Contents available at ScienceDirect

Diabetes Research and Clinical Practice

journal homepage: www.elsevier.com/locate/diabres

International Diabetes Federation

# Female offspring birth weight is associated with Body Mass Index, waist circumference and metabolic syndrome in Latin American women at 10-years postpartum

*Natalie Mueller* [a,b,c,d], *Maria-Luisa Garmendia* [e,*], *Marcela Reyes* [e], *Camila Corvalán* [e], *Ana Pereira* [e], *Ricardo Uauy* [e]

[a] *Institute of Medical Informatics, Biometry, and Epidemiology, Ludwig-Maximilians-University Munich, Marchioninistr. 15, 81377 Munich, Germany*

[b] *ISGlobal, Centre for Research in Environmental Epidemiology (CREAL), Dr. Aiguader 88, 08003 Barcelona, Spain*[1]

[c] *Universitat Pompeu Fabra (UPF), Plaça de la Mercè 10-12, 08002 Barcelona, Spain*

[d] *CIBER Epidemiología y Salud Pública (CIBERESP), Melchor Fernández Almagro 3-5, 28029 Madrid, Spain*

[e] *Institute of Nutrition and Food Technology (INTA), Universidad de Chile, El Líbano 5524, 7830490 Macul, Santiago, Chile*

ARTICLE INFO

*Article history:*
Received 28 December 2016
Received in revised form
12 December 2017
Accepted 26 January 2018
Available online 5 February 2018

*Keywords:*
Birth weight
Latin America
Maternal
Metabolic syndrome
Offspring
Postpartum

ABSTRACT

*Aims:* We aimed to assess whether female offspring birth weight (BW) is associated with anthropometric and metabolic outcomes in Chilean mothers at 10-years postpartum.

*Methods:* We assessed data from 396 Chilean mother-daughter pairs participating in the longitudinal Chilean Growth and Obesity Cohort (GOCS) and Determinants of Breast Cancer Risk (DERCAM) studies. Multivariate linear and logistic regression models were performed to associate female offspring BW with maternal Body Mass Index (BMI), waist circumference, type 2 diabetes mellitus, metabolic syndrome and its components at 10-years postpartum.

*Results:* At 10-years postpartum, 69% of mothers were overweight, 65% had central adiposity and 26% had metabolic syndrome. Adjusted linear regression models showed associations between female offspring BW and (1) maternal BMI (%Δ GM = 4.46; 95% CI 0.25–8.85); and (2) waist circumference (%Δ GM = 3.25; 95% CI 0–6.60). Adjusted logistic regression models showed associations between female offspring BW and (1) maternal metabolic syndrome (OR = 3.48; 95% CI 1.50–8.11); (2) central adiposity (OR = 2.37; 95% CI 1.08–5.22); and (3) hypertriglyceridemia (OR = 3.19; 95% CI 1.40–7.23).

*Conclusions:* Female offspring BW was associated with maternal anthropometric and metabolic outcomes at 10-years postpartum. Our findings add to the emerging evidence that offspring BW might be a potential indicator for future maternal anthropometric and metabolic risks.



* Corresponding author.
E-mail address: mgarmendia@inta.uchile.cl (M.-L. Garmendia).

[1] Present address.

https://doi.org/10.1016/j.diabres.2018.01.029
0168-8227/

## 1. Introduction

The associations between birth weight (BW) and future adulthood risk for cardiovascular and metabolic diseases have been well studied. These associations can be linked to genetic factors [1] as well as environmental exposures during pregnancy [2–4] that possibly trigger epigenetic modifications [5,6]. Studies have also shown that parental body composition has a significant impact on offspring BW [7,8], especially maternal height and weight [9–11].

Recently, there is growing interest in the associations between offspring anthropometric characteristics as risk factors of future parental morbidity and premature death. Research findings suggest a U-shaped relationship between offspring BW and parental insulin sensitivity, type 2 diabetes mellitus and cardiovascular risk [12–16]. Moreover, there seem to be associations between increased offspring BW and risk of obesity as well as mortality in the parents postpartum [17,18].

Until now, research assessing the associations between offspring anthropometry and future parental morbidity focused on Asia, Europe and North America [12,14–19]. Thus, little is known about parents and their offspring in Latin America, despite known differences in lifestyle and genetic predispositions. Chile is an upper-middle income country that has undergone a rapid nutritional transition [20]. According to the Chilean National Health Survey, Chilean women in their reproductive years have a high prevalence of overweight (64%), type 2 diabetes mellitus (10%) and cardiovascular risk factors (37%) [21].

Early identification of risk factors in women – such as possibly offspring anthropometry – for future metabolic morbidity, is of great interest for targeted prevention strategies. The aim of this study was to assess whether offspring BW is associated with adverse anthropometric and metabolic outcomes in Chilean mothers at 10-years postpartum.

## 2. Subjects

In 2006, 594 male and 601 female children born between 2001 and 2002, were recruited for the Chilean Growth and Obesity Cohort Study (GOCS) [22]. All of these children (1) came from six low and middle-income districts from the southern area of Santiago de Chile; (2) were singleton births with a gestational age of 37–42 weeks; and (3) had a BW within the range of 2.5–4.5 kg. The objectives of GOCS are to assess growth trajectories, maturation and early risk factors for future obesity and adverse metabolic outcomes [22].

In 2010, 476 mothers of the GOCS girls were contacted to participate in the longitudinal Determinants of Breast Cancer Risk Study (Determinantes De Riesgo De Cáncer de Mama; DERCAM) to study breast cancer risk factors in mothers and their daughters (mothers of male offspring were not eligible). Of these 476 mothers, 405 mothers met the inclusion criteria and participate in the ongoing DERCAM study [23]. Data for the 2011–2012 DERCAM follow-up were available for 396 women.

## 3. Materials and methods

For the present longitudinal analysis, data of these 396 women were merged with data of their female offspring to study the associations between female offspring BW and maternal anthropometric (BMI; waist circumference) and metabolic outcomes (type 2 diabetes mellitus, metabolic syndrome and its components) at 10-years postpartum.

### 3.1. *Exposure variables*

Data on female offspring BW (kg) were taken from clinical records, where quality was assessed previously, indicating <1% implausible values and plausible variance (GOCS protocol) [24].

### 3.2. *Outcome variables*

#### 3.2.1. *Anthropometric outcomes*

During the 2011–2012 DERCAM follow-up, data on maternal height (cm), weight (kg) and waist circumference (cm) were taken by two trained nutritionists. Women were measured bare-footed and wearing light clothing. Data on the following two anthropometric outcomes were used for the present study:

1. BMI (kg/m$^2$): Maternal weight was assessed using the SECA balance platform (Madison, WI, USA), with increments of 0.10 kg. Height was measured advising the women to stand in upright position, and by using the stadiometer Harpenden 603 (Holtain Ltd., Wales, UK) with increments of 0.10 cm. Height was assumed to have remained constant over the 10-year postpartum period. BMI was classified according to the WHO classification scheme: underweight (BMI < 18.5 kg/m$^2$), normal weight (BMI 18.5–24.9 kg/m$^2$); overweight (BMI 25–29.9 kg/m$^2$); and obese (B MI > 30 kg/m$^2$) [25].
2. Waist circumference (cm): Maternal waist circumference was measured with the woman standing in upright position, just above the iliac crest, using SECA tape measure 201 (Madison, WI, USA).

#### 3.2.2. *Metabolic outcomes*

A 10 ml fasting venous sample was collected during the 2011–2012 DERCAM follow-up. Glycemia and lipid levels were measured. Analyses were conducted at the Institute of Maternal and Child Research (Instituto de Investigaciones Materno Infantil; IDIMI) of the University of Chile. Serum glucose concentrations were measured by using enzymatic colorimetric techniques (HUMAN; Gesellschaft für Biochemica und Diagnostica mbH, Wiesbaden, Germany). Triglycerides were measured by using enzymatic colorimetric techniques (HUMAN). HDL cholesterol was isolated by precipitation with a sodium phosphotungstate and magnesium chloride solution.

The following two metabolic outcomes were studied:

1. Type 2 diabetes mellitus: Self-reported or defined by measured maternal glucose levels >126 mg/dL [26].
2. Metabolic syndrome and its components: Metabolic syndrome was defined by the presence of ≥3 out of 5 metabolic components (ATP III classification) [27]. These components included: (1) ≥88 cm waist circumference (central adiposity); (2) ≥130 mmHg systolic blood pressure or ≥85 mmHg diastolic blood pressure (hypertension); (3) ≥150 mg/dL triglycerides (hypertriglyceridemia), (4) <50 mg/dL HDL cholesterol; and (5) fasting glucose ≥100 mg/dL (hyperglycemia).

### 3.3. Covariates

Maternal self-reported pre-pregnancy and end-of-pregnancy weight data were obtained from a validated 2006 GOCS study questionnaire. Pre-pregnancy BMI and gestational weight gain (GWG; kg) were calculated. Self-reported maternal pregnancy weight appears well correlated with the actual weight [28]. Self-reported data on gestational diabetes mellitus (GDM) were also available from the same questionnaire as well as maternal age at delivery and female offspring gestational age. Data on maternal education (≤8 years = primary education, 8–12 years = secondary education, ≥12 years = higher education) and birth order of the index female offspring (1st child, 2nd–4th child, ≥5th child) were available from a validated 2010 DERCAM questionnaire. Birth order was used as a proxy for parity.

### 3.4. Statistical Methods

Continuous variables were summarized by means, SD and ranges and categorical variables were summarized by frequencies.

Maternal BMI and waist circumference showed skewed distributions and thus were log-transformed. Associations between offspring BW and maternal anthropometric outcomes (BMI and waist circumference) were assessed by multivariate linear regression models. Exponentiated beta coefficients were interpreted as the percent change in the geometric mean of the outcome variable [29].

Multivariate logistic regression models were performed for metabolic outcomes (type 2 diabetes mellitus; metabolic syndrome and its components). All models were adjusted for maternal age at delivery, maternal height, maternal education, parity, gestational age, maternal pre-pregnancy BMI, GWG and GDM. As sensitivity analyses, regressions models were repeated with BW being stratified into tertiles. A p-value < 0.05 was considered as significant. Data were analyzed using Stata version 12.0 (Stata Corporation, College Station, TX).

**Table 1 – Baseline characteristics of 396 mother-daughter pairs (2002–2003).**

| | | Cases (%) | Mean | SD |
|---|---|---|---|---|
| **Women** | | | | |
| Age (years) | | | 29.02 | 6.43 |
| Height (cm) | | | 157.30 | 5.48 |
| *Weight (kg)* | | | | |
| At the beginning of pregnancy (kg) | | | 59.80 | 11.60 |
| *BMI before pregnancy (kg/m$^2$)* | | | | |
| Continuous (kg/m$^2$) | | | 24.01 | 4.34 |
| Underweight | BMI < 18.5 | 19 (5) | | |
| Normal weight | BMI 18.5–24.9 | 228 (60) | | |
| Overweight | BMI 25–29.9 | 98 (26) | | |
| Obese | BMI ≥ 30 | 35 (9) | | |
| At the end of pregnancy (kg) | | | 73.40 | 12.81 |
| Weight gain during pregnancy (kg) | | | 14.00 | 7.70 |
| *Education (%)* | | | | |
| Primary education | | 56 (14) | | |
| Secondary education | | 260 (66) | | |
| Higher education | | 79 (20) | | |
| Gestational diabetes (self-reported) (%) | | 37 (9) | | |
| **Female offspring** | | | | |
| Birth weight (kg) | | | 3.37 | 0.39 |
| Birth length (cm) | | | 49.70 | 1.76 |
| Gestational age (weeks) | | | 39.10 | 1.18 |
| *Delivery order*[a] | | | | |
| 1st child | | 149 (39) | | |
| 2nd–4th child | | 220 (57) | | |
| ≥5th child | | 15 (4) | | |

BMI = Body Mass Index (kg/m$^2$); SD = standard deviation.

[a] Delivery order of the index female offspring was used as a proxy for parity.

### 3.5. Ethics

The GOCS and DERCAM studies were examined and approved by the Institutional Review Board of the Institute of Nutrition and Food Technology (INTA), Universidad de Chile. Written informed consent was obtained from all participants or their guardians.

## 4. Results

### 4.1. Descriptives

At baseline (2002–2003), women were on average 29 years (SD = 6.4), mean height was 157.3 cm (SD = 5.5) and mean weight was 59.8 kg (SD = 11.6) (Table 1). At the onset of pregnancy, 26% of women were overweight and 9% were obese. Mean GWG during pregnancy was 14.0 kg (SD = 7.7) and GDM was self-reported by 9% of women. Mean female offspring BW was 3.4 kg (SD = 0.4) for a mean birth length of 49.7 cm which is within the standards of the WHO Multicentre Growth Reference Study (girls, weight for length: 3.35 kg and 50 cm) [30].

At 10-years postpartum, mean maternal weight was 69.6 kg (SD = 14.0), 39% of women were overweight and 30% were obese (Table 2). Central adiposity (waist circumference ≥ 88 cm) was measured in 65% of women and 79% had low HDL-cholesterol levels, both important contributors to the metabolic syndrome, which was measured in 26% of women.

### 4.2. Maternal anthropometric and metabolic outcomes at 10-years postpartum

Adjusted linear regression models showed associations between female offspring BW and (1) maternal BMI (%Δ GM = 4.46; 95% CI 0.25–8.85); and (2) waist circumference (%Δ GM = 3.25; 95% CI 0–6.60) at 10-years postpartum (Table 3). Adjusted logistic regression models showed associations between female offspring BW and maternal metabolic syndrome (OR = 3.48; CI 95% 1.50–8.11) at 10-years postpartum (Table 4). Among the components of the metabolic syndrome, positive associations were found between BW and (1) central adiposity (OR = 2.37; CI 95% 1.08–5.22) and (2) hypertriglyceridemia (OR = 3.19; CI 95% 1.40–7.23). The relationship between BW and hypertriglyceridemia remained significant after adjusting by current BMI (OR = 3.05; CI 95% 1.33–7.00) (data not shown).

Sensitivity analyses of adjusted stratifications of female offspring BW into tertiles showed that women of female offspring BW in the 3rd tertile (3.51–4.50 kg) were at increased risk for (1) increased BMI (%Δ GM = 4.07; 95% CI 0.15–8.13), (2) increased waist circumference (%Δ GM = 3.40; 95% CI 0.37–6.53) (Fig. 1) and (3) metabolic syndrome (OR = 3.21; 95% CI 1.45–7.13) (Fig. 2) at 10-years postpartum compared to women of female offspring in the 1st tertile (2.50–3.20 kg) (Supplementary Material, Tables S1 and S2).

**Table 2 – Maternal anthropometric and metabolic characteristics at 10-years postpartum (2011–2012) (N=396).**

| | | Cases (%) | Mean | SD |
|---|---|---|---|---|
| **Anthropometry** | | | | |
| Waist circumference (cm) | | | 93.67 | 12.69 |
| *Weight (kg)* | | | 69.57 | 13.99 |
| *BMI (kg/m$^2$)* | | | | |
| Continuous (kg/m$^2$) | | | 28.09 | 5.30 |
| Normal weight | BMI 18.5–24.9 | 123 (31) | | |
| Overweight | BMI 25–29.9 | 154 (39) | | |
| Obese | BMI ≥ 30 | 118 (30) | | |
| **Metabolic characteristics** | | | | |
| Type 2 diabetes mellitus[a] | | 16 (4) | | |
| Metabolic syndrome[b] | | 102 (26) | | |
| Central adiposity[c] | | 259 (65) | | |
| High blood pressure[d] | | 41 (11) | | |
| Hypertriglyceridemia[e] | | 93 (24) | | |
| Low HDL cholesterol[f] | | 306 (79) | | |
| Hyperglycemia[g] | | 49 (13) | | |

BMI = Body Mass Index (kg/m$^2$); Max = maximum value; Min = minimum value; SD = standard deviation.
[a] Self-reported or fasting glycemia ≥ 126 mg/dL.
[b] ≥3 out of 5 components.
[c] Central adiposity: waist circumference ≥ 88 cm.
[d] High blood pressure: ≥130 mm Hg systolic blood pressure or diastolic blood pressure ≥ 85 mmHg.
[e] Hypertriglyceridemia: ≥150 mg/dL triglycerides.
[f] Low HDL cholesterol: <50 mg/dL HDL cholesterol.
[g] Hyperglycemia: fasting glucose ≥ 100 mg/dL.

**Table 3 – Linear regression models between female offspring birth weight and maternal anthropometric outcomes at 10-years postpartum.**

| | BMI (kg/m$^2$) | Waist circumference (cm) |
|---|---|---|
| | %Δ GM<br>β coefficient (95% CI) | %Δ GM<br>β coefficient (95% CI) |
| *Birth weight (kg)* | | |
| Model 1 | 12.98 (8.14–18.00)* | 9.17 (5.71–12.74)* |
| Model 2 | 4.46 (0.25–8.85)* | 3.25 (0.00–6.60)* |

BMI = Body Mass Index (kg/m$^2$); CI = confidence interval;%Δ GM = percent change in geometric mean of the variable.
Model 1: crude.
Model 2: adjusted for maternal age at delivery, maternal height, maternal education, parity, gestational age, maternal pre-pregnancy BMI, maternal gestational weight gain, gestational diabetes mellitus.
* Significant $p < 0.05$.

## 5. Discussion

At 10-years postpartum, 69% of the women had excess body weight and 26% had metabolic syndrome. Increasing female offspring BW was associated with adiposity (BMI and waist circumference) and higher odds for metabolic syndrome (and two of its individual components: central adiposity and hypertriglyceridemia), but was not associated with type 2 diabetes mellitus in Chilean mothers at 10-years postpartum (see Fig. 1 and Fig. 2).

Despite little knowledge on how offspring BW may be associated with the maternal postpartum metabolic risk profile, some of our findings are consistent with previous research. Our associations between BW and maternal BMI, waist circumference and metabolic syndrome agree with results from an Indian cohort of similar size (n = 459) that found mothers of heavier babies to be more obese (measured by BMI and central adiposity), and having a higher prevalence of metabolic syndrome, than mothers of lighter babies at 8-years postpartum [17]. In discrepancy with the Indian cohort, in our study BW was not associated with type 2 diabetes mellitus in the mothers postpartum. However, the association with metabolic syndrome – a risk factor for type 2 diabetes mellitus and cardiovascular events [31,32] – may suggest that our women could potentially be at greater risk to develop type 2 diabetes mellitus in the future. Our women are with a mean age of 39 years relatively young, although the Indian women were even younger. Different genetic predispositions in both populations may contribute to the different results.

As a potential explanation for the found associations between offspring BW and postpartum metabolic outcomes in the Indian women, gestational insulin resistance had been proposed [17]. Maternal insulin resistance is on the one hand associated with insulin-mediated fetal growth and increased BW [16,33], but on the other hand also with maternal BMI and metabolic syndrome postpartum [34–37]. Despite self-reported GDM prevalence in 9% of our women and adjustment hereof, overweight and obese women are more likely to experience decreased insulin sensitivity during pregnancy [38,39]. In the present study, this would apply to 35% of the women. Thus, in our sample the actual gestational insulin resistance and GDM prevalence might have been underestimated.

Female offspring BW was associated apart from an independent association with metabolic syndrome also with two of its individual components. The odds for central adiposity and hypertriglyceridemia were increased in mothers of larger offspring at 10-years postpartum. The association with high triglycerides remained significant after accounting for current BMI. Lipid metabolism is known to change during pregnancy and has been associated on the one hand with fetal intrauterine growth and increased offspring BW and on the other hand with maternal BMI, weight-retention and long-term metabolic disorders postpartum [17,40–43]. As maternal metabolic pre-pregnancy variables were unavailable, baseline levels are unknown. The association between BW and hypertriglyceridemia at 10-years postpartum may in fact be a remain of already high triglyceride levels before and during pregnancy – which is plausible as already 35% of the women had excess weight before pregnancy.

Further explanations for increased BW being associated with maternal anthropometric and metabolic risks postpartum may be found in further maternal pre-pregnancy conditions. Dietary habits and physical activity levels before and during pregnancy might play a role in our associations, but we did not have data on these variables. In the present study, the obtained mean GWG of 14 kg is within the range of the US Institute of Medicine (IOM) and US National Research Council (NRC) weight gain recommendations for normal-weighted women (11.5–16 kg) [44]. However, recommendations for overweight women are 7–11.5 kg and for obese women 5–9 kg (i.e. for 35% of women of our sample). In this regard, excessive GWG, possibly caused by maternal dietary habits and sedentary behavior during pregnancy, has been associated with maternal postpartum risk for increased BMI, central adiposity and weight retention [45–48].

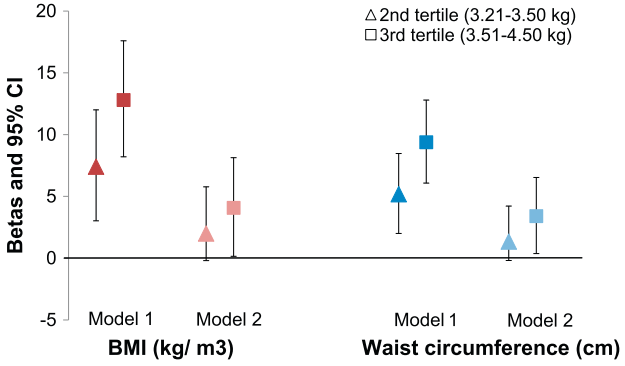
Moreover, as proposed by the Indian study, other disturbances may occur during gestation – either causing a larger fetus, or in 'reverse causation' a genetically-predetermined larger fetus causing the disturbances [17]. Research findings associated increased offspring BW with DNA methylation changes during fetal development and proposed that maternal obesity and overnutrition could be influencing factors [6,49,50]. Whether the fetus can also trigger changes to the maternal epigenome with postpartum consequences is unknown and to our knowledge has not been studied yet.

Offspring BW has commonly been used as an indicator for future offspring health (mainly targeting weight status and cardio-metabolic diseases), but has only to a limited extent

**Table 4 – Logistic regression models between female offspring birth weight and maternal metabolic outcomes at 10-years postpartum.**

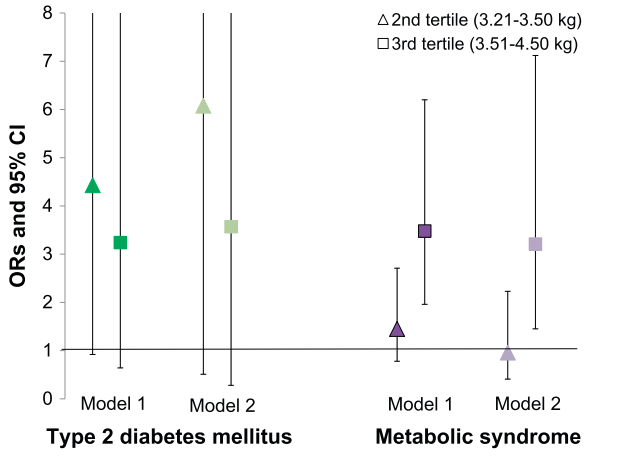
| | Type 2 diabetes mellitus[a] OR (95% CI) | Metabolic syndrome[b] OR (95% CI) | Central adiposity[c] OR (95% CI) | High blood pressure[d] OR (95% CI) | Hipertriglyceridemia[e] OR (95% CI) | Low HDL cholesterol[f] OR (95% CI) | Hyperglycemia[g] OR (95% CI) |
|---|---|---|---|---|---|---|---|
| Model 1 | 1.61 (0.46–5.59) | 3.34 (1.85–6.05)* | 3.61 (2.02–6.45)* | 0.46 (0.19–1.09) | 2.40 (1.33–4.35)* | 2.43 (1.26–4.68)* | 1.74 (0.82–3.68) |
| Model 2 | 1.85 (0.22–15.48) | 3.48 (1.50–8.11)* | 2.37 (1.08–5.22)* | 0.30 (0.09–1.02) | 3.19 (1.40–7.23)* | 1.88 (0.80–4.42) | 1.76 (0.60–5.15) |

CI = confidence interval; OR = odds ratio.
Model 1: crude.
Model 2: adjusted for maternal age at delivery, maternal height, maternal education, parity, gestational age, maternal pre-pregnancy BMI, maternal gestational weight gain, gestational diabetes mellitus.
[a] Self-reported or fasting glycemia ≥126 mg/dL.
[b] ≥3 out of 5 components.
[c] Central adiposity: waist circumference ≥ 88 cm.
[d] High blood pressure: ≥130 mmHg systolic blood pressure or diastolic blood pressure ≥85 mmHg.
[e] Hypertriglyceridemia: ≥150 mg/dL triglycerides.
[f] Low HDL cholesterol: <50 mg/dL HDL cholesterol.
[g] Hyperglycemia: fasting glucose ≥100 mg/dL.
* Significant $p < 0.05$.




**The reference level is the 1st tertile (2.50–3.20 kg).**

**Fig. 1 – Associations between female offspring birth weight tertiles and maternal anthropometric outcomes at 10-years postpartum. The reference level is the 1st tertile (2.50–3.20kg).**




**The reference level is the 1st tertile (2.50–3.20 kg).**

**Fig. 2 – Associations between female offspring birth weight tertiles and maternal metabolic outcomes at 10-years postpartum. The reference level is the 1st tertile (2.50–3.20kg).**

been considered as a potential proxy of future maternal health outcomes. Our findings suggest that offspring BW, even within the normal ranges, has implications for future maternal metabolic health status.

### 5.1. *Limitations and strengths*

To our knowledge, this study is the first Latin American study on the association between female offspring BW and maternal anthropometric and metabolic outcomes at 10-years postpartum. Nonetheless, our study is limited by the fact that data on extreme offspring BW, exceeding the boundaries of 2.5–4.5 kg, were not available. Even stronger associations are expected for BW > 4.5 kg (and also possibly for BW < 2.5 kg as U-shaped associations have been detected before [12,16]). Moreover, many covariates were self-reported (i.e. pre-pregnancy weight, end-of-pregnancy weight, GDM) with a time gap of at least three years (delivery of daughter 2002–2003;

initiation of GOCS study 2006). Hence, re-call bias cannot be ruled out. Additionally, the lack of data on metabolic and other key variables before and during pregnancy (i.e. glucose and insulin levels, dietary intake, physical activity levels) might have led to confounding of associations. Finally, the DERCAM study included only data of women with female offspring, thus it remains inconclusive whether associations hold true for women with male offspring. Strengths of this study include the 10-year follow-up time and the prospective designs of the GOCS and DERCAM studies from which the data were obtained.

### 5.2. *Conclusions*

Female offspring BW was associated with maternal BMI, waist circumference and metabolic syndrome in Chilean mothers at 10-years postpartum. Our findings position offspring BW as a potential proxy for identifying women who are at greater risk for future adverse anthropometric and metabolic outcomes, which appears to be understudied in current research practices.

## Conflict of interest

None.

## Sources of funding

Funding for the longitudinal Chilean GOCS and DERCAM studies was provided by FONDECYT #11100238, Fondecyt # 1120326, Fondecyt # 1130277 and the World Cancer Research Fund 2010/245. Ana Pereira is funded by the Ellison Medical Foundation Grant.

## Acknowledgements

The authors' responsibilities were as follows: NM, MLG, MR, CC and AP designed the study and planned the analyses. NM, MR and MLG conducted the analyses, interpreted findings and wrote the original draft of the manuscript. CC, MR, AP and RU critically reviewed and helped edit the manuscript. All authors approved the final manuscript. MLG is guarantor.

We thank the GOCS and DERCAM study personnel, in particular Daniela Gonzalez and Angela Martinez for their fieldwork coordination. Moreover, we thank David Martinez for statistical advice and Cyntia Manzano for helping with the interpretation of our findings. We are also in debt to all GOCS and DERCAM participants that continue to support our work.

## Appendix A. Supplementary Material

Supplementary data associated with this article can be found, in the online version, at https://doi.org/10.1016/j.diabres.2018.01.029.

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