Pajer KA, et al., J Neonatol Clin Pediatr 2019, 6: 035
DOI: 10.24966/NCP-878X/100035

HSOA Journal of Neonatology and Clinical Pediatrics

Research Article

Different Birth Size Measures are Not Equivalent in Predicting Health Outcomes in Young Women

Kathleen A Pajer[1]*, Pamela J Salsberry[2], William Gardner[3], Patricia B Reagan[4], Muriel Z Fang[5] and Lisa Currie[3]

[1]*University of Ottawa, Department of Psychiatry, Ottawa, Ontario, Canada*

[2]*The Ohio State University, College of Public Health, Columbus, Ohio, USA*

[3]*University of Ottawa, School of Epidemiology and Public Health, Ottawa, Ontario, Canada*

[4]*The Ohio State University, Department of Economics, Columbus, Ohio, USA*

[5]*Freddie Mac. Mclean, Virginia, USA*

Abstract

Objectives

A variety of birth size measures are used in studies investigating the Developmental Origins of Disease and Health (DOHaD) hypothesis. Maternal-fetal medicine research has demonstrated that different birth size measures do not signal the same information about intrauterine growth and development. On this basis, we predict that differences between birth size measures across studies and even within studies will lead to different outcomes, but this question has been inadequately studied. The objective of this study was to investigate whether using different birth size measures can affect relationships between birth size and young adult health outcomes.

Methods

Using a U.S. population sample of 2921 white and African-American females, we tested two hypotheses: 1) different birth size measures will not have the same associations with age at menarche, young adult height, and young adult weight and 2) different categorical birth size measures will not classify the same infants.

Results

Different birth size measures had different strengths of associations with the three health outcomes and the categorical birth size measures identified different infants.

Conclusion

We demonstrate that the choice of birth size measures does affect the predictive relationship between birth size and young adult health outcomes. Moreover, if data from multiple studies with different birth size measures are synthesized (as in a review), it is likely that the data are describing different infants and this may compromise the conclusions that can be drawn. Implications of our findings for DOHaD research are discussed.

Keywords: Birth weight; Body height; Body mass index; Female; Gestational age; Menarche

***Corresponding author:** Kathleen A Pajer, University of Ottawa, Department of Psychiatry, Ottawa, Ontario, Canada Tel: +1 6137377600 X 2723; E-mail: kpajer@cheo.on.ca

Citation: Pajer KA, Salsberry PJ, Gardner W, Reagan PB, Fang MZ, et al. (2019) Different Birth Size Measures are Not Equivalent in Predicting Health Outcomes in Young Women. J Neonatol Clin Pediatr 6: 035.

Received: July 24, 2019; **Accepted:** August 03, 2019; **Published:** August 12, 2019

Copyright: © 2019 Pajer KA, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Introduction

Numerous studies demonstrate a relationship between small birth size and chronic illness in adulthood, e.g. atherosclerotic disease, stroke, hypertension [1], psychopathology [2], and cancer [3]. This relationship is known as the Developmental Origins of Health and Disease hypothesis (DOHaD). In addition to such long-term outcomes, intermediate outcomes on the trajectory to adult disorders exist. Girls who are small at birth reach menarche at a younger age [4-7], are shorter as young adults [8-12], and have more central adiposity in early adulthood [13,14]. These young adult health outcomes are, in turn, associated with an increased risk of adult CVD and breast cancer [15-17].

Although there is support for the DOHaD hypothesis, gaps in our knowledge remain. Many studies have replicated the original findings [18-22], but some have not [23-28]. Using different birth size measures may explain some of the divergence in results. In empirical studies different measures can lead to inconsistent associations between birth size and health outcomes. In reviews, treating all birth size definitions as if they are equivalent markers for IUGR, the hypothesized mechanism for DOHaD, could lead to misclassification errors and misinterpretation of results [29-31]. Unfortunately, the choice of a birth size measure in many epidemiologic studies is not justified with regards to the hypothesized physiological mechanisms and the problem is exacerbated when researchers develop idiosyncratic birth size measures that may have no pathophysiologic relevance to small birth size. Surprisingly, this methodological issue is not well-discussed in the field. For example, an excellent review about methodological limitations in testing the DOHaD hypothesis does not address birth size definitions [32].

The purpose of this study was to use a cohort of girls followed from birth to young adulthood to investigate whether using different birth size measures would affect the relationship between birth size and young adult health outcomes. We tested two hypotheses: 1) different birth size measures will not have the same associations with age at menarche, young adult height and young adult weight and 2) different categorical birth size measures will not classify the same infants.

Materials and Methods

Materials

We used data from the U.S. based National Longitudinal Survey of Youth, 1979 Children and Young Adult Surveys (NLSY79). The NLSY79 enrolled a nationally representative sample of young people living in the U.S. in December 1978, born between 1957 and 1964. Extensive data on these respondents have been collected annually through 1994 and biennially thereafter. Data on biological children born to the women have been collected biennially beginning 1986.

The primary sample inclusion criterion for this study was a daughter born to an African-American or non-Hispanic white woman (hereafter referred to as white) in the NLSY79 before 1993. We focused our study on females because there are sex differences in DOHaD hypothesis outcomes [33-34], the age of menarche is easier to detect than age at spermarche, the age of menarche has been associated with adult chronic disease [35], and age of menarche is associated with small birth size [4-7].

The eligible sample consisted of 2921 girls (white n=1626; African-American n=1295) born to 2035 mothers (white n=1177; African-American n=858). Birth weight, birth length, and gestational age were required for all analyses; 473 girls (16.2% of the sample) were excluded for missing at least one of these measures. Two girls were removed from the sample because they had biologically implausible high birth weights for very short birth lengths. Additionally, some subjects were lost because of missing data in the young adult outcomes. The final sample for analysis of menarche was 2207 (75.6% of eligible sample), for young adult height 2155 (73.8% of eligible sample), and young adult weight 2114 (72.4% of eligible sample). The study sample contained more whites and was slightly better educated than the eligible sample.

Birth size indexes

After extensively reviewing the literature, we selected for comparison the eight most commonly used birth size measures in DOHaD research (Table 1). A birth size measure was included if it had been used in at least two studies. Birth weight, length and gestational age were reported by mothers in the first weeks after delivery. Length and gestational age alone are not used in DOHaD studies, so in this study, they are only included as part of some of the calculated measures. Note that the birth weight percentile, adjusted for GA in female births is based on the work of Oken, et al., [36].

Outcome variables

Three outcome variables were studied: age at menarche, height and weight between the ages of 17-24 years. Age of menarche for participants was first collected from mothers when girls were 8-13 years old. When girls turned 14 years, they were directly asked as a validation process and if they had not experienced menarche, they continued to be asked until they had reached this developmental milestone. Each girl's year and month of birth were used to determine their age of menarche in months, which was then converted to years. Self-reported height was recorded in inches and self-reported weight recorded in pounds when participants were between 17 and 24 years old and post menarche.

Other key variables

Many DOHaD studies have used samples homogenous with regards to race, but race can affect the relationship between birth size and adult health. This is particularly salient in light of well-described differences in African-American and white birth weights, average GA, and birth lengths [37]. African-American and white developmental and somatic differences are significant throughout the hypothesized trajectories for the development of adult disorders: at birth, in adolescence and young adulthood, and in mid-late adulthood [38].

Therefore, we used race as a covariate. Daughters were assigned the race designated by their mothers. These data have been validated in a sub-study that asked the daughters to self-describe their racial/ethnic status and parent and child self-reported race were found to agree.

Data Analysis

To test our first hypothesis, we standardized young adult outcomes and birth size measures. Measures were standardized to a z metric, where z = (y-M)/SD where M and SD are the sample mean and standard deviation. Z scores allowed us to compare the sizes of the associations between birth size indexes and outcomes in the same metrics. We calculated the regressions of each intermediate outcome (age of menarche, young adult height and weight) on each birth size measure listed in table 1, using race as a covariate. We also ran regressions for each outcome/birth size measure combination that included a race by birth size measure interaction. Only one interaction was statistically significant across the twelve regressions, so interactions were not pursued further.

Continuous Variables	
Variable	Definition
Birth weight	Mother reported in pounds and ounces during first interview following the birth; converted to grams
Birth weight percentile, adjusted for gestational age	Weight adjusted for gestational age
Weight/length ratio	Ratio of weight (in grams) to length (meters) as reported above.
Ponderal Index	Relationship between birth weight and birth length: birth weight (kg)/length $(m)^3$
Binary Variables	
Low birth weight	< 2500 grams
Small for Gestational Age (SGA)	Cut-off is $<10^{th}$ percentile based on population curves
Low weight/length ratio	Cut-off is $<10^{th}$ percentile based upon the NLSY study sample distribution
Low Ponderal Index	$<10^{th}$ percentile; percentile determined based on the NLSY study sample distribution

Table 1: Definition of birth size measures.

Our hypothesis was tested by examining the overlap between the four groupings of infants defined by accepted cut points on the four measures of birth size. We analyzed the overlap in two ways. First, for each birth size measure A, we calculated the conditional probability that a baby who was small as defined by A would also be small as defined by an alternative measure B. Second, for each pair of definitions, we calculated the two-by-two table for small vs. not-small according to both definitions. Phi coefficients were calculated. The phi coefficient is the equivalent of a Pearson or coefficient for binary variables. It takes the value 1.0 for perfect agreement between the two variables and the value 0 for chance agreement.

Analyses were performed using R Version 2.15.3 (http://www.r-project.org/). Regressions were calculated using the LME function in the package NLME. All regressions and mean comparisons included random intercepts for mothers to account for siblings in the sample.

Results

Sample descriptive statistics

Table 2 displays the means and standard deviations for the three young adult health outcomes, the continuous birth indexes, and the proportions for the binary variables for birth size. The first and second columns of data show results for whites and African-Americans. The third column presents the data from the whole sample and the fourth displays the p values for the comparison between whites and African-Americans.

As young adults, African-American girls reached menarche earlier, were shorter, and were heavier. African-American infants, however, were lighter and leaner (lower weight/length) than white infants. But they also had larger ponderal indexes (higher weight/length^3). These race differences were in every case highly statistically significant. Therefore, all subsequent analyses include race as a covariate.

Prediction of young adult outcomes by different birth size measures

The results from the series of regressions used to answer this question are summarized in Table 3. This table reports the standardized regression coefficients for the relationships between the birth size measures (continuous and binary) and the young adult outcomes. Because the regression coefficients are standardized, for each young adult outcome we can compare the magnitudes of the effects of different birth size measures.

PI has no consistent relationship with the young adult outcomes: it is statistically significant in only one of 6 regressions and the sign of the coefficient varies. This is substantially different from the pattern of the other birth size variables and we will discuss the latter separately.

The associations between the other three birth size variables: birth weight, birth weight adjusted for gestational age, and weight/length, and the young adult outcomes are consistently positive period that is, smaller babies were shorter and lighter as adults and reached menarche at a younger age. However, the size of the associations among the continuous versions of the birth size variables were on average about 2.5 times larger than the binary versions. Moreover, whereas the continuous versions were always statistically significant, for the binary versions only five of the eight birth size/adult outcome associations were significant.

The strength of association between birth size measures and young adult outcome also varied depending on the outcome. Adult height was most strongly predicted by the birth size variables, followed by adult weight, while age at menarche was the least strongly predicted. For example, being a standard deviation heavier at birth was associated with being a slight 0.05 of a standard deviation older at menarche, compared to being about 0.20 of a standard deviation taller.

Finally, Table 3 shows that for any given adult outcome, there was variation in the strength of association as a function of which birth size variable is used. However, there is no consistent pattern indicating whether one birth size measures best predicts *all* the young adult outcomes.

Different birth size measures to identify groups of infants

We next examined whether the categorical birth size measures would identify the same groups of infants. If so, cross-classification in 2×2 tables should reveal high agreement.

Variable	White Girls (N=1475)	African-American Girls (N=971)	All Girls (N=2446)	p
Young adult outcomes: Mean (SD)				
Age at menarche (mo)	150.2 (14.7)	143.6 (16.3)	147.5 (15.7)	<.0001
Height (cm)	165.2 (7.1)	163.9 (7.4)	164.7 (7.3)	<.0001
Weight (kg)	63.0 (13.5)	68.5 (17.0)	65.3 (15.2)	<.0001
Birth size measures: Mean (SD)				
Birth weight (g)	3339.6 (537.4)	3101.7 (593.3)	3245.2 (572.1)	<.0001
Birth weight for gestational age (%)	53.5 (28.8)	40.4 (29.0)	48.3 (29.6)	<.0001
Birth weight (g)/Birth length (m)	6550.1 (927.3)	6305.9 (1227.3)	6453.1 (1063.1)	<.0001
Ponderal index	25.6 (6.0)	27.5 (14.6)	26.3 (10.3)	<.0001
Binary birth size measures: % Small birth size				
Low birth weight	6.3	13.2	9	<.0001
Low birth weight corrected for gestational age	7.9	18.1	11.9	<.0001
Low birth weight/Birth length	7.8	13.5	10.1	<.0001
Low ponderal index	7.9	13.6	10.1	<.0001

Table 2: Young adult outcomes and birth size measure by participant race: means and standard deviations.

Predictors	Young Adult Outcomes					
	Age at Menarche, N=2207		Height, N=2155		Weight, N=2114	
	Binary	Continuous	Binary	Continuous	Binary	Continuous
Birth weight regressions						
Birth weight	0.016	0.052***	0.092***	0.204***	0.022	0.103**
Birth weight for gestational age (%) regressions						
Birth weight for gestational age (%)	0.039**	0.043***	0.086***	0.237***	0.074*	0.133***
Birth weight/Birth length regressions						
Birth weight/Birth length	0.028	0.055***	0.050**	0.117***	0.034	0.078**
Ponderal index regressions						
Ponderal index	0.037*	-0.016	0.029	-0.032	0.017	0.012
Note: Analyses are clustered by mothers to account for multiple siblings. '*'=p<0.05, '**'=p<0.01, and '***'=p<0.001.						

Table 3: Standardized coefficients for the regression of young adult outcomes on birth size using z-Transformed scores with race as a covariate.

We calculated the probability of an infant being in one group, given that the baby was in another group. We also analyzed the agreement between how the binary variables categorized infants.

The results are displayed in Table 4. Part A of the table shows that the probability of being in the "small" category of each of the indexes, given that that an infant was classified as "small" on another one. The conditional probabilities are all relatively low. Part B shows that agreement in categorizing infants is also poor, with the exception of a phi = 0.73 between infants in the low birth weight group and those in the low birth weight/length ratio group.

Discussion

Variability in birth size measures can be an important challenge in DOHaD research, but is not well-studied. The goals of our study were to determine whether the eight most commonly used research birth size measures equivalently predicted three young adult female health outcomes and whether commonly used categorical birth size measures identified the same girls in their infancies.

We demonstrated three findings of importance to DOHaD researchers. First, the birth size measure used does have an effect on the strength of the association between birth size and young adult health outcomes, which is what we would expect from maternal-fetal medicine research indicating that they are markers of different intrauterine problems. This means that a researcher needs to carefully consider which definition of birth size he or she is going to use for which health outcome. For example, PI may show no relationship with an adult health outcome, but birth size used as a continuous measure may reveal a strong association.

Second, the outcome variable used also matters. Different birth size measures predicted different health outcomes and there was no single birth size definition that predicted all health outcomes. Third, the most commonly used categorical definitions of small birth size classified babies differently. This is particularly important in cross-study syntheses of data (reviews) because the studies reviewed may not be investigating the same infants. This problem can seriously undermine the validity of the conclusion drawn from such reviews this is not a problem that can be detected using the Strengthening the Reporting of Observational Studies in *Epidemiology* (STROBE) methodology for reviews.

What are possible explanations for our findings? The simplest is that although these definitions are assumed to measure the latent variable of IUGR, they are not all doing so. Simple birth weight or length does not necessarily indicate IUGR [39], particularly for late pregnancy growth restriction, as it will result in asymmetrical smallness. SGA and IUGR are often used synonymously, but they are not interchangeable. The category of SGA includes infants who have suffered IUGR, but it also includes neonates who are constitutionally small and there is no way to differentiate between the two. SGA also cannot differentiate between infants suffering IUGR early in pregnancy from those with late onset IUGR.

Because low birth weight, even adjusted for gestational age, may not be a good proxy for IUGR, clinical researchers have looked instead for an index of body composition [40]. Measures that quantify the relationship between soft tissue mass and skeletal growth have been demonstrated to be better proxies for IUGR, e.g. weight/length ratio [41] and the PI [42]. Resnik and Creasy state that PI is the most valid measure of IUGR in term infants [43]. This is of particular importance to DOHaD researchers who often restrict their samples to neonates delivered at term. The distribution of PI has also been found to be similar across races and genders [44].

However, others have disputed this claim, showing that PI does not correlate as highly with triceps skin folds (a standard indicator of fat distribution and thus, intrauterine nutrition) as does weight/length ratio [45].

PI may also help determine the timing of exposure to adverse intrauterine conditions causing IUGR [46]. This was confirmed in a study of serial ultrasound examinations compared with neonatal anthropometric measurements. Decreased birth weight and decreased PI signaled third trimester IUGR. First trimester IUGR produced neonates who had the highest birth weights and PI of the entire IUGR group [39].

These clinical data make it clear that recognizing IUGR is difficult and not only depends on size and timing of birth, but body composition. This highlights the importance of how to use and interpret results from the use of various birth size measures. DOHaD research could be improved by incorporating clinical knowledge into how birth size is defined. Sub-grouping infants in a population study using different measures sequentially could shed more light on epidemiologic studies investigating possible mechanisms.

	Low Birth Weight	Low Birth Weight Corrected For Gestational Age	Low Birth Weight/Birth Length	Low Ponderal Index
Low birth weight	100	61.1	79.6	29
Low birth weight corrected for gestational age	46.2	100	48.6	27.4
Low birth weight/Birth length	71.5	57.7	100	46.3
Low ponderal index	25.8	32.3	46	100

Part A: Probability (%) of low birth size as defined by column, conditional on small birth size as defined by row.

	Low Birth Weight	Low Birth Weight Corrected For Gestational Age	Low Birth Weight/Birth Length	Low Ponderal Index
Low birth weight	1	0.48	0.73	0.2
Low birth weight corrected for gestational age	0.48	1	0.47	0.21
Low birth weight/Birth length	0.73	0.47	1	0.4
Low ponderal index	0.2	0.21	0.4	1

Part B: Phi coefficients for agreement between row and column definitions of small birth size.

Table 4: Identifying the same neonates: Agreement among birth size measures.

For example, first identifying infants who are SGA and then measuring the PI within that group may give investigators a more valid sub-group of IUGR infants.

The second explanation for our findings is that the association between birth size and health outcomes may be differentially mediated or moderated by factors such as postnatal growth rate, childhood stress, or genotype. Epidemiologic studies often don't control for these variables. Bollen and colleagues have proposed an innovative statistical solution using structural equation modeling to partially compensate for the myriad errors associated with using birth size measures, as well the influence of postnatal factors [47].

Although our primary study goal was to compare the effects of different birth size measures on health outcomes, there were some interesting substantive results. Simple (unadjusted) weight/length was the strongest predictor of age of menarche, although every continuous index had a significant positive correlation with this outcome. The binary variable of SGA, previously reported in Reagan, et al., [6] predicted younger age at menarche, a finding similar to that of Morris, et al., [48]. Low PI also predicted young age at menarche.

Continuous birth weight for gestational age was the strongest predictor of young adult height. However, every other variable except PI was also significantly correlated with height. Other researchers in DOHaD studies of young adult stature in females have reported that birth weight and length were positively correlated with later stature [8,11].

Birth size was positively associated with weight in young adulthood and the continuous variable of weight for gestational age was the strongest predictor. The direction of this association perhaps appears to contradict the DOHaD hypothesis, but our findings are similar to the results reported by Labayen, et al., when they focused the relationship between birth weight and late adolescent weight [13]. When they further investigated birth weight and later body composition, e.g., fat distribution, they discovered that birth weight was inversely associated with anthropometric markers of central adiposity. Similarly, Breukhoven and colleagues did not find a negative correlation between small sizes at birth or prematurity and young adult weight, but with Dual Energy X-ray Absorptiometry (DEXA) scanning, were able to detect higher central fat mass in the participants who had been preterm and smaller [14].

There were limitations in our goal to investigate the effects of different birth size measures in DOHaD research. The most significant is that we were not studying the typical adult outcomes of cardiovascular disease, hypertension, stroke, or diabetes. It is possible that different birth size measures would have had uniform associations with these adult outcomes, although we think this is doubtful. Second, birth size data and outcome data were self-reported. We cannot determine in what directions this may have influenced our results. Finally, we did not study males and therefore cannot generalize our results to them.

The gold standard for defining IUGR is direct serial measurements of fetal development *in utero*. However, these methods are difficult and expensive to do on a population basis, so we expect that many researchers will continue to use anthropomorphic data standardly available at delivery to investigate the DOHaD hypothesis. Our findings suggest that researchers should choose birth size measures depending on their hypotheses. Sequential categorization of infants may best define a valid group of IUGR infants or the use of structural equation modeling as described by Bollen may help mitigate experimental error in using birth size measures. Those researchers doing a systematic or meta-analytic review of the literature should not synthesize data across different birth size measures as such studies are likely not investigating the same infants. Instead, data should be analyzed in subgroups by the birth size measure used.

Ethics: The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national guidelines on human experimentation (NIH) and with the Helsinki Declaration of 1975, as revised in 2008, and has been approved by the Institutional Review Board at The Ohio State University.

Acknowledgement

Financial support: This work was supported by a grant from the U.S. National Institutes of Health (NIH): NR009384, Salsberry and Reagan, Co-PIs.

Conflicts of Interest

All authors have no conflicts of interest to disclose.

References

1. Barker DJ, Thornburg KL (2013) The obstetric origins of health for a lifetime. Clin Obstet Gynecol 56: 511-519.
2. Roseboom TJ, Painter RC, van Abeelen AF, Veenendaal MV, de Rooij SR (2011) Hungry in the womb: what are the consequences? Lessons from the Dutch famine. Maturitas 70:141-145.
3. Silva Idos S, De Stavola B, McCormack V, Collaborative Group on PreNatal Risk Factors and Subsequent Risk of Breast Cancer (2008) Birth size and breast cancer risk: Re-analysis of individual participant data from 32 studies. PLoS Med 5: 193.
4. Opdahl S, Nilsen TI, Romundstad PR, Vanky E, Carlsen SM, et al. (2008) Association of size at birth with adolescent hormone levels, body size and age at menarche: Relevance for breast cancer risk. Br J Cancer 99: 201-206.
5. Romundstad PR, Vatten LJ, Nilsen TI, Holmen TL, Hsieh CC, et al. (2003) Birth size in relation to age at menarche and adolescent body size: implications for breast cancer risk. Int J Cancer 105: 400-403.
6. Reagan PB, Salsberry PJ, Fang MZ, Gardner WP, Pajer K (2012) African-American/white differences in the age of menarche: Accounting for the difference. Soc Sci Med 75:1263-1270.
7. Sloboda DM, Hart R, Doherty DA, Pennell CE, Hickey M (2007) Age at menarche: Influences of prenatal and postnatal growth. J Clin Endocrinol Metab 92: 46-50.
8. Pietilainen KH, Kaprio J, Rasanen M, Winter T, Rissanen A, et al. (2001) Tracking of body size from birth to late adolescence: Contributions of birth length, birth weight, duration of gestation, parents' body size, and twinship. Am J Epidemiol 154: 21-29.
9. Euser AM, Finken MJ, Keijzer-Veen MG, Hille ET, Wit JM, et al. (2005) Associations between prenatal and infancy weight gain and BMI, fat mass, and fat distribution in young adulthood: A prospective cohort study in males and females born very preterm. Am J Clin Nutr 81: 480-487.
10. Loos RJ, Fagard R, Beunen G, Derom C, Vlietinck R (2001) Birth weight and blood pressure in young adults: A prospective twin study. Circulation 104: 1633-1638.
11. Loos RJ, Beunen G, Fagard R, Derom C, Vlietinck R (2002) Birth weight and body composition in young women: A prospective twin study. Am J Clin Nutr 75: 676-682.
12. Gigante DP, Horta BL, Lima RC, Barros FC, Victora CG (2006) Early life factors are determinants of female height at age 19 years in a population-based birth cohort (Pelotas, Brazil). J Nutr1 36: 473-478.
13. Labayen I, Moreno LA, Ruiz JR, Gonzalez-Gross M, Warnberg J, et al. (2008) Small birth weight and later body composition and fat distribution in adolescents: The Avena study. Obesity 16: 1680-1686.
14. Breukhoven PE, Kerkhof GF, Willemsen RH, Hokken-Koelega AC (2012) Fat mass and lipid profile in young adults born preterm. J Clin Endocrinol Metab 97: 1294-1302.
15. Canoy D, Beral V, Balkwill A, Wright FL, Kroll ME, et al. (2015) Age at menarche and risks of coronary heart and other vascular diseases in a large UK cohort. Circulation 131: 237-244.
16. Paajanen TA, Oksala NK, Kuukasjarvi P, Karhunen PJ (2010) Short stature is associated with coronary heart disease: A systematic review of the literature and a meta-analysis. Eur Heart J 31: 1802-1809.
17. Stevens J, Truesdale KP, Wang CH, Cai J, Erber E (2012) Body mass index at age 25 and all-cause mortality in whites and African Americans: The Atherosclerosis Risk in Communities study. J Adolesc Health 50: 221-227.
18. Barker DJ (1998) *In utero* programming of chronic disease. Clin Sci (Lond) 95: 115-128.
19. Gluckman PD, Cutfield W, Hofman P, Hanson MA (2005) The fetal, neonatal, and infant environments-the long-term consequences for disease risk. Early Hum Dev 81: 51-59.
20. Gluckman PD, Hanson MA (2004) Living with the past: Evolution, development, and patterns of disease. Science 305: 1733-1736.
21. Rich-Edwards JW, Stampfer MJ, Manson JE, Rosner B, Hankinson SE, et al. (1997) Birth weight and risk of cardiovascular disease in a cohort of women followed up since 1976. BMJ 315: 396-400.
22. Barker DJ (1991) The intrauterine origins of cardiovascular and obstructive lung disease in adult life. The Marc Daniels Lecture 1990. J R Coll Physicians Lond 25: 129-133.
23. Tu YK, West R, Ellison GT, Gilthorpe MS (2005) Why evidence for the fetal origins of adult disease might be a statistical artifact: The "reversal paradox" for the relation between birth weight and blood pressure in later life. Am J Epidemiol 161: 27-32.
24. Schluchter MD (2003) Publication bias and heterogeneity in the relationship between systolic blood pressure, birth weight, and catch-up growth--a meta analysis. J Hypertens 21: 273-279.
25. Huxley R, Neil A, Collins R (2002) Unravelling the fetal origins hypothesis: Is there really an inverse association between birthweight and subsequent blood pressure? Lancet 360: 659-665.
26. Stein AD, Conlisk A, Torun B, Schroeder DG, Grajeda R, et al (2002) Cardiovascular disease risk factors are related to adult adiposity but not birth weight in young Guatemalan adults. J Nutr 132: 2208-2214.
27. Osler M, Lund R, Kriegbaum M, Andersen AM (2009) The influence of birth weight and body mass in early adulthood on early coronary heart disease risk among Danish men born in 1953. Eur J Epidemiol 24: 57-61.
28. Whincup PH, Kaye SJ, Owen CG, Huxley R, Cook DG, et al. (2008) Birth weight and risk of type 2 diabetes: A systematic review. JAMA 300: 2886-2897.
29. von Bonsdorff ME, von Bonsdorff MB, Martikainen J, Salonen M, Kajantie E, et al. (2017) Body size at birth and coronary heart disease-related hospital care in adult men - findings from the Helsinki Birth Cohort Study. Ann Med 49: 126-133.
30. Andersen LG, Angquist L, Eriksson JG, Forsen T, Gamborg M, et al. (2010) Birth weight, childhood body mass index and risk of coronary heart disease in adults: Combined historical cohort studies. PloS One 5: 14126.
31. Hoffman DJ, Reynolds RM, Hardy DB (2017) Developmental origins of health and disease: Current knowledge and potential mechanisms. Nutr Rev 75: 951-970.
32. Sharma D, Shastri S, Farahbakhsh N, Sharma P (2016) Intrauterine growth restriction - part 1. J Matern Fetal Neonatal Med 29: 3977-3987.
33. Sharma D, Farahbakhsh N, Shastri S, Sharma P (2016) Intrauterine growth restriction - part 2. J Matern Fetal Neonatal Med 29: 4037-4048.
34. Figueras F, Gratacos E (2014) Update on the diagnosis and classification of fetal growth restriction and proposal of a stage-based management protocol. Fetal Diagn Ther 36: 86-98.
35. Gage SH, Munafo MR, Davey Smith G (2016) Causal inference in developmental origins of health and disease (DOHaD) research. Annu Rev Psychol 67: 567-585.
36. Ojeda NB, Intapad S, Alexander BT (2014) Sex differences in the developmental programming of hypertension. Acta Physiol 210: 307-316.
37. Intapad S, Ojeda NB, Dasinger JH, Alexander BT (2014) Sex differences in the developmental origins of cardiovascular disease. Physiology 29: 122-132.

38. Mueller NT, Duncan BB, Barreto SM, Chor D, Bessel M, et al (2014) Earlier age at menarche is associated with higher diabetes risk and cardiometabolic disease risk factors in Brazilian adults: Brazilian Longitudinal Study of Adult Health. Cardiovasc Diabetol 13: 22.

39. Oken E, Kleinman KP, Rich-Edwards J, Gillman MW (2003) A nearly continuous measure of birth weight for gestational age using a United States national reference. BMC Pediatr 3: 6.

40. Bryant AS, Worjoloh A, Caughey AB, Washington AE (2010) Racial/ethnic disparities in obstetric outcomes and care: Prevalence and determinants. Am J Obstet Gynecol 202: 335-343.

41. Kuzawa CW, Sweet E (2009) Epigenetics and the embodiment of race: Developmental origins of US racial disparities in cardiovascular health. Am J Hum Biol 21: 2-15.

42. Hemachandra AH, Klebanoff MA (2006) Use of serial ultrasound to identify periods of fetal growth restriction in relation to neonatal anthropometry. Am J Hum Biol 18: 791-797.

43. Barker DJ (2000) *In utero* programming of cardiovascular disease. Theriogenology 53: 555-574.

44. Fok TF, Hon KL, Ng PC, Wong E, So HK, et al. (2009) Use of anthropometric indices to reveal nutritional status: Normative data from 10,226 Chinese neonates. Neonatology 95: 23-32.

45. Khoury MJ, Berg CJ, Calle EE (1990) The ponderal index in term newborn siblings. Am J Epidemiol 132: 576-583.

46. Resnik R, Creasy RK (2010) Intrauterine growth restriction. In: Robert K Creasy, Robert Resnik, Jay D Iams, Charles J Lockwood, Thomas R Moore, Michael F Greene (eds.). Maternal-Fetal Medicine (6th edn). Elsevier, Philadelphia, USA.

47. Dombrowski MP, Berry SM, Johnson MP, Saleh AA, Sokol RJ (1994) Birth weight-length ratios, ponderal indexes, placental weights, and birth weight-placenta ratios in a large population. Arch Pediatr Adolesc Med 148: 5085-12.

48. Braga TD, Lima Mde C (2002) Weight/length ratio: Is it a good index to assess the nutritional status of full-term newborns? J Pediatr 78: 219-224.

49. Landmann E, Reiss I, Misselwitz B, Gortner L (2006) Ponderal index for discrimination between symmetric and asymmetric growth restriction: Percentiles for neonates from 30 weeks to 43 weeks of gestation. J Matern Fetal Neonatal Med 19: 157-160.

50. Bollen KA, Noble MD, Adair LS (2013) Are gestational age, birth weight, and birth length indicators of favorable fetal growth conditions? A structural equation analysis of Filipino infants. Stat Med 32: 2950-2961.

51. Morris DH, Jones ME, Schoemaker MJ, Ashworth A, Swerdlow AJ (2010) Determinants of age at menarche in the UK: Analyses from the Breakthrough Generations Study. Br J Cancer 103: 1760-1764.

Journal of Anesthesia & Clinical Care

Journal of Addiction & Addictive Disorders

Advances in Microbiology Research

Advances in Industrial Biotechnology

Journal of Agronomy & Agricultural Science

Journal of AIDS Clinical Research & STDs

Journal of Alcoholism, Drug Abuse & Substance Dependence

Journal of Allergy Disorders & Therapy

Journal of Alternative, Complementary & Integrative Medicine

Journal of Alzheimer's & Neurodegenerative Diseases

Journal of Angiology & Vascular Surgery

Journal of Animal Research & Veterinary Science

Archives of Zoological Studies

Archives of Urology

Journal of Atmospheric & Earth-Sciences

Journal of Aquaculture & Fisheries

Journal of Biotech Research & Biochemistry

Journal of Brain & Neuroscience Research

Journal of Cancer Biology & Treatment

Journal of Cardiology & Neurocardiovascular Diseases

Journal of Cell Biology & Cell Metabolism

Journal of Clinical Dermatology & Therapy

Journal of Clinical Immunology & Immunotherapy

Journal of Clinical Studies & Medical Case Reports

Journal of Community Medicine & Public Health Care

Current Trends: Medical & Biological Engineering

Journal of Cytology & Tissue Biology

Journal of Dentistry: Oral Health & Cosmesis

Journal of Diabetes & Metabolic Disorders

Journal of Dairy Research & Technology

Journal of Emergency Medicine Trauma & Surgical Care

Journal of Environmental Science: Current Research

Journal of Food Science & Nutrition

Journal of Forensic, Legal & Investigative Sciences

Journal of Gastroenterology & Hepatology Research

Journal of Gerontology & Geriatric Medicine

Journal of Genetics & Genomic Sciences

Journal of Hematology, Blood Transfusion & Disorders

Journal of Human Endocrinology

Journal of Hospice & Palliative Medical Care

Journal of Internal Medicine & Primary Healthcare

Journal of Infectious & Non Infectious Diseases

Journal of Light & Laser: Current Trends

Journal of Modern Chemical Sciences

Journal of Medicine: Study & Research

Journal of Nanotechnology: Nanomedicine & Nanobiotechnology

Journal of Neonatology & Clinical Pediatrics

Journal of Nephrology & Renal Therapy

Journal of Non Invasive Vascular Investigation

Journal of Nuclear Medicine, Radiology & Radiation Therapy

Journal of Obesity & Weight Loss

Journal of Orthopedic Research & Physiotherapy

Journal of Otolaryngology, Head & Neck Surgery

Journal of Protein Research & Bioinformatics

Journal of Pathology Clinical & Medical Research

Journal of Pharmacology, Pharmaceutics & Pharmacovigilance

Journal of Physical Medicine, Rehabilitation & Disabilities

Journal of Plant Science: Current Research

Journal of Psychiatry, Depression & Anxiety

Journal of Pulmonary Medicine & Respiratory Research

Journal of Practical & Professional Nursing

Journal of Reproductive Medicine, Gynaecology & Obstetrics

Journal of Stem Cells Research, Development & Therapy

Journal of Surgery: Current Trends & Innovations

Journal of Toxicology: Current Research

Journal of Translational Science and Research

Trends in Anatomy & Physiology

Journal of Vaccines Research & Vaccination

Journal of Virology & Antivirals

Archives of Surgery and Surgical Education

Sports Medicine and Injury Care Journal

International Journal of Case Reports and Therapeutic Studies

Submit Your Manuscript: http://www.heraldopenaccess.us/Online-Submission.php

Herald Scholarly Open Access, 2561 Cornelia Rd, #205, Herndon, VA 20171, USA.
Tel: +1 202-499-9679; E-mail: info@heraldsopenaccess.us
http://www.heraldopenaccess.us/