

Supplemental Material

| Supplemental Table 1. Coefficients of variation and assay type for each biomarker | | |
|---|------------------|---|
| Biomarker | Range of CVs (%) | Assay |
| CRP | 0.3 - 9.5 | Highly sensitive immunoturbidimetric assay ¹ or high-sensitivity latex-enhanced immunonephelometric assay ² |
| IL-6 | 1.9 - 15.3 | Enzyme-linked immunosorbent assay (R&D Systems, Minneapolis, MN) |
| HbA _{1c} | 1.2 - 1.6 | Turbidimetric immunoinhibition immunoassay (Roche Diagnostics, Indianapolis, IN) |
| ICAM-1 | 2.3 - 8.9 | Enzyme-linked immunosorbent assay (R&D Systems, Minneapolis, MN) |
| HDL-C | 1.3 - 6.6 | Measured enzymatically ³ |
| LDL-C | 1.3 - 6.7 | Measured enzymatically ³ |
| Triglycerides | 1.2 - 10.4 | Measured enzymatically ⁴ |
| Total Cholesterol | 1.0 - 6.2 | Measured enzymatically ⁵ |

¹Roche Diagnostics, Indianapolis, IN; or Denka Seiken, Tokyo, Japan

²Dade-Behring, Newark, DE

³Roche Diagnostics, Indianapolis, IN; or Genzyme, Cambridge, MA; or Abbot Laboratories, Abbot Park, IL

⁴Roche Diagnostics, Indianapolis, IN; or Genzyme, Cambridge, MA; or Thermo Fisher Scientific, Oy, Finland

⁵Roche Diagnostics, Indianapolis, IN; or Genzyme, Cambridge, MA; or Abbot Laboratories, Abbot Park, IL; or Thermo Fisher Scientific, Oy, Finland

Supplemental Table 2. Age-standardized characteristics of participants by history of pregnancy complications among controls

| | Only Normotensive (n=3,428) | Ever Hypertensive Disorder of Pregnancy (n=354) | Normotensive | |
|---|--------------------------------|--|------------------------|-------------------------|
| | | | Only Term (n=3,037) | Ever Preterm (n=388) |
| Age at first birth in years, ¹ mean (SD) | 26.5 (4.3) | 26.8 (4.4) | 26.6 (4.2) | 26.4 (4.6) |
| Age at blood draw ¹ | | | | |
| <40 years | 16.4 | 18.6 | 16.1 | 19.1 |
| 40 to <45 years | 34.9 | 38.7 | 35.7 | 29.1 |
| ≥45 years | 48.7 | 42.7 | 48.2 | 51.8 |
| White | 97.8 | 97.7 | 97.8 | 97.7 |
| Years between first birth and blood draw, mean (SD) | 17.6 (6.6) | 17.4 (6.5) | 17.6 (6.5) | 17.6 (7.0) |
| Characteristics at blood draw: | | | | |
| Smoking at blood draw | | | | |
| Past or never smoker | 93.8 | 92.0 | 94.1 | 90.7 |
| Current smoker | 6.2 | 8.0 | 5.9 | 9.3 |
| Alcohol consumption in month prior to blood draw | | | | |
| No drinks in past month | 32.2 | 42.6 | 31.7 | 36.1 |
| Moderate drinker in past month | 58.6 | 49.8 | 58.7 | 57.0 |
| Heavy drinker in past month | 9.2 | 7.7 | 9.5 | 7.0 |
| Menopausal status at blood draw | | | | |
| Pre-menopausal | 82.4 | 80.2 | 82.5 | 81.1 |
| Post-menopausal | 10.3 | 9.7 | 10.3 | 10.3 |
| Unknown | 7.4 | 10.2 | 7.2 | 8.6 |
| Post-menopausal hormone use at blood draw | 15.8 | 20.6 | 15.7 | 17.3 |
| History of infertility at blood draw | 6.7 | 7.8 | 6.2 | 9.9 |
| Parity at blood draw | | | | |
| 1 birth | 14.6 | 15.2 | 14.9 | 11.2 |
| ≥2 births | 85.5 | 84.8 | 85.1 | 88.7 |
| Potential Confounders: | | | | |
| Pre-pregnancy BMI | | | | |
| Underweight (<18.5 kg/m ²) | 2.1 | 2.3 | 2.1 | 2.0 |
| Normal weight (18.5-24.9 kg/m ²) | 89.3 | 79.0 | 89.4 | 88.9 |
| Overweight (25-29.9 kg/m ²) | 7.3 | 13.3 | 7.2 | 8.3 |
| Obese (≥30 kg/m ²) | 1.2 | 5.4 | 1.3 | 0.8 |
| Pre-pregnancy Alternative Healthy Eating Index | | | | |
| First quintile (unhealthiest) | 20.7 | 22.7 | 20.7 | 20.8 |
| Fifth quintile (healthiest) | 18.2 | 16.9 | 17.9 | 20.8 |
| Strenuous physical activity, age 18-22 years | | | | |
| Never | 30.7 | 31.7 | 30.7 | 30.5 |
| 10-12 months per year | 10.5 | 10.7 | 10.2 | 13.1 |

Values are percentages unless otherwise specified and are standardized to the age distribution of the study population. Values of polytomous variables may not sum to 100% due to rounding. Characteristics at blood draw were matching factors in sub-studies included in the analysis

¹ Value is not age adjusted

Supplemental Table 3. Percent difference in post-pregnancy biomarkers and 95% confidence intervals comparing women with only normotensive pregnancies to women with a history of a hypertensive disorder of pregnancy (HDP) among controls

| | Normotensive Only | Ever HDP |
|---|----------------------|----------------------|
| CRP | n=1,821 | n=176 |
| CRP level, mg/L, median (IQR) | 0.79 (0.37, 1.95) | 1.31 (0.51, 2.48) |
| Model 1 | ref | 32.4 (12.8, 55.4) |
| Model 2 | ref | 29.4 (10.4, 51.7) |
| IL-6 | n=1,621 | n=152 |
| IL-6 level, pg/mL, median (IQR) | 0.88 (0.62, 1.32) | 1.11 (0.74, 1.63) |
| Model 1 | ref | 16.7 (5.5, 29.1) |
| Model 2 | ref | 14.0 (3.2, 26.1) |
| HbA_{1c} | n=792 | n=93 |
| HbA _{1c} , %, median (IQR) | 5.38 (5.21, 5.53) | 5.38 (5.21, 5.48) |
| Model 1 | ref | -0.1 (-1.0, 0.8) |
| Model 2 | ref | -0.3 (-1.2, 0.6) |
| ICAM-1 | n=1,093 | n=109 |
| ICAM-1, ng/mL, median (IQR) | 231.5 (207.3, 261.2) | 244.1 (213.5, 273.6) |
| Model 1 | ref | 4.1 (-0.6, 9.2) |
| Model 2 | ref | 2.8 (-1.8, 7.7) |
| HDL-C | n=812 | n=96 |
| HDL-C level, mg/dL, median (IQR) | 58.8 (51.0, 69.1) | 56.2 (47.0, 66.5) |
| Model 1 | ref | -2.9 (-8.1, 2.6) |
| Model 2 | ref | -2.2 (-7.2, 3.2) |
| LDL-C | n=812 | n=96 |
| LDL-C level, mg/dL, median (IQR) | 111.8 (92.7, 130.0) | 109.3 (89.7, 129.8) |
| Model 1 | ref | -1.6 (-7.3, 4.5) |
| Model 2 | ref | -2.3 (-7.9, 3.7) |
| Triglycerides | n=1,254 | n=150 |
| Triglyceride level, mg/dL, median (IQR) | 85.3 (65.0, 121.2) | 86.2 (67.4, 131.5) |
| Model 1 | ref | 3.2 (-4.8, 11.8) |
| Model 2 | ref | -0.2 (-7.7, 7.9) |
| Total Cholesterol | n=2,085 | n=224 |
| Total cholesterol, mg/dL, median (IQR) | 190.3 (171.2, 213.1) | 193.4 (167.9, 214.3) |
| Model 1 | ref | 0.0 (-2.4, 2.4) |
| Model 2 | ref | -0.5 (-2.9, 1.9) |

Model 1 is adjusted for the following criteria for sample selection for laboratory analysis: age at blood draw, race, menopausal status at blood draw, smoking at blood draw, alcohol intake at blood draw, post-menopausal hormone use at blood draw, and history of infertility at blood draw.

Model 2 is additionally adjusted for pre-pregnancy BMI, diet, and physical activity, and parity at blood draw.

The null value comparing ever HDP to only normotensive is 0.0 percent difference.

Supplemental Table 4. Percent difference in post-pregnancy biomarkers and 95% confidence intervals among women with no history of HDP, comparing women with only term deliveries to women with a history of preterm deliveries among controls

| | Only Term (≥37 weeks) | Ever Preterm (<37 weeks) | Ever Moderate Preterm (≥32 to <37 weeks) | Ever Very Preterm (<32 weeks) |
|--|--------------------------|-----------------------------|---|----------------------------------|
| CRP | n=1,623 | n=198 | n=154 | n=44 |
| CRP level, mg/L, median (IQR) | 0.79 (0.36, 2.03) | 0.81 (0.40, 1.68) | 0.81 (0.42, 1.72) | 0.70 (0.35, 1.37) |
| Model 1 | ref | -5.2 (-18.3, 10.1) | -0.4 (-15.3, 17.2) | -20.2 (-42.2, 10.4) |
| Model 2 | ref | -4.2 (-17.4, 11.1) | 0.2 (-14.7, 17.8) | -18.2 (-40.4, 12.5) |
| IL-6 | n=1,442 | n=179 | n=140 | n=39 |
| IL-6 level, pg/mL, median (IQR) | 0.88 (0.62, 1.33) | 0.89 (0.63, 1.32) | 0.87 (0.61, 1.31) | 0.96 (0.71, 1.36) |
| Model 1 | ref | 1.6 (-8.1, 12.3) | 0.8 (-10.0, 12.9) | 4.6 (-14.2, 27.4) |
| Model 2 | ref | 1.7 (-8.0, 12.5) | 0.7 (-10.2, 12.8) | 5.8 (-13.2, 29.0) |
| HbA_{1C} | n=706 | n=84 | n=65 | n=19 |
| HbA _{1C} , %, median (IQR) | 5.38 (5.21, 5.53) | 5.41 (5.24, 5.53) | 5.42 (5.21, 5.53) | 5.38 (5.26, 5.53) |
| Model 1 | ref | 0.2 (-0.8, 1.2) | 0.2 (-0.9, 1.4) | 0.2 (-1.2, 1.6) |
| Model 2 | ref | 0.2 (-0.8, 1.1) | 0.2 (-1.0, 1.3) | 0.1 (-1.3, 1.5) |
| ICAM-1 | n=967 | n=125 | n=92 | n=33 |
| ICAM-1, ng/mL, median (IQR) | 231.5 (207.6, 260.0) | 231.2 (203.6, 265.5) | 225.7 (201.1, 263.2) | 246.1 (220.7, 278.6) |
| Model 1 | ref | 1.6 (-2.3, 5.7) | 0.3 (-4.1, 4.9) | 5.5 (-2.2, 13.8) |
| Model 2 | ref | 1.6 (-2.4, 5.7) | 0.6 (-3.8, 5.2) | 4.4 (-3.2, 12.5) |
| HDL-C | n=722 | n=90 | n=70 | n=20 |
| HDL level, mg/dL, median (IQR) | 58.7 (50.6, 68.7) | 59.5 (51.7, 70.8) | 59.7 (51.4, 71.0) | 57.1 (52.1, 70.5) |
| Model 1 | ref | 2.5 (-2.8, 8.1) | 1.8 (-4.3, 8.2) | 5.0 (-4.9, 15.9) |
| Model 2 | ref | 2.8 (-2.6, 8.5) | 2.1 (-3.9, 8.6) | 5.2 (-5.0, 16.6) |
| LDL-C | n=722 | n=90 | n=70 | n=20 |
| LDL level, mg/dL, median (IQR) | 111.5 (92.0, 130.0) | 112.8 (96.3, 131.2) | 111.3 (94.6, 126.1) | 117.3 (106.9, 135.4) |
| Model 1 | ref | 2.8 (-2.3, 8.2) | 2.0 (-3.8, 8.1) | 5.7 (-3.1, 15.3) |
| Model 2 | ref | 2.5 (-2.6, 7.9) | 1.8 (-4.0, 7.9) | 5.0 (-3.6, 14.3) |
| Triglycerides | n=1,112 | n=141 | n=108 | n=33 |
| Triglycerides, mg/dL, median (IQR) | 85.3 (65.0, 121.7) | 85.0 (61.6, 117.3) | 83.8 (61.3, 114.8) | 100.7 (70.2, 134.7) |
| Model 1 | ref | -4.5 (-12.1, 3.8) | -6.8 (-15.3, 2.6) | 3.5 (-10.2, 19.3) |
| Model 2 | ref | -4.2 (-11.7, 4.0) | -6.3 (-14.8, 3.0) | 3.3 (-10.1, 18.8) |
| Total Cholesterol | n=1,848 | n=235 | n=175 | n=60 |
| Total Cholesterol, mg/dL, median (IQR) | 190.3 (170.9, 213.2) | 191.5 (174.5, 213.1) | 189.3 (172.2, 213.1) | 199.1 (181.0, 213.3) |
| Model 1 | ref | 0.4 (-1.7, 2.6) | -0.1 (-2.5, 2.4) | 1.9 (-1.9, 5.7) |
| Model 2 | ref | 0.4 (-1.7, 2.5) | 0.1 (-2.4, 2.6) | 1.2 (-2.5, 5.1) |

Model 1 is adjusted for the following criteria for sample selection for laboratory analysis: age at blood draw, race, menopausal status at blood draw, smoking at blood draw, alcohol intake at blood draw, post-menopausal hormone use at blood draw, and history of infertility at blood draw.

Model 2 is additionally adjusted for pre-pregnancy BMI, diet, and physical activity, and parity at blood draw.

The null value comparing ever preterm groups to only term is 0.0 percent difference.

