TITLE: Influence of maternal adiposity, preterm birth and birth weight centiles on early childhood obesity in an Indigenous Australian pregnancy-through-to-early-childhood cohort study

Authors: Pringle, K.G.*[1,2,3] Lee, Y.Q.*[1,2,3] Weatherall, L.[3] Keogh, L.[3] Diehm C.[3,4] Roberts C.T.[5] Eades S.[6] Brown A.[7] Smith, R.[1,8,] Lumbers, E.R.[1,2] Brown, L.J.[4,9] Collins, C.E.[9,10] Rae, K.M.[1,3,4,8,11]

*Joint first authors

Author Affiliations:

1. Priority Research Centre in Reproductive Sciences, University of Newcastle, Australia;
2. School of Biomedical Sciences and Pharmacy, University of Newcastle, Australia
3. Gomeroi gaaynggal Centre, Faculty of Health and Medicine, University of Newcastle, Australia;
4. Department of Rural Health, University of Newcastle, Australia;
5. Adelaide Medical School and Robinson Research Institute, University of Adelaide, Adelaide, South Australia;
6. Aboriginal Health, Baker IDI Heart and Diabetes Institute, Melbourne, Victoria
7. Aboriginal Research Unit, South Australian Health & Medical Research Institute, Adelaide, South Australia;
8. Mothers and Babies Research Centre, Hunter Medical Research Institute, Newcastle, Australia
9. Priority Research Centre of Physical Activity and Nutrition, University of Newcastle, Australia
10. School of Health Sciences, University of Newcastle, Australia

11. Priority Research Centre for Generational Health and Ageing, University of Newcastle, Australia

Corresponding author:
Dr Kirsty Pringle
Hunter Medical Research Institute
Lot 1 Kookaburra Circuit, New Lambton Heights NSW 2305, Australia
T: +61 2 4042 0372
E: Kirsty.Pringle@newcastle.edu.au

Abstract

Childhood obesity rates are higher among Indigenous compared to non-Indigenous Australian children. It has been hypothesised that early-life influences beginning with the intrauterine environment predict the development of obesity in the offspring. The aim of this paper was to assess, in 227 mother–child dyads from the Gomeroi gaaynggal cohort, associations between prematurity, Gestation Related-Optimal Weight (GROW) centiles, maternal adiposity (percentage body fat, visceral fat area), maternal non-fasting plasma glucose levels (measured at mean gestational age of 23.1 weeks) and offspring BMI and adiposity (abdominal circumference, subscapular skinfold thickness) in early childhood (mean age 23.4 months). Maternal non-fasting plasma glucose concentrations were positively associated with infant birth weight (P=0.005) and GROW customised birth weight centiles (P=0.008). There was a significant association between maternal percentage body fat (P=0.02) and visceral fat area (P=0.00) with infant body weight in early childhood. BMI in early childhood was significantly higher in offspring born preterm compared with those born at term (P=0.03). GROW customised birth weight centiles was significantly associated with body weight (P=0.01), BMI (P=0.007) and abdominal circumference (P=0.039) at early childhood. Our findings suggest that being born preterm, large for gestational age or exposed to an obesogenic intrauterine environment and higher maternal non-fasting plasma glucose concentrations are associated with increased obesity risk in early childhood. Future strategies should aim to reduce the prevalence of overweight/obesity in women of child-bearing age and emphasise the importance of optimal glycemia during pregnancy, particularly in Indigenous women.

Keywords: Pregnancy, Maternal obesity, Preterm birth, Indigenous, childhood obesity.

Introduction

The prevalence of obesity worldwide has more than doubled between 1980 and 2014,[1] and is now a global health issue. Not only is obesity more prevalent in adults, but the prevalence of infant, childhood and adolescent obesity is increasing at an alarming rate around the world, affecting many low- and middle-income countries. In 2014, an estimated 41 million children under 5 years of age were overweight (body mass index (BMI) ≥ 85th percentile and less than the 95th percentile) or obese (BMI ≥ 95th percentile); a dramatic increase from 32 million globally in 1990.[2,3] In Australia, 26% of children aged 5–14 are considered overweight or obese [4] and Aboriginal and Torres Strait Islander children (aged 2–14 years) are more likely than non-Indigenous children to be overweight or obese (30% vs 25%).[5] It is undeniable that being overweight or obese in childhood and adolescence has adverse health consequences, increasing the likelihood of many health problems in adult life, including cardiovascular disease, cancer, diabetes, osteoarthritis, and chronic kidney disease.[6-8]

The intrauterine environment can have long-lasting consequences for the infant related to obesity and future development of chronic disease.[9,10] Being born premature (≤37 weeks gestation) or small at birth (below the 10th percentile for gestational age) is associated with greater adiposity and an increased risk of being overweight or obese throughout all stages of life and contributes to the increased risk of metabolic disease, cardiovascular disease and diabetes in adult life.[11-18] Furthermore, low birth weight (LBW) premature infants exhibit 'catch up growth' in the early years of their life and experience a steep gain in weight.[19] Excess weight gain during infancy increases the likelihood of developing chronic diseases such as obesity, cardiovascular disease and diabetes as an adult.[20,21]

Maternal overweight or obesity and maternal hyperglycemia (including gestational diabetes) also increases the likelihood of offspring obesity during infancy, childhood and later in life,[22-28] and may 'program' later cardio-metabolic health in offspring.[29] In the Helsinki Birth Cohort Study of individuals born during 1934–44, higher maternal BMI was associated with greater adiposity [28], and an increased risk of cardiovascular disease (hazard ratio (HR) 1.026; P=0.002), type 2 diabetes (HR 1.04; P=0.004) among offspring.[30] This emphasises the importance of ensuring the optimal nutritional health of women of reproductive age and early preventive interventions for overweight and obesity.

The Aboriginal and Torres Strait Islander peoples of Australia (or the Indigenous community) are one of the most socially disadvantaged populations in the country. They continue to experience poorer health outcomes and a life expectancy 10 years lower than non-Indigenous Australians due to generations of social and economic disadvantage.[31] The high rates and burden of preventable chronic disease is a significant contributor to premature mortality and the large disparity in life expectancy. Indigenous mothers are 1.6 times more likely to be overweight or obese, as well as 1.6 times and 3.5 times more likely to have gestational diabetes and pre-existing diabetes, respectively, than non-Indigenous mothers.[32] A recent systematic review reported that up to 22% of Indigenous infants aged 2-4 years are overweight or obese.[33] 14% of Indigenous Australian babies are born preterm, compared with 8% of babies of non-Indigenous mothers, and 14.1% are born small for gestational age, compared with 9.1% of babies of non-Indigenous mothers.[32]

Examination of the associations between being born preterm or exposed to an obesogenic intrauterine environment and risk of childhood obesity has direct relevance for the Aboriginal and Torres Strait Islander population, given the elevated rates of preterm birth, LBW, maternal

obesity and chronic diseases.[5,34] This link has been explored within other populations, but current evidence for an association in Aboriginal and Torres Strait Islander Australians is lacking.[35]

Therefore, the objectives of the current study were: (i) to determine any associations between maternal adiposity or non-fasting plasma glucose and offspring BMI and adiposity in early childhood (1-3 years); and (ii) to determine any associations between preterm birth or Gestation Related-Optimal Weight (GROW) centiles and offspring BMI and adiposity in early childhood (1-3 years) in Indigenous Australian children.

Methods

Ethics:

The Gomeroi gaaynggal program has received ethics approval from the Hunter New England Human Research Ethics Committee (Ref. No. 08/05/21/4.01), New South Wales Human Research Ethics Committee (Ref. No.HREC/08/HNE/129) and Aboriginal Health and Medical Research Ethics Committee (Ref. No. 654/08).

Study design and Setting:

The Gomeroi gaaynggal ArtsHealth program is a prospective pregnancy through to childhood longitudinal cohort where mothers and their infants are followed until the child reaches 5 years of age. The study is based at two locations in New South Wales (NSW), Australia. These are the rural community of Tamworth, NSW, and the smaller remote community of Walgett, NSW. Further details of the Gomeroi gaaynggal study have been published elsewhere.[36]

Participants:

Pregnant women who identifed as Indigenous Australians or who were carrying an Indigenous infant were eligible to participate. The study has been recruiting since 2010 and recruitment is ongoing at the time of publication. Pregnant women are eligible to participate at any time in gestation. Participants are eligible to consent provided they were at least 16 years of age. If under 16 years, consent is also required from their guardian. Recruitment is undertaken by Indigenous research assistants in antenatal clinics in each community who spend time explaining the study to the potential participant and any family members. The additional time spent in recruitment is a cultural necessity and many participants will not consent to the study unless this time is taken. This additional time assists in building trustful relationships between the research team and the participant and is an essential component to long term engagement in the study. Women also provide written consent to participate in the follow-up study.

Timing of study visits:

While every effort was made to see study participants at every study visit, this was not always feasible. Study visits were timed to see participants once per trimester. For the purpose of this study maternal measures (non-fasting plasma glucose, body fat percentage and visceral fat area) were collected at their first visit, regardless of when in gestation this occurred. Follow up visits with infants occured at 3 (range 1.6-4.3 months), 6 (4.5-7.8 months), 9 (8-10.8 months) and 12 (11.4-18.4 months) months in the first year of life and annually until the child reached 5 years. For the purpose of this analysis, we have only included data from follow-up visits with infants up until the age of 3 years (ranges of 2 and 3 years of 19-29.9 months and 33.1-43.3 months, respectively). Data collected at each time point for pregnant women and their offspring participating in the Gomeroi gaaynggal study is outlined in Supplementary Table S1. More detailed information has been published elsewhere.[36]

161 ***Measures***

162 *Pregnancy and delivery measures:*

163 All participants were asked to provide information on their obstetric history and self-report
164 other pre-existing conditions including diabetes, asthma and hypertension. Maternal BMI was
165 calculated from measured height (ht) and self-reported pre-pregnancy weight (wt) at their first
166 visit during pregnancy [wt(kg)/ht(m^2)] and each participant was subsequently categorized as
167 being underweight (BMI <18.5 kg/m^2), normal weight (BMI 18.5-24.9 kg/m^2), overweight
168 (BMI 25.0-29.9 kg/m^2) or obese (BMI ≥30.0 kg/m^2) according to World Health Organization
169 categories.[37] Height was measured to the nearest 0.1 cm and weight to the nearest 0.1 kg. For
170 participants who could not recall their pre-pregnancy weight, their pre-pregnancy BMI was
171 calculated using weight measured at less than 12 weeks' gestation.

172

173 All participants had their body composition (percentage body fat and visceral fat area) obtained
174 at each study visit using the InBody 720^{TM} body composition bio-impedance scales (Biospace
175 Co., Seoul, South Korea). InBody 720 (Biospace, Korea) is a multi-frequency body
176 composition analyzer with 4 pairs of electrodes (octapolar technology) embedded into the
177 handles (thumb and palm electrodes) and floor scale (ball of foot and heel electrodes) of the
178 analyzer. By using low and high frequency electric currents which flow at different rates
179 through the body, depending on body composition,[38] the impedance measures are used to
180 estimate total body water, fat free mass, % body fat and other body composition components.[39]
181 Participants step onto the foot electrodes barefoot and stand still until body weight is measured.
182 Then the participants are asked to grasp the hand electrode cables and hold the thumb and palm
183 electrode gently. Hands are held approximately 15º away from the body and the participant is
184 asked to stay still until measurements are complete. Numerous previous studies have evaluated
185 the reliability and accuracy of using different reference methods to determine body

composition, for example bioelectrical impedance analysis (BIA) and dual energy x-ray absorptiometry (DXA), or in different populations.[40-44] Maternal blood samples were collected at each antenatal visit, centrifuged and non-fasting plasma glucose was tested via the Abbott Architect Automated analyser. Fasting blood sugars and oral glucose tolerance test (OGTT) are currently not accessible in this study, thus the non-fasting plasma glucose measured during routine antenatal visits were reported and used.

Gestational age and estimated date of delivery were calculated by a qualified ultrasonographer using a Portable Phillips CX50 Ultrasound unit with a convex 5MHz tranducer at the first study visit during pregnancy. Birth weight, length and head circumference measures were taken from the data recorded by hospital staff at the time of delivery. A birth weight centile was calculated for the infant using the GROW Customised Birth Weight Centile calculator.[45] This calculator individually adjusts for gestational age, maternal height, weight, parity, ethinicity and infant sex. Where variables were missing, e.g. maternal height, partial customization was undertaken automatically in the calculator by using an estimate or population average.

Postpartum infant measures:

An Accredited Practicing Dietitian (APD) with a Level 1 Anthropometry certification from the International Society for the Advancement of Kinanthropometry (ISAK) undertook all anthropometry measures of mothers and their infants. Using Harpenden skinfold calipers (Baty International, RH15 9LR, England, CE 0120), infant skinfold thicknesses were measured at the following sites: subscapular, biceps, iliac crest, front thigh and medial calf. Circumferences were measured at infant's head, mid-upper arm, abdomen, mid-thigh and calf. Skinfold thicknesses were taken sequentially and then repeated in that same order. If two skinfold measurements differed by more than 0.5mm, a third measurement was repeated. The two

measurements that were within 0.5mm of each other were averaged and used for the analysis. Infant weight was measured in light clothing to the nearest 0.01kg using digital baby scales (model BD-590; Tanita Corporation, Tokyo, Japan) and infant length was measured crown-to-heel without shoes to the nearest 0.1 cm using a recumbent length board (model MZ 10027; Wedderburn, Germany) if they were unable to stand. Once able to stand, the infant was weighed in light clothing to the nearest 0.01kg using the InBody Scales and infant standing height was measured without shoes to the nearest 0.1 cm using a wall-mounted stadiometer with a head board (model 0123; Seca, Germany) with the child's head positioned in the Frankfort plane. The definition of overweight and obesity at age two-three years was defined using the International Obesity Task Force cut-offs for BMI, which defines BMI according to age-and gender-specific z-score cut-points for children.[46]

Nutritional assessment of infant:

Measures of dietary intake of infants are collected via the Infant Feeding Recall (IFR) form. It collects information on initiation and duration of breastfeeing and if infants have regularly consumed and age of initiaition of the following items: infant formula, cow's milk, milk substitutes and solid foods. This information is collected at each postpartum follow-up visit.

Statistical Analysis

Statistical analyses were performed using the statistical software package Intercooled Stata, version 14 (Stata Corp LP, College Station, Texas, USA). Variables used in the analyses were tested for normality. P values <0.05 were considered statistically significant.

Chi-square statistics for categorical data were used to compare the birth outcomes between male and female infants. 2-sample t-tests or the Kruskal-Wallis test for continuous data were

used to compare offspring anthropometry measurements at 1-3 years in preterm and term infants. Analysis of variance testing, with Bonferroni correction for multiple comparisons, were undertaken to assess the differences in offspring anthropometry measurements at 1-3 years between small for gestational age (SGA), large for gestational age (LGA) and appropriately grown for gestational age (AGA) infants.

Multiple linear regression models were used to assess how much the maternal characteristics (percentage body fat, visceral fat and non-fasting plasma glucose) during pregnancy explain the variation in offspring anthropometry measurements at birth and at 1-3 years, while adjusting for maternal height, smoking and fetal sex. Similarly, multiple linear regression models were performed to assess how offspring GROW birth weight centiles explain the variation in offspring anthropometry measurements at 1-3 years, while adjusting for maternal height, smoking and fetal sex. Adjusted R^2 values and coefficients (95% CI) are reported, with $R^2 \geq 0.26$ considered large, ≥ 0.13– <0.26 medium and ≤ 0.02 small.[47]

Results

Maternal characteristics

The maternal charcteristics of the participants are outlined in Table 1. The mean maternal age of the particpants was 25.56 ± 6.09 years (mean ± SD) at the time of consent (n=226). 6.5% (n=8/123) of mothers were underweight (BMI <18.5kg/m^2), 24.4% (n=30/123) were within the normal weight range (BMI 18.5-24.99 kg/m^2) and 69.1% (n=85/123) were overweight/obese (BMI ≥25.0kg/m^2). The proportion who self-reported smoking during pregnancy was 27.3% (n=62/227). Within the cohort, 1.8% (n=4/227) had pre-existing type I diabetes, 3% (n=7/227) had type II diabetes, and 11.1% (n=25/227) developed gestational diabetes mellitus (GDM) during their pregnancy.

The median maternal non-fasting plasma glucose levels were 4.1 (3.7, 4.95) mmol/L [median (interquartile range)] (n=184), measured at a mean gestational age of 23.1 weeks (range 8-40.4). For trimester 1 (mean gestational age of 11.1 weeks), the median maternal non-fasting plasma glucose levels were 4.55 mmol/L (IQR: 4, 5.3, n=14). For trimester 2 (mean gestational age of 20.3 weeks), the median maternal non-fasting plasma glucose levels were 4 mmol/L (IQR: 3.6, 4.8, n=116). For trimester 3 (mean gestational age of 32.1 weeks), the median maternal non-fasting plasma glucose levels was 4.4 mmol/L (IQR: 3.9, 5, n=54).

To assess maternal adiposity, we examined measures of percentage body fat and visceral fat area at the first antenatal study visit. The mean percentage body fat of pregnant women in the cohort was 41.3% (SD 12.75, n=133) and the mean visceral fat area was 163.31cm^2 (SD: 96.8, n=132), both measured at mean 23.7 weeks gestation, (range 5.8-38.7 weeks).

Birth Outcomes

As of August 2017, there were 245 infants born from the Gomeroi gaaynggal cohort with known birth outcomes, 18 of these were twins and were excluded from further analyses. Of the singleton infants (n=227), 58.6% of were male. The mean birth weight, length, head circumference and gestational age at delivery of infants in the cohort are detailed in Table 2. There was no significant difference in the mean gestational age at delivery, birth weight, length, GROW customised birth weight centile, or head circumference between male and female infants (Table 2). A total of 11.9% of singleton infants were born preterm (n=27/227) with the rate tending to be higher among male infants; 15% of male (20/133) and 7.5% of female (7/94) infants were born preterm (P=0.082).

Of all infants, 14.3% were born small for gestational age (32/223) and rates were similar between male and female offspring (13.8% and 15%, respectively, P=0.80). Conversely, 19.7% of babies were born large for gestational age (44/223) with rates in female and male infants being similar (23.6% and 16.9%, respectively, P=0.21). The majority of the babies (64%) were delivered by normal vaginal birth.

Association between maternal body composition and non-fasting plasma glucose in pregnancy and offspring birth outcomes

There were no associations between maternal percentage body fat or visceral fat area and offspring birth weight or length (Table 3). In contrast, maternal non-fasting plasma glucose concentrations were positively associated with infant birth weights (P=0.005) and GROW adjusted birth weight centiles (P=0.008), but not with gestational age at delivery nor infant length at birth.

Infant anthropometry measurements from birth to 3 years

The mean infant anthropometry measurements at 3, 6 and 9 months and early childhood anthropometry measurements at 1, 2 and 3 years are outlined in Supplementary Table S2. Overall there was little difference between male and female anthropometry measurements up to 3 years of age. Using the BMI cut-off points sourced from Cole et al.,[46] at 2-years follow-up, the majority of the children (n=27/36, 75%) were within the normal weight range, 8% (n= 3/36) were underweight, and 16% (n= 6/36) were overweight or obese. At 3-years follow-up, 68.8% (n=11/16) were within the normal weight range while 31.3% (n=5/16) were overweight or obese. Mean anthropometric measures (weight-for-age percentiles, lengh-for-age percentiles, head circumference-for-age percentiles) of infants indicate appropriate growth trajectories with no apparent stunting or wasting (Supplementary Figures S1 and S2).

311

312 *Infant dietary intake*

313 Of the whole cohort, infant feeding data was available for 96/227 infants and indicates that 20
314 infants were never breast-fed (20.8%), 76 (79.2%) were breast-fed, with 27 (35.5%) of these
315 infants breast-fed and formula-fed concurrently. Of those who were breast-fed, 47 (61.8%)
316 were breastfed for ≤ 3 months, 3 (3.9%) were breastfed for between 4-6 months, and 26
317 (34.2%) were breastfed for ≥ 6 months.

318

319 *Association between gestation at delivery and birth weight on offspring anthropometry*
320 *measurements at 1-3 years of age*

321 To assess the impact of preterm delivery and birth weight on early childhood growth, data from
322 follow up visits between 1-3 years were pooled and repeated measures on the same offspring
323 were removed, using only data from the latest follow up visit. The mean age of early childhood
324 follow-up was 23.4 months. Overall 73 infants had at least 1 follow up visit between 1 and 3
325 years of age; 7 of these were born preterm. There was no difference in height, weight,
326 abdominal circumference or subscapular skinfold thickness at 1-3 years of age in infants born
327 preterm or term (Table 4). However, BMI in early childhood (1-3 years) was significantly
328 higher in offspring born preterm compared with those born at term (P=0.03, Table 4).

329

330 Being born small or large for gestational age significantly affected early childhood weight, and
331 abdominal circumference (ANOVA, Table 5). After testing for multiple comparisons, children
332 who were born SGA had significantly lower body weights (P=0.004) and abdominal
333 circumferences (P=0.008) than children born LGA at mean age of 23.4 months. Children who
334 were born LGA had significantly higher body weight in early childhood than those who were
335 born AGA (P=0.001). Table 6 summarises the adjusted linear regression analyses between

GROW customised birth weight centiles and early childhood anthropometry measurements (1-3 years). In the adjusted regression model (adjusted for smoking, fetal sex and maternal height), GROW customised birth weight centiles significantly explained the variation in body weight, BMI and abdominal circumference in early childhood (1-3 years).

Association between maternal adiposity and non-fasting plasma glucose levels in pregnancy on offspring anthropometry measurements at 1-3 years of age

Table 7 summarizes the adjusted linear regression analyses between maternal percentage body fat, visceral fat area and non-fasting plasma glucose and early childhood anthropometry measurements (1-3 years). In the adjusted regression model (adjusted for smoking, fetal sex and maternal height), maternal percentage body fat significantly explained the variation in infant body weight while maternal visceral fat area significantly explained the variation in infant body weight and height.

Discussion

A consistent body of evidence demonstrates that being overweight or obese in childhood and adolescence has adverse consequences on overall health and leads to premature mortality and increased physical morbidity in adulthood.[48] Identification of early-life risk factors for developing obesity in Indigenous Australian children is therefore essential for the development of public health interventions and policy to reduce childhood obesity in this high risk population group. Although there have been previous descriptive reports from the Gomeroi Gaaynggal cohort outlining the various maternal determinants of pregnancy outcomes, including inflammation, cigarette smoke exposure, and pre-pregnancy BMI,[49,50] none have reported on the associations between maternal adiposity, preterm birth or birth weight and early childhood weight status, as has been examined in the current study.

361

362 This study demonstrates in an Australian Indigenous population cohort, that being born preterm
363 is associated with an increase in BMI in early childhood (mean age 23.4 months) placing these
364 preterm infants on a trajectory for an increased risk of metabolic disease in later life. Although
365 an association of this type has been demonstrated in a variety of populations,[16-18] this has never
366 before been investigated in Indigenous Australian infants. ~12% of Indigenous Australian
367 infants in this cohort and 14.3% of Indigenous Australian babies nationally were born preterm,
368 compared with 8.3% of babies of non-Indigenous mothers.[32] This significant disparity is of
369 great concern. The risk factors for preterm birth, which include smoking during pregnancy,
370 poor nutrition and psychosocial stress related to economic disadvantage, are more prevalent in
371 Indigenous women. Thus, the importance of prioritising health for Indigenous women during
372 the prenatal and antenatal periods cannot be over-emphasised.

373

374 We have also demonstrated, for the first time, that being born large for gestational age is
375 associated with higher BMI in early childhood (mean age 23.4 months) among Aboriginal and
376 Torres Strait Islander children. The association between birth weight and early childhood BMI
377 is similar to that reported in a large systematic review of 282 studies which demonstrated that
378 high infant birth weight is consistently associated with later childhood obesity.[51] Kapral *et al.*
379 demonstrated that there is a 70–130% increased risk of overweight or obesity among children
380 of high birth weight (HBW) compared to children of normal birth weight.[52] Furthermore, it has
381 been demonstrated that children who are LGA at birth and exposed to an intrauterine
382 environment of either maternal diabetes or obesity are at increased risk of developing metabolic
383 syndrome.[52] Boney *et al*. highlighted that children born LGA have an increased risk of
384 metabolic syndrome diagnosis by age 11 years (HR 2.19, 95% CI: 1.25-3.82; *P*=.01).[29] In the
385 current cohort, there is a higher percentage of infants who are of LGA (19.7%) compared to

386 those born SGA (14.3%). The rate of Indigenous infants who were SGA in the current cohort
387 is similar to that reported nationally (14.1%) and is 1.5 times higher than that for non-
388 Indigenous infants (9.1%).[32] To the best of our knowledge, there is currently no available
389 information regarding the rate of LGA in Indigenous and non-Indigenous Australian babies
390 nationally to compare with. Being born LGA is also associated with adverse long-term health
391 outcomes such as obesity, cancer, asthma and diabetes.[53] Increased attention to and follow-up
392 of Indigenous children who are born at higher birth weights is therefore warranted. Since there
393 is a relatively low sample size in the current study, results should be interpreted with caution.
394 Ideally the prevalence of both SGA and LGA should be examined in a larger cohort with infant
395 measurements also adjusted for gestational age.
396
397 In this prospective follow-up study of mothers and offspring from the Gomeroi gaaynggal
398 cohort, we found that maternal adiposity, measured as percentage body fat and visceral fat area,
399 are positively associated with early childhood weight, up to a mean age of two years. In the
400 literature, maternal pre-pregnancy BMI or obesity is positively associated with children's
401 overweight or obesity risk,[22,54] and there is also compelling evidence from animal studies that
402 maternal obesity alters offspring phenotype in a similar way.[55-57] However, our study was
403 unable to find an association between maternal percentage body fat, visceral fat area and
404 offspring abdominal circumference or subscapular skinfold thickness at a mean age of two
405 years. The relatively small cohort and the early childhood follow-up age of 1-3 years may have
406 limited our ability to detect an association, thus longer term follow-up and increase in cohort
407 size of the Gomeroi gaaynggal cohort will endeavor to answer this question. The relatively
408 small sample size together with characteristics related to socioeconomic indices, family
409 income, educational level, maternal smoking during pregnancy, and duration of breastfeeding
410 are potential confounding variables which may limit the ability to detect relationships as

411 statistically significant in the current study. From a recent systematic review,[54] it is clear that
412 the majority of studies assessed the relationship between pre-pregnancy BMI and the off-
413 spring's body composition in terms of childhood adiposity obtained by indirect methods, for
414 example dual energy X-ray absorptiometry (DEXA). Further research that assesses the
415 association between maternal body composition (other than maternal weight and BMI) and the
416 offspring's body composition obtained by skinfold thickness are required, especially in lower
417 socioeconomic communities where certain factors, such as cost and accessibility, limit the use
418 of reference laboratory methods.
419
420 According to the developmental over-nutrition hypothesis, higher concentrations of glucose,
421 free fatty acids, and amino acids are delivered to the developing fetus, resulting in permanent
422 alterations in appetite control, neuroendocrine functioning and/or energy metabolism in the
423 developing fetus.[58] Additionally, not only are the infants larger at birth, they have a higher risk
424 of adiposity in later life.[25,59,60] The relationship between maternal glycaemia and obesity in the
425 offspring is of interest. In line with this association, our study has shown a positive correlation
426 between maternal non-fasting plasma glucose concentrations at a mean gestational age of 23
427 weeks and offspring birth weight and GROW customised birth weight centile. However, we
428 did not detect any association between maternal non-fasting plasma glucose levels in
429 pregnancy and early childhood BMI or adiposity. Similarly, the Belfast Hyperglycemia and
430 Adverse Pregnancy Outcome (HAPO) follow-up study found little association between
431 maternal plasma glucose (fasting glucose p= 0.08; 1-h glucose P=0.22; 2-h glucose P=0.36)
432 during pregnancy at 28 weeks' and obesity in 2 year old offspring.[61] It is possible that the
433 relationship between maternal diabetes and later childhood adiposity only becomes evident at
434 a later age,[62] thus further prospective studies with longer term follow-up are required. Some
435 previous studies have reported that intrauterine exposure to maternal hyperglycemia (i.e.

436 gestational diabetes) is associated with greater levels of abdominal fat in older children and
437 adolescent youth [26,62,63] and is also associated with greater risk of adverse health consequences
438 such as type 2 diabetes and cardiovascular disease.[64] For example, the Pima Indian population
439 has been studied extensively due to their high rates of chronic disease. The strongest risk factor
440 predicting obesity development in this population is intrauterine exposure to maternal diabetes,
441 independent of maternal obesity and infant birth weight.[65] In a study of almost 10,000 children,
442 Hillier *et al*. found that the highest quartile of maternal hyperglycaemia on the 50-g 1-h glucose
443 challenge test during pregnancy, was associated with a significantly higher level of childhood
444 obesity (85th and 95th percentiles) when compared with the lowest quartile of glucose
445 concentration ($P_{trend}< 0.0001$).[66] In this cohort, 15.9% of the women developed gestational
446 diabetes or had pre-existing diabetes during pregnancy, placing the infants at increased risk of
447 being born LGA, developing obesity in early childhood, and increasing the risk of metabolic
448 disease in later life.
449
450 This is of concern given the high rates of, and increasing trends in, both obesity and diabetes
451 among Aboriginal and Torres Strait Islander women of reproductive age.[32] Potentially, this
452 incurs intergenerational cycle of increased risk of obesity and metabolic syndrome in their
453 offspring. Our findings suggest that to reduce the disease and mortality burden among the next
454 generation of Aboriginal and Torres Strait Islander children is to improve the health of their
455 mothers. This would require accessible, affordable, effective and culturally-acceptable
456 antenatal care which include social and psychological support for the Indigenous women
457 during pregnancy.
458
459 BMI is a commonly used measure of adiposity in clinical and epidemiological studies. It can
460 be used to estimate the prevalence of obesity within a population and to assist in developing

public health and nutrition policy and to prioritise interventions. Although universal BMI cut-off points were used in this study, caution must be exercised when BMI cut-off points derived from other populations are used to define overweight and obesity amongst Indigenous people. Future research should determine the appropriateness of these cut-off points in Indigenous Australians from different communities, since there is a wide variation in body composition between them.[67,68]

Our study has several strengths and limitations. To our knowledge, this is the largest Indigenous community-based birth cohort study in New South Wales, with birth records obtained from the hospital. The collection of biochemical and anthropometric data in the pregnancy and follow-up study were undertaken with adherence to a research study protocol. However, this study also has some limitations. A notable one is that the sample size at follow-up was relatively small, and the population only comprised of women from a rural town in New South Wales, so the conclusions may not be generalizable to all Indigenous women. Several reasons for lack of full retention of all women postpartum include: participants from this cohort moving away from the study locations, the time constraints on the mother and the lack of incentives for continued participation. Given the unpredictable nature of infants and the number of measures to be collected, it is not always possible to obtain all measures at a given time. This project however, provides a useful benchmark for the growth trajectory of Indigenous infants in this community, enhancing our knowledge of where to target public health interventions and policies to address the current gaps.

Conclusion

In conclusion, we identified a statistically significant association between being born preterm and an increased risk of developing obesity in early childhood within the current cohort of

Indigenous women and their infants. Given that 12% of Indigenous Australian infants in this cohort are born preterm, this is likely to increase their risk for chronic diseases later in life and action needs to be taken to improve their birth outcomes. This study also shows that maternal non-fasting plasma glucose concentrations are positively associated with birth weight centiles and that Indigenous infants born large for gestational age or from mothers with increased body fat are at increased risk of obesity in early childhood. Future studies should therefore work with Indigenous communities to design appropriate interventions aimed at reducing maternal adiposity and plasma glucose levels prior to pregnancy to ensure optimal metabolic health for future generations.

Acknowledgements

The authors wish to pay their respects to Elders past and present, and extend that respect to any Indigenous readers. The authors of the paper would like to acknowledge the Gomeroi gaaynggal Aboriginal Steering committee for their ongoing advice for the Gomeroi gaaynggal studies. Shalem Yiner-Lee Leemaqz has assisted the investigators with software issues related to management of the dataset. The authors would like to gratefully recognize the women and children who dedicate their time to participate in the Gomeroi gaaynggal study.

Author Contributions

This primary author/s for this paper were KGP, YQL and KMR. Statistical analysis of the paper was undertaken by YQL and all other authors had input into editing the paper.

Funding

This work was supported by the National Health and Medical Research Council (Grant numbers 569239, APP1026733, APP1063123). YQL is supported by a Susan Alberti PhD

Scholarship, KGP is supported by an ARC Future Fellowship (FT150100179) and CE Collins is supported by an NHMRC Senior Research Fellowship and a Faculty of Health and Medicine Gladys M Brawn Senior Fellowship.

References

1. Centers for Disease Control and Prevention. Overweight and obesity. 2017 [cited 2017 August 25, 2017]; Available from: https://www.cdc.gov/obesity/index.html
2. UNICEF, WHO, Bank. W. Levels and trends in child malnutrition. 2015.
3. WHO Multicentre Growth Reference Study Group. WHO child growth standards based on length/height, weight and age. *Acta Paediatrica*. 2006;Suppl 450, 76-85.
4. Australian Institute of Health and Welfare. Australia's health 2016. Canberra: 2016 Contract No.: Cat. no. AUS 199.
5. Australian Bureau of Statistics. Australian Aboriginal and Torres Strait Islander Health Survey: First Results, Australia, 2012-2013. Canberrra: Australian Bureau of Statistics, 2013.
6. Ng M, Fleming T, Robinson M, et al. Global, regional, and national prevalence of overweight and obesity in children and adults during 1980–2013: a systematic analysis for the Global Burden of Disease Study. *Lancet*. 2014;384, 766-781.
7. Llewellyn A, Simmonds M, Owen C, Woolacott N. Childhood obesity as a predictor of morbidity in adulthood: a systematic review and meta-analysis. *Obesity Reviews*. 2016;17, 56-67.
8. Umer A, Kelley G, Cottrell L, et al. Childhood obesity and adult cardiovascular disease risk factors: a systematic review with meta-analysis. *BMC Public Health*. 2017 17(1), 683.
9. Barker D. Developmental origins of adult health and diseases. *J Epidemiol Community Health*. 2004;58, 114-115.
10. Warner M, Ozanne S. Mechanisms involved in the developmental programming of adulthood diseases. . *Biochem J*. 2010;427, 333-347.
11. Whincup PH, Kaye SJ, Owen CG, et al. Birth weight and risk of type 2 diabetes: a systematic review. *Jama*. 2008;300(24), 2886-2897.
12. Huxley R, Owen CG, Whincup PH, et al. Is birth weight a risk factor for ischemic heart disease in later life? *The American journal of clinical nutrition*. 2007;85(5), 1244-1250.
13. Huxley RR, Shiell AW, Law CM. The role of size at birth and postnatal catch-up growth in determining systolic blood pressure: a systematic review of the literature. *Journal of hypertension*. 2000;18(7), 815-831.
14. Li Y, Ley SH, VanderWeele TJ, et al. Joint association between birth weight at term and later life adherence to a healthy lifestyle with risk of hypertension: a prospective cohort study. *BMC medicine*. 2015;13, 175.
15. Kajantie E, Osmond C, Barker DJ, Eriksson JG. Preterm birth--a risk factor for type 2 diabetes? The Helsinki birth cohort study. *Diabetes Care*. 2010;33(12), 2623-2625.
16. Thomas EL, Parkinson JR, Hyde MJ, et al. Aberrant adiposity and ectopic lipid deposition characterize the adult phenotype of the preterm infant. *Pediatric research*. 2011;70(5), 507-512.
17. Euser AM, Finken MJ, Keijzer-Veen MG, et al. Associations between prenatal and infancy weight gain and BMI, fat mass, and fat distribution in young adulthood: a prospective cohort study in males and females born very preterm. *The American journal of clinical nutrition*. 2005;81(2), 480-487.
18. Mathai S, Derraik JG, Cutfield WS, et al. Increased adiposity in adults born preterm and their children. *PLoS One*. 2013;8(11), e81840.
19. Casey P. Growth of low birth weight preterm children. *Semin Perinatol*. 2008;32, 20-27.
20. Gluckman PD, Hanson MA, Cooper C, Thornburg KL. Effect of in utero and early-life conditions on adult health and disease. *N Engl J Med*. 2008;359(1), 61-73.

21. Martin A, Connelly A, Bland R, Reilly J. Health impact of catch-up growth in low-birth weight infants: systematic review, evidence appraisal, and meta-analysis. *Matern Child Nutr*. 2017;13(1).
22. Yu Z, Han S, Zhu J, et al. Pre-pregnancy body mass index in relation to infant birth weight and offspring overweight/ obesity: a systematic review and meta-analysis. *PLoS One*. 2013;8, e61627.
23. Poston L. Maternal obesity, gestational weight gain and diet as determinants of offspring long term health. *Best practice & Research Clinical Endocrinology & Metabolism*. 2012;26, 627–639.
24. Philipps L, Santhakumaran S, Gale C, et al. The diabetic pregnancy and offspring BMI in childhood: a systematic review and meta-analysis. *Diabetologia*. 2011;54(8), 1957-1966.
25. Dabelea D, Hanson R, Lindsay R, al. e. Intrauterine exposure to diabetes conveys risks for type 2 diabetes and obesity: a Study of Discordant Sibships. *Diabetes*. 2000;49(12), 2208-2211.
26. Crume TL, Ogden L, West NA, et al. Association of exposure to diabetes in utero with adiposity and fat distribution in a multiethnic population of youth: the Exploring Perinatal Outcomes among Children (EPOCH) Study. *Diabetologia*. 2011;54(1), 87-92.
27. Metzger BE. Long-term outcomes in mothers diagnosed with gestational diabetes mellitus and their offspring. . *Clinical Obstetrics and Gynaecology*. 2007;50(4), 972-979.
28. Eriksson J, Sandboge S, Salonen M, Kajantie E, Osmond C. Maternal weight in pregnancy and offspring body composition in late adulthood: findings from the Helsinki Birth Cohort Study (HBCS). . *Ann Med*. 2015;47, 94-99.
29. Boney C, Verma A, Tucker R, Vohr B. Metabolic Syndrome in Childhood: Association with Birth weight, Maternal Obesity and Gestational Diabetes Mellitus. *Pediatrics*. 2005;115(3), e290-e296.
30. Eriksson J, Sandboge S, Salonen M, Kajantie E, Osmond C. Longterm consequences of maternal overweight in pregnancy on offspring later health: findings from the Helsinki Birth Cohort Study. *Ann Med* 2014;46, 434-438.
31. Australian Institute of Health and Welfare. The health and welfare of Australia's Aboriginal and Torres Strait Islander peoples 2015. Canberra: AIHW.
32. Australian Institute of Health and Welfare. Australia's mothers and babies 2014—in brief. Canberra: Australian Institute of Health and Welfare,, 2016 Contract No.: Cat no. PER 87.
33. Dyer SM, et al. Prevalence and characteristics of overweight and obesity in indigenous Australian children: A systematic review. *Crit Rev Food Sci Nutr*. 2017;57(7), 13565-11376.
34. Vos T, Barker B, Begg S, Stanley L, Lopez AD. Burden of disease and injury in Aboriginal and Torres Strait Islander Peoples: the Indigenous health gap. *International journal of epidemiology*. 2009;38(2), 470-477.
35. McNamara BJ, Gubhaju L, Chamberlain C, Stanley F, Eades SJ. Early life influences on cardio-metabolic disease risk in aboriginal populations--what is the evidence? A systematic review of longitudinal and case-control studies. *International journal of epidemiology*. 2012;41(6), 1661-1682.
36. Ashman AM, Collins CE, Weatherall L, et al. A cohort of Indigenous Australian women and their children through pregnancy and beyond: the Gomeroi gaaynggal study. *Journal of developmental origins of health and disease*. 2016;7(4), 357-368.

634 37. World Health Organisation. Global Strategy on Diet, Physical Activity and Health.
635 2016; Available from: http://www.who.int/dietphysicalactivity/childhood_what/en/.
636 38. Dehghan M, Merchant AT. Is bioelectrical impedance accurate for use in large
637 epidemiological studies? *Nutrition journal*. 2008;7, 26.
638 39. Ellis KJ, Bell SJ, Chertow GM, et al. Bioelectrical impedance methods in clinical
639 research: a follow-up to the NIH Technology Assessment Conference. *Nutrition*
640 *(Burbank, Los Angeles County, Calif)*. 1999;15(11-12), 874-880.
641 40. Pietrobelli A, Rubiano F, St-Onge MP, Heymsfield SB. New bioimpedance analysis
642 system: improved phenotyping with whole-body analysis. *European journal of clinical*
643 *nutrition*. 2004;58(11), 1479-1484.
644 41. Neovius M, Hemmingsson E, Freyschuss B, Udden J. Bioelectrical impedance
645 underestimates total and truncal fatness in abdominally obese women. *Obesity (Silver*
646 *Spring, Md)*. 2006;14(10), 1731-1738.
647 42. Gibson AL, Holmes JC, Desautels RL, Edmonds LB, Nuudi L. Ability of new octapolar
648 bioimpedance spectroscopy analyzers to predict 4-component-model percentage body
649 fat in Hispanic, black, and white adults. *The American journal of clinical nutrition*.
650 2008;87(2), 332-338.
651 43. Volgyi E, Tylavsky FA, Lyytikainen A, et al. Assessing body composition with DXA
652 and bioimpedance: effects of obesity, physical activity, and age. *Obesity (Silver Spring,*
653 *Md)*. 2008;16(3), 700-705.
654 44. Bedogni G, Malavolti M, Severi S, et al. Accuracy of an eight-point tactile-electrode
655 impedance method in the assessment of total body water. *European journal of clinical*
656 *nutrition*. 2002;56(11), 1143-1148.
657 45. Gardosi J, Francis A. Customised Weight Centile Calculator. GROW version 6.7.8.2
658 (AU). *Gestation Network, wwwgestationnet*. 2017.
659 46. Cole TJ, et al. Establishing a standard definition for child overweight and obesity
660 worldwide: international survey. *BMJ*. 2000;320(7244), 1240-1243.
661 47. Cohen J. Statistical Power Analysis for the Behavior Science. 1988. Lawrance Eribaum
662 Association: Hillsdale, NJ, USA.
663 48. Reilly JJ, Kelly J. Long-term impact of overweight and obesity in childhood and
664 adolescence on morbidity and premature mortality in adulthood: systematic review.
665 *International journal of obesity (2005)*. 2011;35(7), 891-898.
666 49. Pringle KG, Weatherall L, Roberts TC, et al. The Gomeroi Gaaynggal Cohort: A
667 Preliminary Study of the Maternal Determinants of Pregnancy Outcomes in Indigenous
668 Australian Women. *J Preg Child Health*. 2015; 3:211.
669 50. Pringle KG, Rae K, Weatherall L, et al. Effects of maternal inflammation and exposure
670 to cigarette smoke on birth weight and delivery of preterm babies in a cohort of
671 indigenous Australian women. *Frontiers in immunology*. 2015;6, 89.
672 51. Woo Baidal JA, Locks LM, Cheng ER, et al. Risk Factors for Childhood Obesity in the
673 First 1,000 Days: A Systematic Review. *Am J Prev Med*. 2016;50(6), 761-779.
674 52. Kapral N, Miller SE, Scharf RJ, Gurka MJ, DeBoer MD. Associations between
675 birthweight and overweight and obesity in school-age children. *Pediatr Obes*. 2017;
676 doi: [Epub ahead of print].
677 53. Hadfield RM, Lain SJ, Simpson JM, et al. Are babies getting bigger? An analysis of
678 birthweight trends in New South Wales, 1990-2005. *The Medical journal of Australia*.
679 2009;190(6), 312-315.
680 54. Castillo-Laura H, Santos IS, Quadros LC, Matijasevich A. Maternal obesity and
681 offspring body composition by indirect methods: a systematic review and meta-
682 analysis. *Cadernos de saude publica*. 2015;31(10), 2073-2092.

683 55. Long N, George L, Uthlaut A, et al. Maternal obesity and increased nutrient intake
684 before and during gestation in the ewe results in altered growth, adiposity, and glucose
685 tolerance in adult offspring. *J Anim Sci*. 2010;88, 3546-3553.
686 56. McCurdy C, Bishop J, Williams S, et al. Maternal high-fat diet triggers lipotoxicity in
687 the fetal livers of nonhuman primates. *J Clin Invest*. 2009;119, 323-335.
688 57. Samuelsson A, Matthews P, Argenton M, et al. Diet-induced obesity in female mice
689 leads to offspring hyperphagia, adiposity, hypertension, and insulin resistance: a novel
690 murine model of developmental programming. *Hypertension*. 2008;51, 383-392.
691 58. Drake A, Reynolds R. Impact of maternal obesity on offspring obesity and
692 cardiometabolic disease risk. *Reproduction*. 2010;140, 387-398.
693 59. Clausen TD, Mathiesen ER, Hansen T, et al. High prevalence of type 2 diabetes and
694 pre-diabetes in adult offspring of women with gestational diabetes mellitus or type 1
695 diabetes: the role of intrauterine hyperglycemia. *Diabetes Care*. 2008;31(2), 340-346.
696 60. Boerschmann H, Pflüger M, Henneberger L, Ziegler A, Hummel S. revalence and
697 predictors of overweight and insulin resistance in offspring of mothers with gestational
698 diabetes mellitus. *Diabetes Care*. 2010;33(8), 1845-1849.
699 61. Pettitt DJ, McKenna S, McLaughlin C, et al. Maternal glucose at 28 weeks of gestation
700 is not associated with obesity in 2-year-old offspring: the Belfast Hyperglycemia and
701 Adverse Pregnancy Outcome (HAPO) family study. *Diabetes Care*. 2010;33, 1219-
702 1223.
703 62. Krishnaveni GV, Hill JC, Leary SD, et al. Anthropometry, glucose tolerance, and
704 insulin concentrations in Indian children: relationships to maternal glucose and insulin
705 concentrations during pregnancy. *Diabetes Care*. 2005;28(12), 2919-2925.
706 63. Wright CS, Rifas-Shiman SL, Rich-Edwards JW, et al. Intrauterine exposure to
707 gestational diabetes, child adiposity, and blood pressure. *American Journal of*
708 *Hypertension*. 2009;22(2), 215-220.
709 64. Bergman RN, Kim SP, Catalano KJ, et al. Why visceral fat is bad: mechanisms of the
710 metabolic syndrome. *Obesity*. 2006;14(Suppl 1), 16S-19S.
711 65. Dabelea D, Pettitt D. Intrauterine diabetic environment confers risks for type 2 diabetes
712 mellitus and obesity in the offspring, in addition to genetic susceptability. *J Pediatric*
713 *Endocrinol Metab*. 2001;14, 1085-1091.
714 66. Hillier T, Pedula K, Schmidt M, et al. Childhood Obesity and Metabolic Imprinting:
715 The ongoing effects of maternal hyperglycemia. *Diabetes Care*. 2007;30(9), 2287-
716 2292.
717 67. Wang Z, Hoy W, McDonald S. Body mass index in aboriginal Australians in remote
718 communities. *Australian and New Zealand journal of public health*. 2000;24(6), 570-
719 575.
720 68. Adegbija O, Hoy WE, Wang Z. Waist circumference values equivalent to body mass
721 index points for predicting absolute cardiovascular disease risks among adults in an
722 Aboriginal community: a prospective cohort study. *BMJ open*. 2015;5(11), e009185.
723

724

Figure Legends

Supplementary Figure S1. (A) Weight, (B) Length and (C) Head Circumference Growth Trajectories of full-term female infants. Data are presented as means (filled circle) ± S.D. n = 82-86, 16, 21, 12, 14-15, 11, and 9 at 3, 6, and 9 months, 1, 2 and 3 years, respectively.

Supplementary Figure S2. (A) Weight, (B) Length and (C) Head Circumference Growth Trajectories of full-term male infants. Data are presented as means (filled circle) ± S.D. n = 106-111, 16, 13, 18-19, 26-27, 21-22, and 6 at 3, 6, and 9 months, 1, 2 and 3 years, respectively.

Table 1. Maternal characteristics**.**

Variables	Values*
Maternal age at consent (years) (n=226)	25.56 ± 6.09
Pre-pregnancy BMI status (n=123)	
Underweight (<18.5 kg/m^2) (%)	8 (6.5)
Normal weight (18.5-24.99 kg/m^2) (%)	30 (24.4)
Overweight/obese (≥25.0kg/m^2) (%)	85 (69.1)
Smoked during pregnancy (n=227) (%)	62 (27.3)
Pre-existing type I diabetes (n=227) (%)	4 (1.8)
Pre-existing type II diabetes (n=227) (%)	7 (3)
Gestational diabetes mellitus (n=227) (%)	25(11.1)

*Values are mean ± SD or *n* (%)

Table 2. Birth outcomes of Indigenous infants (n=227) in the Gomeroi gaaynggal cohort study.

	n	Mean	SD	p
Gestational Age at delivery (weeks)				
All infants	224	38.82	2.31	
Male	130	38.65	2.66	
Female	94	39.06	1.71	0.19
Birth weight (g)				
All infants	224	3292.00	633.30	
Male	131	3302.9	644.9	
Female	93	3276.7	619.8	0.76
GROW Customised Birth Weight Centile				
All infants	224	53.78	33.50	
Male	131	54.1	32.12	
Female	93	53.32	35.6	0.86
Birth length (cm)				
All infants	209	49.34	2.53	
Male	121	49.46	2.53	
Female	88	49.18	2.39	0.41
Head Circumference (cm)				
All infants	218	34.43	2.12	
Male	125	34.53	1.96	
Female	93	34.3	2.31	0.44

SD = standard deviation

Table 3. Associations between maternal measures of adiposity and glucose levels and birth outcomes.

	Percentage Body Fat					Visceral Fat Area (cm^2)					Non-fasting Plasma Glucose (mmol/L)				
	n	Coefficient	95% CI	R^2	P	n	Coefficient	95% CI	R^2	P	n	Coefficient	95% CI	R^2	P
Birth weight (g)	129	1.87	-7.11,10.85	0.05	0.68	128	0.63	-0.54,1.80	0.06	0.29	166	134.31*	40.85,227.77	0.11	0.005
GA at delivery (weeks)	130	-0.01	-0.035,0.024	0.004	0.7	129	-0.002	-0.005,0.002	0.008	0.41	167	-0.107	-0.4,0.19	0.003	0.47
GROW Customised Birth Weight Centile	129	0.092	-0.38,0.56	0.002	0.7	128	0.041	-0.02,0.10	0.02	0.19	166	6.44	1.67,11.2	0.06	0.008
Birth length (cm)	120	0.02	-0.02,0.054	0.05	0.35	119	0.002	-0.00,0.007	0.04	0.51	157	0.16	-0.21,0.53	0.06	0.38

Adjusted for smoking, fetal sex, maternal height. GA = gestational age. CI = confidence interval. R^2 = partial correlation coefficient.
*Interpreted as one unit increase in maternal non-fasting plasma glucose is associated with 134.3g increase in birth weight.

Table 4. Associations between preterm delivery and early childhood anthropometry measurements at 1-3 years.

	All Infants			Term			Preterm			
	n	**Mean**	**SD**	**n**	**Mean**	**SD**	**n**	**Mean**	**SD**	**P**
Age (months)	72	23.36	9.31	65	24	9.69	7	23.36	9.31	0.87
Weight (kg)	70	12.59	4.30	63	12.57	2.86	7	12.87	4.29	0.80
Height (cm)	69	85.07	9.35	62	85.42	9.23	7	81.96	10.58	0.36
BMI (kg/m^2)	68	17.29	1.76	61	17.13	1.65	7	18.64	2.24	0.03
Abdominal Circumference (cm)	64	50.34	4.52	58	50.12	4.43	6	52.42	5.32	0.24
Subscapular Skinfold Thickness (mm)	58	8.43	2.98	53	8.45	3.00	5	8.26	3.14	0.89

Adjusted for sex, maternal height, maternal smoking in pregnancy.

Table 5. Associations between SGA and LGA and early childhood anthropometry measurements at 1-3 years.

	All Infants			AGA			SGA			LGA			*ANOVA*
	n	Mean	SD	n	Mean	SD	n	Mean	SD	n	Mean	SD	P
Age (months)	70	23.63	9.55	53	23.18	9.64	7	20.54	6.67	10	28.2	10.03	0.21
GA at delivery (weeks)	221	38.83	2.32	145	39.08	1.61	32	38.62	2.61	44	38.14	3.63	0.055
Weight (kg)	68	12.55	3.00	52	12.13	2.19	6	10.91	2.72	10	15.68*^	4.70	0.00
Height (cm)	67	84.76	9.27	52	84.23	8.67	6	80.49	8.05	9	90.72	11.59	0.07
BMI (kg/m^2)	66	17.34	1.76	51	17.22	1.67	6	16.53	1.25	9	18.56	2.16	0.052
Abdominal Circumference (cm)	62	50.35	4.60	46	50	3.64	6	47.00	3.47	10	53.96^	6.9	0.01
Subscapular Skinfold Thickness (mm)	56	8.42	3.03	43	8.26	2.51	4	6.73	1.73	9	9.93	4.97	0.17

* Denotes significant difference to AGA; ^ denotes significant difference to SGA.
GA = gestational age. SGA = small for gestational age. LGA = large for gestational age. AGA = appropriate for gestational age.

Table 6. Associations between GROW customised birth weight centile and early childhood anthropometry measurements at 1-3 years.

	GROW Customised Birth Weight Centile				
	n	**Coefficient**	**95% CI**	**R^2**	**P**
Weight (kg)	63	0.03	0.008,0.06	0.11	0.01
Height (cm)	62	0.05	-0.03,0.14	0.05	0.18
BMI (kg/m^2)	61	0.02	0.006,0.035	0.12	0.007
Abdominal Circumference (cm)	58	0.04	0.002,0.076	0.10	0.039
Subscapular Skinfold Thickness (mm)	53	0.02	-0.002,0.051	0.10	0.07

Adjusted for smoking, fetal sex, maternal height. CI = confidence interval. R^2 = partial correlation coefficient.

Table 7. Associations between maternal adiposity and non-fasting plasma glucose levels and early childhood anthropometry measurements at 1-3 years.

	Percentage Body Fat					Visceral Fat Area					Non-fasting Plasma Glucose (mmol/L)				
	n	**Coefficient**	**95% CI**	**R^2**	**P**	**n**	**Coefficient**	**95% CI**	**R^2**	**P**	**n**	**Coefficient**	**95% CI**	**R^2**	**P**
Weight (kg)	52	0.11	0.02,0.20	0.10	0.02	52	0.02	0.01,0.03	0.19	0.00	63	0.60	-0.22,1.41	0.03	0.15
Height (cm)	50	0.25	-0.024,0.52	0.06	0.07	50	0.06	0.02,0.10	0.18	0.00	62	1.89	-0.64,4.42	0.05	0.14
BMI (kg/m^2)	50	0.03	-0.02,0.09	-0.003	0.22	50	0.00	-0.01,0.01	-0.03	0.64	61	-0.05	-0.53,0.43	-0.003	0.84
Abdominal Circumference (cm)	48	0.12	-0.03,0.25	0.07	0.12	48	0.02	-0.00,0.03	0.08	0.10	58	0.65	-0.58,1.88	0.04	0.29
Subscapular Skinfold Thickness (mm)	43	0.05	-0.05,0.15	0.06	0.29	43	0.01	-0.01,0.02	0.07	0.25	53	-0.07	-0.92,0.78	0.03	0.87

Adjusted for smoking, fetal sex, maternal height. CI = confidence interval. R^2 = partial correlation coefficient.

Supplementary Table S1. Data collected of mothers and offspring at each study visit for the Gomeroi gaaynggal cohort.

Data collected	Pregnancy			Postnatal							
	1T	2T	3T	3m	6m	9m	1y	2y	3y	4y	5y
Maternal											
Anthropometry											
InBody weight and body composition	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Height	✓	✓	✓								
Pre-pregnancy weight (self-reported)	✓	✓	✓								
Samples collected											
Blood	✓	✓	✓		✓		✓	✓	✓	✓	✓
Urine	✓	✓	✓		✓		✓	✓	✓	✓	✓
Saliva	✓	✓	✓								
Blood pressure	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Dietary intake											
24 hr recall	✓			✓	✓	✓	✓	✓	✓	✓	✓
Australian Eating Survey (AES)			✓		✓		✓	✓	✓	✓	✓
Other											
Demographic and health questionnaire	✓			✓	✓	✓	✓	✓	✓	✓	✓
Psychosocial survey	✓										
Offspring											
Fetal ultrasound scan	✓	✓	✓								
Anthropometry											
Length or height, weight, skinfold thicknesses and girths				✓	✓	✓	✓	✓	✓	✓	✓
Samples collected											
Urine				✓	✓	✓	✓	✓	✓	✓	✓
Dietary intake											
Australian child and adolescent eating survey (ACAES)								✓	✓	✓	✓
24 hr recall						✓	✓	✓	✓	✓	✓
Current feeding practices questionnaire				✓	✓	✓	✓	✓	✓	✓	✓
Infant feeding questionnaire				✓	✓	✓	✓	✓	✓	✓	✓
Other											
Demographic and health questionnaire				✓	✓	✓	✓	✓	✓	✓	✓

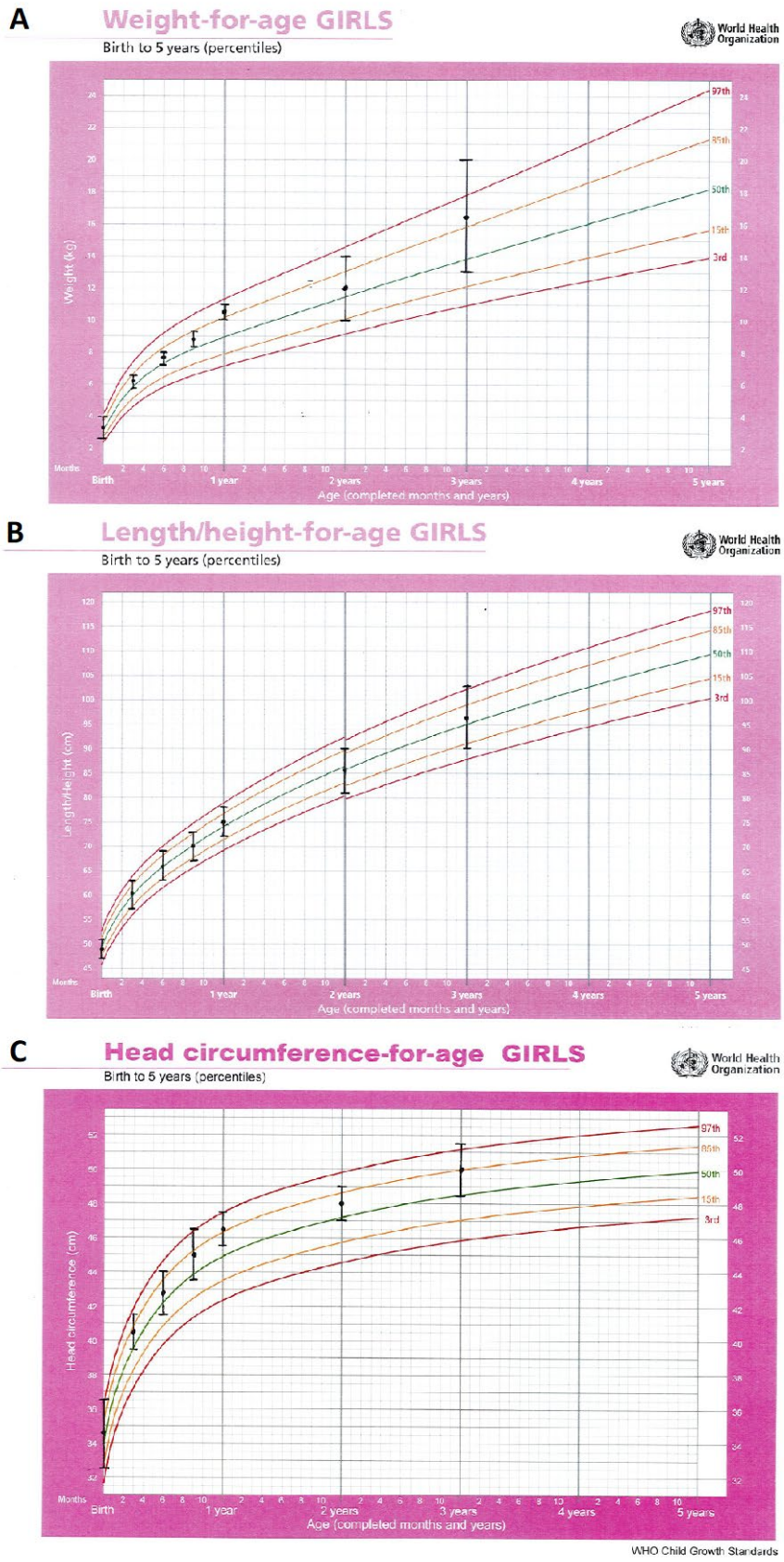
T: trimester. m: months. y: years.

Supplementary Table S2. Infant and early childhood anthropometry measurements.

		3 months			6 months			9 months			1 year			2 years			3 years		
		n	Mean	SD	n	Mean	SD	n	Mean	SD	n	Mean	SD	n	Mean	SD	n	Mean	SD
Age (months)		36	3.43	0.58	37	6.07	1.07	34	9.50	0.85	46	13.84	1.93	38	25.11	2.63	18	**37.34**	**2.96**
Weight (kg)	All infants	36	6.17	0.99	36	7.81	1.09	34	8.95	1.18	44	10.38	1.31	37	12.72	1.64	17	16.13	14.55
	Male	17	6.37	0.60	16	7.98	1.14	20	9.09	1.20	28	10.29	1.31	26	12.98	1.57	8	15.62	2.52
	Female	19	6.00	1.23	20	7.66	1.06	14	8.75	1.18	16	10.55	1.42	11	12.11	1.72	9	16.59	3.59
Height (cm)	All infants	36	60.80	2.43	36	66.99	3.37	34	70.99	3.49	44	76.94	3.59	36	87.00	4.43	17	96.60	5.32
	Male	17	61.51	2.05	16	68.38	3.59	20	72.11	3.26	28	76.94	3.53	25	87.65	4.31	8	96.70	5.00
	Female	19	60.16	2.61	20	65.89*	2.80	14	69.4*	3.27	16	75.58	3.63	11	85.50	4.53	9	96.51	5.89
BMI (kg/m2)	All infants	36	16.62	1.93	36	17.32	2.54	33	17.81	1.92	44	17.75	1.77	36	16.81	1.55	16	17.28	1.97
	Male	17	16.80	1.07	16	16.99	1.44	19	17.58	1.97	28	17.33	1.46	25	16.94	1.62	7	16.88	2.16
	Female	19	16.45	2.49	20	17.58	1.59	14	18.14	1.86	16	18.47*	2.05	11	16.50	1.41	9	17.59	1.88
Head Circumference	All infants	36	40.65	1.20	36	43.24	1.72	33	45.00	1.50	44	46.88	1.57	35	48.55	1.61	17	49.82	1.6
(cm)	Male	17	41.26	0.99	16	43.83	1.91	19	45.35	1.27	29	47012	1.69	24	48.86	1.69	8	50.36	1.68
	Female	19	40.1*	1.12	20	42.77	1.43	14	44.52	1.70	15	46.41	1.23	11	47.87	1.22	9	49.35	1.45
Abdominal	All infants	36	41.51	2.65	34	44.85	4.12	33	46.83	3.33	44	48.48	3.85	29	49.88	3.11	17	54.06	5.20
Circumference	Male	17	41.87	2.65	15	43.77	2.34	19	46.91	2.67	28	47.97	3.56	20	50.54	2.89	8	52.18	3.55
	Female	19	41.18	5.33	19	45.71	4.99	14	46.74	4.17	16	49.36	4.57	9	48.42	3.25	9	55.74	6.03
mid-upper arm	All infants	36	13.89	1.19	33	15.05	2.13	33	15.92	1.37	44	16.35	1.30	29	16.54	1.08	17	17.08	3.27
circumference	Male	17	14.00	0.96	14	15.51	1.19	19	15.92	1.12	28	16.19	1.22	20	16.76	1.08	8	15.89	3.94
	Female	19	13.79	1.39	19	14.71	2.59	14	15.92	1.69	16	16.65	1.48	9	16.04	0.96	9	18.14	2.28
mid-thigh	All infants	36	21.11	2.12	33	25.04	3.01	33	25.54	2.86	44	26.47	3.42	29	26.76	2.23	17	29.09	6.80
	Male	17	21.21	1.68	14	24.34	2.75	19	25.01	2.49	28	25.94	2.22	20	27.37	2.30	8	27.77	9.12
	Female	19	21.03	2.50	19	25.56	3.16	14	26.25	3.25	16	27.40	2.53	9	25.39*	1.32	9	30.26	4.07
calf	All infants	36	16.24	2.48	33	18.19	1.99	33	18.82	1.89	44	19.74	1.95	29	20.39	1.35	17	21.57	2.52
	Male	17	16.34	1.30	14	18.26	2.11	19	18.49	1.84	28	19.58	2.20	20	20.58	1.36	8	21.10	2.27
	Female	19	16.15	3.23	19	18.13	1.96	14	19.27	1.94	16	20.02	1.44	9	19.97	1.30	9	22.00	2.79
subscapular skinfold	All infants	30	7.66	1.35	32	8.19	1.26	30	7.98	2.10	39	7.94	2.33	25	7.84	2.00	16	9.43	4.28
thickness	Male	14	7.84	1.40	14	7.50	1.26	17	7.34	1.49	26	7.67	2.38	18	7.87	2.03	7	7.89	3.07
	Female	16	7.50	1.33	18	8.73	2.13	13	8.82	2.52	13	8.47	2.24	7	7.77	2.06	9	10.63	4.86
bicep	All infants	32	6.18	1.49	32	7.02	2.05	28	7.97	3.09	40	7.15	2.51	26	8.01	2.94	15	8.81	3.40
	Male	14	6.34	1.03	14	5.59	1.26	16	7.72	3.55	26	6.90	2.60	18	8.34	3.12	6	9.55	3.71
	Female	18	6.06	1.78	18	8.13*	1.87	12	8.32	2.47	14	7.63	2.37	8	7.26	2.51	9	8.31	3.42
thigh	All infants	29	16.85	3.01	29	18.23	3.95	29	19.13	3.77	39	18.21	4.26	23	16.72	3.29	14	17.47	5.55
	Male	14	17.14	3.44	12	16.53	3.41	17	18.67	3.91	26	17.28	4.45	17	16.87	3.30	7	17.70	4.03
	Female	15	16.58	15.11	17	19.43	3.95	12	19.78	3.64	13	20.07	3.25	6	16.28	3.53	7	17.24	7.09
iliac crest	All infants	29	6.63	1.28	30	7.61	2.01	29	7.16	2.08	39	6.76	2.83	25	6.13	2.12	14	9.89	8.24
	Male	15	6.88	1.50	13	7.09	1.64	17	6.66	1.70	25	6.42	2.30	18	5.78	2.02	7	10.90	11.67
	Female	14	6.67	0.96	17	8.01	2.22	12	8.98	2.36	14	7.38	3.61	7	7.04	2.24	7	8.87	2.92
medial calf	All infants	27	12.59	2.08	29	14.72	3.45	25	15.49	3.42	36	13.26	3.25	25	12.11	2.29	14	11.04	2.71
	Male	12	12.66	2.68	13	12.88	2.31	16	14.42	3.15	23	12.57	3.38	18	12.03	1.88	7	11.56	0.74
	Female	15	12.54	1.56	16	16.22*	3.56	9	17.40	3.17	13	14.49	2.70	7	12.31	3.29	7	10.51	3.83

*P<0.05: significantly different between male and female

Supplementary Figure S1. Weight, Length and Head Circumference Growth Trajectories of full-term female infants.



Supplementary Figure S2. Weight, Length and Head Circumference Growth Trajectories of full-term male infants.