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Sex-specific associations of birth weight with measures of adiposity in mid-to-late adulthood: the Brazilian Longitudinal Study of Adult Health (ELSA-Brasil)

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Abstract

BACKGROUND/OBJECTIVES: To investigate sex-specific associations of birth weight with body mass index (BMI), waist circumference (WC) and waist-to-hip ratio (WHR) in mid-to-late adulthood.

SUBJECTS/METHODS: ELSA-Brasil is a multicenter cohort study of adults aged 35–74 years affiliated with universities or research institutions of six capital cities in Brazil. After exclusions,

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AUTHOR CONTRIBUTIONS

MIS and BBD conceived the study, interpreted the data and prepared the final manuscript. VL, GR, MCS and AV analyzed and interpreted the data and prepared the final manuscript. NTM interpreted the data and prepared the final manuscript. SMB and IMB conceived the study and assisted in drafting the manuscript. SMAM, MJMF and LJA assisted in drafting the manuscript. All authors approved the final manuscript.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

we investigated 11 636 participants. Socio-demographic factors and birth weight were obtained by interview. All anthropometry was directly measured at baseline. We categorized birth weight as low (≤ 2.5 kg); normal (2.5–4 kg) and high (≥ 4 kg). We performed analysis of covariance (ANCOVA) for continuous outcomes and ordinal logistic regression for categorical adiposity outcomes. We examined interaction on the multiplicative scale by sex and by race.

RESULTS: High birth weight uniformly predicted greater overall and central obesity in men and women. However, low (vs normal) birth weight, in ANCOVA models adjusted for participant age, family income, race, education, maternal education, and maternal and paternal history of diabetes, was associated with lower BMI, WC and WHR means for men, but not for women ($P_{\text{interaction}} = 0.01, <0.0001$ and <0.0001 , respectively). In similarly adjusted ordinal logistic regression models, odds of obesity (odds ratio (OR) = 0.65, 0.46–0.90) and of being in the high (vs low) tertile of WC (OR = 0.66, 0.50–0.87) and of WHR (OR = 0.79, 0.60–1.03) were lower for low (vs normal) birth weight men, but trended higher (BMI: OR = 1.18, 0.92–1.51; WC: OR = 1.21, 0.97–1.53; WHR: OR = 1.44, 1.15–1.82) for low (vs normal) birth weight women.

CONCLUSIONS: In this Brazilian sample of middle-aged and elderly adults who have lived through a rapid nutritional transition, low birth weight was associated with adult adiposity in a sex-specific manner. In men, low birth weight was associated with lower overall and central adult adiposity, while in women low birth weight was generally associated with greater central adiposity.

INTRODUCTION

The number of overweight and obese adults has increased from 857 million in 1980 to 2.1 billion in 2013, making this global epidemic one of the greatest public health challenges facing our generation. Rates in low- and middle-income countries seem to be rising faster than high-income countries.¹ In the Brazilian scenario, 57%, or 82 million adults, have excess weight, and women are more affected than men.²

Multiple lines of evidence suggest an *in utero* provenance for overall and central adult obesity. Compared with adults born with normal birth weight (2.5–4 kg), those born with high birth weight (>4.0 kg) are at greater risk of becoming overweight or obese as an adult, but the association between low birth weight (<2.5 kg) and adult obesity is less clear.³ The association between low birth weight and adult obesity may be obscured by sex differences. Famine studies show that *in utero* caloric deprivation is associated with adult adiposity in a sex-specific manner, with stronger associations in women than in men.^{4–6} To the best of our knowledge, cohort studies have not comprehensively evaluated sex differences in the association of low birth weight with measures of overall and central adiposity in middle-aged and elderly adults.

To address this issue, we examined sex-specific associations of birth weight with measures of body mass index (BMI), waist circumference and waist-to-hip ratio in middle-aged and elderly Brazilian men and women, born at a time of food insecurity and now living in a notably obesogenic environment.

MATERIALS AND METHODS

Study design and population

This investigation is based on cross-sectional data from the Brazilian Longitudinal Study of Adult Health (ELSA-Brasil), a multicenter cohort enrolling participants from 2008 to 2010 investigates diabetes, cardiovascular diseases and other related chronic conditions. We invited active and retired employees of selected public institutions of higher education and research located in six capital cities to participate, as previously detailed.^{7,8} From a total of 15 105 ELSA participants, we excluded 2228 lacking information on birth weight, 915 who indicated twin births or prematurity, 6 lacking waist circumference, hip circumference or BMI, and 320 lacking data on covariates, leaving 11 636 in the analytic sample. The institutional review boards of the six institutions conducting the study approved ELSA-Brasil. We obtained written informed consent from all participants.

Exposure assessment

At baseline exam, we asked participants to recall their weight at birth as '<2.5 kg', '2.5–4 kg', '>4 kg', or as 'I do not know'. These first three categories were defined as low birth weight, normal birth weight and high birth weight, respectively.

Covariate assessment

History of paternal diabetes was ascertained by asking participants 'Was your father diagnosed with diabetes?' and history of maternal diabetes as 'Was your mother diagnosed with diabetes?'. Participants who answered, 'I don't know' to either of these parental history of diabetes questions were categorized as 'no' for each respective covariate in this analysis. Maternal educational attainment was ascertained by asking participants 'What was the highest level of education that your mother completed?'. Prematurity was assessed by asking participants, 'Were you born preterm?'.

Outcome ascertainment

We obtained several anthropometric measures using internationally standardized protocols.⁹ Waist circumference and weight were measured when fasting and with an empty bladder at the research clinics. During measurement, participants dressed in standardized clothing without eyeglasses and other personal objects. We measured height to the nearest 0.1 cm (Seca-SE-216, Hamburg, Germany). We obtained waist and hip circumferences with a 150-cm inelastic measuring tape (Mabis-Gulick, Waukegan, IL, USA), waist circumference being obtained at the midpoint between the inferior edge of the costal border and the iliac crest, in the mid axillar line, and hip circumference at the maximum posterior protrusion of the gluteus muscles, when viewed laterally. We measured body weight with an electronic scale with maximum capacity of 300 kg (Toledo, São Bernardo do Campo, Brazil). Quality control measures were uniform across all centers.¹⁰ BMI was calculated as measured weight (kg) divided by measured height squared (m^2). We defined waist-to-hip ratio as the ratio of these two circumferences.

Data analysis

We describe socio-demographic and anthropometric characteristics of participants with absolute and relative frequencies for categorical variables and means (standard deviations) for continuous ones. We compared adjusted means of adiposity measures across birth weight categories with analysis of covariance (ANCOVA). We fit ordinal logistic regression (partial proportional odds) models to evaluate the relationship between birth weight (three ordinal categories, with the middle one (2.5–4 kg) as the reference category) and adiposity measures (also three ordinal categories, with the lowest as the reference category). For overweight and obesity, we adopted conventional cutoffs established by the World Health Organization.¹¹ For waist circumference and waist-to-hip ratio, we used tertiles as cutoffs are not consensual and even those recommended for waist circumference in the definition of the metabolic syndrome differ according to population groups.¹² We tested interactions with sex and race (white vs non-white). We conducted all statistical analyses with SAS version 9.3 (SAS Institute Inc., Cary, NC, USA), and defined statistical significance at $P < 0.05$.

RESULTS

Our sample of 11 636 participants comprised 5254 men and 6382 women. The mean age was 51.3 (s.d.: 8.8) years and net monthly family income per capita was R\$1452.25 (interquartile range: R\$726.13–R\$2282.25). Low birth weight (<2.5 kg) was reported by 608 (5.3%) and high birth weight (>4 kg) by 911 (7.9%) participants. More than half (54.9%) of participants reported white race/skin color (the typical approach to classifying ethnicity in Brazil), while 27.1% reported brown ('pardo'), and 15.0% black, 2.2% Asian origin and 0.9% declared themselves Amerindian. More than half of the sample (55.9%) had a university degree, while only 6.9% of their mothers reached this level of educational attainment. Maternal history of diabetes was reported by 2355 (20.2%) participants, and paternal history of diabetes by 1555 (13.4%) participants.

In Table 1, we present baseline characteristics separately for men and women according to birth weight categories. For both sexes, birth weight was positively associated with white race/skin color, participant educational attainment and the educational achievement of the participant's mother. Participants who reported a high birth weight were more likely to have parents with a history of diabetes. Those reporting a low birth weight were more likely to have a maternal history of diabetes. Among men only, birth weight was inversely associated with age at baseline.

In ANOVA, we found statistically significant interactions between sex and birth weight categories (all P -values for interaction < 0.05), and thus performed all additional analyses stratified by sex. We found no evidence of interaction between race/ethnicity (white vs non-white) and birth weight categories in relation to adult adiposity outcomes ($P_{\text{interaction}}$: BMI = 0.44, waist circumference = 0.34; waist-to-hip ratio = 0.12).

Table 2 presents multivariable adjusted means of BMI, waist circumference and waist-to-hip ratio across birth weight categories. In men, we found means of all three adiposity measures increased monotonically with higher birth weight categories. Among women, instead of linearity, J- or U-shaped patterns were seen. Compared to women with normal birth weight,

those with high birth weight had higher mean values for all adiposity measures. Compared to women with normal birth weight, those with low birth weight had similar BMI and waist circumference means, but a higher mean waist-to-hip ratio (Figure 1). Statistical testing demonstrated significant sex differences comparing those with low to normal weight (BMI: $P_{\text{interaction}} = 0.01$; waist circumference and waist-to-hip ratio: $P_{\text{interaction}} < 0.0001$), but not comparing those with high to normal weight ($P_{\text{interaction}} \geq 0.18$).

Similar sex-specific patterns were observed when we analyzed adiposity outcomes using ordinal logistic regression models (Table 3). Among men, greater odds of adult overall and central obesity occurred with each higher category of birth weight. Among women, however, when compared to those with normal birth weight, those with both low and high birth weight had higher odds, frequently statistically significant, of being in the highest level of each adiposity outcome, producing, again, J- or U-shaped patterns. For low birth weight women, this difference was statistically significant for waist-to-hip ratio. Figure 2 illustrates these sex-specific categorical analyses, presenting the odds of obesity (vs normal weight) and those of being in the third (vs first) tertile of waist circumference and waist-to-hip ratio. Once again, there were sex differences comparing those with low to normal weight (BMI: $P_{\text{interaction}} = 0.004$; waist circumference: $P_{\text{interaction}} = 0.0008$ and waist-to-hip ratio: $P_{\text{interaction}} = 0.005$), but not comparing those with high to normal weight ($P_{\text{interaction}} \geq 0.20$).

In sensitivity analyses that excluded 87 participants (48 obese, 27 overweight and 12 with normal BMI) who reported having undergone bariatric surgery, the results were not appreciably different from the main results including these participants.

DISCUSSION

In this sample of middle-aged and elderly Brazilians 35–74 years, born from 1936 to 1973, we found a sex-specific pattern of associations of low but not high birth weight with adult measures of overall and central adiposity. In men, low birth weight was generally associated with lower overall and central adult adiposity, while in women low birth weight was generally associated with higher levels of adiposity. Those with high birth weight, consistent with findings from a large systematic review,¹³ had greater odds of adult overweight and obesity (57–87% greater), and these associations were generally similar for men and women.

The sex-specific association between low birth weight and adult overall and central adiposity has not, to our knowledge, been comprehensively reported in cohorts of middle-aged or elderly adults. A systematic review reported a decreased odds of overweight/obesity (odds ratio (OR) = 0.67; 95% confidence interval (CI) = 0.59–0.76) for those with low birth weight (<2500 g).¹³ However, in sensitivity analyses of only those studies with adult participants, lower odds for future excess weight were not seen (OR = 0.97; 95% CI = 0.79–1.20). In this systematic review, results in adults were not presented separately by sex. In fact, we could find no reports in the literature investigating sex-specific adiposity outcomes of low birth weight for middle-aged and elderly adults, the age range at which overall and central obesity are usually associated with their common cardiometabolic complications.

An investigation of 3 72 542 middle-aged UK women, but no men, showed a U-shaped relationship between birth weight and obesity at middle age.¹⁴ In comparison to those with normal birth weight, those with low birth weight had 26% greater odds of obesity (OR = 1.26; 95% CI = 1.23–1.29) and those with high birth weight had 33% greater odds of obesity (OR = 1.33; 95% CI = 1.30–1.37). A Brazilian birth cohort that followed participants until 30 years of age found that women with low birth weight, but not men, had greater visceral fat content.¹⁵ A study of Chinese adolescents found a U-shaped association of birth weight with BMI and waist circumference, the latter being statistically significant only in girls.¹⁶ Adolescent Spanish girls presented smaller associations of birth weight, assessed as weight for gestational age, with measures of body composition than boys, although only linear relationships across the entire birth weight spectrum were reported.¹⁷

Our findings suggest sex-specific responses to intrauterine adversity that influence the development of overall and central obesity. Similar to our findings, sex differences have been reported from several studies of survivors of famines. Middle-aged women conceived during the Dutch Famine of 1944–1945,⁴ the Nigerian Biafran Famine,⁵ the Great Depression in Reykjavik (1930–1934)⁶ and the Great Chinese Famine^{18,19} have a greater prevalence of overweight and obesity than men.

In terms of biologic mechanisms that may underlie the associations we report, growing evidence shows that intrauterine adversity not only restricts fetal growth but also alters gene expression in a manner that may increase future risk of adiposity and metabolic diseases.²⁰ Consistent with our findings, the current literature suggests that these epigenetic marks are sex specific.^{21–24}

These sex-specific findings may also be interpreted within a larger framework of sexually-dimorphic, species-specific gestational strategies to cope with environmental adversity.^{25–27} This framework suggests that our findings may represent the long-term effects of fetal programming evolved through natural selection to produce alternative survival strategies for boys and girls in the setting of intrauterine growth restriction. In a number of non-human mammalian species, a greater fraction of females are born in gestations complicated by poor nutrition or a poor habitat.²⁸ Some^{29–31} but not all³² studies of famine also report a drop in the male-to-female ratio of births. A Brazilian study of low birth weight infants showed neonatal mortality in boys to be 67% greater than that in girls.³³

There are limitations to our study that merit mention. Birth weight was ascertained by interview through self-report. However, if an ELSA participant was uncertain about his or her birth weight, he or she was encouraged to investigate it further and report back later to the clinic. Additionally, care was taken to limit low birth weight to causes related to intrauterine growth restriction (for example, those reporting premature or twin birth were excluded from analyses), and several cohort studies have shown moderate correlations between estimated and recorded birth weight ($r = 0.64$ – 0.83).^{34–36} A subsample of the *Nurse's Health Study II* found that 70% of referred values fell into the correct birth weight categories written in birth certificates.³⁷ Another limitation is missing data; we were only able to conduct analyses in the 84% of participants self-reported their birth weight. Although potential confounders, such as maternal educational attainment, were controlled for in our

multivariable analysis, we also cannot rule out influence from unmeasured or residual confounding. Finally, as our study participants were recruited from higher education institutes they may be of higher socioeconomic status than other contemporary Brazilian adults.

Our study also has several strengths, including its generalizability to populations in low- and middle-income countries. The majority of the world's population is currently undergoing a rapid nutritional transition. ELSA participants were born between 1930 and 1970, and thus lived through the mid-1900s during which food insecurity was common, as well as through the more recent period in which obesity has been highly prevalent. This study is the first, to our knowledge, to examine the association of birth weight with measures of obesity in middle-aged and elderly adults within this context of a rapid nutritional transition. Additionally, adult anthropometry in ELSA was carefully measured following internationally standardized techniques.

In conclusion, birth weight was associated with measures of overall and central adiposity in a sex-specific manner, suggesting a positive linear association in men and J- or U-shaped associations in women. Sex stratification in future studies of fetal programming may help to uncover novel sex-dependent responses to the *in utero* environment that may lead to adult metabolic disease.

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REFERENCES

1. Ng M, Fleming T, Robinson M, Thomson B, Graetz N, Margono C 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 2013. *Lancet* 2014; 384: 766–781. [PubMed: 24880830]
2. Instituto Brasileiro de Geografia e Estatística. Pesquisa Nacional de Saúde: 2013. Ciclos de vida: Brasil e grandes regiões. IBGE: Rio de Janeiro, Brazil, 2015.
3. Yu ZB, Han SP, Zhu GZ, Zhu C, Wang XJ, Cao XG et al. Birth weight and subsequent risk of obesity: a systematic review and meta-analysis: Birth weight in relation to obesity. *Obes Rev* 2011; 12: 525–542. [PubMed: 21438992]
4. Ravelli AC, van Der Meulen JH, Osmond C, Barker DJ, Bleker OP. Obesity at the age of 50 y in men and women exposed to famine prenatally. *Am J Clin Nutr* 1999; 70: 811–816. [PubMed: 10539740]
5. Hult M, Tornhammar P, Ueda P, Chima C, Bonamy A-KE, Ozumba B et al. Hypertension, diabetes and overweight: looming legacies of the Biafran famine. *PLoS One* 2010; 5: e13582. [PubMed: 21042579]
6. Imai CM, Halldorsson TI, Gunnarsdottir I, Gudnason V, Aspelund T, Jonsson G et al. Effect of birth year on birth weight and obesity in adulthood: comparison between subjects born prior to and during the great depression in Iceland. *PLoS One* 2012; 7: e44551. [PubMed: 22957081]
7. Aquino EML, Barreto SM, Bensenor IM, Carvalho MS, Chor D, Duncan BB et al. Brazilian Longitudinal Study of Adult Health (ELSA-Brasil): objectives and design. *Am J Epidemiol* 2012; 175: 315–324. [PubMed: 22234482]

8. Schmidt MI, Duncan BB, Mill JG, Lotufo PA, Chor D, Barreto SM et al. Cohort Profile: Longitudinal Study of Adult Health (ELSA-Brasil). *Int J Epidemiol* 2015; 44: 68–75. [PubMed: 24585730]
9. Lohman TG, Roche AF, Martorell R. Anthropometric Standardization Reference Manual. Human Kinetics Books: Champaign, IL, USA, 1988.
10. Schmidt MI, Griep RH, Passos VM, Luft VC, Goulart AC, Menezes GM de S et al. [Strategies and development of quality assurance and control in the ELSA-Brasil]. *Rev Saúde Pública* 2013; 47(Suppl 2): 105–112. [PubMed: 24346727]
11. World Health Organization The Use and Interpretation of Anthropometry: Report of a WHO Expert Committee. WHO: Geneva, Switzerland, 1995.
12. Alberti KGMM, Eckel RH, Grundy SM, Zimmet PZ, Cleeman JI, Donato KA et al. Harmonizing the metabolic syndrome: a joint interim statement of the International Diabetes Federation Task Force on Epidemiology and Prevention; National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; and International Association for the Study of Obesity. *Circulation* 2009; 120: 1640–1645. [PubMed: 19805654]
13. Schellong K, Schulz S, Harder T, Plagemann A. Birth weight and long-term overweight risk: systematic review and a meta-analysis including 643,902 persons from 66 studies and 26 countries globally. *PLoS ONE* 2012; 7: e47776. [PubMed: 23082214]
14. Yang TYO, Cairns BJ, Beral V. On behalf of the Million Women Study Collaborators Association between birthweight and obesity in adult females. *J Epidemiol Community Health* 2010; 64: A18–A19.
15. Araújo de França GV, Lucia Rolfe ED, Horta BL, Gigante DP, Yudkin JS, Ong KK et al. Associations of birth weight, linear growth and relative weight gain throughout life with abdominal fat depots in adulthood: the 1982 Pelotas (Brazil) birth cohort study. *Int J Obes* 2016; 40: 14–21.
16. Tam CHT, Wang Y, Luan J, Lee HM, Luk AOY, Tutino GE et al. Non-linear relationship between birthweight and cardiometabolic risk factors in Chinese adolescents and adults. *Diabet Med* 2015; 32: 220–225. [PubMed: 25388749]
17. Labayen I, Moreno LA, Ruiz JR, González-Gross M, Wärnberg J, Breidenassel C et al. Small birth weight and later body composition and fat distribution in adolescents: the AVENA study. *Obesity* 2008; 16: 1680–1686. [PubMed: 18464751]
18. Fung WW-Y. Early Childhood Malnutrition and Adult Obesity: Evidence from the 1959–61 China Famine. and University Mimeograph 2009 Available from http://cahnrs-cms.wsu.edu/ses/seminars/Documents/PastSeminarsPapers/Obesity_WinnieFung.pdf.
19. Luo Z, Mu R, Zhang X. Famine and overweight in China. *Rev Agric Econ* 2006; 28: 296–304.
20. Saffery R, Novakovic B. Epigenetics as the mediator of fetal programming of adult onset disease: what is the evidence? *Acta Obstet Gynecol Scand* 2014; 93: 1090–1098. [PubMed: 24835110]
21. Tobi EW, Lumey LH, Talens RP, Kremer D, Putter H, Stein AD et al. DNA methylation differences after exposure to prenatal famine are common and timing- and sex-specific. *Hum Mol Genet* 2009; 18: 4046–4053. [PubMed: 19656776]
22. Inoshita M, Numata S, Tajima A, Kinoshita M, Umehara H, Yamamori H et al. Sex differences of leukocytes DNA methylation adjusted for estimated cellular proportions. *Biol Sex Differ* 2015; 6: 11. [PubMed: 26113971]
23. Hall E, Volkov P, Dayeh T, Esguerra JLS, Salö S, Eliasson L et al. Sex differences in the genome-wide DNA methylation pattern and impact on gene expression, microRNA levels and insulin secretion in human pancreatic islets. *Genome Biol* 2014; 15: 522. [PubMed: 25517766]
24. Yousefi P, Huen K, Davé V, Barcellos L, Eskenazi B, Holland N. Sex differences in DNA methylation assessed by 450 K BeadChip in newborns. *BMC Genomics* 2015; 16: 911. [PubMed: 26553366]
25. DiPietro JA, Voegtline KM. The gestational foundation of sex differences in development and vulnerability. *Neuroscience* 2015; e-pub ahead of print 29 July 2015; doi:10.1016/j.neuroscience.2015.07.068.

26. Trivers RL, Willard DE. Natural selection of parental ability to vary the sex ratio of offspring. *Science* 1973; 179: 90–92. [PubMed: 4682135]
27. Sandman CA, Glynn LM, Davis EP. Is there a viability-vulnerability tradeoff? Sex differences in fetal programming. *J Psychosom Res* 2013; 75: 327–335. [PubMed: 24119938]
28. Clutton-Brock TH, Iason GR. Sex ratio variation in mammals. *Q Rev Biol* 1986; 61: 339–374. [PubMed: 3532167]
29. Hernández-Julián R, Mansour H, Peters C. The effects of intrauterine malnutrition on birth and fertility outcomes: evidence from the 1974 Bangladesh famine. *Demography* 2014; 51: 1775–1796. [PubMed: 25189157]
30. Mu R, Zhang X. Why does the Great Chinese Famine affect the male and female survivors differently? Mortality selection versus son preference. *Econ Hum Biol* 2011; 9: 92–105. [PubMed: 20732838]
31. Song S Does famine influence sex ratio at birth? Evidence from the 1959–1961 Great Leap Forward Famine in China. *Proc Biol Sci* 2012; 279: 2883–2890. [PubMed: 22456881]
32. Lumey LH, Stein AD, Susser E. Prenatal famine and adult health. *Annu Rev Public Health* 2011; 32: 237–262. [PubMed: 21219171]
33. Ribeiro AM, Guimarães MJ, Lima M de C, Sarinho SW, Coutinho SB. [Fatores de risco para mortalidade neonatal em crianças com baixo peso ao nascer]. *Rev Saúde Pública* 2009; 43: 246–255. [PubMed: 19225697]
34. Sanderson M, Williams MA, White E, Daling JR, Holt VL, Malone KE et al. Validity and reliability of subject and mother reporting of perinatal factors. *Am J Epidemiol* 1998; 147: 136–140. [PubMed: 9457002]
35. Troy LM, Michels KB, Hunter DJ, Spiegelman D, Manson JE, Colditz GA et al. Self-reported birthweight and history of having been breastfed among younger women: an assessment of validity. *Int J Epidemiol* 1996; 25: 122–127. [PubMed: 8666479]
36. Kemp M, Gunnell D, Maynard M, Smith GD, Frankel S. How accurate is self reported birth weight among the elderly? *J Epidemiol Community Health* 2000; 54: 639. [PubMed: 10890878]
37. Curhan GC, Chertow GM, Willett WC, Spiegelman D, Colditz GA, Manson JE et al. Birth weight and adult hypertension and obesity in women. *Circulation* 1996; 94: 1310–1315. [PubMed: 8822985]

Figure 1.

Adjusted mean values of BMI, waist circumference and the waist-to-hip ratio for men and women (women = black, men = gray). Values were adjusted through ANCOVA for study center, age, family income, participant race, participant education, education of participant's mother, mother had diabetes and father had diabetes. *P*-value for the interaction between low birth weight and sex was on BMI = 0.01, on waist circumference <0.0001 and on waist-to-hip ratio <0.0001; and for high birth weight and sex on these same outcomes: 0.33, 0.18 and 0.42, respectively.

Figure 2.

Adjusted OR of obesity (BMI), high waist circumference (3rd vs 1st tertile) and high waist-to-hip ratio (3rd vs 1st tertile) for men and women (women=black, men=gray). Values were adjusted through ordinal logistic regression models for study center, age, family income, participant race, participant education, education of participant's mother, whether the participant's mother had diabetes and whether the participant's father had diabetes. *P*-value for the interaction between low birth weight and sex was on obesity =0.004, on high vs low tertile waist circumference=0.0008 and on high vs low tertile waist-to-hip ratio =0.005; and for high birth weight and sex on these same outcomes: 0.43, 0.64 and 0.54, respectively.

Table 1.
Characteristics of 11 636 adult participants from ELISA-Brazil, according to sex and birth weight

Characteristic ^a	Birth weight categories							
	Men				Women			
	<2.5 kg (n = 277)	2.5–4 kg (n = 4447)	>4 kg (n = 530)	P-value	<2.5 kg (n = 346)	2.5–4 kg (n = 5642)	>4kg (n = 394)	P-value
Age	52.6±9.0	51.4±9.1	50.4±9.0	0.0049	51.9±8.2	51.3±8.7	51.1±8.3	0.3547
Race/color								
White	116 (41.9)	2 478 (55.7)	319 (60.1)	<0.0001	165 (47.7)	3073 (54.5)	232 (58.9)	0.0299
Brown	97 (35.0)	1301 (29.3)	136 (25.7)		104 (30.1)	1427 (25.3)	90 (22.8)	
Black	47 (17.0)	553 (12.4)	62 (11.7)		66 (19.1)	949 (16.8)	64 (16.2)	
Asian origin	10 (3.6)	75 (1.7)	3 (0.6)		11 (3.2)	152 (2.7)	6 (1.5)	
Amerindian	7 (2.5)	40 (0.9)	10 (1.9)		0 (0.0)	41 (0.7)	2 (0.5)	
School achievement								
<Complete primary	35 (12.6)	261 (5.9)	28 (5.3)	<0.0001	17 (4.9)	135 (2.4)	9 (2.3)	0.0022
Primary	42 (15.2)	325 (7.3)	28 (5.3)		22 (6.4)	248 (4.4)	12 (3.0)	
Secondary	112 (40.4)	1489 (33.5)	157 (29.6)		134 (38.7)	1951 (34.6)	127 (32.2)	
University	88 (31.8)	2372 (53.3)	317 (59.8)		173 (50.0)	3308 (58.6)	246 (62.4)	
Mother's schooling								
<Complete primary	190 (68.6)	2375 (53.4)	259 (48.9)	<0.0001	218 (63.0)	3093 (54.8)	208 (52.8)	0.0339
Primary	40 (14.4)	893 (20.1)	113 (21.3)		57 (16.5)	1176 (20.8)	78 (19.8)	
Secondary	40 (14.4)	861 (19.4)	109 (20.6)		55 (15.9)	981 (17.4)	83 (21.1)	
University	7 (2.5)	318 (7.1)	49 (9.2)		16 (4.6)	392 (6.9)	25 (6.3)	
Mother had diabetes								
Yes	59 (21.3)	861 (19.4)	128 (24.1)	0.0282	76 (22.0)	1110 (19.7)	121 (30.7)	<0.0001
Father had diabetes								
Yes	16 (5.8)	552 (12.4)	72 (13.6)	0.0027	50 (14.4)	802 (14.2)	63 (16.0)	0.6223
Body mass index (kg m ⁻²)	26.3±4.7	27.0±4.2	28.1±4.7	<0.0001	27.1±5.2	27.0±5.0	28.5±5.9	<0.0001
Waist circumference	92.4±11.5	95.3±11.5	98.2±12.5	<0.0001	88.1±3.0	87.4±12.3	91.8±14.5	<0.0001
Waist-to-hip ratio	0.94±0.07	0.95±0.07	0.95±0.07	0.2393	0.86±0.08	0.85±0.07	0.86±0.08	<0.0001

Abbreviation: ELISA-Brazil, Brazilian Longitudinal Study of Adult Health.

^aMean ± s.d. or N (%).

Table 2.

Adjusted^a means (and 95% confidence intervals) of body mass index, waist circumference and waist-to-hip ratio, according to sex and birth weight categories in adults 35–70 years of age in ELSA-Brasil

Birth weight categories	Body mass index, kg m ⁻²	Waist circumference, cm	Waist-to-hip ratio
<i>Men</i>			
<2.5 kg	26.7 (26.1–27.2)	94.0 (92.6–95.5)	0.95 (0.94–0.96)
2.5–4 kg	27.6 (27.4–27.9)	97.5 (97.0–98.1)	0.96 (0.96–0.97)
>4 kg	28.9 (28.5–29.4)	100.7 (99.6–101.8)	0.97 (0.96–0.97)
<i>Women</i>			
<2.5 kg	27.7 (27.2–28.3)	90.2 (88.9–91.6)	0.87 (0.87–0.88)
2.5–4 kg	27.7 (27.5–28.0)	89.8 (89.1–90.4)	0.86 (0.86–0.87)
> 4 kg	29.3 (28.8–29.8)	94.0 (92.7–95.3)	0.87 (0.86–0.88)

Abbreviation: ELSA-Brasil, Brazilian Longitudinal Study of Adult Health.

^aAnalysis of covariance adjusted for study center, sex, age, family income, race, education, education of mother, mother had diabetes and father had diabetes.

Table 3.

Associations^a of birth weight categories with body mass index (BMI), waist circumference and waist-to-hip ratio categories according to sex in adults 35–70 years of age in ELSA-Brasil

Birth weight categories	25 BMI<30 kg m ⁻² vs <25 kg m ⁻²	BMI 30kg m ⁻² vs <25 kg m ⁻²
	OR (95% CI)	OR (95% CI)
<i>Men</i>		
<2.5 kg	0.66 (0.51–0.85)	0.65 (0.46–0.90)
2.5–4 kg	1 (reference)	1 (reference)
>4 kg	1.59 (1.29–1.96)	1.88 (1.54–2.30)
<i>Women</i>		
<2.5 kg	1.00 (0.80–1.26)	1.18 (0.92–1.51)
2.5–4 kg	1 (reference)	1 (reference)
>4 kg	1.61 (1.29–2.02)	1.67 (1.34–2.08)
	<i>Waist circumference 2nd vs 1st tertile</i>	<i>Waist circumference 3rd vs 1st tertile</i>
	OR (95% CI)	OR (95% CI)
<i>Men</i>		
<2.5 kg	0.61 (0.47–0.79)	0.66 (0.50–0.87)
2.5–4 kg	1 (reference)	1 (reference)
<4 kg	1.42 (1.16–1.75)	1.71 (1.41–2.06)
<i>Women</i>		
<2.5 kg	0.90 (0.71–1.14)	1.21 (0.97–1.53)
2.5–4 kg	1 (reference)	1 (reference)
>4 kg	1.48 (1.16–1.87)	1.82 (1.48–2.25)
	<i>Waist-to-hip ratio 2nd vs 1st tertile</i>	<i>Waist-to-hip ratio 3rd vs 1st tertile</i>
	OR (95% CI)	OR (95% CI)
<i>Men</i>		
<2.5 kg	0.63 (0.49–0.83)	0.79 (0.60–1.03)
2.5–4 kg	1 (reference)	1 (reference)
>4 kg	1.08 (0.89–1.33)	1.33 (1.09–1.62)
<i>Women</i>		
<2.5 kg	1.61 (1.24–2.10)	1.44 (1.15–1.82)
2.5–4 kg	1 (reference)	1 (reference)
>4 kg	1.21 (0.96–1.53)	1.21 (0.97–1.52)

Abbreviations: CI, confidence interval; ELSA-Brasil, Brazilian Longitudinal Study of Adult Health; OR, odds ratio. Cutoffs for tertiles of waist circumference: men 90 and 99.6 cm; women 81.2 and 91.9 cm; cutoffs for tertiles of waist-to-hip ratio: men 0.919 and 0.978; women 0.812 and 0.877.

^a Ordinal logistic regression models adjusted for study center, age, family income, participant race, participant education, education of participant's mother, mother had diabetes and father had diabetes. Statistically significant associations are presented in bold.