Published in final edited form as:

Epidemiology. 2011 September ; 22(5): 724–730. doi:10.1097/EDE.0b013e318225c960.

Preconception cardiovascular risk factors and pregnancy outcome

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Abstract

Background—Pregnancy-related cardiovascular conditions are associated with both poorer pregnancy outcomes and cardiovascular disease later in life. Little is known about the relationship between preconception cardiovascular risk factor levels and pregnancy complications.

Methods—Data from the Cardiovascular Risk in Young Finns Study were linked with birth registry data for 1142 primiparous women. Age-standardized levels of total cholesterol, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, triglycerides, blood pressure, insulin, and glucose from the study visit prior to last menstrual period were calculated. These factors were examined as predictors of gestational age, preterm birth (<37 weeks), birthweight, low birthweight (<2500 g), small-for-gestational-age (weight <10th percentile for gestational age), hypertensive disorders of pregnancy, and gestational diabetes, using linear and Poisson regression with adjustment for age, body mass index, smoking, and socioeconomic status.

Results—Higher triglycerides were associated with a higher risk of hypertensive disorders (adjusted risk ratio [aRR]= 1.42 [95% confidence interval (CI) = 0.90–2.23]), pre-eclampsia (1.70 [1.08–2.65]), and gestational diabetes (1.68 [1.25–2.25]). After removing women with pregnancy complications (n=30), the estimated aRR for the association between systolic blood pressure and preterm birth was 1.23 (95% CI= 0.99–1.54); for HDL-c and low birthweight, 0.97 (0.73–1.28); for diastolic blood pressure and small-for-gestational-age, 0.98 (0.81–1.20); and for systolic blood pressure and small-for-gestational-age, 1.18 (0.97–1.45).

Conclusions—High lipid levels before pregnancy predict an increased risk of pre-eclampsia and gestational diabetes. Reported associations between these pregnancy complications and later cardiovascular disease of the mother are probably explained, at least in part, by maternal conditions that precede pregnancy. Interventions to improve cardiovascular health before pregnancy may reduce risk of pregnancy complications.

Poor cardiovascular health puts a woman at risk for poor birth outcomes. Hypertensive disorders of pregnancy are a leading cause of growth retardation and indicated preterm

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birth,^{1,2} and even within the normal range, elevated blood pressure is associated with preterm birth.³ Both elevated and low cholesterol have been associated with spontaneous preterm birth.^{4–6} Glucose intolerance has been associated with preterm birth,⁷ although higher glucose levels are generally associated with larger birthweights.⁸

It has also become clear that conditions arising during pregnancy can predict a woman's cardiovascular risk status after pregnancy. Women who deliver a preterm or low birthweight infant have a higher risk of cardiovascular disease,⁹ elevated blood pressure, and insulin resistance later in life.¹⁰ Women who develop pre-eclampsia have elevated blood pressure and lipids after pregnancy^{11,12} and are at higher risk of developing diabetes^{12,13} metabolic syndrome¹⁴ and cardiovascular disease.¹⁵ Women who develop gestational diabetes during pregnancy are at increased risk of later diabetes¹³ – independent of family history, preconception glycemia, and body mass index (BMI).¹⁶ It is not clear whether these women are at higher constitutional risk for cardiovascular disease, which is revealed during pregnancy, or whether pregnancy induces this higher cardiovascular risk.

Given these associations, it is plausible that a woman's cardiovascular health even prior to her pregnancy could predict her birth outcomes. This is the case for clinical conditions: women with chronic hypertension who become pregnant are at higher risk of pre-eclampsia,^{17,18} preterm birth,^{18,19} small-for-gestational-age,¹⁸ and gestational diabetes,²⁰ while women with diabetes who become pregnant are at higher risk of pre-eclampsia.¹⁷ A few previous articles have addressed the relationship between pre-pregnancy cardiovascular risk factors and birth outcomes. The Nord-Trøndelag health study found that higher lipids and blood pressure prior to pregnancy were associated with developing pre-eclampsia.²¹ Another Norwegian study found that higher blood pressure was associated with lower birthweight for gestational age, while higher cholesterol and glucose were associated with higher birthweight for gestational age.²² Triglycerides had an inverse association with birthweight for gestational age in women with lower BMI and a positive association in women with higher BMI.²² The CARDIA study found that women in the lowest and highest quartiles of cholesterol were at increased risk of preterm birth,²³ but preterm risk was not increased with triglycerides, low-density lipoprotein (LDL-c), or high-density lipoprotein (HDL-c).

The purpose of our analysis was to further assess the relationship between pre-pregnancy cardiovascular risk factors and pregnancy health in a cohort with a wide age representation. We hypothesized that women with more adverse cardiovascular risk factors would be at greater risk for pre-eclampsia, gestational diabetes, shortened gestation and reduced birthweight. We further hypothesized that associations with gestational age and birthweight would hold even in the absence of pre-eclampsia or gestational diabetes.

Methods

Source population

The methods for the Cardiovascular Risk in Young Finns study have been described in detail previously.²⁴ Briefly, 3596 children and adolescents aged 3–18 years, randomly chosen from population registers, were enrolled in 1980. Follow-up assessments were conducted every three years between 1980 and 1992, and then in 2001 and 2007. Retention rates for women were 81% in 1983, 72% in 1986, 68% for clinical examinations in 2001, and 66% for 2007. There was no difference in baseline cholesterol, blood pressure, or BMI between those lost to follow-up and those continuing to participate.²⁴

Data from the cardiovascular study cohort were merged with the Finnish national birth registry. The birth registry contains information on every birth in Finland since 1987,

including data on the pregnancy. Of the 1832 women originally enrolled in the Cardiovascular Risk in Young Finns study, 1323 had a pregnancy in the birth registry; 1316 had at least one singleton in the registry. The study visit prior to the pregnancy was defined as the last visit before the recorded last menstrual period (LMP). (If no LMP was recorded [n=130], it was estimated as being 10 weeks prior to the first prenatal visit [the mean time for first prenatal visit in the data]). Any women whose previous study visit by this definition could have occurred early in the pregnancy (n=3) was omitted. Of the remaining women, 1310 had at least one pregnancy that occurred after a previous study visit (6 women had incomplete data on the dates of their pregnancy). We further excluded women with type 1 diabetes (n=7) or suspected familial hypercholesterolemia (defined as cholesterol>9 mmol/l, n=11). Among these women, 1160 were primiparous. The data were further limited to primiparous women with complete information on birthweight, gestational age, lipids, and blood pressure, leaving 1142 for analysis.

Exposure measures

At each visit, a fasting blood draw was conducted. Cholesterol, HDL-c, LDL-c, triglycerides, and insulin were measured at each visit, and glucose measurement was added in 2001. Details of the lipids, glucose, and insulin measurement protocols have been published previously; measures were corrected because of changes in determination methods.^{25,26} Blood pressure was measured in a sitting position after 5 minutes' rest, using a random-zero sphygmomanometer (Hawksley & Sons Ltd, Lancin, UK). The fifth Korotkoff phase was used as the sign of diastolic blood pressure. Readings were performed at least three times on each subject, and the mean of the three used for analysis.

A summary variable was created for those above the 90th percentile for any 3 of the following: LDL-c, systolic or diastolic blood pressure, triglycerides, and insulin, or below the 10th percentile for HDL-c.

Outcome measures

The birth registry data include direct reports of some medical information, as well as up to 10 spaces to record diagnoses using ICD-9 and ICD-10 codes. We analyzed three pregnancy complications: overall hypertensive disorders of pregnancy, pre-eclampsia, and gestational diabetes. Overall hypertensive disorders of pregnancy were defined as any hypertensive disorder specified as having begun during pregnancy, or an eclamptic disorder (ICD-9 codes 6423–6427, ICD-10 codes O12–O15). Pre-eclampsia was defined as a recorded diagnosis of eclampsia (n=1) as well as ICD-9 codes 6424–6427 and ICD-10 codes O11, O12, O14, and O15. Gestational diabetes was defined as failing a glucose tolerance test, ICD-9 code 6488, or ICD-10 code O24. Preterm birth was defined as birth at <37 weeks' gestation, low birthweight as weight <2500 g, and small-for-gestational-age as weight below the 10th percentile for gestational age, with percentiles based on this study population.

Additional covariates

Smoking was categorized as never reported, pre-pregnancy only, and during pregnancy, using data from the birth registry and the study data. A socioeconomic status variable was created, based on a combination of occupational status reports at 3 times: first, reported socioeconomic status based on occupational status in 2001 (manual/lower-grade non-manual/higher-grade non-manual); second, socioeconomic status in 2007; and third, parental occupational socioeconomic status as a child. Data to create this variable were missing for 34% of the study population, and so multiple imputation using PROC MI and PROC MIANALYZE in SAS (SAS, Cary, NC) was implemented to create the final adjusted models. Data from the birth registry were used to measure age at delivery and parity. Data on pre-pregnancy weight in

the birth registry were missing for the majority of study participants, and so we used BMI at the study visit.

Analytic methods

Risk factor levels (total cholesterol, HDL-c, LDL-c, triglycerides, systolic blood pressure, diastolic blood pressure, insulin, glucose) were age-standardized. Multivariable models (linear for continuous outcomes; Poisson with robust variance for dichotomous outcomes²⁷ [log-linear models failed to converge]) were created, adjusting the results for potential confounders: age, smoking, BMI, and socioeconomic status. Pregnancy complications (hypertensive disorders, pre-eclampsia, and gestational diabetes), preterm birth, low birthweight, small-for-gestational-age, gestational age, and birthweight at first pregnancy were the outcomes, and each cardiovascular risk factor was examined as a predictor. We also ran the birthweight and gestational age models after removing women who had suffered complications. Quadratic terms were examined to assess nonlinear relationships. Statistical interaction with BMI was also assessed using a product term.

The variable time between study visit and pregnancy was addressed in two ways. First, we adjusted for this time gap to determine whether it changed the results. This variable was not predictive and was omitted from final models. Second, results were assessed in the subset of pregnancies that occurred within five, two, and one year(s) of a study visit.

The original study was approved by the local ethics committees. The data linkage and analysis were approved by the Medical Birth Register and the Institutional Review Board of Tulane University.

Results

Most women included in this analysis had their first birth in their twenties or early thirties (Table 1). Eleven percent had smoked during pregnancy, and 86% were married or living with a partner. One-quarter were classified as working a manual-labor job as adults. Four percent of the infants were low birthweight and 6% preterm, and between 0.5 and 1.5% of women were reported to have had the pregnancy complications of interest. Median time between the study visit and the pregnancy was 7.4 years. The proportion of women who gave birth were similar for those in the highest quartiles of 3 risk factors or more at age 18 and those in the lower quartiles (75 vs. 79%, $p=0.40$).

The associations of cardiovascular risk factors with complications of pregnancy are given in Table 2 and with birth outcomes in Table 3. The strongest associations were for triglycerides and pregnancy complications, and for systolic blood pressure and preterm birth/small-for-gestational-age. When women with pregnancy complications were excluded from the analyses, the effect estimates were similar. Exclusion of women with pre-eclampsia caused the largest change in effect. Results were similar for continuous outcomes, with the strongest association found for the relationships of blood pressure with gestational age and with birthweight (eTable 1, <http://links.lww.com>).

Previous studies have indicated U-shaped relationships of cardiovascular risk factors with pregnancy complications and adverse pregnancy outcomes; for example, the risk of complications is higher with both high and low cholesterol.²³ Our data were consistent with a quadratic relationship between blood pressure and gestational diabetes (p for Wald test of quadratic term for systolic blood pressure=0.01, for diastolic blood pressure 0.07) as well as between glucose and gestational diabetes ($p=0.04$), between diastolic blood pressure and low birthweight ($p=0.03$), and between systolic blood pressure and small-for-gestational-age ($p=0.01$). For example, women were at increased risk of low birthweight if they were in

either the lowest quartile (adjusted risk ratio [aRR]= 1.5 [95% confidence interval (CI)= 0.56–4.1] or the highest quartile (2.1 [0.83–5.5]) of diastolic blood pressure compared with the second quartile. There was also a suggestion of a quadratic relationship between triglycerides and small-for-gestational-age ($p=0.06$) and between low birthweight and glucose ($p=0.08$). All other relationships were $p>0.10$ for the quadratic term.

Previous studies had found that the relationships between cardiovascular risk factors and birth outcomes were stronger in women with higher BMIs.²² This generally did not hold in our data (eTable 2, <http://links.lww.com>). For pregnancy complications, the effect estimate for the association of LDL-c and gestational diabetes was stronger among overweight women ($BMI>25$). However, other associations did not indicate heterogeneity or were in the direction of weaker or protective effects in women who were overweight, although these results were imprecise. For birth outcomes, among women who were overweight, higher triglycerides were associated with an elevated risk of small-for-gestational-age (aRR= 1.36 [95% CI= 1.12–1.67]) but not among women with lower BMI (0.87 [0.69–1.11]; p for product term <0.01). A similar but less precise pattern was seen for the relationship between blood pressure and low birthweight.

Results limiting the data to those within a certain time before the pregnancies are given in the Figure, limited to those without the listed complications (sample size did not allow for examining dichotomous outcomes). Confidence intervals overlap widely for all comparisons.

Discussion

Our data suggest an association of pre-pregnancy lipids with pre-eclampsia and gestational diabetes. Magnussen and colleagues²¹ similarly found that pre-pregnancy lipids were associated with pre-eclampsia, but also found a strong relationship of blood pressure with pre-eclampsia. These findings suggest that the associations^{9–15} found between pregnancy complications and later cardiovascular disease are due, at least in part, to underlying or pre-existing cardiovascular health that predates the pregnancy.

Our data are also consistent with the hypothesis that some pre-pregnancy cardiovascular risk factors, especially blood pressure, predict preterm birth and low birthweight. This is broadly consistent with previous studies. We corroborate Romundstad et al.²² in finding that higher blood pressure was associated with lower birthweight. However, in our data, higher cholesterol and triglycerides were associated with lower birthweight, while those authors found that cholesterol and triglycerides were associated with higher birthweight. They also reported that triglycerides had an inverse association with birthweight in lower-BMI women, and most of our study participants had fairly low BMIs.²² Even so, many of our results are imprecise and can only be said to be inconsistent with a protective effect. Larger studies will be required to confirm these possible associations.

Strengths of our study include the prospective design and ability to link to the national birth registry, allowing essentially complete follow-up and independent data collection for those who have given birth. One limitation of this analysis is that many women's reproductive lifespan had not yet been completed; some women may yet give birth. Mean age at first birth in Finland is 28;²⁸ the youngest study participant was 30 in 2007.

Another limitation is that data on weight gain during pregnancy were not available. It is also possible that residual confounding—for example, by socioeconomic status—might contribute to these results, although adjustment for standard risk factors did not materially change the effect estimates.

Prior validation studies have found that 64% to 75% of diagnoses of pre-eclampsia and abnormal glucose tolerance are recorded in the birth registry.²⁹ The reported incidence of these complications among our study population was low (even for a group that was fairly young, healthy, and lean) and indicates possible under-reporting. A previous study of Finnish doctors, teachers, and general obstetric patients found a 0.9%–3.2% incidence of pre-eclampsia, for instance.³⁰ The recorded cases are likely to be the most severe. It is possible that the relationships between cardiovascular risk factors and birth outcomes that remained after excluding women with known complications were due to undiagnosed, milder cases.

Possible mechanisms for the elevated risk seen with gestational age and birthweight include unreported or subclinical pre-eclampsia. In addition, higher lipids or blood pressure may indicate an adverse cardiovascular profile that reduces placental perfusion or function independent of preeclampsia.²³ Uteroplacental vasculopathy, such as histopathologic lesions and intravascular coagulation, has been found in several adverse pregnancy conditions including preterm birth and fetal growth restriction, and is associated with dyslipidemia and insulin resistance.³¹ Our study adds to the body of research suggesting that improving women's cardiovascular health at younger ages might also help improve pregnancy outcomes.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

Thanks to Gerald Berenson for facilitating this collaboration and to the reviewers for helpful comments on the analysis.

Funding:

The Cardiovascular Risk in Young Finns study was supported financially by the Academy of Finland (grants 117797, 126925, and 121584), Social Insurance Institution of Finland, Turku University Foundation, special federal grants for Turku University Central Hospital, Juho Vainio Foundation, Finnish Foundation of Cardiovascular Research, Finnish Cultural Foundation, and Orion Farnos Research Foundation.

This work was supported by the National Institute of Child Health And Human Development (K12HD043451 to EWH).

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Figure.

Change in birth outcomes and 95% confidence interval (horizontal bars) with a 1-standard deviation change in the pre-conception cardiovascular risk factor level by length of time between measurement and pregnancy, adjusted for age, BMI, smoking, and socioeconomic status (primiparous women in the Cardiovascular Risk in Young Finns study, 1987–2007). SBP indicates systolic blood pressure; DBP, diastolic blood pressure.

Table 1

Characteristics^a of Primiparous women in the Cardiovascular Risk in Young Finns study (n = 1142), 1987–2007.

Characteristics assessed at visit prior to first included pregnancy; mean (SD), range		
Total cholesterol (mmol/L)	5.1 (0.9), 2.2–8.4	
LDL-c (mmol/L)	3.1 (0.8), 0.5–6.3	
HDL-c (mmol/L)	1.6 (0.3), 0.6–2.5	
Triglycerides (mmol/L)	1.0 (0.4), 0.3–4.7	
Systolic blood pressure (mmHg)	113.2 (11.36), 80.7–166.7	
Diastolic blood pressure (mmHg)	67.2 (9.5), 33.0–104.7	
Glucose (mmol/L)	4.6 (0.5), 3.1–6.3	
Insulin (mU/L)	10.5 (5.5), 1.5–42.5	
Birth outcome		
Birthweight (g); mean (SD), range	3452 (533), 445–5000	
Gestational age (weeks); mean (SD), range	39.8 (1.9), 23.3–43.1	
Low birthweight (<2500 g)		
Yes	41	(4)
No	1101	(96)
Preterm birth (<37 weeks)		
Yes	67	(6)
No	1075	(94)
Gestational hypertension		
Yes	15	(1)
No	1127	(99)
Pre-eclampsia/eclampsia		
Yes	7	(1)
No	1135	(99)
Pregnancy complications		
Gestational diabetes		
Yes	16	(1)
No	1126	(99)
Age at first study visit (1980; years)		
3	124	(11)
6	200	(18)
9	223	(20)
12	230	(20)
15	205	(18)
18	160	(14)
Age at time of prior study visit (years)		
3–11	108	(10)
12–18	560	(49)
19–24	328	(29)

>24	146	(13)
Age at time of first birth (years)		
15–22	190	(17)
23–28	556	(49)
29–34	329	(29)
>34	67	(6)
Childhood socioeconomic position		
Lower	335	(43)
Middle	299	(38)
Higher	147	(19)
Social class of participant as adult (2001), based on occupational status		
Manual	202	(24)
Lower-grade non-manual	472	(56)
Higher-grade non-manual	165	(20)
BMI category at prior study visit (among those >15 years old)		
Underweight	263	(30)
Normal	510	(57)
Overweight	105	(12)
Obese	14	(2)
Smoking during pregnancy		
None	976	(87)
Quit in first trimester	29	(3)
Smoked later than first trimester or throughout pregnancy	121	(11)
Marital status at birth		
Married	612	(54)
Living with partner	360	(32)
Single	165	(15)
Number of prenatal visits		
≤10	60	(5)
11–20	920	(81)
>20	156	(14)

* No may not add to total due to missing data. % may not add to 100 due to rounding.

^aNo. (%) unless otherwise specified,

Table 2

Association of pre-conception cardiovascular risk factors levels and pregnancy complications^a in primiparous women in the Cardiovascular Risk in Young Finns study (n=1142), 1987–2007.

	Gestational hypertension				Pre-eclampsia				Gestational diabetes			
	Unadjusted		Adjusted ^b		Unadjusted		Adjusted ^b		Unadjusted		Adjusted ^b	
	RR	(95% CI)	RR	(95% CI)	RR	(95% CI)	RR	(95% CI)	RR	CI	RR	95% CI
Cholesterol	0.97	(0.56–1.71)	0.95	(0.55–1.66)	1.63	(0.94–2.84)	1.52	(0.87–2.66)	1.58	(1.05–2.38)	1.51	(1.01–2.25)
HDL-c	1.19	(0.68–2.09)	1.27	(0.78–2.07)	1.08	(0.57–2.03)	1.17	(0.64–2.15)	0.77	(0.41–1.44)	0.76	(0.45–1.31)
LDL-c	0.77	(0.43–1.37)	0.75	(0.43–1.30)	1.32	(0.75–2.33)	1.22	(0.65–2.30)	1.48	(0.99–2.21)	1.44	(1.00–2.07)
Triglycerides	1.48	(0.98–2.26)	1.42	(0.90–2.23)	1.90	(1.25–2.90)	1.70	(1.08–2.65)	1.64	(1.31–2.06)	1.68	(1.25–2.25)
Systolic blood pressure	1.12	(0.71–1.78)	1.03	(0.58–1.84)	1.33	(0.86–2.04)	1.28	(0.71–2.29)	1.10	(0.86–1.41)	1.06	(0.75–1.50)
Diastolic blood pressure	0.74	(0.47–1.17)	0.68	(0.40–1.15)	0.75	(0.32–1.77)	0.64	(0.22–1.87)	1.14	(0.90–1.44)	1.12	(0.81–1.55)
Glucose (n=844)	0.83	(0.47–1.48)	0.80	(0.45–1.40)	0.79	(0.32–1.94)	NC		1.46	(0.98–2.16)	1.38	(0.92–2.06)
Insulin	1.24	(0.88–1.77)	1.16	(0.75–1.79)	1.27	(0.88–1.83)	1.10	(0.70–1.75)	1.27	(0.97–1.67)	1.27	(0.94–1.73)

^aRelative increase in risk associated with one standard deviation (standardized for age at measurement)

^badjusted for age, BMI, smoking, and socioeconomic status
Could not be calculated because model failed to converge

Table 3

Association of pre-conception cardiovascular risk factors levels and birth outcomes^a in primiparous women in the Cardiovascular Risk in Young Finns study, 1987–2007.

	Preterm birth			Low birthweight			Small-for-gestational-age					
	Unadjusted		Adjusted ^b	Unadjusted		Adjusted ^b	Unadjusted		Adjusted ^b			
	RR	(95% CI)	RR	(95% CI)	RR	(95% CI)	RR	CI	RR	95% CI		
All women (n=1142)												
Cholesterol	1.10	(0.84–1.44)	1.11	(0.84–1.46)	1.36	(0.98–1.90)	1.38	(0.98–1.94)	0.97	(0.79–1.20)	0.99	(0.81–1.21)
HDL-c	0.96	(0.75–1.21)	0.92	(0.73–1.17)	0.99	(0.75–1.32)	0.97	(0.74–1.27)	0.93	(0.75–1.15)	0.94	(0.76–1.16)
LDL-c	1.11	(0.85–1.44)	1.13	(0.86–1.48)	1.34	(0.95–1.88)	1.37	(0.97–1.93)	0.97	(0.79–1.20)	0.99	(0.81–1.21)
Triglycerides	1.07	(0.83–1.37)	1.10	(0.84–1.42)	1.17	(0.88–1.56)	1.20	(0.88–1.64)	1.06	(0.87–1.30)	1.04	(0.84–1.28)
Systolic blood pressure	1.23	(1.01–1.51)	1.28	(1.05–1.57)	1.26	(0.93–1.71)	1.31	(0.97–1.76)	1.19	(0.97–1.44)	1.17	(0.96–1.43)
Diastolic blood pressure	1.16	(0.91–1.48)	1.19	(0.94–1.53)	1.12	(0.78–1.60)	1.14	(0.80–1.63)	1.00	(0.81–1.22)	0.99	(0.81–1.21)
Glucose (n=844)	0.99	(0.74–1.33)	1.01	(0.76–1.34)	1.12	(0.80–1.56)	1.14	(0.82–1.57)	0.90	(0.66–1.24)	0.88	(0.64–1.21)
Insulin	1.15	(0.90–1.47)	1.25	(0.98–1.59)	1.07	(0.79–1.47)	1.15	(0.85–1.56)	0.96	(0.77–1.21)	0.95	(0.76–1.20)
3 or more factors >90th percentile	1.90	(0.73–4.93)	2.48	(0.91–6.79)	0.75	(0.11–5.29)	0.89	(0.12–6.33)	1.56	(0.67–3.59)	1.41	(0.61–3.25)
Limited to women without gestational hypertension, pre-eclampsia, and gestational diabetes (n=1112)												
Cholesterol	1.11	(0.84–1.48)	1.13	(0.84–1.49)	1.41	(0.99–2.01)	1.43	(1.00–2.05)	0.99	(0.80–1.22)	1.01	(0.82–1.24)
HDL-c	0.95	(0.73–1.22)	0.92	(0.72–1.18)	0.99	(0.73–1.34)	0.97	(0.73–1.28)	0.92	(0.74–1.15)	0.94	(0.76–1.17)
LDL-c	1.15	(0.88–1.51)	1.17	(0.89–1.54)	1.44	(1.02–2.03)	1.46	(1.03–1.74)	0.99	(0.80–1.22)	1.01	(0.82–1.23)
Triglycerides	0.96	(0.73–1.26)	0.98	(0.74–1.30)	1.03	(0.75–1.41)	1.05	(0.75–1.46)	1.06	(0.86–1.31)	1.04	(0.84–1.29)
Systolic blood pressure	1.19	(0.96–1.48)	1.23	(0.99–1.54)	1.20	(0.85–1.69)	1.24	(0.88–1.74)	1.20	(0.98–1.46)	1.18	(0.97–1.45)
Diastolic blood pressure	1.16	(0.90–1.50)	1.19	(0.92–1.54)	1.12	(0.76–1.65)	1.15	(0.78–1.68)	0.99	(0.81–1.21)	0.98	(0.81–1.20)
Glucose (n=817)	1.03	(0.75–1.43)	1.04	(0.76–1.41)	1.22	(0.84–1.77)	1.23	(0.86–1.75)	0.89	(0.65–1.24)	0.87	(0.63–1.20)
Insulin	1.18	(0.92–1.51)	1.27	(0.99–1.63)	1.10	(0.79–1.53)	1.18	(0.85–1.63)	0.96	(0.77–1.21)	0.95	(0.76–1.20)
3 or more factors >90th percentile	2.10	(0.80–5.47)	2.63	(0.96–7.21)	0.85	(0.12–6.06)	0.99	(0.14–7.03)	1.61	(0.70–3.71)	1.46	(0.64–3.35)