4) |
| Neonatal death | 28 | (0.1%) | 0 | – | 6 | (0.7%) | 17 | (0.8%) |
| | Ref. | – | – | – | 5.4 | (2.2–12.9) | 6.2 | (3.4–11.3) |

Data expressed as $n$, (%) and RR (95% CI).

to both non-SGA infants. Infants who were classified as SGA by both criteria had the greatest risk of perinatal death (RR 11.4, 95% CI 8.5–15.2).

The PAR of SGA-related perinatal death using full customisation was higher for all definitions of SGA (below the third, fifth and tenth centiles) when compared with ultrasound-and-gender customisation (Figure 2). Using the standard definition of SGA (below the tenth centile), 6.8% more perinatal deaths were attributable to $SGA_{full}$ infants (PAR 49.8%) compared with $SGA_{us}$ infants (PAR 43.0%).

## Discussion

We report updated coefficients and ten new ethnicity coefficients for a customised birthweight centile calculator in a large, multiethnic contemporary cohort of New Zealand women. We have demonstrated that the full customisation model identifies SGA infants that have significantly increased odds of perinatal death compared with SGA infants identified by a partial model, customised for ultrasound and gender alone. Full customisation identified an additional group of at-risk SGA infants ($SGA_{full}$ only $n$ = 888), who were not identified using ultrasound-and-gender customisation. These newly identified SGA infants have a greater than four-fold increased risk of perinatal death when compared with non-SGA infants. Full customisation also resulted in a clinically important 6.8% increase in PAR of SGA-related perinatal death, compared with ultrasound-and-gender customisation ($SGA_{full}$ 49.8%; $SGA_{us}$ 43.0%). These findings support our hypothesis that excluding the effects of pathological factors and adjusting for maternal characteristics in a full customisation model better identifies SGA infants who are at risk of perinatal mortality than an ultrasound-and-gender customisation model.

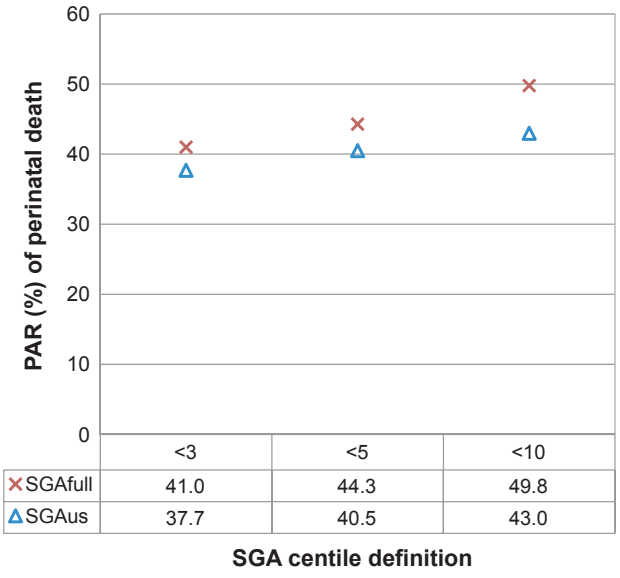


**Figure 2.** Population-attributable risk (PAR %) of SGA-related perinatal death by SGA centile definition for full customisation ($SGA_{full}$) and ultrasound-and-gender customisation ($SGA_{us}$).

Infants who were identified as SGA by the previous New Zealand centile calculator have been shown to have an increased risk of perinatal morbidity and mortality,[8] but at the time those coefficients were generated much of the data required for the model were not routinely collected. Of 11 423 eligible participants in the previous study, 6459 (56.6%) were excluded because of missing height and/or weight data.[13] It is possible that non-random missing data could have contributed to bias in the previous study, such as women with specific pregnancy complications being more likely to have had height and weight measured. This potential bias in the previous study may explain the differences in some ethnicity coefficients reported in the current study. The correction of such bias by using updated and more complete data has resulted in a model that is likely to more accurately reflect the characteristics of our current obstetric population. Additionally, we are now able to account for the pathological effects of smoking, diabetes, hypertensive disease and APH in the calculation of optimal birthweight. Smoking, hypertensive disease and APH are associated with fetal growth restriction,[14–16,29] and diabetes

is associated predominantly with increased fetal growth.[30] By including pathological variables in the initial regression model but not including the coefficients for these pathological variables in the calculation of TOW, the resulting optimal birthweight reference range can be considered to be exclusive of pathology, i.e. a reference range for a non-smoker, non-diabetic with no hypertensive disease or APH. Another method to achieve this optimal birthweight reference range would be to exclude all women with these pathological features from the initial regression model; however, excluding such a large number of women would inevitably introduce non-systematic bias into the model. The adjustment to exclude pathological variables described above allows for the calculation of a more accurate true optimal birthweight.

Consistent with previous studies, the full customisation model explains significantly more variability in birthweight than the ultrasound-and-gender model ($R^2$ statistic 0.31 and 0.18, respectively, $P < 0.001$).[11,26] The low $R^2$ value, even for the full customisation model, illustrates that the majority of variability in birthweight is not explained by variables included in this model. Other models that have attempted to predict birthweight with large numbers of variables, in addition to those used in full customisation, have not resulted in substantial increases in predictive value, and the majority of determinants of birthweight are still unknown.[31]

Sceptics of customised birthweight centiles have suggested that the addition of maternal characteristics does not add further benefit to a model that adjusts for an intrauterine fetal weight reference and infant gender.[6,11,12] Hutcheon et al.[11] compared a modified full customisation model with the Hadlock ultrasound-based model, and found no difference in risk of stillbirth or early neonatal death. Their Swedish cohort from 1992 to 2001 was predominantly European and non-obese, as was the low-risk white American cohort used to derive the Hadlock fetal growth standard.[27] Additionally, the risk of perinatal death was not investigated in infants who were SGA by a single criterion only. Similarly, in an analysis based on a low-risk, predominantly white American cohort from more than 20 years ago, Zhang et al.[32] compared infants who were classed as SGA (below the fifth centile) by the Hadlock ultrasound-based reference with those classed as SGA by full customisation, and found a similar risk of adverse perinatal outcomes in infants classed as SGA by either criteria (SGA by ultrasound, RR 2.68, 95% CI 2.00–3.58; SGA by full customisation RR 3.13, 95% CI 2.34–4.18). Consistent with our findings, however, they also showed an increased risk of adverse perinatal outcome in infants who were classed as SGA by full customisation alone (RR 2.09, 95% CI 0.96–4.54), but not in infants who were classed as SGA by the ultrasound-based reference alone (RR 1.04, 95% CI 0.42–2.55).

Recently, Mikolajczyk et al.[33] published a method of birthweight customisation for global populations that presented stepwise analyses of adverse perinatal outcomes in SGA infants defined using increasing numbers of explanatory variables. In these non-European populations, customisation using the Hadlock ultrasound-based fetal weight reference alone consistently over-diagnosed SGA, with rates of SGA as high as 60%. Adjustment of the Hadlock model for country resulted in improved identification of SGA infants at risk of adverse perinatal outcomes (RR 2.87, 95% CI 2.73–3.01), compared with Hadlock alone (RR 1.59, 95% CI 1.43–1.66), but the addition of maternal variables (height, weight and parity) to the adjusted model did not further improve the detection of at-risk SGA infants. As participating countries in this study have relatively homogenous populations, the adjustment for country can be considered a surrogate adjustment for ethnicity, and the mean maternal characteristics (height, weight and parity) of that population. Subsequent adjustment for maternal characteristics in addition to country would not therefore be expected to substantially improve the performance of the model. As a result, Mikolajczyk et al. have demonstrated that adjustment for maternal characteristics using the surrogate of country, improves the detection of adverse perinatal outcomes over Hadlock ultrasound customisation alone.

In our ethnically diverse population with a high proportion of overweight and obese women, there was considerable agreement in classification between full and ultrasound-and-gender customisation with 24 412 (94%) infants classed as either non-SGA or SGA by both criteria. This degree of agreement is to be expected, as classification changes between models will only occur in infants that have a customised birthweight centile close to the tenth centile by either model. Customisation of birthweight by either model identified SGA infants who were at risk of perinatal death; however, full customisation identified a higher risk population of SGA infants with a significantly increased odds of perinatal death compared with SGA infants defined by the ultrasound-and-gender model ($SGA_{us}$, OR 2.1, 95% CI 1.4–3.3; $SGA_{full}$, OR 5.6, 95% CI 3.6–8.7, $P = 0.02$).

The majority of perinatal deaths occurred in infants where the classifications were concordant (both non-SGA and both SGA $n = 182$, 91%), and the highest risk of perinatal death occurred in the majority group of SGA infants who were classed as SGA by both criteria ($n = 2183$, 44 per 1000 total births, RR 11.4, 95% CI 8.5–15.2). However, the infants who were newly identified as SGA by the full customisation model ($SGA_{full}$, only $n = 888$, i.e. 24% of all SGA infants), were a high-risk group with a greater than four-fold increased risk of perinatal death compared with non-SGA infants. In contrast, infants who were $SGA_{us}$ alone ($n = 676$, 18%) did not have an increased risk of

perinatal death compared with non-SGA infants. These findings suggest full customisation better identifies true growth restriction than ultrasound-and-gender customisation.

Further support for the advantages of full customisation was the higher PAR of SGA-related perinatal death when compared with the ultrasound-and-gender model. As PAR standardises risk comparisons by accounting for different numbers of 'exposed' pregnancies (infants identified as SGA by each model), direct comparisons between models can be made. Using a definition of SGA as infants born below the tenth centile, the full customisation model resulted in a PAR of SGA-related perinatal deaths that was 6.8% higher than was calculated by ultrasound and gender alone, which we believe is a clinically important increase.

As with previous analyses of customised birthweight standards, the applicability of our findings to clinical practice is limited to the identification of these at-risk SGA infants at birth, when no intervention is possible other than postnatal monitoring.

The current study used prospectively collected hospital data, with robust data cleaning.[17] Overall, 9% of the eligible study population had missing data. It is possible that the women with these missing data are non-random; however, with >90% complete data and large study numbers, this is unlikely to have a significant impact on our results. Additionally, some of the new ethnicity groups had small numbers, particularly the Fijian ($n$ = 192) and Latin American ($n$ = 158) groups. As a result, these groups may not fully reflect the characteristics of their respective ethnicities; however, separate coefficients based on smaller numbers will still estimate ethnicity characteristics better than combining women of diverse ethnicities into a heterogeneous 'Other' group.

Despite our large study population of 25 976 women, our sample is smaller than some other studies that have investigated maternal characteristics in birthweight customisation.[11,26] As perinatal death is a rare event, there were only 19 perinatal deaths in the subgroup analyses of SGA infants where classifications did not agree ($SGA_{us}$ only and $SGA_{full}$ only). The major advantage of the current study population over previous cohorts is the heterogeneity of maternal characteristics, particularly ethnicity and maternal body mass index. It would be ideal if the subgroup analyses we have performed could be repeated in a larger multi-ethnic population to confirm our study findings.

## Conclusion

New customised birthweight centile coefficients have been created using data from a large updated birth cohort, with the addition of new ethnicities to better reflect our current obstetric population.

We have shown that a full customisation model that excludes the effects of pathological factors, and adjusts for maternal characteristics, identifies SGA infants that are at higher risk of perinatal death than a partial customisation model that adjusts for ultrasound and gender alone. Additionally, the group of infants identified as SGA by full customisation alone have a greater than four-fold increased risk of perinatal death, whereas infants identified by ultrasound-and-gender customisation alone do not have an increased risk of perinatal death. Furthermore, this full customisation model increases the PAR of SGA-related perinatal death by 6.8%. The inclusion of maternal characteristics and pathological variables in a birthweight customisation model is therefore of clinical utility.

### Disclosure of interests

None to declare.

### Contribution to authorship

NA helped conceive the study design, cleaned data, performed the statistical analysis with assistance from AS and drafted the article. LS provided data, interpreted analyses and reviewed the article. LM conceived the initial study design, helped interpret data and reviewed the article. AS provided previous study data, wrote the statistical programme and provided statistical advice. All authors have approved the final version of the article.

### Details of ethics approval

Ethical approval for this study was gained from the Northern X Regional Ethics Committee (NTX/09/179/EXP).

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