HHS Public Access

Author manuscript

Ann Epidemiol. Author manuscript; available in PMC 2017 September 01.

Published in final edited form as:

Ann Epidemiol. 2016 September ; 26(9): 643–647. doi:10.1016/j.annepidem.2016.07.013.

Birth Weight was longitudinally associated with Cardiometabolic Risk Markers in Mid-Adulthood

Fawaz Mzayek[a], **J Kennedy Cruickshank**[b], **Doris Amoah**[a], **Sathanur Srinivasan**[c], **Wei Chen**[c], and **Gerald S Berenson**[c,d]

[a]Division of Epidemiology, Biostatistics and Environmental Health, University of Memphis School of Public Health, Memphis, TN, USA

[b]Cardiovascular Medicine Group, Diabetes and Nutritional Science Division, King's College, London, UK

[c]Center of Cardiovascular Health, Department of Epidemiology, Tulane University School of Public Health and Tropical Medicine, New Orleans, LA, USA

[d]Louisiana State University Health Sciences Center, Section of Cardiology, LSU, New Orleans, LA, USA

Abstract

Purpose—Birth weight (BW) is associated with risk of cardiovascular (CV) disease. The findings form studies examined the association of BW with metabolic markers of CV risk were inconsistent and controversial. We examined the association of BW with insulin resistance and blood lipids using repeated measures up to mid-adulthood.

Methods—Data from seven screenings of the Bogalusa Heart Study—a longitudinal study of cardiovascular risk factors in Bogalusa, LA, are analyzed using generalized estimation equations method. Participants with birth data and at least one measurement of study outcomes between 18–44 years of age (n=2,034) were included.

Results—BW is inversely associated with insulin resistance, triglycerides and total cholesterol (P<0.01 for all). For 1-kg decrease in BW, insulin resistance increased by 2.3 units, 95% CI = 0.7, 3.9; triglycerides by 8.7 mg/dL, 95% CI = 4.9, 12.4 and total cholesterol by 5.4 mg/dL, 95% CI = 1.8, 9.1. The association of body mass with adult blood lipids levels is weaker in persons with low- vs. normal BW.

Conclusions—The study provides strong evidence of an inverse relationship of BW with adulthood cardiometabolic risk profile. Persons born with low BW are maybe less responsive to preventive interventions aiming at weight reduction.

Corresponding author: Fawaz Mzayek, MD, PhD, School of Public Health, University of Memphis, Robison Hall, Room 300, Memphis, TN 38152, Phone: 1 901 678-1662, fmzayek@memphis.edu.

Keywords

Birth weight; cardiovascular risk; cholesterol; insulin resistance; HOMA-IR; lipids; triglycerides

INTRODUCTION

A large body of evidence has accumulated indicating a relationship between in utero growth restriction (IUGR) and the development of many disorders later in life, including increased insulin resistance and type 2 diabetes mellitus, hypertension, and adverse blood lipid profile. [1–4] According to the hypothesis of early origins of adult disease, adverse prenatal pressures stimulate fetal responses that permanently alter the "programming" of many of its physiologic systems, thus predisposing the individual to various diseases later in life. [5,6] Low birth weight (BW) at or near term is the most commonly used surrogate measure of IUGR and has been related to increased cardiovascular mortality, presumably due to its adverse effect on many cardiovascular risk factors acting later in life. [6–8] The epidemiologic evidence clearly points to an inverse association between BW and many hemodynamic CV risk markers, especially systolic blood pressure (BP) and pulse pressure (PP). [9–11] The findings are less consistent, however, for markers of cardiometabolic risk, such as blood lipids and lipoproteins and insulin resistance. [12–17]

Additionally, some authors questioned these findings citing the lack of adjustment for important confounders, such as socioeconomic status (SES) and lifestyle variables. [12,18] Others have questioned the interpretation of an effect of BW from statistical models concurrently relating birth- and current body mass to later CV risk factors, arguing that these models actually test the effect of *change* of body mass from birth rather than the effect of size at birth. [18] This notion has profound public health implications as it shifts the emphasis from prenatal to postnatal growth.

In this paper, we examine the association of BW with levels of markers of cardiometabolic risk (serum lipids and lipoproteins and insulin resistance), using repeated measurements from young to mid-adulthood that were collected by the Bogalusa Heart Study (BHS). To address the aforementioned points, three analytical approaches are used: 1) testing the associations of BW with later markers of cardiometabolic risk without adjusting for BMI; 2) testing the associations of BW with later markers of cardiometabolic risk adjusting for BMI and other important socioeconomic, behavioral and familial variables; 3) testing the association of repeated measures of BMI with later markers of cardiometabolic risk in persons with low BW (BW <2500g) vs. those with normal BW (BW ≥2500g). Modeling the association of BW and repeated measures of body mass with metabolic markers of CV risk allows assessing the effect of the total burden of the change of body mass over time on various risk factors. Additionally, comparing the association of BMI with the outcomes in individuals of low- vs. normal BW allows assessing the heterogeneity, or lack of, of the effect of weight gain over time on CV risk factors in the two groups.

This study aims to reexamine the hypothesized association of low BW with an adverse metabolic CV risk profile later in life, while addressing the issues of adjusting for BMI and

adequate controlling for important confounding factors such as lifestyle and familial variables.

MATERIALS AND METHODS

Participants

The BHS is a longitudinal study following a bi-ethnic cohort (65% White, 35% African American) from Bogalusa, LA, to examine the natural development of CV disease. A detailed description of the demographic characteristics of the community, as well as the overall design of the study, has been published elsewhere. [19] This study utilized data of seven screenings of BHS performed during participants' early to mid-adulthood (age range: 18–44 years). Birth data were collected from birth certificates that were obtained from the Office of Health Statistics in New Orleans, LA. Of the 2,301 participants who were eligible to be included in this analysis, BW was available on 2,274 (98.8%) of them. Singletons with complete birth data and at least one measurement of markers of CV risk after the age of 18 years were eligible for the study (n=2,274). Birth data were obtained from birth certificates. Exclusion criteria included having type 1 diabetes mellitus (n=6); having congenital heart disease (n=4); failed to fast (n=3) and premature birth (n=226) leaving 2,034 participants (89.4%) who were included in this analysis.

Informed consent was obtained from the parents during childhood screenings and from the participants during adulthood screenings. The study was approved by the institutional review board at Tulane University in New Orleans, USA.

Procedures

Height was measured manually to the nearest 1 mm and weight to the nearest 0.1 kg, both as the mean of two measurements. Body mass index (BMI) was calculated from the formula = weight (kg)/height^2 (meter). Birth weights were obtained from birth certificates and were then converted into kilograms (1 ounce ≈ 0.028 kg).

All lab tests were done after overnight fasting. Serum total cholesterol and triglycerides measurements were performed using enzymatic procedures on Hitachi 902 Automatic Analyzer (Roche Diagnostics, Indianapolis, IN). Low-density lipoprotein cholesterol (LDL-C), and high-density lipoprotein cholesterol (HDL-C) levels were determined by a combination of heparin-calcium precipitation and agar-agarose gel electrophoresis. Plasma immunoreactive insulin levels were measured by a commercial radio-immunoassay kit (Phadebas, Pharmacia Diagnostics, Piscataway, NJ). Serum glucose level was measured as part of a multiple chemistry profile. Homeostasis model assessment (HOMA-IR)—calculated as [fasting insulin (μU/ml) × fasting glucose (mmol/L)/22.5]—was used to measure insulin resistance. [20] The World Health Organization definition for low BW, <2500 g, was adopted for this study. Prematurity was defined as gestational age less than 37 weeks.

Income was defined as the last self-reported annual income and was classified into two categories: <$45 000 and ≥$45 000. Smoking status was defined as the last information available about smoking and was coded into two categories: non/former-smokers and current smokers. Alcohol consumption was defined as the last information available about drinking

and was coded into three categories: none/less than one drink per week, 2–4 drinks per week, and >4 drinks per week. Family history of cardiovascular disease was defined as having a parent who had a heart attack, a stroke, a bypass surgery, or an angioplasty or who died of a heart attack or stroke. This variable was coded as 2 if both parents had a history of CV disease, as 1 if one parent had a history of CV disease, and as 0 if neither parent had a history of CV disease. Available information on the familial and lifestyle variables ranged from 70 percent for income to 99 percent for smoking status.

Statistical analyses

De-identified data of the outcome and the independent variables from the seven files pertaining to the seven Bogalusa Heart Study screenings of young adults between 1988 and 2001 were linked to the file containing birth outcomes data, indexed on the unique ID number, and keeping the chronological order of the data.

The outcome variables were HOMA-IR, triglycerides, total cholesterol, low density lipoprotein (LDL) cholesterol, or high density lipoprotein (HDL) cholesterol. The generalized estimation equation (GEE) method was used to analyze the data. GEE methods account for within-subject correlation, due to repeated measurements, and between-subject variation due to the individual differences among the participants. For each outcome, the correlation structure between the repeated measures was examined using Pearson's correlation. Based on this analysis exchangeable working correlation matrix was defined for all models. All the dependent variables deviated from normality and were skewed to the right. Therefore, the inverse Gaussian distribution was selected for all models, resulting in much better fits to the data than the normal distribution, as measured by quasi likelihood under independence criterion (QIC). Two models were run for each outcome: the minimally-adjusted model included BW, age, sex and race as the independent variables, whereas the full model additionally included BMI, income, smoking status, alcohol drinking and parental history of CV disease. BW was entered in the models as a continuous variable. Age and BMI were entered as time-variant variables to adjust for their effect as they changed over time. To examine whether BW interacts with body mass, the models were rerun in those with BW <2,500 g vs. ≥2,500 g and the coefficients of BMI in the two groups were compared. Two-tailed tests were used in all analyses with a significance level set to 0.01 to control for multiple testing. All analyses were conducted by using SPSS statistical package, version 21.0 (SPSS, Inc., Chicago, Illinois).

RESULTS

The mean number of screenings per subject is 2.5 (range 1–7). The sample is 65% white and 45% men. Table 1 shows the comparison of main birth outcomes by gender and race.

In minimally-adjusted models, BW is borderline associated with later serum triglycerides and total cholesterol levels (b=−5.0, p=0.03 and b=−3.4, p=0.07, respectively). The results of the full models are presented in Table 2.

Birth weight and insulin resistance

Birth weight is inversely associated with insulin resistance. For every 1 kg increase in BW, HOMA-IR decreases by an average of 2.3 units. Men have lower HOMA-IR levels than women (b=−2.1). Individuals with lower income or higher BMI have higher HOMA-IR levels (b=2.5 and b=2.6, respectively). Individuals with no parental history of CV disease have lower HOMA-IR levels than those with a history of CV disease in both parents (b=−5.1). Never/ex-smokers and non-drinkers have higher HOMA-IR levels than current smokers (b=2.7). Age is inversely associated with HOMA-IR levels (b=−0.5) (Table 2).

Birth weight and serum triglycerides

Birth weight is inversely associated with levels of serum triglycerides. For every 1 kg increase in BW, serum triglycerides decrease by an average of 8.7 mg/dL. Age and BMI are positively associated with triglycerides and (b=1.1 and b=3.8, respectively). Men and Caucasians have higher concentration of triglycerides than women and African Americans (b=4.4 and b=18.8, respectively). Non/ex-smokers have lower triglycerides levels than current smokers (b=−8.2).

Birth weight and total-, LDL-, and HDL-cholesterol

Birth weight is inversely associated with later levels of total cholesterol. For every 1 kg increase in BW, total cholesterol decreases by an average of 5.4 mg/dL. Age and BMI are positively associated with total cholesterol (b=1.0 and b=1.7, respectively). Caucasians have higher levels of total cholesterol than African Americans (b=6.9). BW also is inversely associated with levels of LDL-cholesterol, but at the <0.05 significance level. For every 1 kg increase of BW LDL-cholesterol decreases by an average of 4.6 mg/dL. Age and BMI are positively associated with LDL-cholesterol (b=0.3 and b=1.7, respectively). Men and Caucasians have higher levels of LDL-cholesterol than women and African Americans (b=4.3 and b=11.1, respectively). Individuals with no parental history of CV disease have lower levels of LDL-cholesterol than those with a history of CV disease in both parents (b=−3.2). BW is not independently associated with HDL-cholesterol. Age and BMI are inversely associated with HDL-cholesterol (b=−0.1 and b=−0.5, respectively). Men and Caucasians have lower levels of HDL-cholesterol than women and African Americans (b=−7.6 and b=−6.5, respectively). Non/ex-smokers have higher levels of HDL-cholesterol than current smokers (b=2.7). Categories of alcohol drinking are inversely associated with levels of HDL-cholesterol (b=−10.6 and b=−6.3, respectively).

To assess whether the effect of BW on the outcomes is homogenous across its range, we repeated the analysis in subgroups with BW below and above 3.3 kg (50% percentile) for the three significant outcomes (HOMA-IR, triglycerides and total cholesterol). The coefficients of BW in both subgroups were similar and in the same direction to those obtained from the total sample (HOMA-IR: b=−4.1 and −2.7; triglycerides: b=−14 and −6.7; total cholesterol: b=−2.8 and −5.6, for BW ≤ 3.3 kg and BW > 3.3 kg, respectively, p<0.05 for all).

To assess whether BW interacts with later BMI on cardiometabolic risk profile, the interaction term (BW × BMI) was tested in the full model for all the outcomes. With the exception of HOMA-IR, the interaction was significant in all models (p<0.01 for all). To

evaluate this interaction, the effect of BMI on cardiometabolic risk outcomes was compared between the subgroups of low BW (<2,500 g) vs. normal BW (≥2,500 g). The comparison shows that, with the exception of insulin resistance, the coefficient of BMI is 2–4 times larger in the normal BW group compared to the low BW one (Table 3).

DISCUSSION

In this population, low BW is associated with an adverse metabolic profile later in adulthood that is characterized by higher levels of insulin resistance, triglycerides, and total- and LDL-cholesterol. For each 1 kg (2.2 lb) lower BW, insulin resistance, triglycerides, total- and LDL-cholesterol increased by 2.3 units, 8.7 mg/dL, 5.4 mg/dL and 4.6 mg/dL, respectively. Moreover, comparing the relationship of BW with these outcomes in individuals below and above the 50% percentile of BW (3.3 kg) shows that the effects of BW on later HOMA-IR and triglycerides levels tend to be stronger in the lower BW group, while the opposite is true for total cholesterol. These results agree with findings from other studies which found an inverse association of BW with insulin resistance, [21–23] and with blood lipids. [24–26] These findings emphasize the need for optimum nutrition and medical care during pregnancy.

The finding that BW is inversely associated with insulin resistance later in life agrees with the observed association of low BW with increased risk of type 2 diabetes that is consistently observed in studies in different populations [4,27,28]. Many studies found that the highest risk of increased insulin resistance and diabetes is conveyed by a combination of low BW with an accelerated weight gain early in life (catch up growth). [23,27,29] In this study, BMI was analyzed as a time-variant variable, i.e., the models adjusted for the trajectory of BMI change over time. BMI change significantly predicts later HOMA-IR, but its effect is similar in individuals with low- vs. normal BW (table 3). Therefore, and unlike the case of BW with early weight gain, our data provides no evidence of an interaction between BW and later change in body mass on risk of insulin resistance. In this model, the finding of an inverse association of age with insulin resistance was unexpected. This may be because age-HOMA-IR relation is non-linear. Another possibility is that this could be a chance finding because when the analysis was restricted to individuals older than 25 years of age the findings for all the outcomes remained essentially the same and the coefficient of age on HOMA-IR became positive but statistically insignificant.

The inverse association of BW with serum triglycerides is one of the most consistently reported finding.[13] The finding of a strong inverse association of BW with serum triglycerides levels later in life provides additional evidence of an adverse role of low BW on insulin resistance since increased triglycerides levels is one of the criteria for diagnosing metabolic syndrome. This finding also has important implications for public health, especially in African Americans, given the ease of measuring this risk factor, its association with metabolic syndrome, and its high prevalence, along with low BW, among African Americans. [30,31]

The inverse associations of BW with total- and LDL-cholesterol levels agree with findings from many other studies. [23,32,33] However, the association of BW with later cholesterol levels is also controversial, as several studies reported either a very small or no effect of

BW. [12,13,25] Some studies reported this association in men only. [26,33] Our results, using repeated measurements, support the inverse association between BW and cholesterol levels.

Table 3 shows that the effect of body mass (as BMI) on blood lipids is less pronounced in persons of low BW; that is the influence of body mass in determining adulthood lipids levels is smaller in persons with low BW. One explanation could be that other, low BW-related mechanisms play a role in determining lipids levels in persons born small in size. That is, the heterogeneous effect of body mass on lipid levels between those of low- vs. normal BW indicates that starting lower on the continuum of body size from birth to adulthood involves different mechanisms affecting later lipids levels. This suggests that in persons with low BW interventions targeting body weight may produce smaller improvements in blood lipids than that expected in persons with normal BW, which reemphasizes the role of prenatal growth and, consequently the importance of adequate health care during pregnancy.

In this population, parental history of CV disease independently predicts insulin resistance and total cholesterol in adulthood. The association is inverse and graded, but the difference between one vs. both parents is not significant. The important implication for risk-classification is that individuals born small with a familial history of CV disease have a greater risk of CV disease.

Some authors pointed out the small effect of low BW on metabolic markers of CV disease risk implying little or no clinical significance. [12,13,26] Taken individually, these changes may not be clinically significant. However, these differences are in the population average. Small changes on the population average carry more overall effect than individual differences. Moreover, BW affects many hemodynamic and metabolic markers of CV risk—effects that start early and continue throughout life. [8,9,25,26] The long duration and the combined impact of those multiple risk factors could explain the observed association of low BW with increased CV morbidity and mortality. [7,34]

This study has some limitations: there are no data on early postnatal growth to assess its effect on the study's outcomes, [35] which we found previously in a small sample to be associated with blood pressure [36]; only the last available information on smoking and drinking habits is used to adjust for their effects, which may not reflect the real burden of these factors on the outcomes; the number of persons with low BW is small, which means that the subgroup analysis described in Table 3 must be interpreted with caution. This study has several strengths: an adequate sample size; repeated measures of the outcomes spanning a long period of time; the adjustment for important confounders; the ascertainment of BW from birth certificates, and the use of advanced analytical methods.

CONCLUSIONS

Taken together, these findings provide additional evidence of the role of prenatal factors in predisposing the individual to diabetes and coronary heart disease later in life and, consequently, reemphasize the need for proper prenatal care. Additionally, timely and more intensive preventive programs, that specifically target insulin resistance and blood lipids, are needed in persons born small in size

Acknowledgments

The authors thank the people of Bogalusa, LA, and the staff of the Bogalusa Heart Study for their hard work and dedication.

FUNDING

This work was supported by grants from National Institute of Environmental Health Sciences (grant number ES-021724), and from the National Institute on Aging (grant number AG-16592).

List of Abbreviations

BMI	Body mass index
CV	Cardiovascular
GEE	Generalized estimation equations
HDL-cholesterol	High density lipoprotein cholesterol
HOMA-IR	Homeostasis model assessment insulin resistance
LDL-cholesterol	Low density lipoprotein cholesterol
SES	Socio-economic status

References

1. Lackland DT, Egan BM, Ferguson PL. Low birth weight as a risk factor for hypertension. J Clin Hypertens (Greenwich). 2003; 5(2):133–6. [PubMed: 12671326]
2. Newsome CA, Shiell AW, Fall CH, Phillips DI, Shier R, Law CM. Is birth weight related to later glucose and insulin metabolism?--A systematic review. Diabet Med. 2003; 20(5):339–48. [PubMed: 12752481]
3. Fall CH, Osmond C, Barker DJ, Clark PM, Hales CN, Stirling Y, Meade TW. Fetal and infant growth and cardiovascular risk factors in women. Bmj. 1995; 310(6977):428–32. [PubMed: 7873947]
4. Song Y, Huang Y-T, Song Y, Hevener A, Ryckman K, Qi L, LeBlanc E, Kazlauskaite R, Brennan K, Liu S. Birthweight, mediating biomarkers and the development of type 2 diabetes later in life: a prospective study of multi-ethnic women. Diabetologia. 2015; 58(6):1220–1230. [PubMed: 25567102]
5. Class QA, Rickert ME, Lichtenstein P, D'Onofrio BM. Birth Weight, Physical Morbidity, and Mortality: A Population-based Sibling-Comparison Study. Am J Epidemiol. 2013
6. Risnes KR, Vatten LJ, Baker JL, Jameson K, Sovio U, Kajantie E, Osler M, Morley R, Jokela M, Painter RC, Sundh V, Jacobsen GW, Eriksson JG, Sorensen TI, Bracken MB. Birthweight and mortality in adulthood: a systematic review and meta-analysis. Int J Epidemiol. 2011; 40(3):647–61. [PubMed: 21324938]
7. Lawlor DA, Davey Smith G, Ebrahim S. Birth weight is inversely associated with coronary heart disease in post-menopausal women: findings from the British women's heart and health study. J Epidemiol Community Health. 2004; 58(2):120–5. [PubMed: 14729890]
8. Mzayek F, Sherwin R, Hughes J, Hassig S, Srinivasan S, Chen W, Berenson GS. The association of birth weight with arterial stiffness at mid-adulthood: the Bogalusa Heart Study. J Epidemiol Community Health. 2009; 63(9):729–33. [PubMed: 19429574]
9. Mzayek F, Hassig S, Sherwin R, Hughes J, Chen W, Srinivasan S, Berenson G. The association of birth weight with developmental trends in blood pressure from childhood through mid-adulthood: the Bogalusa Heart study. Am J Epidemiol. 2007; 166(4):413–20. [PubMed: 17525085]

10. Gamborg M, Andersen PK, Baker JL, Budtz-Jorgensen E, Jorgensen T, Jensen G, Sorensen TI. Life course path analysis of birth weight, childhood growth, and adult systolic blood pressure. Am J Epidemiol. 2009; 169(10):1167–78. [PubMed: 19357327]
11. Fagerudd J, Forsblom C, Pettersson-Fernholm K, Saraheimo M, Waden J, Ronnback M, Rosengard-Barlund M, Af Bjorkesten CG, Thorn L, Wessman M, Groop PH. Birth weight is inversely correlated to adult systolic blood pressure and pulse pressure in type 1 diabetes. Hypertension. 2004; 44(6):832–7. [PubMed: 15492128]
12. Huxley R, Owen CG, Whincup PH, Cook DG, Colman S, Collins R. Birth weight and subsequent cholesterol levels: exploration of the “fetal origins” hypothesis. Jama. 2004; 292(22):2755–64. [PubMed: 15585736]
13. Lauren L, Jarvelin MR, Elliott P, Sovio U, Spellman A, McCarthy M, Emmett P, Rogers I, Hartikainen AL, Pouta A, Hardy R, Wadsworth M, Helmsdal G, Olsen S, Bakoula C, Lekea V, Millwood I. Relationship between birthweight and blood lipid concentrations in later life: evidence from the existing literature. Int J Epidemiol. 2003; 32(5):862–76. [PubMed: 14559765]
14. Murtaugh MA, Jacobs DR Jr, Moran A, Steinberger J, Sinaiko AR. Relation of birth weight to fasting insulin, insulin resistance, and body size in adolescence. Diabetes Care. 2003; 26(1):187–92. [PubMed: 12502679]
15. Simental-Mendia LE, Castaneda-Chacon A, Rodriguez-Moran M, Guerrero-Romero F. Birth-weight, insulin levels, and HOMA-IR in newborns at term. BMC Pediatr. 2012; 12:94. [PubMed: 22770114]
16. Byberg L, McKeigue PM, Zethelius B, Lithell HO. Birth weight and the insulin resistance syndrome: association of low birth weight with truncal obesity and raised plasminogen activator inhibitor-1 but not with abdominal obesity or plasma lipid disturbances. Diabetologia. 2000; 43(1): 54–60. [PubMed: 10663216]
17. Stein AD, Conlisk A, Torun B, Schroeder DG, Grajeda R, Martorell R. Cardiovascular disease risk factors are related to adult adiposity but not birth weight in young guatemalan adults. J Nutr. 2002; 132(8):2208–14. [PubMed: 12163664]
18. Cole TJ. Modeling postnatal exposures and their interactions with birth size. J Nutr. 2004; 134(1): 201–4. [PubMed: 14704319]
19. Foster TA, Voors AW, Webber LS, Frerichs RR, Berenson GS. Anthropometric and maturation measurements of children, ages 5 to 14 years, in a biracial community--the Bogalusa Heart Study. Am J Clin Nutr. 1977; 30(4):582–91. [PubMed: 851088]
20. Ikeda Y, Suehiro T, Nakamura T, Kumon Y, Hashimoto K. Clinical significance of the insulin resistance index as assessed by homeostasis model assessment. Endocr J. 2001; 48(1):81–6. [PubMed: 11403106]
21. Lawlor DA, Riddoch CJ, Page AS, Anderssen SA, Froberg K, Harro M, Stansbie D, Smith GD. The association of birthweight and contemporary size with insulin resistance among children from Estonia and Denmark: findings from the European Youth Heart Study. Diabet Med. 2005; 22(7): 921–30. [PubMed: 15975109]
22. Park E. Birth weight was negatively correlated with plasma ghrelin, insulin resistance, and coenzyme Q10 levels in overweight children. Nutr Res Pract. 2010; 4(4):311–6. [PubMed: 20827347]
23. Bavdekar A, Yajnik CS, Fall CH, Bapat S, Pandit AN, Deshpande V, Bhave S, Kellingray SD, Joglekar C. Insulin resistance syndrome in 8-year-old Indian children: small at birth, big at 8 years, or both? Diabetes. 1999; 48(12):2422–9. [PubMed: 10580432]
24. Kuzawa CW, Adair LS. Lipid profiles in adolescent Filipinos: relation to birth weight and maternal energy status during pregnancy. Am J Clin Nutr. 2003; 77(4):960–6. [PubMed: 12663298]
25. Owen CG, Whincup PH, Odoki K, Gilg JA, Cook DG. Birth weight and blood cholesterol level: a study in adolescents and systematic review. Pediatrics. 2003; 111(5 Pt 1):1081–9. [PubMed: 12728092]
26. Skidmore PM, Hardy RJ, Kuh DJ, Langenberg C, Wadsworth ME. Birth weight and lipids in a national birth cohort study. Arterioscler Thromb Vasc Biol. 2004; 24(3):588–94. [PubMed: 14715646]

27. Ruiz-Narvaez EA, Palmer JR, Gerlovin H, Wise LA, Vimalananda VG, Rosenzweig JL, Rosenberg L. Birth weight and risk of type 2 diabetes in the black women's health study: does adult BMI play a mediating role? Diabetes Care. 2014; 37(9):2572–8. [PubMed: 25147255]

28. Whincup PH, Kaye SJ, Owen CG, Huxley R, Cook DG, Anazawa S, Barrett-Connor E, Bhargava SK, Birgisdottir BE, Carlsson S, de Rooij SR, Dyck RF, Eriksson JG, Falkner B, Fall C, Forsen T, Grill V, Gudnason V, Hulman S, Hypponen E, Jeffreys M, Lawlor DA, Leon DA, Minami J, Mishra G, Osmond C, Power C, Rich-Edwards JW, Roseboom TJ, Sachdev HS, Syddall H, Thorsdottir I, Vanhala M, Wadsworth M, Yarbrough DE. Birth weight and risk of type 2 diabetes: a systematic review. Jama. 2008; 300(24):2886–97. [PubMed: 19109117]

29. Fagerberg B, Bondjers L, Nilsson P. Low birth weight in combination with catch-up growth predicts the occurrence of the metabolic syndrome in men at late middle age: the Atherosclerosis and Insulin Resistance study. J Intern Med. 2004; 256(3):254–9. [PubMed: 15324369]

30. Martin, J.; Hamilton, B.; Osterman, M.; Curtin, S.; Mathews, T. National Vital Statistics Reports. Atlanta: CDC; 2013.

31. Miller M, Stone NJ, Ballantyne C, Bittner V, Criqui MH, Ginsberg HN, Goldberg AC, Howard WJ, Jacobson MS, Kris-Etherton PM, Lennie TA, Levi M, Mazzone T, Pennathur S. Triglycerides and cardiovascular disease: a scientific statement from the American Heart Association. Circulation. 2011; 123(20):2292–333. [PubMed: 21502576]

32. Barker DJ, Martyn CN, Osmond C, Hales CN, Fall CH. Growth in utero and serum cholesterol concentrations in adult life. Bmj. 1993; 307(6918):1524–7. [PubMed: 8274921]

33. Ziegler B, Johnsen SP, Thulstrup AM, Engberg M, Lauritzen T, Sorensen HT. Inverse association between birth weight, birth length and serum total cholesterol in adulthood. Scand Cardiovasc J. 2000; 34(6):584–8. [PubMed: 11214012]

34. Koupilova I, Leon DA, McKeigue PM, Lithell HO. Is the effect of low birth weight on cardiovascular mortality mediated through high blood pressure? J Hypertens. 1999; 17(1):19–25. [PubMed: 10100089]

35. Fabricius-Bjerre S, Jensen RB, Faerch K, Larsen T, Molgaard C, Michaelsen KF, Vaag A, Greisen G. Impact of birth weight and early infant weight gain on insulin resistance and associated cardiovascular risk factors in adolescence. PLoS One. 6(6):e20595.

36. Cruickshank JK, Mzayek F, Liu L, Kieltyka L, Sherwin R, Webber LS, Srinavasan SR, Berenson GS. Origins of the "black/white" difference in blood pressure: roles of birth weight, postnatal growth, early blood pressure, and adolescent body size: the Bogalusa heart study. Circulation. 2005; 111(15):1932–7. [PubMed: 15837946]

Table 1

Composition and Birth Characteristics of the Study Population, by Gender and Ethnicity, The Bogalusa Heart Study, 1973–2001

Race/Gender	No.	%[a]	Mean (SD) Birth weight (kg)	Low birth weight (<2500 g)		Premature (<37 week)	
				No.	%[b]	No.	%[b]
Caucasian	1320	65%	3.4 (0.5)	42	3.2%	59	4.5%
Men	601	30%	3.5 (0.5)	14	1.1%	32	2.4%
Women	719	35%	3.4 (0.5)	28	2.2%	27	2.1%
African American	715	35%	3.1 (0.5)	68	9.5%	61	8.5%
Men	315	15%	3.2 (0.5)	27	3.8%	30	4.2%
Women	400	20%	3.1 (0.5)	41	5.7%	31	4.3%
All	2035	100%	3.3 (0.5)	110	5.4%	120	5.9%

[a] = percent of grand total;

[b] = percent within ethnic group

Table 2

Regression of Metabolic Markers of Cardiovascular Risk on Birth Weight, The Bogalusa Heart Study, 1973–2001

Outcome and predictors	Coefficient (*b*)	95% confidence interval
HOMA-IR (n=1313)		
Birth weight (Kg)	−2.3	−3.9, −0.7[b]
Age (years)	−0.5	−0.6, −0.4[b]
BMI (kg/m^2)	2.6	2.4, 2.8[b]
Gender		
Men	−2.1	−3.8, −0.4[a]
Women[d]		
Parental history of CV disease[c]		
None	−5.1	−9.8, −0.5[a]
Both parents[d]		
Smoking		
Never/Ex	2.7	0.8, 4.6[b]
Current[†]		
Income		
<$45,000/year	2.5	0.7, 4.2[b]
≥$45,000/year[d]		
Triglycerides (n=1402)		
Birth weight (kg)	−8.7	−12.4, −4.9[b]
Age (years)	1.1	0.8, 1.3[b]
BMI (kg/m^2)	3.8	3.3, 4.3[b]
Gender		
Men	4.4	0.5, 8.4[a]
Women[d]		
Race		
Caucasian	18.8	15.0, 22.7[b]
African American[d]		
Smoking		
Never/Ex	−8.2	−12.4, −4.1[b]
Current[†]		
Total cholesterol (n=1915)		
Birth Weight (kg)	−5.4	−9.1, −1.8[b]
Age (years)	1.0	0.8, 1.1[b]
BMI (kg/m^2)	1.7	1.5, 2.0[b]
Race		

Outcome and predictors	Coefficient (*b*)	95% confidence interval
Caucasian	6.9	3.2, 10.6[a]
African American[d]		
LDL-cholesterol (n=1346)		
Birth weight (kg)	−4.6	−8.2, −0.9[a]
Age (years)	0.3	0.2, 0.5[b]
BMI (kg/m^2)	1.7	1.4, 1.9[b]
Gender		
Men	4.3	1.0, 7.6[a]
Women[d]		
Race		
Caucasian	11.1	7.5, 14.8[b]
African American[d]		
Parental history of CV disease[c]		
None	−3.2	−9.0, 2.7[a]
Both parents[d]		
HDL-cholesterol (n=1769)		
Birth weight (kg)	0.2	−0.8, 1.3
Age (years)	−0.1	−0.2, −0.0[a]
BMI (kg/m^2)	−0.5	−0.6, −0.4[b]
Gender		
Men	−7.6	−8.6, −6.7[b]
Women[d]		
Race		
Caucasian	−6.5	−7.9, −5.2[b]
African American[d]		
Smoking		
Never/ex	2.7	1.7, 3.7[b]
Current[d]		
Drinking		
None <1 drink/week	−10.6	−13.9, −7.2[b]
2–4 drinks/week	−6.3	−10.0, −2.5[b]
>4 drinks/week[d]		

BMI = body mass index; CI = confidence interval; HDL-cholesterol = High density lipoprotein cholesterol; HOMA-IR = homeostasis model assessment insulin resistance; LDL-cholesterol = Low density lipoprotein cholesterol.

[a] $p<0.05$,

[b] $p<0.01$,

[c] = p-value is for the trend,

[d] = reference category.

Models are adjusted for age, BMI, gender, race, income, smoking status, alcohol drinking and parental history of CV disease. The differences in the actual numbers included in each model are due to missing values on covariates

Table 3

Comparison of the Association of BMI on Metabolic Markers of Cardiovascular Risk in Persons with Low vs. Normal Birth Weight, The Bogalusa Heart Study, 1973–2001

Outcome	Coefficient of BMI (95% CI)[a]	
	<2,500 g	≥2,500 g
HOMA-IR	2.7 (1.2, 4.1)	2.6 (2.4, 2.8)
Triglycerides (mg/dL)	2.3 (0.3, 2.9)	4.1 (3.5, 4.5)
Total cholesterol (mg/dL)	0.8 (0.0, 1.8)	1.8 (1.5, 2.0)
LDL-cholesterol (mg/dL)	0.6 (−0.1, 1.3)	1.7 (1.4, 1.9)
HDL-cholesterol (mg/dL)	−0.1 (−0.4, 1.7)	−0.5 (−0.6, −0.4)

BMI = body mass index; CI = confidence interval; HDL-cholesterol = High density lipoprotein cholesterol; HOMA-IR = homeostasis model assessment insulin resistance; LDL-cholesterol = Low density lipoprotein cholesterol.

[a] = Adjusted for age, gender and race