Beyond birth weight:

Alternate ways of representing how the fetal environment relates to adult blood pressure*

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Abstract

The Developmental Origins of Adult Disease (DOHaD) paradigm holds that the prenatal environment affects not only birth outcomes, but also adult health outcomes. As DOHaD research has advanced it is a good time to critically examine often-used measures of fetal conditions and their performance in empirical research. In this study, we draw on data from the Cebu Longitudinal Health and Nutrition Study to analyze different measures of fetal conditions and assess how well they predict young adult blood pressure and we compare individual measures to factor score approaches based on latent measures of fetal conditions to see what differences result. Overall, we find that factor scores improve the performance of fetal measures. Further, a latent variable, favorable fetal growth conditions, does well in predicting systolic blood pressure of males and females while a ponderal index is best at predicting diastolic blood pressure for males.

1. Introduction

The Developmental Origins of Adult Disease (DOHaD) paradigm holds that the prenatal environment has important effects not only on birth outcomes, but also on adult health outcomes such as cardiovascular diseases, and type 2 diabetes (Barker 2004; Barker 2005; Gluckman and Hanson 2006). Following early work showing elevated mortality hazard ratios for adults at the lowest and highest end of

the birth weight distribution (Barker, Winter, Osmond, Margetts, and Simmonds 1989), many studies have found inverse or U-shaped associations of birth weight with levels of adult risk factors (such as blood pressure, reviewed in (Gluckman and Hanson 2006), (Adair and Dahly 2005; Mu, Wang, Sheng, Zhao, Li, Hu, and Tao 2012)), insulin resistance (Raghupathy, Antonisamy, Geethanjali, Saperia, Leary, Priya, Richard, Barker, and Fall 2010; Yajnik and Deshmukh 2008), or dyslipidemia (Lauren, Jarvelin, Elliott, Sovio, Spellman, McCarthy, Emmett, Rogers, Hartikainen, Pouta, Hardy, Wadsworth, Helmsdal, Olsen, Bakoula, Lekea, and Millwood 2003; Lawlor, Owen, Davies, Whincup, Ebrahim, Cook, and Davey Smith 2006). Owing to the difficulty of directly measuring the fetal environment, most human epidemiologic studies rely on birth weight as a sensitive, but non-specific proxy measure of the fetal environment. However, the use of birth weight for this type of analysis has been criticized for many reasons (Gillman 2002). Birth weight reflects multiple factors that contribute to shortened gestation and/or to fetal growth restriction, both of which result in lower weight at birth. When analyzing birth weight in the context of DOHaD, it is important to note that fetal growth and size at birth are not synonymous. Size represents some factors that may not relate to adult disease risk, and some determinants of adult outcomes may be unrelated to size at birth (Gillman 2002). Further, birth weight does not reflect the degree to which a fetus has met its growth potential: an average birth weight infant born to a tall mother may have suffered some level of fetal growth restriction. Thus, using only birth weight may result in misclassification of infants as growth-restricted. This has led one group of researchers to advocate for customized fetal growth charts which

consider maternal height, pre-pregnancy weight, parity, ethnicity and baby's sex to customize fetal growth curves and distinguish physiologic or constitutional vs. pathologic smallness (Gardosi 2004; Gardosi 2006).

Despite its limitations, many studies will continue to use birth weight as a proxy for the fetal environment owing to the ease of obtaining these data from existing records or measuring it in new studies. In addition, birth length and gestational age are measured with considerably more error. Measurement error for all of these indicators is rarely considered in analyses of how size at birth relates to later health outcomes. Even less considered is that the DOHaD considers the fetal growth conditions more broadly and birth weight, length, and gestational age are just indicators of these fetal conditions considered more generally.

As DOHaD research has advanced it is a good time to critically examine oftenused measures of fetal conditions and their performance in empirical research. While birth weight is the most frequently used indicator, fetal conditions measures have also included birth length (Eriksson 2005), measures of body proportions such as BMI or ponderal index (weight/length³) (Barker, Osmond, Simmonds, and Wield 1993; Law, Gordon, Shiell, Barker, and Hales 1995), gestational age, and measures of placental size and morphology (Barker and Thornburg 2013). The later health outcomes studied in relation to early life are at least as diverse as the fetal measures and include indicators of glucose metabolism, dyslipidemia, blood pressure, inflammatory markers, and a host of related diseases including hypertension, cardiovascular disease, diabetes, and cancer, among others (Gluckman and Hanson 2006). Here, we focus on young adult blood pressure, owing to its contribution as a key risk factor for cardiovascular disease mortality worldwide, and well established biological plausibility of early life effects (Bagby 2009; Barker, Bagby, and Hanson 2006) and the extensive literature that has developed around the relationship of birth weight to blood pressure. We evaluate alternate indictors of the quality of the fetal environment, including birth length, gestational age, and ponderal index with the goal of comparing their performance in predicting blood pressure. Our analysis pays particular attention to 2 key issues: First, all measures of birth size and gestational age contain measurement error related to measuring instruments, human recording or reporting mistakes, and other factors. Even "well-behaved" random errors can bias the coefficient estimates of the health effects of not only the fetal environment indicators, but also of the other control variables that are part of the analysis. This happens even if the control variables are free of error (Bollen, 1989). For this reason, we will estimate some models that attempt to minimize measurement error.

Second, birth weight, birth length, and gestational age, are imperfect indicators of more fundamental genetic, environmental, and epigenetic factors that influence fetal growth and susceptibility to later disease. The presumption is that a lower birth weight or length, or shortened gestation duration mark a poor fetal environment. In our analysis we build on recent work (identifying reference removed) that treats favorable fetal growth conditions (FFGC) as a latent variable. We thus have two primary purposes in this paper: (1) we analyze different ways to represent fetal conditions and assess how well they predict young adult blood pressure and (2) we compare individual measures to factor score approaches to FFGC to see what, if any, differences result. We use an excellent longitudinal data set from Cebu, Philippines to examine these issues. Our goal is to provide insights into the best way to represent fetal conditions when testing the DOHaD hypothesis. The results should prove relevant beyond our specific data.

Data and Variables

We use data from the Cebu Longitudinal Health and Nutrition Survey (CLHNS), a community based birth cohort that recruited more than 3000 mothers during pregnancy, then followed their offspring into adulthood (Adair, Popkin, Akin, Guilkey, Gultiano, Borja, Perez, Kuzawa, McDade, and Hindin 2011). These panel data were collected in months 6-7 of pregnancy, shortly after birth, bimonthly for two years, and during multiple later follow-up surveys.

Blood Pressure. The primary outcomes in this analysis are systolic and diastolic blood pressure for respondents at age 21 (N=1,885). Trained medical technologists used mercury sphygmomanometers with appropriate cuff sizes to take 3 readings after the respondent had a 10-minute, seated rest. We use the average of the three readings of systolic and diastolic blood pressure. We excluded 73 women who were pregnant at the time of the survey, leaving us with an analysis sample of 1,812. A small amount of missing data in the covariates is addressed in our analysis with Casewise Maximum Likelihood estimators that make use of all of the available data (Arbuckle 1996).

Birth Measures. We have two measures of newborn weight. Infants were weighed immediately after birth by birth attendants. Those born in hospitals or maternity centers were weighed on the facility's scales, while those born at home were, in most cases, weighed on project scales provided to birth attendants. Place of delivery, use of the project scale, and timing of measurement relative to birth were recorded. After notification of a birth, highly trained CLHNS staff conducted home visits to weigh infants on Salter dial-faced scales and measure recumbent length using custom-made length boards. Gestational age in weeks was estimated from the mother's report of the date of her last menstrual period (LMP). If the LMP date was missing, if there were pregnancy complications, or if the infant was born weighing less than 2500 g, trained nurses conducted Ballard tests to assess gestational age (Ballard, Novak, and Driver 1979; Sasidharan, Dutta, and Narang 2009). We used the natural log transformation of these gestational age measures to lessen extreme values in the analyses and multiplied these log-transformed scores by 100 to increase the magnitude of the units. For one set of analyses we rely on single-item measures like those used in most epidemiologic studies, including weight measured by birth attendants and gestational age from mothers' LMP date.

For a second set of analyses, we developed measurement models that specify birth weight, birth length, and gestational age as latent variables, and incorporate the multiple measures of birth weight and gestational age as well as variables that influenced these measures (timing of measurements, type of scale). We use these measurement models to construct factor scores for birth weight, birth length, and gestational age.

Factor scores are predicted values for an underlying latent variable using the factor score regression method (Thomson, 1939). The regression method is by far the most common method for estimating factor scores. It maximizes the correlation between the factor scores and the latent variable they reflect. In our analysis, these correlations are quite high. The correlation between latent birth weight and the factor scores for birth weight is 0.97, between latent birth length and the factors score for birth length is 0.92, and between latent gestational age and the factor scores for gestational age is 0.84. The reported correlations are weighted averages of the correlations between the factor scores and the latent variables across the different patterns of missing data. The proportion of cases with the given pattern of missing data determines the weights.

We also developed a second-order measurement model in which latent birth weight, birth length, and gestational age are, together, treated as indicators of a second-order latent factor variable that we call "favorable fetal growth conditions (FFGC)". We construct factor scores for latent FFGC to compare the performance of the individual components of fetal conditions with the more general measure. We constructed the factor scores for FFGC from two models. One model includes the characteristics of the mother and their impact on FFGC using the model in (identifying reference omitted). The second model matches the first except we exclude the mother's characteristics in forming the factor scores. These two different methods to constructing factor scores were highly correlated (r = 0.99). In this paper we report only the results with factor scores constructed without the mother's characteristics. The correlation between latent FFGC and these factor scores for FFGC is 0.95.

Finally, we used the ponderal index (birth weight (kg)/birth length (m)³) as a measure of relative weight that is uncorrelated with length but highly correlated with measures of adiposity (Fok, Hon, Ng, Wong, So, Lau, Chow, and Lee 2009). A comparable measure was derived using the factor scores for latent birth weight and for the latent birth length.

Other covariates include whether the participant's mother was primiparous, along with adult age at measurement, weight, height, and waist circumference as continuous variables ; smoking (natural log of the frequency plus 1). We also include an index of urbanicity of the place of residence (Dahly and Adair 2007) and several measures of socioeconomic status, including household income (natural logged), housing material (light, mixed, or strong), and ownership of selected assets (house or land, livestock and consumer goods (e.g., televisions, electric fans, computers), and a weighted average of indicators for owning different types of vehicles (1 = bikes, 2 = motorbikes, 3 = cars, trucks, or jeepneys). All of the measures of SES are available for the year of birth (i.e., the families' SES) and 2005, when blood pressure was measured.

3.4 Descriptive Statistics

Table 1 provides the descriptive statistics for the blood pressure and fetal/birth measures along with the other covariates. We use the natural log transformation of gestational age in the analysis, but report both the untransformed and 100*log

transformed gestational age in the table. Since the measurement models used to construct the factor scores scale the latent fetal conditions to single measures (i.e., latent birth weight is scaled to birth weight), their mean values are similar to those for the actual measures of birth weight, birth length, and gestational age. There is somewhat less variation in the factor scores (e.g., their standard deviations are smaller than those for the single measures). Similarly, the measurement model for FFGC is scaled to birth weight and thus has a roughly similar metric to it as is apparent from the means of 3.05 for women and 3.10 for men.

Over the 2 decades represented with by our data, the study area became more urbanized, and household wealth and income increased. Adult prevalence of overweight and obesity were low in this population of 21 year olds (9.9% of males and 7.5% of females had a BMI>25 kg/m²), but the males are already showing signs of early development of elevated blood pressure (17.6% of males, and 2.1% of females had prehypertension or hypertension as defined by the International Diabetes Federation cut-point of 130/85 (Federation 2006)).

[TABLE 1 ABOUT HERE]

Analysis Methods

To explore the performance of different approaches to measuring fetal conditions, we consider the following 11 model specifications: (1) birth weight alone, (2) factor score of birth weight alone, (3) birth length alone, (4) factor score of birth length alone, (5) gestational age alone, (6) factor score of gestational age alone, (7) birth weight, birth length, and gestational age together, (8) factor scores of birth weight, birth length, and gestational age together, (9) ponderal index, (10) factor scores version of ponderal index, (11) factor scores of FFGC. All models include the full set of control variables discussed in the previous section. Across these model specifications, we can make several types of comparison. First, we can compare each single measure to its corresponding factor score. Factor scores will have less measurement error than a measure by itself. Thus, we can determine what difference it makes to use a factor score that has a lower portion of measurement error than does the single measure. Second, we can see how measures that capture different dimensions of fetal growth, including linear growth and relative weight or adiposity relate to adult blood pressure. Third, we can evaluate the utility of the factor score for FFGC that is intended to capture the overall quality of the fetal environment. Our criteria for comparisons include evaluation of the magnitude and precision of estimates and of model fit, using the BIC (Raftery 1995; Schwarz 1978) where smaller values indicate a better model fit.

We estimate sex-stratified models for systolic and diastolic blood pressure. In a later section, we report diagnostics and sensitivity analyses for the best fitting models.

Systolic Blood Pressure (tables 2 and 3)

[TABLEs 2 and 3 ABOUT HERE]

Among females, none of the coefficients of the single measures (birth weight, birth length, and gestational age) individually are significantly associated with systolic blood pressure, but each of their corresponding factor score versions have statistically significant negative coefficients. This suggests that lessening the measurement error in these variables by using factor scores improves the results. However, when all of the factor score measures are entered simultaneously (model 8), none are associated with systolic blood pressure, likely reflecting high collinearity among these factor scores, which makes it difficult to estimate the unique influence of each variable. FFGC is inversely related to systolic blood pressure. We also note that the R-squares are roughly the same to two significant digits for all the models in Table 2. However, the BIC suggests that model fit is superior when fetal conditions are represented by the FFGC factor score and the factor score for birth weight.

Among males, both versions of birth weight are inversely associated with systolic blood pressure, except in model 8 that includes birth weight, birth length, and gestational age factor scores. The birth weight factor score estimate is larger and more precise. The ponderal index factor score and FFGC each have statistically significant negative coefficients in predicting systolic blood pressure. The lowest BIC is for the model with the ponderal index factor score (model 10).

Diastolic Blood Pressure, (tables 4 and 5)

[TABLEs 4 and 5 ABOUT HERE]

Among females, we find no statistically significant coefficients for any of the measures of fetal conditions in that their confidence intervals contain zero. The BICs suggest that the model with gestational age factor score alone and the model with FFGC are preferred over the others, but they are only slightly better than the models with individual measures of fetal conditions (models 1 through 5) and the models with the Ponderal index (models 9 and 10) and the coefficients lack significance.

[TABLE 4 ABOUT HERE]

Among males, raw birth weight is inversely related to adult diastolic blood pressure only when birth length and gestational age are included in the model (model 7). This is not true for the corresponding factor score. Both versions of the ponderal index are inversely associated with diastolic blood pressure (models 9 and 10), but the coefficient on the factor score version is much larger and more precise. The BIC indicates that the best fitting model is the one with the ponderal index based on factor scores (model 10).

Sensitivity Analysis

For the sensitivity analyses we focus on the best fitting models for each blood pressure and male/female combination and conduct additional regression diagnostics. We examined differences in results when adult weight and waist circumference were log transformed, explored non-linear relationships of measures of fetal conditions with adult blood pressure using higher order terms and augmented component plus residual plots (ACPR plots), a form of a partial residual plot. We also checked studentized residuals, Cook's D, DFITS, and DFBETAs for indications of influential cases (Belsely, Kuh, & Welsh, 1980).

Alternate representations of adult weight and waist circumference (log transformed values) did not change any of the results. Similarly, alternate specifications of the form of the fetal conditions variables failed to improve model fit and led to the same conclusions. Influence analysis flagged 2-4% of cases, depending on the outcome, but dropping those cases from the models did not alter the pattern or magnitude of associations.

Because the factor scores for gestational age had the lowest correlation with the latent variable (r = 0.84), we estimated models that fixed the reliability of the factor scores to 0.71 (=0.84²) to determine whether the lower reliability of the factor scores for gestational age had any influence on our results. We found that fixing the reliability had minimal effect on the estimates for gestational age and for any of the other covariates with significant effects on systolic or diastolic blood pressure for men and women.

Discussion

Scholars interested in relating fetal conditions to adult health have many choices for how to measure and represent those conditions. Direct measurement of the fetal environment is not possible, so we rely most often on indirect measures in the form of variables that represent fetal growth. While more studies are using fetal ultrasound measurements to better characterize fetal growth, there is still a strong reliance on birth outcome measures, particularly for large epidemiologic studies. In this paper we use high quality data from a birth cohort study to compare the results obtained using a variety of possible indicators to predicting young adult blood pressure. We did this with the intent of answering several questions.

The first question is: does taking measurement error into account through the use of factor scores for birth weight, length and gestational age change our estimates of how these birth measures relate to adult blood pressure? In our regression models we found that the choice of measure could make a difference in the size and precision of estimates and thus our judgment of whether associations were significant or not. For instance, raw measures of birth weight, length and gestational age were unrelated to systolic blood pressure in females, but their corresponding factor scores were strongly negatively related. This is likely due to the lower levels of measurement error present in the factor scores compared to the use of single indicators. The most extreme instance is the case of gestational age. In (identifying reference omitted) gestational age measured by self-reported last period had very low reliability (about .10). The factor score prediction of gestational age was far more reliable (greater than .8) and this led to a much stronger effect for the factor score than for the uncorrected measure.

A second question is whether measures that capture different dimensions of fetal growth relate differently to adult blood pressure. Weight, length, and ponderal index reflect different influences at different periods of gestation and may therefore be expected to have different implications for later health. For example, adiposity, reflected in the ponderal index at birth, is predicted by maternal diet (Blumfield, Hure, MacDonald-Wicks, Smith, Simpson, Giles, Raubenheimer, and Collins 2012). Our results suggest that thinness is important for male blood pressure, and is captured by birth weight adjusted for birth length, or by ponderal index, with the latter shown to have better model fit. This finding on the importance of thinness is consistent with studies showing how thinness at birth relates to later health in other populations (Law et al. 1995; Phillips, Barker, Hales, Hirst, and Osmond 1994) When gestational age is added to a model that includes birth weight and length, we are essentially asking a question about being small for gestational age rather than preterm. Without GA in the model, we are testing the effects of small size, irrespective of whether smallness results from being born early or being born small for gestational age.

The FFCG latent variable is a more global indicator of the quality of the fetal environment, and indeed, conceptually what our DOHaD models are trying to capture, since we know that growth itself may not be causally related to adverse health outcomes (Gillman 2002), but may represent the true underlying causes. This suggests that use of a latent variable may be most appropriate in DOHaD modeling. For women, the best performing single measure in our regression analysis is the factor score prediction variable FFGC. Given the abstract nature of the fetal conditions that lie behind the fetal origins hypothesis, researchers should make a more conscientious attempt to take account of the measurement error in their variables rather than to do nothing but to refer to them as "proxies" for the latent variable. Direct modeling with latent variables also is a desirable way that explicitly considers all the measurement error in the variables.

Another general finding is that our fetal measures were more successful in predicting systolic blood pressure than diastolic blood pressure. For females, none of the fetal measures were statistically significant whereas for males only the ponderal index was.

We end with a cautionary note. As we said in the introduction, there are many possible measures of fetal conditions and many possible health outcomes to consider. We looked at a variety of ways to represent the fetal environment but there are more that might be considered. The same is true of the health outcomes. Our focus was on blood pressure, but there is a key need to determine whether our results generalize beyond the measures and data set that we examine. Our findings suggest that such further examination would be worth the effort.

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Tables

Table 1. Descriptive statistics for blood pressure, fetal conditions, and covariates separately	y for
women and men.	

	V	Vomen (N =	822)		Men (N = 990)		
			Std.			Std.	
	Ν	Mean/Pr	Dev.	Ν	Mean/Pr	Dev.	
Systolic blood pressure	822	99.40	10.11	990	112.18	10.68	
Diastolic blood pressure	822	68.20	8.52	990	76.50	9.32	
Birth weight (kg)	820	2.97	0.42	990	3.04	0.45	
Birth weight (fac score kg)	822	3.05	0.37	990	3.11	0.39	
Birth length (cm)	820	49.04	2.07	990	49.54	2.12	
Birth length (fac score cm)	822	48.36	1.59	990	48.69	1.65	
Gestational age (weeks)	770	39.38	2.79	921	38.88	2.76	
Gestational age (100x(log* weeks))	770	367.08	7.14	921	365.78	7.26	
Gestational age (fac score weeks)	822	38.97	0.68	990	39.06	0.73	
Gestationl age (fac score 100x(log* weeks))	822	366.26	1.75	990	366.50	1.88	
Ponderal index (kg/m^3)	820	25.15	2.39	990	24.96	2.56	
Ponderal index (fac score)	822	26.83	1.42	990	26.76	1.56	
FFGC (fac score)	822	3.05	0.35	990	3.10	0.37	
First pregnancy (1 = yes)	822	0.22	0.41	990	0.22	0.41	
Birth household income (log*)	815	5.18	0.98	976	5.19	0.95	
Birth housing material: light	822	0.44	0.50	990	0.43	0.50	
Birth housing material: mixed	822	0.38	0.49	990	0.40	0.49	
Birth housing material: strong	822	0.19	0.39	990	0.17	0.37	
Birth urbanicity	822	29.28	12.83	990	29.81	12.84	
Birth own home (1 = yes)	822	0.74	0.44	990	0.73	0.44	
Birth own land (1 = yes)	822	0.18	0.38	990	0.16	0.37	
Birth own vehicles (index)	822	0.05	0.13	990	0.06	0.15	
Birth own livestock (index)	822	0.26	0.27	990	0.25	0.26	
Birth own consumer goods (index)	822	0.13	0.18	990	0.14	0.20	
Adult age	822	21.47	0.31	990	21.48	0.30	
Adult smoking (log*)	822	0.06	0.28	990	0.88	1.04	
Adult weight	822	46.34	8.11	990	56.07	9.41	
Adult height	822	15.12	0.55	990	16.31	0.58	
Adult waist size	820	67.92	7.45	988	72.16	7.53	
Adult household income (log*)	819	6.05	0.87	987	5.93	0.89	
Adult housing material: light	821	0.22	0.41	989	0.24	0.43	
Adult housing material: mixed	821	0.57	0.50	989	0.57	0.50	
Adult housing material: strong	821	0.22	0.41	989	0.20	0.40	
Adult urbanicity	821	41.24	13.08	989	40.99	13.59	

Adult own home (1 = yes)	822	0.84	0.37 99	0.85	0.35
Adult own land (1 = yes)	822	0.39	0.49 99	0.40	0.49
Adult own vehicles (index)	822	0.25	0.41 99	0.26	0.39
Adult own livestock (index)	822	0.16	0.22 99	0.17	0.21
Adult own consumer goods (index)	822	0.38	0.21 99	0.36	0.21

Notes:

* log = natural log. We multiplied by 100 to improve the numerical stability of the estimates.

	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)	(10)	(11)
birth weight	-1.46 (-0.06)						-1.32 (05)				
	[-3.14,0.21]						[-3.66,1.02]				
birth weight (fs)		-2.41* (09)						-5.91 (22)			
		[-4.29,-0.52]						[-19.40,7.58]			
birth length			-0.22 (05)				-0.02 (004)				
			[-0.56,0.12]				[-0.49,0.46]				
birth length (fs)				-0.53* (08)				-0.16 (03)			
				[-0.97,-0.09]				[-1.15,0.83]			
gestational age					-0.04 (03)		-0.03 (02)				
					[-0.13,0.06]		[-0.12,0.07]				
gestational age (fs)						-0.48* (08)		0.87 (.15)			
						[-0.88,-0.09]		[-1.95,3.69]			
ponderal index									-0.12 (03)		
									[-0.40,0.15]		
ponderal index (fs)										-0.35 (05)	
										[-0.82,0.11]	
FFGC (fs)											-2.58* (09)
											[-4.56,-0.60]
Ν	822	822	822	822	822	822	822	822	822	822	822
R-sq	0.16	0.17	0.16	0.16	0.16	0.16	0.16	0.17	0.16	0.16	0.17
BIC	22.975	19.681	24.272	20.442	25.244	20.197	36.123	32.672	25.143	23.711	19.428

Table 2. Estimates from linear models regressing blood pressure on measures of fetal conditions and covariates; Female, Systolic blood pressure.

Unstandardized coefficients. Standardized estimates in parentheses. 95% confidence intervals in brackets. (fs) = factor scores.

* p<0.05; ** p<0.01; *** p<0.001

	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)	(10)	(11)
birth weight	-1.85* (08)						-3.19** (14)				
	[-3.35,-0.35]						[-5.29,-1.09]				
birth weight (fs)		-2.29** (08)						-2.02 (07)			
		[-4.01,-0.56]						[-15.98,11.95]			
birth length			-0.06 (01)				0.42 (.09)				
			[-0.39,0.26]				[-0.04,0.88]				
birth length (fs)				-0.32 (05)				0.94 (.15)			
				[-0.74,0.10]				[-0.01,1.89]			
gestational age					-0.02 (01)		-0.004 (002)				
					[-0.11,0.07]		[-0.10, 0.09]				
gestational age (fs)						-0.48** (09)		-0.80 (07)			
						[-0.84,-0.12]		[-3.71, 2.12]			
ponderal index									-0.38** (09)		
									[-0.63,-0.13]		
ponderal index (fs)										-0.70*** (- .10)	
										[-1.11,-0.29]	
FFGC (fs)											-2.30* (08)
											[-4.12,-0.49]
Ν	990	990	990	990	990	990	990	990	990	990	990
R-sq	0.13	0.13	0.13	0.13	0.13	0.13	0.14	0.14	0.14	0.14	0.13
BIC	30.594	29.665	36.251	34.154	36.224	29.568	41.094	39.576	27.538	25.163	30.242

Table 3. Estimates from linear models regressing blood pressure on measures of fetal conditions and covariates; Male, Systolic blood pressure.

Unstandardized coefficients. Standardized estimates in parentheses. 95% confidence intervals in brackets. (fs) = factor scores.

* p<0.05; ** p<0.01; *** p<0.001

	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)	(10)	(11)
birth weight	-0.52 (03)						-0.42 (02)				
	[-1.96,0.92]						[-2.44,1.59]				
birth weight (fs)		-1.06 (05)						1.34 (.06)			
		[-2.69,0.57]						[-10.29,12.97]			
birth length			-0.08 (02)				-0.01 (003)				
			[-0.38,0.21]				[-0.42,0.40]				
birth length (fs)				-0.22 (04)				0.03 (.01)			
				[-0.60,0.16]				[-0.83,0.88]			
gestational age					-0.02 (02)		-0.02 (02)				
					[-0.11,0.06]		[-0.10,0.06]				
gestational age (fs)						-0.23 (05)		-0.53 (11)			
						[-0.57,0.11]		[-2.96,1.90]			
ponderal index									-0.05 (01)		
									[-0.29,0.19]		
ponderal index (fs)										-0.18 (03)	
										[-0.58,0.22]	
FFGC (fs)											-1.13 (05)
											[-2.84,0.58]
Ν	822	822	822	822	822	822	822	822	822	822	822
R-sq	0.12	0.12	0.12	0.12	0.21	0.13	0.12	0.13	0.12	0.12	0.12
BIC	59.71	58.575	59.898	58,905	59.835	58.451	72,902	71.812	60.051	59.454	58.531

Table 4. Estimates from linear models regressing blood pressure on measures of fetal conditions and covariates; Female, Diastolic blood pressure.

Unstandardized coefficients. Standardized estimates in parentheses. 95% confidence intervals in brackets. (fs) = factor scores.

* p<0.05; ** p<0.01; *** p<0.001

	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)	(10)	(11)
birth weight	-1.31 (06)						-2.20* (11)				
	[-2.64,0.02]						[-4.06,-0.34]				
birth weight (fs)		-1.26 (05)						3.46 (.15)			
		[-2.78,0.27]						[-8.90,15.81]			
birth length			-0.05 (01)				0.30 (.07)				
			[-0.34,0.24]				[-0.11,0.70]				
birth length (fs)				-0.13 (02)				0.79 (.14)			
				[-0.50,0.24]				[-0.05,1.63]			
gestational age					-0.03 (02)		-0.02 (01)				
					[-0.11,0.05]		[-0.10,0.07]				
gestational age (fs)						-0.28 (06)		-1.61 (33)			
						[-0.60,0.04]		[-4.19,0.97]			
ponderal index									-0.26* (07)		
									[-0.48,-0.04]		
ponderal index (fs)										-0.48** (08)	
										[-0.84,-0.12]	
FFGC (fs)											-1.20 (05)
											[-2.81,0.40]
Ν	990	990	990	990	990	990	990	990	990	990	990
R-sq	0.11	0.11	0.11	0.11	0.11	0.11	0.11	0.11	0.11	0.11	0.11
BIC	55,441	56.56	59.054	58,659	58,718	56,181	67.074	65,924	53,805	52.39	57.01

Table 5. Estimates from linear models regre	ssing blood pro	ssure on measures of fetal	conditions and covariates	: Male	. Diastolic blood	pressure
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Unstandardized coefficients. Standardized estimates in parentheses. 95% confidence intervals in brackets. (fs) = factor scores.

* p<0.05; ** p<0.01; *** p<0.001