GROW documentation

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This document describes the application of the customised growth potential to assess fetal size and growth, using the **Gestation Related Optimal Weight (GROW**) software.

GROW – Customised Weight Centiles
- to calculate birthweight centiles individually or in bulk for whole databases;

GROW – Customised Growth Charts
- to plot fundal height and estimated fetal weight.

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1. Introduction

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The customised growth chart concept was developed initially in Nottingham in the early 1990s[1]. While recognising the importance of growth for fetal well being, we became increasingly aware that existing charts were not useful for clinical assessment in a heterogeneous maternity population.

Over time, we have been able to test the concept of adjustable or customised assessment of growth and birthweight from many different perspectives. A recent review article includes a summary of the concept and rationale for customised growth charts and an update on their current clinical application.[2]

The project has been fortunate to benefit from a number of dedicated researchers, statisticians and programmers over the years, who are acknowledged in various referenced publications. I would particularly like to acknowledge the long time, ongoing help of Andre Francis, statistician and friend. But while the strengths of the method, supporting evidence and implementation are thanks to the efforts of many collaborators, any weaknesses are entirely my own responsibility.

We hope that you find our software useful for the assessment of fetal growth and birth weight. We are continuing to seek to improve it, and feedback is always welcome, so please do not hesitate to get in touch.

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The software can be referenced as follows, with the relevant version ('x') of the software used:

Birthweight or fetal weight centiles:
Gardosi J, Williams A, Hugh O, Francis A. Customised Centile Calculator. GROW version x, Year. Gestation Network, www.gestation.net

Antenatal growth charts:
Gardosi J, Williams A, Hugh O, Francis A. Customised Growth Chart - GROW version x, Year. Gestation Network, www.gestation.net

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2. General concepts

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The software allows the generation of an individual or 'customised' standard by adjusting for physiological factors which are known to affect fetal growth. The pregnancy characteristics are entered to calculate the **Term Optimal Weight (TOW, Section 3)**. This is the weight that the baby is predicted to achieve in the absence of pathological influences. The calculation of TOW is centred on 40.0 weeks (280 days).

Through this point TOW, the proportionality curve is plotted to delineate how this weight is expected to be reached in a normal pregnancy (see section 5). This gives an individually adjusted **Gestation Related Optimal Weight (GROW)** curve. Around this optimal line, the normal variation can be calculated and limits such as the 10th and 90th centile lines drawn. Thus, neonatal weights from previous pregnancies, as well as fundal height measurements or fetal weight estimations in the current pregnancy, can be seen in relation to individually adjusted optimal weight limits.

There are 3 underlying **principles for GROW-percentiles**:

1. Weights are assessed in reference to a standard that is **individually adjusted** for physiological pregnancy variables (maternal height, weight, parity and ethnic group); e.g. at 40 weeks, a 3000g baby is small for an average size mother but may be normal for a small mother. Postnatally, the standard is also adjusted for the sex of the baby.
2. The standard is **'optimised' to obtain the growth potential**, i.e. pathological variables such as smoking and diabetes are excluded. For example, expected term baby weight for a mother who smokes is calculated as if she was a non-smoker so that, if her baby's growth ***is*** affected, the growth or weight deficit is more likely to be identified.
3. Optimal weight is calculated using a **fetal** rather than a **neonatal** weight standard. Preterm neonatal weights are abnormal by definition, and have often been affected by fetal growth restriction preceding spontaneous or iatrogenic preterm delivery. Eg. at 32 weeks, a 1500g baby would fall within normal birth weight limits, but is small according to a 32 week fetal weight standard derived from pregnancies which have gone on to normal delivery at term.

3. Calculating the Optimal Weight

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The main non-pathological factors affecting birth weight are **gestational age, maternal height, maternal weight at booking, parity, ethnic group and sex of the baby** [1]. Coefficients to adjust for these variables were originally derived from a dataset of around 30,000 ultrasound dated deliveries. They allow calculation of an expected birth weight for each pregnancy, and the 'customised' percentile of a fetal or neonatal weight in relation to this expected endpoint.

An alternative method to adjust for such variables is to calculate the individual birth weight ratio (IBR).[3–5] IBR follows principle 1 above, i.e. adjusts for individual variation, but does not optimise (principle 2) or apply a fetal weight standard (principle 3).

Other physiological variables such as **paternal height**, unless extreme, have a relatively minor effect [6]. **Maternal age** usually appears to play no significant role once parity is adjusted for.

In pre-2009 versions, adjustment for maternal weight was made within **BMI limits** of 20-30 only, which approximately represented the 10th and 90th centiles of the BMI distribution in the population at the time. Since then, it has become apparent that the polynomial coefficients derived in the multivariable regression analysis were robust enough to be applicable across the whole BMI range, and better reflected adverse perinatal outcome. Extreme limits (BMI <15, >50) were programmed into the software because of rareness of such data and likelihood of erroneous entry.

Pathological factors such as **smoking, social deprivation, pre-eclampsia or diabetes** were also included in the analysis to define the effect they had on the weight constant, but then excluded i.e. not used to adjust the term optimal weight, even if the condition was present. The purpose is not to predict a pathological birthweight, but to determine the 'term optimal weight' (TOW) as an ideal standard, against which the actual fetal or neonatal weight can be assessed - in order to better identify if – for example in the case of smoking – the growth was indeed affected. TOW is calculated for day 280, the median and modal length of pregnancy in our population[7].

4. Coefficients for calculating the term optimal weight (TOW) Contents

Coefficients are derived from suitable databases using a multiple regression model centred on median gestational age, the largest ethnic group, average maternal height and weight at booking, and first pregnancy (para 0). In addition, gender is listed as an 'average' i.e. sex-neutral. The regression model has a constant to which weight is added or subtracted for each of the variables, according to the formula

TOW = constant + htao + wtao + ethao + parao + sexao

where 'ao' are add-ons, respectively, for

ht = maternal height
wt = maternal weight at booking (first visit)
eth = ethnic origin
par = parity and
sex = gender of fetus/neonate, if known

Coefficients

The original coefficients were derived from a Nottingham database (1987-1991; n=30,000) [7] and are reproduced here for illustration only, as they have **since been superseded**.

Name of coefficient		Contribution in grams
Constant		3478.4
Maternal height (*median 162.3 cm*) deviation		
	for each cm	+7.8
Maternal weight (*median 64.3 kg*) deviation:		
	for each kg	+8.7
	for each kg^2	-0.117
	for each kg^3	+0.00072
Ethnic origin (*default European incl British Isles and those of European origin elsewhere. eg Australia, Canada, USA*)		
	Indian Subcontinent	-186.0
	African Caribbean	-127.5
	Other	-65.2
Parity at beginning of pregnancy (*default para 0*)		
	Para 1	+108.0
	Para 2	+148.6
	Para 3	+149.9
	Para 4 or more	+149.8
Sex of fetus/neonate (*default 'average' i.e. sex neutral*)		
	Male	+58.4
	Female	-58.4

SE of model = 389.0, giving CV = 0.11

Since then, sets of coefficients have been developed for databases from over 30 countries totalling in excess of 4 million pregnancies. Some sets of coefficients published from the various countries include Australia[8], New Zealand[9], United States[10], Ireland[11], Spain[12], Sweden[13], Slovenia[14] and Iran[15] .

The extent of the data allow us now to derive **ethnic specific sets of coefficients**; thereby, we can adjust for maternal size etc variation for each ethnicity or country of origin. Where data for individual ethnic groups are not yet available, regional coefficients can be used. The new global GROW charts and calculators now incorporate over 130 ethnic and regional sets of coefficients.

Additional datasets are welcome for analysis of country specific coefficients. The data fields required for analysis can be viewed here.

5. Proportionality curve

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Once the TOW (term optimal weight, predicted for median gestation) is calculated, it is combined with a proportionality growth function to determine the optimal weight at all gestations. This function transforms the average weights at all gestations to a percent of term weight in that pregnancy. The proportionality principle can be used retrospectively (birthweight to fetal weight) or to project fetal weight to predict birth weight. [7,16]

Reviews of published formulae for fetal weight gain suggest that most follow a similar pattern, or growth dynamic, although the endpoints (term weights) may vary. [17,18] Our standard formula is derived from Hadlock's fetal weight equation [19] which has been converted into a proportionality formula [6] expressing percent term weight at different gestations, as follows:

$$\% \text{ weight} = \exp(0.578 + 0.332 * GA - 0.00354 * GA^2) / \exp(0.578 + 0.332 * GM - 0.00354 * GM^2)$$

where GA is gestational age between 10 and 42 weeks and GM is median gestation of the model.

6. Normal range

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The normal limits of weight for all gestations are calculated from the coefficient of variation (CV) of the TOW. It is derived from the SD and Mean (Constant) of the population through the regression model, and defined as: $CV (\%) = \dfrac{SD * 100}{Mean}$

For the original UK database[7], SD = 389 and Mean = 3478 giving CV = 11%.

The centile limits are derived using Z scores. For example, the 90th and 10th centiles are represented by $z = \pm 1.28$.

This gives: $z * CV = \pm 1.28 * 11\% = \pm 14\%$;

Thus: 90^{th} centile = TOW + 14%
10^{th} centile = TOW – 14%

For example, the 10-90 centile range for a TOW of 3500g is 3500±14%, i.e. range 3010-3990g.

The effect of using the CV is that the range designated as 'normal' becomes narrower for lower TOWs and wider for higher TOWs. Thus, a small baby is allowed a smaller range of normal variation in absolute terms. The method compensates for the positive skewness of the distribution of birth weight.

The proportionality weight equation is fitted through the three term points: TOW, TOW+14% and TOW–14%. This defines the 50^{th}, 90^{th} and 10^{th} centile lines respectively for the gestation period 24 to 42 weeks. This principle is used in the applications described in the following sections. More recently, we have added 97^{th} and 3^{rd} centile lines to the chart.

As databases vary in background and pathologies recorded, our models apply a uniform coefficient of variation of 11% to reflect a general population that is free of pathology.

7. GROW - Customised Centiles

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This module allows a customised weight-for-gestational age centile to be determined for previous babies, and for estimated fetal weights and birth weight in the current pregnancy.

The calculators are provided in two forms:

- Individual Centile Calculator (ICC), a web-based application, for case-by-case use.
- Bulk Centile Calculator (BCC), in spreadsheet format, for whole databases.

Precise gestational age (at birth, or at the time of EFW measurement) needs to be entered. Gestational age can be calculated with the 'Gestational Age Calculator' - see section 10 below.

The applications can also be used for an estimated fetal weight (EFW) centile when the sex of the baby is not known. When other variables are missing or unobtainable - e.g. maternal height - partial customisation can be undertaken by entering an estimate or population average. In the BCC, this is done automatically when a variable is omitted.

The application can also be used to investigate stillbirth weights. If outcome = fetal death is entered, the calculator automatically deducts 2 days from the gestational age, as an approximation of the average fetal death-to-delivery interval [20].

The centile calculator is also integral to the customised growth chart, to calculate centiles from previous pregnancies as a history of small or large babies will be relevant for care in the current pregnancy. The centiles are calculated for the corresponding parity of the mother at the *beginning* of the respective pregnancy.

NB: No adjustment is made for maternal weight if it was different in a previous pregnancy; if the weight is considered to have been significantly different, we recommend that previous birthweight centiles are calculated separately for the respective maternal variables.

8. GROW – Customised Growth Charts

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The GROW customised chart module allows the generation of antenatal charts. After entering the pregnancy data through the 'Mother details', 'Baby details' and 'EDD' sub-routines, the chart is generated on screen and can be printed out in early pregnancy.

It shows

- a summary of the pregnancy details and the BMI calculated from maternal height and weight
- previous babies' birthweight centiles
- centile lines as above
- on the x-axis, the EDD and the day and month for each week of gestation
- two y-axes:

  left axis: fundal height (FH, in cm),

  right axis: estimated fetal weight (EFW, in g)

The relationship between weight and fundal height is described by a formula derived from a study of 325 pregnancies[21], showing a relationship in the third trimester of the form

$$\ln(EFW) = 10.6857 - 100.25/SFH$$

where EFW is in grams and SFH is in cms.

Linked to weight, fundal height norms are therefore also customised according to pregnancy characteristics, thereby allowing for individual variation. Multivariate analysis showed that maternal characteristics such as parity and weight were significantly associated with fundal height values in the third trimester [22].

The chart can be attached to the mother's hand held maternity notes – e.g. the Pregnancy Notes www.preg.info – and used for fetal growth monitoring in the community, provided the pregnancy is considered low risk. From 26-28 weeks onwards, we recommend serial (2- 3 weekly) fundal height measurement with a non-elastic tape, preferably by the same care provider. The measurement should start from the variable point (the fundus) to the fixed point (upper border of the symphysis pubis), along the longitudinal axis of the uterus (which should *not* be corrected to the mid-line).

The fundal height should be plotted using an 'x' symbol. If the slope / trajectory through consecutive plots is not between those defined by the 90th and 10th centile lines on the chart, fetal biometry by ultrasound scan is recommended. It is important to assess liquor volume (which affects fundal height) and measure fetal biometry parameters to calculate estimated fetal weight (EFW). This can then be plotted using an 'o' symbol. If the baby is small, or its growth velocity is slower than the 3rd centile line on the chart, further investigation such as Doppler flow measurements are recommended. Subsequent management will depend on these results and clinical considerations, and can include repeated ultrasound and Doppler or delivery.

GROW charts can be used for screening for intrauterine growth restriction (IUGR) and macrosomia. A controlled study of community growth screening suggests that serial plotting of fundal height on customised charts increases the detection rate of growth abnormalities while decreasing the rate of unnecessary referrals for further investigation. [23] A subsequent audit in the West Midlands has confirmed these findings. [24] Ultrasound EFWs plotted in normal pregnancies are more likely to stay within customised GROW limits than if general limits for the whole population are used - i.e. customisation of fetal weight reduces the false positive diagnosis of SGA/'IUGR'. [25] The use of customised charts is recommended by RCOG guidelines.[26]

9. GRAW – Population Average Growth Charts

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GRAW (Gestation Related Average Weight) uses a simplified version of the GROW method, to generate a **population average** growth chart for countries where there is insufficient data to derive individually adjustable coefficients. Contact us for details.

10. Gestational Age Calculation

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Accurate pregnancy dating is a central requirement for any weight centile assessment. The 'Calculate EDD' function within GROW has options for entering:

1 - the last menstrual period (LMP), to which 280 days are added to determine the expected date of delivery (EDD);

2 - scan measurements from which the EDD is calculated according to standard references for 1st trimester CRL[27] , or for 2nd trimester BPD [28] or HC[29];

We recommend that ultrasound dates be used, where possible, *without* allowance for the LMP. There are considerable discrepancies between even 'certain' menstrual dates and scan dates [30,31], and many analyses have suggested that ignoring menstrual history altogether improves the accuracy of pregnancy dates. [32–34]

11. References

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