Online Supporting Material

A prospective study of artificially sweetened beverage intake and cardiometabolic health among women at high risk

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Supplementary Figure 1. Sample flow diagram.



| Continuous Outcomes | Artificially Sweetened Beverage Intake in Pregnancy (1996-2002) | | | | |
|----------------------------------|---|-------------------|--------------------|-----------------------|------------|
| $(2012-2014)^{1,2}$ | <1 serving / mo | 1-4 serving / m | o 2-6 serving / wk | ≥ 1 serving / day | <i>P</i> - |
| . , | C | C | 0 | 0 1 | Trend |
| HbA _{1C} | 0.0 (Reference) | 0.0 (-3.9,4.1) | 4.3 (-0.1,8.9) | 9.9 (1.2,19.3) | 0.01 |
| Fasting Glucose | 0.0 (Reference) | -3.1 (-12.7,7.5) | 4.9 (-2.5,12.9) | 7.3 (-5.1,21.3) | 0.18 |
| Fasting Insulin | 0.0 (Reference) | 22.5 (0.5,49.3) | 21.8 (-0.1,48.5) | -11.0 (-38.3,28.4) | 0.49 |
| C-Peptide | 0.0 (Reference) | 9.7 (-7.0,29.4) | 6.0 (-8.4,22.6) | -10.7 (-30.8,15.2) | 0.33 |
| HOMA-IR | 0.0 (Reference) | 23.0 (1.1,49.7) | 26.6 (2.7,56.2) | -5.5 (-33.4,34.1) | 0.73 |
| HOMA-B | 0.0 (Reference) | 22.2 (-5.0,57.2) | 11.0 (-12.9,41.5) | -22.0 (-51.6,25.7) | 0.25 |
| Triglycerides | 0.0 (Reference) | 2.2 (-11.5,18.1) | 7.2 (-6.3,22.5) | 3.7 (-13.6,24.6) | 0.64 |
| HDL | 0.0 (Reference) | 2.1 (-5.5,10.4) | -2.3 (-9.4,5.3) | -2.9 (-12.9,8.3) | 0.48 |
| LDL | 0.0 (Reference) | -5.5 (-15.4,5.6) | -3.1 (-12.8,7.6) | -2.7 (-16.8,13.9) | 0.81 |
| BMI | 0.0 (Reference) | 0.4 (-4.4,5.4) | -0.5 (-5.0,4.2) | -0.1 (-7.7,8.2) | 0.94 |
| Waist Circumference | 0.0 (Reference) | 2.0 (-1.2,5.4) | 1.3 (-1.8,4.5) | 1.3 (-3.4,6.2) | 0.69 |
| Visceral Adipose Tissue | 0.0 (Reference) | 1.9 (-46.2,93.2) | 9.0 (-38.5,93.4) | 6.6 (-43.4,100.9) | 0.81 |
| Mean Arterial Pressure | 0.0 (Reference) | 2.1 (-2.0,6.4) | 0.7 (-3.3,4.9) | -0.6 (-5.8,4.9) | 0.71 |
| CRP | 0.0 (Reference) | 25.5 (-18.1,92.4) | 6.9 (-26.6,55.9) | 30.0 (-21.7,116.0) | 0.41 |
| ALT ³ | 0.0 (Reference) | -7.3 (-24.9,14.4) | 13.7 (-14.7,51.6) | -6.8 (-32.9,29.3) | 0.80 |
| AST ³ | 0.0 (Reference) | -3.8 (-20.3,16.1) | 1.4 (-18.8,26.5) | 0.2 (-21.6,28.2) | 0.90 |
| AST:ALT Ratio ³ | 0.0 (Reference) | 3.8 (-11.5,21.8) | -10.9 (-25.7,6.8) | 7.6 (-14.4,35.2) | 0.62 |
| Liver Fat Percent ^{3,4} | 0.0 (Reference) | 4.1 (-23.0,40.6) | 52.5 (6.8,117.7) | 18.5 (-23.9,84.6) | 0.42 |
| GGT ³ | 0.0 (Reference) | 7.7 (-23.5,51.7) | 7.7 (-25.3,55.3) | 8.0 (-36.2,82.6) | 0.82 |
| Bilirubin ³ | 0.0 (Reference) | -9.7 (-35.0,25.6) | -16.1 (-38.6,14.7) | -3.3 (-36.9,48.1) | 0.96 |
| Binary Outcomes ⁵ | | | | | |
| (2012-2014) | | | | | |
| Hyperglycemia | 1.00 (Reference) | 1.42 (0.25,8.16) | 1.73 (0.41,7.35) | 2.66 (0.41,17.16) | 0.30 |
| Type 2 Diabetes | 1.00 (Reference) | 1.21 (0.50,2.95) | 1.28 (0.55,2.97) | 1.10 (0.27,4.44) | 0.87 |
| Hypertriglyceridemia | | | | | |
| Obesity | 1.00 (Reference) | 1.87 (0.38,9.06) | 1.53 (0.34,6.77) | 3.92 (0.69,22.29) | 0.12 |
| Elevated ALT ³ | 1.00 (Reference) | 0.61 (0.26,1.45) | 1.00 (0.47,2.11) | 0.83 (0.35,2.00) | 0.91 |
| Elevated AST:ALT | ` | | | | |
| Ratio ³ | | | | | |
| Elevated Liver Fat | | | | | |
| Score ^{3,6} | | | | | |

Supplementary Table 1. Consumption of artificially sweetened beverages during pregnancy and adjusted associations with cardiometabolic outcomes 9-16 years later among women with a history of gestational diabetes and with pre-pregnancy normal weight at baseline (n=251).

HDL, high-density lipoprotein; HOMA-IR, Homeostatic model assessment for insulin resistance; HOMA-B, Homeostatic model assessment for β -cell function; LDL, low-density lipoprotein.

¹Continuous outcomes were log-transformed. Results are presented as the percent difference (95% confidence interval) calculated as the exponentiated beta coefficient from the adjusted linear regression model, subtracting 1 and multiplying by 100.

² Analyses adjusted for index pregnancy characteristics including maternal age, pre-pregnancy BMI, parity, education, smoking, pre-pregnancy chronic diseases, moderate/vigorous physical activity, alternative healthy eating index-2010, intake of tea, and intake of coffee. Multiple imputation with 20 replicates was used for missing exposure and covariate data. Missing exposure and covariate data were multiply imputed. Boldfaced indicates estimates that are significant at P < 0.05.

³ Outcomes related to liver function exclude women with habitual alcohol intake at follow-up of > 24 g/d, approximately equivalent to 2 standard drinks/d.

⁴ Calculated liver fat percent = $10^{(-0.805+0.282 * \text{metabolic syndrome (yes=1; no=0)} + 0.078 * T2DM (yes=2; no=0) + 0.525 * log(fs-insulin[mU/L]) + 0.521 * log(fs-AST[U/L]) - 0.454 * log(AST/ALT))$

⁵ Binary outcomes are presented as the relative risk (95% confidence interval) calculated from a Poisson regression model with robust error variance. The following definitions were used for the Binary outcomes: elevated ALT, \geq 19.0 U/L; elevated AST:ALT ratio, ratio \geq 2; Liver fat score, > -0.640; hypertriglyceridemia, triglycerides \geq 200 mg/dL; hyperglycemia, fasting glucose \geq 7.0 mmol/l; type 2 diabetes, HbA_{1C} \geq 6.5%, fasting glucose \geq 7.0 mmol/l, or 2-hour oral glucose tolerance test glucose \geq 11.1 mmol/l or self-report of physician diagnosis; obesity, BMI \geq 30.0 kg/m².

⁶ Liver Fat Score=-2.89 +1.18*metabolic syndrome(yes=1/no=0) +0.45*T2DM(yes=1/no=0) +insulin(mU/L) +0.04*AST(U/L) -0.94*AST/ALT.

| Continuous | Habitual Artificially Sweetened Beverage Intake at Follow Up (2012-2014) | | | | | |
|----------------------------------|--|--------------------|-------------------|----------------------|-----------------|--|
| Outcomes | < 1 serving / mo | 1-4 serving / mo | 2-6 serving / wk | \geq 1 serving / d | P -Trend | |
| $(2012-2014)^{1,2}$ | C | C | 0 | 0 | | |
| HbA _{1C} | 0.0 (Reference) | -1.5 (-4.3,1.2) | 3.8 (0.3,7.4) | 13.8 (3.2,25.5) | 0.007 | |
| Fasting Glucose | 0.0 (Reference) | 2.1 (-2.9,7.4) | 2.7 (-4.1,9.9) | 15.1 (-2.6,36.0) | 0.11 | |
| Fasting Insulin | 0.0 (Reference) | 6.9 (-12.8,31.0) | 14.1 (-4.9,37.0) | -24.8 (-59.2,38.6) | 0.34 | |
| C-Peptide | 0.0 (Reference) | 4.9 (-8.8,20.8) | 1.6 (-10.8,15.7) | -15.3 (-40.4,20.4) | 0.32 | |
| HOMA-IR | 0.0 (Reference) | 10.1 (-10.3,35.3) | 21.5 (-0.1,47.7) | -14.0 (-49.1,45.4) | 0.52 | |
| HOMA-B | 0.0 (Reference) | -2.8 (-22.5,22.0) | -2.2 (-20.0,19.5) | -40.5 (-74.6,39.4) | 0.24 | |
| Triglycerides | 0.0 (Reference) | -1.7 (-12.9,10.9) | 13.6 (1.3,27.3) | 10.3 (-11.9,38.1) | 0.36 | |
| HDL | 0.0 (Reference) | 0.5 (-6.7,8.3) | 0.4 (-6.4,7.7) | -2.1 (-14.3,12.0) | 0.74 | |
| LDL | 0.0 (Reference) | -4.0 (-14.0,7.2) | 0.7 (-7.6,9.8) | -5.9 (-17.2,6.9) | 0.42 | |
| BMI | 0.0 (Reference) | 1.3 (-2.9,5.6) | -0.9 (-5.6,4.0) | 9.4 (-3.4,23.9) | 0.16 | |
| Waist Circumference | 0.0 (Reference) | 2.2 (-1.5,5.9) | -0.3 (-3.1,2.5) | 3.6 (-1.4,8.9) | 0.22 | |
| Visceral Adipose | 0.0 (Reference) | 42.4 (-17.6,146.0) | -3.5 (-40.0,55.4) | 24.2 (-42.5,168.1) | 0.71 | |
| Tissue | | | | | 0.71 | |
| Mean Arterial | 0.0 (Reference) | 2.6 (-2.0,7.3) | 0.8 (-2.6,4.2) | 4.4 (-2.1,11.4) | 0.24 | |
| Pressure | | | | | 0.24 | |
| CRP | 0.0 (Reference) | -14.8 (-40.1,21.1) | 10.1 (-21.6,54.7) | 12.9 (-36.0,99.3) | 0.57 | |
| ALT ³ | 0.0 (Reference) | -4.1 (-25.9,24.1) | 10.4 (-8.9,33.7) | 6.1 (-21.4,43.1) | 0.69 | |
| AST ³ | 0.0 (Reference) | -5.3 (-22.4,15.6) | 1.3 (-11.6,16.1) | 1.7 (-19.8,29.0) | 0.81 | |
| AST:ALT Ratio ³ | 0.0 (Reference) | -1.3 (-17.1,17.6) | -8.3 (-20.2,5.5) | -4.1 (-21.3,16.8) | 0.77 | |
| Liver Fat Percent ^{3,4} | 0.0 (Reference) | -6.0 (-31.6,29.3) | 30.7 (0.3,70.3) | -5.8 (-42.8,55.2) | 0.74 | |
| GGT ³ | 0.0 (Reference) | 27.7 (-14.4,90.3) | 14.4 (-11.3,47.6) | 11.6 (-26.5,69.5) | 0.85 | |
| Bilirubin ³ | 0.0 (Reference) | 10.2 (-19.2,50.3) | -0.9 (-25.2,31.2) | -14.2 (-35.9,14.9) | 0.19 | |
| Binary Outcomes ⁵ | | | | | | |
| (2012-2014) | | | | | | |
| Hyperglycemia | 1.00 (Reference) | 1.82 (0.32,10.50 | 2.57 (0.71,9.38) | 5.13 (1.16,22.73) | 0.04 | |
| Type 2 Diabetes | 1.00 (Reference) | 1.64 (0.66,4.03) | 1.81 (0.88,3.74) | 0.51 (0.09,2.84) | 0.28 | |
| Hypertriglyceridemia | | | | | | |
| Obesity | 1.00 (Reference) | 0.87 (0.17,4.37) | 0.94 (0.24,3.78) | 2.37 (0.68,8.33) | 0.08 | |
| Elevated ALT ³ | 1.00 (Reference) | 0.39 (0.12,1.21) | 1.20 (0.74,1.94) | 1.09 (0.55,2.16) | 0.56 | |
| Elevated AST:ALT | | | | | | |
| Ratio ³ | | | | | | |
| Elevated Liver Fat | 1.00 (Reference) | | | | | |
| Score ^{3,6} | | | | | | |

Supplementary Table 2. Consumption of artificially sweetened beverages during the past year and adjusted associations with cardiometabolic outcomes among women with a history of gestational diabetes and with pre-pregnancy normal weight at baseline (n=251).

Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase; BMI, body mass index; HDL, high-density lipoprotein; HOMA-IR, Homeostatic model assessment for insulin resistance; HOMA-B, Homeostatic model assessment for β-cell function; LDL, low-density lipoprotein.

¹Continuous outcomes were log-transformed. Results are presented as the percent difference (95% confidence interval) calculated as the exponentiated beta coefficient from the adjusted linear regression model, subtracting 1 and multiplying by 100.

² Analyses adjusted for index pregnancy characteristics including maternal age, pre-pregnancy BMI, parity, education, smoking, pre-pregnancy chronic diseases, moderate/vigorous physical activity, alternative healthy eating index-2010, intake of tea, and intake of coffee. Multiple imputation with 20 replicates was used for missing exposure and covariate data. Missing exposure and covariate data were multiply imputed. Boldfaced indicates estimates that are significant at P<0.05.

³ Outcomes related to liver function exclude women with habitual alcohol intake at follow-up of > 24 g/d, approximately equivalent to 2 standard drinks/d.

⁴ Calculated liver fat percent = $10^{(-0.805+0.282 * \text{metabolic syndrome (yes=1; no=0)} + 0.078 * T2DM (yes=2; no=0) + 0.525 * log(fs-insulin[mU/L]) + 0.521 * log(fs-AST[U/L]) - 0.454 * log(AST/ALT))$

⁵ Binary outcomes are presented as the relative risk (95% confidence interval) calculated from a Poisson regression model with robust error variance. The following definitions were used for the Binary outcomes: elevated ALT, \geq 19.0 U/L; elevated AST:ALT ratio, ratio \geq 2; Liver fat score, > -0.640; hypertriglyceridemia, triglycerides \geq 200 mg/dL; hyperglycemia, fasting glucose \geq 7.0 mmol/l; type 2 diabetes, HbA_{1C} \geq 6.5%, fasting glucose \geq 7.0 mmol/l, or 2-hour oral glucose tolerance test glucose \geq 11.1 mmol/l or self-report of physician diagnosis; obesity, BMI \geq 30.0 kg/m².

⁶ Liver Fat Score=-2.89 +1.18*metabolic syndrome(yes=1/no=0) +0.45*T2DM(yes=1/no=0) +insulin(mU/L) +0.04*AST(U/L) -0.94*AST/ALT.

| Continuous Outcomes | nuous Outcomes Habitual Artificially Sweetened Beverage Intake at Follow Up (2012-2014) | | | | |
|----------------------------------|---|--------------------|--------------------|----------------------|------------|
| (2012-2014) ^{1, 2} | < 1 serving / mo | 1-4 serving / mo | 2-6 serving / wk | \geq 1 serving / d | <i>P</i> - |
| . , | C | 0 | 0 | 0 | Trend |
| HbA _{1C} | 0.0 (Reference) | -0.3 (-5.0,4.6) | 3.1 (-0.8,7.1) | 6.9 (0.8,13.4) | 0.03 |
| Fasting Glucose | 0.0 (Reference) | 0.1 (-5.7,6.4) | 5.3 (-1.1,12.1) | 7.8 (-1.3,17.8) | 0.16 |
| Fasting Insulin | 0.0 (Reference) | -3.8 (-20.9,16.9) | -8.3 (-22.6,8.6) | -10.3 (-30.0,15.0) | 0.54 |
| C-Peptide | 0.0 (Reference) | -2.3 (-15.0,12.4) | -6.7 (-17.6,5.5) | -13.3 (-27.1,3.2) | 0.14 |
| HOMA-IR | 0.0 (Reference) | -3.6 (-22.5,20.0) | -3.4 (-19.8,16.4) | -4.1 (-25.8,24.0) | 0.86 |
| HOMA-B | 0.0 (Reference) | -4.6 (-20.9,15.2) | -17.2 (-30.8,-1.0) | -20.4 (-41.5,8.5) | 0.29 |
| Triglycerides | 0.0 (Reference) | -4.7 (-18.0,10.8) | 0.7 (-11.4,14.5) | 3.0 (-14.0,23.5) | 0.63 |
| HDL | 0.0 (Reference) | 4.3 (-3.5,12.7) | 1.5 (-5.6,9.1) | 2.8 (-6.1,12.6) | 0.75 |
| LDL | 0.0 (Reference) | -9.9 (-19.3,0.4) | -4.9 (-13.1,4.0) | -1.2 (-11.4,10.1) | 0.50 |
| BMI | 0.0 (Reference) | 2.1 (-2.3,6.7) | -1.3 (-5.0,2.5) | 0.1 (-4.3,4.8) | 0.94 |
| Waist Circumference | 0.0 (Reference) | 2.1 (-1.4,5.7) | -0.4 (-3.2,2.5) | 1.4 (-2.2,5.2) | 0.48 |
| Visceral Adipose Tissue | 0.0 (Reference) | -7.1 (-43.3,52.2) | -10.6 (-39.2,31.5) | -14.5 (-45.0,33.0) | 0.57 |
| Mean Arterial Pressure | 0.0 (Reference) | 1.7 (-2.5,6.0) | 0.9 (-2.3,4.2) | 4.0 (-0.2,8.3) | 0.07 |
| CRP | 0.0 (Reference) | -17.7 (-46.1,25.8) | -17.2 (-40.8,15.8) | -16.8 (-44.1,23.9) | 0.68 |
| ALT ³ | 0.0 (Reference) | -6.1 (-24.9,17.4) | -2.1 (-17.7,16.4) | -5.3 (-22.2,15.3) | 0.68 |
| AST ³ | 0.0 (Reference) | -11.4 (-26.5,6.9) | -6.2 (-17.5,6.6) | -7.5 (-20.3,7.3) | 0.67 |
| AST:ALT Ratio ³ | 0.0 (Reference) | -5.7 (-17.7,7.9) | -3.4 (-14.5,9.0) | -2.7 (-15.2,11.8) | 0.99 |
| Liver Fat Percent ^{3,4} | 0.0 (Reference) | -10.2 (-35.4,24.9) | 8.5 (-17.2,42.2) | -6.1 (-31.2,28.2) | 0.63 |
| GGT ³ | 0.0 (Reference) | -8.8 (-39.4,37.2) | -18.9 (-37.1,4.7) | -12.4 (-34.4,16.9) | 0.77 |
| Bilirubin ³ | 0.0 (Reference) | 9.2 (-17.4,44.3) | 8.9 (-11.6,34.1) | 1.2 (-18.3,25.2) | 0.63 |
| Binary Outcomes ⁵ | | | | | |
| (2012-2014) | | | | | |
| Hyperglycemia | 1.00 (Reference) | 1.13 (0.34,3.77) | 1.73 (0.69,4.36) | 1.58 (0.50,4.93) | 0.67 |
| Type 2 Diabetes | 1.00 (Reference) | 1.08 (0.54,2.15) | 1.31 (0.79,2.15) | 1.23 (0.69,2.16) | 0.74 |
| Hypertriglyceridemia | 1.00 (Reference) | 0.57 (0.12,2.73) | 1.35 (0.55,3.29) | 1.01 (0.36,2.84) | 0.90 |
| Obesity | 1.00 (Reference) | 0.99 (0.66,1.49) | 1.01 (0.73,1.41) | 1.02 (0.71,1.47) | 0.87 |
| Elevated ALT ³ | 1.00 (Reference) | 0.72 (0.42,1.23) | 1.00 (0.70,1.42) | 0.93 (0.63,1.38) | 0.98 |
| Elevated AST:ALT | | | | | |
| Ratio ³ | | | | | |
| Elevated Liver Fat | 1.00 (Reference) | 1.03 (0.57,1.85) | 1.25 (0.79,1.98) | 1.13 (0.70,1.82) | 0.89 |

Supplementary Table 3. Consumption of artificially sweetened beverages during the past year and adjusted associations with cardiometabolic outcomes among women with a history of gestational diabetes who were consumers of ASB during pregnancy 9-16 years prior (n=358).

Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase; BMI, body mass index; HDL, high-density lipoprotein; HOMA-IR, Homeostatic model assessment for insulin resistance; HOMA-B, Homeostatic model assessment for β -cell function; LDL, low-density lipoprotein.

¹Continuous outcomes were log-transformed. Results are presented as the percent difference (95% confidence interval) calculated as the exponentiated beta coefficient from the adjusted model, subtracting 1 and multiplying by 100.

² Analyses adjusted for current characteristics including maternal age, parity, education, smoking, moderate/vigorous physical activity, alternative healthy eating index-2010, intake of tea, and intake of coffee, and pre-pregnancy chronic diseases at the index pregnancy. Multiple imputation with 20 replicates was used for missing exposure and covariate data. Boldfaced indicates estimates that are significant at P<0.05.

³ Outcomes related to liver function exclude women with habitual alcohol intake > 24 g/d, approximately equivalent to 2 standard drinks/d.

⁴ Calculated liver fat percent = $10^{(-0.805+0.282 * \text{metabolic syndrome (yes=1; no=0)} + 0.078 * T2DM (yes=2; no=0) + 0.525 * log(fs-insulin[mU/L]) + 0.521 * log(fs-AST[U/L]) - 0.454 * log(AST/ALT))$

⁵ Binary outcomes are presented as the relative risk (95% confidence interval). The following definitions were used for the Binary outcomes: elevated ALT, \geq 19.0 U/L; elevated AST:ALT ratio, ratio \geq 2; Liver fat score, > -0.640; hypertriglyceridemia, triglycerides \geq 200 mg/dL; hyperglycemia, fasting glucose \geq 7.0 mmol/l; type 2 diabetes, HbA_{1C} \geq 6.5%, fasting glucose \geq 7.0 mmol/l, or 2-hour oral glucose tolerance test glucose \geq 11.1 mmol/l or self-report of physician diagnosis; obesity, BMI \geq 30.0 kg/m². ⁶ Liver Fat Score=-2.89 +1.18*metabolic syndrome(yes=1/no=0) +0.45*T2DM(yes=1/no=0) +insulin(mU/L) +0.04*AST(U/L) -0.94*AST/ALT.

Supplementary Table 4. Consumption of artificially sweetened beverages during the past year and adjusted associations with cardiometabolic outcomes among women with a history of gestational diabetes and without prevalent chronic diseases at follow-up (n=363).

| Continuous Outcomes Habitual Artificially Sweetened Beverage Intake at Follow Up (2012-2014) | | | | | |
|--|------------------|--------------------|-------------------|----------------------|-------|
| $(2012-2014)^{1,2}$ | < 1 serving / mo | 1-4 serving / mo | 2-6 serving / wk | \geq 1 serving / d | Р- |
| | - | - | | | Trend |
| HbA _{1C} | 0.0 (Reference) | -1.2 (-3.7,1.3) | 1.6 (-0.7,4.0) | 2.1 (-2.8,7.1) | 0.38 |
| Fasting Glucose | 0.0 (Reference) | 1.6 (-2.5,6.0) | 1.6 (-2.3,5.6) | 0.3 (-7.2,8.4) | 0.92 |
| Fasting Insulin | 0.0 (Reference) | 7.4 (-7.4,24.6) | -2.4 (-13.8,10.5) | -9.2 (-24.5,9.3) | 0.20 |
| C-Peptide | 0.0 (Reference) | 4.8 (-6.4,17.2) | -3.0 (-12.0,7.0) | -0.7 (-13.5,14.0) | 0.81 |
| HOMA-IR | 0.0 (Reference) | 7.9 (-8.4,27.1) | -1.2 (-13.9,13.4) | -8.3 (-26.3,14.0) | 0.31 |
| HOMA-B | 0.0 (Reference) | 5.6 (-8.7,22.1) | -5.7 (-16.7,6.8) | -8.4 (-24.9,11.7) | 0.33 |
| Triglycerides | 0.0 (Reference) | -0.1 (-11.4,12.5) | 4.4 (-5.6,15.6) | 7.2 (-11.5,29.7) | 0.50 |
| HDL | 0.0 (Reference) | 3.1 (-3.9,10.7) | 1.6 (-4.5,8.1) | -2.8 (-11.5,6.7) | 0.38 |
| LDL | 0.0 (Reference) | -4.5 (-12.6,4.2) | -1.6 (-8.2,5.4) | -0.3 (-11.6,12.4) | 0.84 |
| BMI | 0.0 (Reference) | 2.9 (-0.9,6.9) | 0.5 (-3.5,4.8) | 3.5 (-5.3,13.2) | 0.55 |
| Waist Circumference | 0.0 (Reference) | 2.5 (-0.5,5.6) | -0.2 (-2.6,2.3) | 0.7 (-3.2,4.8) | 0.97 |
| Visceral Adipose | 0.0 (Reference) | 22.7 (-22.8,94.9) | 7.9 (-26.8,59.1) | 10.3 (-33.0,81.8) | 0 00 |
| Tissue | | | | | 0.88 |
| Mean Arterial Pressure | 0.0 (Reference) | 1.4 (-1.9,4.8) | -0.2 (-3.0,2.7) | 4.1 (-0.7,9.2) | 0.11 |
| CRP | 0.0 (Reference) | -6.5 (-32.8,30.1) | -7.0 (-30.1,23.7) | -8.4 (-39.1,37.8) | 0.77 |
| ALT ³ | 0.0 (Reference) | -8.1 (-21.7,7.9) | 5.6 (-9.0,22.7) | 6.7 (-12.0,29.3) | 0.38 |
| AST ³ | 0.0 (Reference) | -18.1 (-27.8,-7.0) | -4.8 (-15.6,7.3) | 4.0 (-12.5,23.8) | 0.19 |
| AST:ALT Ratio ³ | 0.0 (Reference) | -10.8 (-21.8,1.6) | -9.9 (-19.7,1.1) | -2.5 (-16.1,13.4) | 0.67 |
| Liver Fat Percent ^{3,4} | 0.0 (Reference) | -14.5 (-35.3,12.8) | -0.6 (-20.4,24.2) | 5.6 (-22.6,44.1) | 0.49 |
| GGT ³ | 0.0 (Reference) | 2.6 (-24.3,39.2) | -8.6 (-25.9,12.6) | 5.4 (-18.6,36.3) | 0.59 |
| Bilirubin ³ | 0.0 (Reference) | 12.2 (-12.9,44.6) | -5.8 (-20.7,11.9) | -5.0 (-24.5,19.6) | 0.50 |
| Binary Outcomes ⁵ | | | | | |
| (2012-2014) | | | | | |
| Hyperglycemia | 1.00 (Reference) | 1.64 (0.42,6.42) | 1.14 (0.29,4.39) | 0.94 (0.21,4.29) | 0.66 |
| Type 2 Diabetes | 1.00 (Reference) | 1.09 (0.39,3.09) | 1.01 (0.41,2.49) | 0.66 (0.22,2.02) | 0.35 |
| Hypertriglyceridemia | 1.00 (Reference) | 0.67 (0.17,2.61) | 0.86 (0.28,2.66) | 1.28 (0.40,4.12) | 0.43 |
| Obesity | 1.00 (Reference) | 1.17 (0.79,1.74) | 1.10 (0.78,1.55) | 1.12 (0.72,1.74) | 0.84 |
| Elevated ALT ³ | 1.00 (Reference) | 0.60 (0.33,1.12) | 0.98 (0.65,1.49) | 1.09 (0.67,1.76) | 0.33 |
| Elevated AST:ALT | | | | | |
| Ratio ³ | | | | | |
| Elevated Liver Fat | 1.00 (Reference) | 0.78 (0.30,2.00) | 1.13 (0.55,2.33) | 1.06 (0.48,2.33) | 0.76 |
| Score ^{3,6} | . , , | | | | 0.70 |

Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase; BMI, body mass index; HDL, high-density lipoprotein; HOMA-IR, Homeostatic model assessment for insulin resistance; HOMA-B, Homeostatic model assessment for β-cell function; LDL, low-density lipoprotein.

¹Continuous outcomes were log-transformed. Results are presented as the percent difference (95% confidence interval) calculated as the exponentiated beta coefficient from the adjusted model, subtracting 1 and multiplying by 100.

² Analyses adjusted for current characteristics including maternal age, parity, education, smoking, moderate/vigorous physical activity, alternative healthy eating index-2010, intake of tea, and intake of coffee, and pre-pregnancy chronic diseases at the index pregnancy. Multiple imputation with 20 replicates was used for missing exposure and covariate data. Boldfaced indicates estimates that are significant at P<0.05.

³ Outcomes related to liver function exclude women with habitual alcohol intake > 24 g/d, approximately equivalent to 2 standard drinks/d.

⁴ Calculated liver fat percent = $10^{(-0.805+0.282 * \text{metabolic syndrome (yes=1; no=0)} + 0.078 * T2DM (yes=2; no=0) + 0.525 * log(fs-insulin[mU/L]) + 0.521 * log(fs-AST[U/L]) - 0.454 * log(AST/ALT))$

⁵ Binary outcomes are presented as the relative risk (95% confidence interval). The following definitions were used for the Binary outcomes: elevated ALT, \geq 19.0 U/L; elevated AST:ALT ratio, ratio \geq 2; Liver fat score, > -0.640; hypertriglyceridemia, triglycerides \geq 200 mg/dL; hyperglycemia, fasting glucose \geq 7.0 mmol/l; type 2 diabetes, HbA_{1C} \geq 6.5%, fasting glucose \geq 7.0 mmol/l, or 2-hour oral glucose tolerance test glucose \geq 11.1 mmol/l or self-report of physician diagnosis; obesity, BMI \geq 30.0 kg/m². ⁶ Liver Fat Score=-2.89 +1.18*metabolic syndrome(yes=1/no=0) +0.45*T2DM(yes=1/no=0)

+insulin(mU/L) +0.04*AST(U/L) -0.94*AST/ALT.

Supplementary Table 5. Long-term consumption patterns of artificially sweetened beverages from pregnancy 9-16 years earlier to the past year and adjusted associations with current cardiometabolic outcomes among women with a history of gestational diabetes and with pre-pregnancy normal weight at baseline (n=251).

| | \leq 4 Serving / mo | \leq 4 Servings / mo | \geq 2 Servings / wk | \geq 2 Serving / wk |
|----------------------------------|---------------------------|------------------------|------------------------|-----------------------|
| | in Pregnancy and | in Pregnancy and | and ≤ 4 Servings | in Pregnancy and |
| Continuous Outcomes | at Follow-up | \geq 2 Servings / wk | per / at Follow-up | at Follow-up |
| $(2012-2014)^{1,2}$ | | at Follow-up | | |
| HbA _{1C} | 0.0 (Reference) | 2.4 (-1.6,6.7) | 1.0 (-2.2,4.3) | 11.5 (5.0,18.4) |
| Fasting Glucose | 0.0 (Reference) | -0.7 (-9.3,8.6) | -0.5 (-5.9,5.3) | 10.8 (1.1,21.4) |
| Fasting Insulin | 0.0 (Reference) | -1.4 (-24.5,28.8) | 4.1 (-17.0,30.6) | 10.4 (-16.7,46.4) |
| C-Peptide | 0.0 (Reference) | -2.0 (-17.6,16.6) | 1.2 (-14.7,20.1) | -4.3 (-20.4,15.0) |
| HOMA-IR | 0.0 (Reference) | 2.4 (-20.6,32.0) | 3.9 (-18.4,32.2) | 22.7 (-7.4,62.5) |
| HOMA-B | 0.0 (Reference) | -8.7 (-34.5,27.2) | 3.1 (-17.8,29.3) | -12.4 (-38.6,25.0) |
| Triglycerides | 0.0 (Reference) | 11.4 (-3.3,28.4) | 0.9 (-13.4,17.6) | 16.4 (1.3,33.7) |
| HDL | 0.0 (Reference) | 1.5 (-6.9,10.6) | -1.4 (-10.7,8.8) | -3.0 (-10.6,5.2) |
| LDL | 0.0 (Reference) | -1.1 (-10.4,9.3) | -3.3 (-15.5,10.7) | 0.3 (-10.0,11.7) |
| BMI | 0.0 (Reference) | 2.5 (-4.5,9.9) | 2.2 (-3.1,7.7) | 0.2 (-4.7,5.4) |
| Waist Circumference | 0.0 (Reference) | -0.5 (-3.7,2.8) | 1.0 (-3.0,5.1) | 1.0 (-2.4,4.4) |
| Visceral Adipose | 0.0 (D of sum as) | -6.4 (-45.4,60.5) | 16.1 (-52.5,183.9) | -4.5 (-43.5,61.2) |
| Tissue | 0.0 (Reference) | | | |
| Mean Arterial Pressure | 0.0 (Reference) | -0.5 (-4.5,3.8) | -2.4 (-6.8,2.1) | 1.2 (-3.0,5.6) |
| CRP | 0.0 (Reference) | 3.3 (-32.4,57.8) | -8.3 (-39.9,39.9) | 25.7 (-14.4,84.5) |
| ALT ³ | 0.0 (Reference) | 13.4 (-9.0,41.3) | 13.8 (-20.5,63.0) | 14.6 (-8.8,44.1) |
| AST ³ | 0.0 (Reference) | 7.1 (-9.7,27.0) | 8.1 (-15.4,38.1) | 2.8 (-12.4,20.7) |
| AST:ALT Ratio ³ | 0.0 (Reference) | -5.5 (-19.4,10.7) | -5.0 (-24.4,19.2) | -10.3 (-24.2,6.2) |
| Liver Fat Percent ^{3,4} | 0.0 (Reference) | 4.3 (-26.1,47.3) | 17.7 (-15.0,63.0) | 51.3 (6.3,115.3) |
| GGT ³ | 0.0 (Reference) | 16.5 (-18.8,67.1) | 19.3 (-24.8,89.2) | 7.3 (-22.9,49.2) |
| Bilirubin ³ | 0.0 (Reference) | -14.2 (-37.7,18.2) | -25.2 (-47.9,7.3) | -15.8 (-37.8,14.0) |
| Binary Outcomes ⁵ | | | | |
| (2012-2014) | | | | |
| Hyperglycemia | | | | |
| Type 2 Diabetes | 1.00 (Reference) | 1.79 (0.64,4.96) | 1.31 (0.41,4.13) | 1.71 (0.67,4.34) |
| Hypertriglyceridemia | | | | |
| Obesity | | | | |
| Elevated ALT ³ | 1.00 (Reference) | 1.34 (0.74,2.43) | 0.88 (0.31,2.46) | 1.34 (0.72,2.51) |
| Elevated AST:ALT | | | | |
| Ratio ³ | | | | |
| Elevated Liver Fat | | | | |
| Score ^{3,6} | | | | |

Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase; BMI, body mass index; HDL, high-density lipoprotein; HOMA-IR, Homeostatic model assessment for insulin resistance; HOMA-B, Homeostatic model assessment for β-cell function; LDL, low-density lipoprotein.

¹Continuous outcomes were log-transformed. Results are presented as the percent difference (95% confidence interval) calculated as the exponentiated beta coefficient from the adjusted model, subtracting 1 and multiplying by 100.

² Analyses adjusted for current characteristics including maternal age, parity, education, smoking, moderate/vigorous physical activity, alternative healthy eating index-2010, intake of tea, and intake of coffee, and pre-pregnancy chronic diseases at the index pregnancy. Multiple imputation with 20 replicates

was used for missing exposure and covariate data. Boldfaced indicates estimates that are significant at P < 0.05.

³ Outcomes related to liver function exclude women with habitual alcohol intake > 24 g/d, approximately equivalent to 2 standard drinks/d.

 $^{4} Calculated liver fat percent = 10^{(-0.805+0.282 * metabolic syndrome (yes=1; no=0) + 0.078 * T2DM (yes=2; no=0) + 0.525 * log(fs-insulin[mU/L]) + 0.521 * log(fs-AST[U/L]) - 0.454 * log(AST/ALT))$

⁵ Binary outcomes are presented as the relative risk (95% confidence interval). The following definitions were used for the Binary outcomes: elevated ALT, \geq 19.0 U/L; elevated AST:ALT ratio, ratio \geq 2; Liver fat score, > -0.640; hypertriglyceridemia, triglycerides \geq 200 mg/dL; hyperglycemia, fasting glucose \geq 7.0 mmol/l; type 2 diabetes, HbA_{1C} \geq 6.5%, fasting glucose \geq 7.0 mmol/l, or 2-hour oral glucose tolerance test glucose \geq 11.1 mmol/l or self-report of physician diagnosis; obesity, BMI \geq 30.0 kg/m². ⁶ Liver Fat Score=-2.89 +1.18*metabolic syndrome(yes=1/no=0) +0.45*T2DM(yes=1/no=0) +insulin(mU/L) +0.04*AST(U/L) -0.94*AST/ALT.

Supplementary Table 6. Long-term consumption patterns of artificially sweetened beverages from pregnancy 9-16 years earlier to the past year and adjusted associations with current cardiometabolic outcomes among women with a history of gestational diabetes and without prevalent chronic diseases at follow-up (n=363).

| Continuous Outcomes | \leq 4 Serving / mo | \leq 4 Servings / mo | \geq 2 Servings / wk | \geq 2 Serving / wk |
|----------------------------------|-----------------------|------------------------|------------------------|-----------------------|
| (2012-2014) ^{1, 2} | in Pregnancy and | in Pregnancy and | and ≤ 4 Servings | in Pregnancy and |
| | at Follow-up | \geq 2 Servings / wk | per / at Follow-up | at Follow-up |
| | | at Follow-up | | |
| HbA _{1C} | 0.0 (Reference) | 3.2 (-0.1,6.6) | 1.6 (-1.2,4.4) | 2.2 (-0.5,5.0) |
| Fasting Glucose | 0.0 (Reference) | 0.5 (-4.2,5.4) | 0.1 (-4.1,4.6) | 1.0 (-3.4,5.7) |
| Fasting Insulin | 0.0 (Reference) | -5.1 (-18.7,10.8) | 5.1 (-10.8,23.9) | -4.7 (-17.1,9.5) |
| C-Peptide | 0.0 (Reference) | -6.1 (-17.1,6.3) | -0.4 (-12.5,13.4) | -2.2 (-11.7,8.4) |
| HOMA-IR | 0.0 (Reference) | -3.7 (-19.0,14.5) | 5.6 (-12.0,26.7) | -3.9 (-17.7,12.3) |
| HOMA-B | 0.0 (Reference) | -7.7 (-21.0,7.9) | 2.8 (-11.7,19.8) | -6.9 (-19.2,7.4) |
| Triglycerides | 0.0 (Reference) | 13.6 (0.2,28.9) | 7.7 (-6.3,23.9) | 2.7 (-9.0,16.0) |
| HDL | 0.0 (Reference) | -0.8 (-8.3,7.4) | -4.7 (-12.4,3.7) | -3.2 (-9.5,3.5) |
| LDL | 0.0 (Reference) | 0.5 (-6.9,8.6) | -1.2 (-10.7,9.3) | -0.8 (-8.7,7.8) |
| BMI | 0.0 (Reference) | 1.5 (-4.3,7.6) | 3.4 (-0.9,7.8) | 1.4 (-2.6,5.7) |
| Waist Circumference | 0.0 (Reference) | -1.4 (-4.2,1.5) | 1.2 (-2.1,4.7) | 0.6 (-2.3,3.5) |
| Visceral Adipose Tissue | 0.0 (Reference) | 6.1 (-31.3,63.8) | 12.7 (-32.9,89.2) | 7.4 (-31.8,69.3) |
| Mean Arterial Pressure | 0.0 (Reference) | 0.1 (-3.4,3.7) | -3.0 (-6.3,0.4) | -1.2 (-4.3,2.1) |
| CRP | 0.0 (Reference) | 1.2 (-28.5,43.2) | 34.7 (-3.5,88.0) | 7.5 (-20.9,46.1) |
| ALT ³ | 0.0 (Reference) | 13.7 (-2.7,32.8) | 9.4 (-10.5,33.8) | 12.4 (-6.0,34.3) |
| AST ³ | 0.0 (Reference) | 3.0 (-10.8,19.0) | 0.8 (-14.2,18.4) | 7.6 (-5.7,22.7) |
| AST:ALT Ratio ³ | 0.0 (Reference) | -9.4 (-20.4,3.2) | -7.9 (-21.3,7.7) | -4.3 (-16.6,9.9) |
| Liver Fat Percent ^{3,4} | 0.0 (Reference) | 11.1 (-14.3,43.9) | 4.1 (-22.0,38.8) | 7.1 (-16.9,38.1) |
| GGT ³ | 0.0 (Reference) | 7.1 (-17.7,39.4) | 24.7 (-6.9,67.1) | 0.4 (-21.3,28.1) |
| Bilirubin ³ | 0.0 (Reference) | -16.6 (-31.8,2.1) | -22.6 (-37.8,-3.7) | -19.4 (-33.4,-2.6) |
| Binary Outcomes ⁵ | | | | |
| (2012-2014) | | | | |
| Hyperglycemia | 1.00 (Reference) | 1.05 (0.29,3.84) | 1.14 (0.30,4.30) | 0.79 (0.21,3.03) |
| Type 2 Diabetes | 1.00 (Reference) | 1.27 (0.51,3.13) | 1.22 (0.42,3.54) | 0.69 (0.26,1.87) |
| Hypertriglyceridemia | 1.00 (Reference) | 1.52 (0.52,4.48) | 0.94 (0.25,3.51) | 0.87 (0.29,2.59) |
| Obesity | 1.00 (Reference) | 1.03 (0.69,1.53) | 1.49 (0.98,2.27) | 1.38 (0.95,1.99) |
| Elevated ALT ³ | 1.00 (Reference) | 1.37 (0.84,2.23) | 1.23 (0.70,2.17) | 1.24 (0.74,2.08) |
| Elevated AST:ALT | 1.00 (Reference) | 0.86 (0.28,2.66) | 0.56 (0.13,2.46) | 1.18 (0.41,3.40) |
| Ratio ³ | | | | |
| Elevated Liver Fat | 1.00 (Reference) | 1.38 (0.68,2.77) | 1.04 (0.43,2.55) | 1.15 (0.53,2.51) |
| Score ^{3,6} | | | | |

Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase; BMI, body mass index; CI, confidence interval; HDL, high-density lipoprotein; HOMA-IR, Homeostatic model assessment for insulin resistance; HOMA-B, Homeostatic model assessment for β -cell function; LDL, low-density lipoprotein; MET, metabolic equivalent.

¹Continuous outcomes were log-transformed. Percent difference was calculated as the exponentiated beta coefficient from the adjusted model, subtracting 1 and multiplying by 100.

 2 Analyses adjusted for current characteristics including maternal age, parity, education, smoking, moderate/vigorous physical activity, alternative healthy eating index-2010, intake of tea, and intake of coffee, and pre-pregnancy chronic diseases at the index pregnancy. Multiple imputation with 20 replicates was used for missing exposure and covariate data. Boldfaced indicates estimates that are significant at P < 0.05.

³ Outcomes related to liver function exclude women with habitual alcohol intake > 24 g/d, approximately equivalent to 2 standard drinks/d.

⁴ The following definitions were used for the Binary outcomes: elevated ALT, \geq 19.0 U/L; elevated AST:ALT ratio, ratio \geq 2; elevated liver fat score, >-0.640; hypertriglyceridemia, triglycerides \geq 200 mg/dL; hyperglycemia, fasting glucose \geq 7.0 mmol/l; type 2 diabetes, HbA1c \geq 6.5%, fasting glucose \geq 7.0 mmol/l, or 2-hour oral glucose tolerance test glucose \geq 11.1 mmol/l or self-report of physician diagnosis; obesity, BMI \geq 30.0 kg/m².

| Continuous Outcomes | Up (2012-2014) | | | | |
|----------------------------------|------------------|--------------------|--------------------|----------------------|-------|
| (2012-2014) ^{1,2} | < 1 serving / mo | 1-4 serving / mo | 2-6 serving / wk | \geq 1 serving / d | Р- |
| | | | | | Trend |
| HbA _{1C} | 0.0 (Reference) | -0.4 (-3.0,2.3) | 2.5 (0.1,5.0) | 6.3 (2.0,10.8) | 0.006 |
| Fasting Glucose | 0.0 (Reference) | 0.5 (-3.2,4.4) | 3.5 (-0.8,8.0) | 6.2 (-0.4,13.2) | 0.12 |
| Fasting Insulin | 0.0 (Reference) | 6.8 (-7.0,22.5) | -3.0 (-14.7,10.3) | -7.0 (-23.7,13.3) | 0.39 |
| C-Peptide | 0.0 (Reference) | 4.2 (-5.3,14.6) | -2.7 (-10.8,6.2) | -6.5 (-17.6,6.1) | 0.24 |
| HOMA-IR | 0.0 (Reference) | 7.3 (-7.7,24.7) | 1.9 (-11.1,17.0) | -0.9 (-18.8,20.9) | 0.74 |
| HOMA-B | 0.0 (Reference) | 4.2 (-9.2,19.7) | -12.8 (-24.3,0.3) | -17.6 (-35.4,4.9) | 0.15 |
| Triglycerides | 0.0 (Reference) | -1.4 (-11.0,9.3) | 3.4 (-5.8,13.5) | 4.1 (-9.1,19.2) | 0.59 |
| HDL | 0.0 (Reference) | 3.4 (-2.2,9.3) | 1.4 (-3.7,6.9) | 0.4 (-6.3,7.5) | 0.80 |
| LDL | 0.0 (Reference) | -4.5 (-11.3,2.9) | -3.1 (-8.9,2.9) | -0.8 (-8.7,7.7) | 0.76 |
| BMI | 0.0 (Reference) | 2.8 (-0.4,6.2) | 0.7 (-2.2,3.6) | 1.9 (-3.4,7.6) | 0.66 |
| Waist Circumference | 0.0 (Reference) | 2.5 (-0.1,5.1) | 0.4 (-1.6,2.4) | 0.9 (-1.9,3.7) | 0.87 |
| Visceral Adipose | 0.0 (Reference) | 11.7 (-21.6,59.3) | 8.3 (-20.3,47.1) | -5.1 (-35.7,40.1) | 0.57 |
| Tissue | | | | | |
| Mean Arterial Pressure | 0.0 (Reference) | -0.4 (-3.3,2.6) | -0.3 (-2.5,2.1) | 0.4 (-2.8,3.7) | 0.72 |
| CRP | 0.0 (Reference) | -2.3 (-27.0,30.7) | -8.5 (-27.5,15.5) | -13.8 (-36.1,16.3) | 0.40 |
| ALT ³ | 0.0 (Reference) | 6.1 (-9.9,24.9) | 7.3 (-5.8,22.2) | 4.9 (-10.0,22.4) | 0.86 |
| AST ³ | 0.0 (Reference) | -10.0 (-20.9,2.5) | -4.1 (-13.0,5.7) | -4.0 (-14.8,8.3) | 0.95 |
| AST:ALT Ratio ³ | 0.0 (Reference) | -15.3 (-24.8,-4.5) | -10.2 (-18.2,-1.5) | -8.7 (-18.3,2.0) | 0.71 |
| Liver Fat Percent ^{3,4} | 0.0 (Reference) | -1.4 (-22.3,25.1) | 6.9 (-11.9,29.7) | 1.0 (-20.6,28.3) | 0.93 |
| GGT ³ | 0.0 (Reference) | 14.1 (-14.8,53.0) | -5.5 (-21.9,14.3) | 3.2 (-17.6,29.3) | 0.82 |
| Bilirubin ³ | 0.0 (Reference) | 9.7 (-8.7,31.9) | 1.0 (-12.9,17.1) | -3.9 (-18.1,12.7) | 0.33 |
| Binary Outcomes ⁵ | | | | | |
| (2012-2014) | | | | | |
| Hyperglycemia | 1.00 (Reference) | 1.11 (0.46,2.65) | 1.67 (0.84,3.32) | 1.41 (0.63,3.17) | 0.76 |
| Type 2 Diabetes | 1.00 (Reference) | 1.05 (0.67,1.66) | 1.22 (0.86,1.74) | 1.05 (0.72,1.55) | 0.81 |
| Hypertriglyceridemia | 1.00 (Reference) | 0.48 (0.14,1.70) | 1.28 (0.64,2.56) | 1.18 (0.53,2.63) | 0.63 |
| Obesity | 1.00 (Reference) | 1.24 (0.90,1.70) | 1.18 (0.91,1.54) | 1.24 (0.92,1.67) | 0.41 |
| Elevated ALT ³ | 1.00 (Reference) | 0.96 (0.65,1.43) | 1.19 (0.90,1.58) | 1.12 (0.81,1.53) | 0.68 |
| Elevated AST:ALT | 1.00 (Reference) | 0.29 (0.07,1.14) | 0.51 (0.24,1.08) | 0.63 (0.24,1.62) | 0.88 |
| Ratio ³ | · / | | | | |
| Elevated Liver Fat | 1.00 (Reference) | 1.16 (0.73,1.82) | 1.28 (0.88,1.87) | 1.24 (0.84,1.83) | 0.56 |
| $Score^{3,6}$ | × , | | | | |

Supplementary Table 7. Consumption of artificially sweetened beverages *including* coffee and tea with added artificial sweeteners during the past year and adjusted associations with cardiometabolic outcomes among women with a history of gestational diabetes (n=607).

Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase; BMI, body mass index; Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase; BMI, body mass index; HDL, high-density lipoprotein; HOMA-IR, Homeostatic model assessment for insulin resistance; HOMA-B, Homeostatic model assessment for β-cell function; LDL, low-density lipoprotein.

¹Continuous outcomes were log-transformed. Results are presented as the percent difference (95% confidence interval) calculated as the exponentiated beta coefficient from the adjusted model, subtracting 1 and multiplying by 100.

² Analyses adjusted for current characteristics including maternal age, parity, education, smoking, moderate/vigorous physical activity, alternative healthy eating index-2010, intake of tea, and intake of coffee, and pre-pregnancy chronic diseases at the index pregnancy. Multiple imputation with 20 replicates was used for missing exposure and covariate data. Boldfaced indicates estimates that are significant at P<0.05.

³ Outcomes related to liver function exclude women with habitual alcohol intake > 24 g/d, approximately equivalent to 2 standard drinks/d.

⁴ Calculated liver fat percent = $10^{(-0.805+0.282 * \text{metabolic syndrome (yes=1; no=0)} + 0.078 * T2DM (yes=2; no=0) + 0.525 * log(fs-insulin[mU/L]) + 0.521 * log(fs-AST[U/L]) - 0.454 * log(AST/ALT))$

⁵ Binary outcomes are presented as the relative risk (95% confidence interval). The following definitions were used for the Binary outcomes: elevated ALT, \geq 19.0 U/L; elevated AST:ALT ratio, ratio \geq 2; Liver fat score, > -0.640; hypertriglyceridemia, triglycerides \geq 200 mg/dL; hyperglycemia, fasting glucose \geq 7.0 mmol/l; type 2 diabetes, HbA_{1C} \geq 6.5%, fasting glucose \geq 7.0 mmol/l, or 2-hour oral glucose tolerance test glucose \geq 11.1 mmol/l or self-report of physician diagnosis; obesity, BMI \geq 30.0 kg/m². ⁶ Liver Fat Score=-2.89 +1.18*metabolic syndrome(yes=1/no=0) +0.45*T2DM(yes=1/no=0)

+insulin(mU/L) +0.04*AST(U/L) -0.94*AST/ALT.

| <u> </u> | Artificially Swee | tened Beverage In | take in Pregnancy | (1996-2002) | / |
|----------------------------------|-------------------|--------------------|--------------------|------------------------|-------|
| Continuous Outcomes | v | 0 | | | Р- |
| $(2012-2014)^{1,2}$ | < 1 serving / mo | 1-4 serving / mo | 2-6 serving / wk | ≥ 1 serving / day | Trend |
| HbA _{1C} | 0.0 (Reference) | -2.3 (-11.7,8.1) | 6.7 (-4.5,19.3) | 7.2 (-11.7,30.2) | 0.40 |
| Fasting Glucose | 0.0 (Reference) | -4.0 (-18.7,13.4) | 13.0 (-5.5,35.2) | 11.3 (-15.4,46.4) | 0.33 |
| Fasting Insulin | 0.0 (Reference) | 12.2 (-31.0,82.4) | 16.5 (-27.2,86.4) | -1.1 (-49.3,93.1) | 0.80 |
| C-Peptide | 0.0 (Reference) | 6.3 (-24.4,49.3) | 3.3 (-28.1,48.5) | 11.7 (-40.9,111.0) | 0.78 |
| HOMA-IR | 0.0 (Reference) | 8.0 (-37.8,87.5) | 25.6 (-27.5,117.4) | 9.0 (-45.4,117.5) | 0.89 |
| HOMA-B | 0.0 (Reference) | 22.9 (-22.3,94.3) | 0.9 (-36.0,58.8) | -15.0 (-66.8,118.0) | 0.55 |
| Triglycerides | 0.0 (Reference) | 4.2 (-25.4,45.5) | 7.6 (-24.6,53.6) | 12.5 (-39.3,108.6) | 0.75 |
| HDL | 0.0 (Reference) | 7.7 (-9.9,28.7) | 0.8 (-17.4,23.2) | 9.3 (-15.4,41.2) | 0.59 |
| LDL | 0.0 (Reference) | -16.0 (-39.0,15.7) | -3.1 (-23.5,22.8) | 7.4 (-25.7,55.1) | 0.42 |
| BMI | 0.0 (Reference) | 5.7 (-5.5,18.2) | -1.1 (-11.6,10.7) | 2.7 (-11.8,19.6) | 0.99 |
| Waist Circumference | 0.0 (Reference) | 4.5 (-3.5,13.2) | 2.2 (-6.4,11.5) | 3.3 (-9.3,17.6) | 0.87 |
| Visceral Adipose Tissue | 0.0 (Reference) | | | | |
| Mean Arterial Pressure | 0.0 (Reference) | 3.0 (-9.5,17.2) | 2.9 (-5.5,11.9) | 1.1 (-17.0,23.1) | 0.99 |
| CRP | 0.0 (Reference) | 31.7 (-53.4,272.1) | -8.5 (-62.9,125.7) | 10.0 (-76.3,409.9) | 0.97 |
| ALT ³ | 0.0 (Reference) | 0.3 (-40.1,67.8) | 13.7 (-25.5,73.7) | 76.0 (2.5,202.3) | 0.02 |
| AST ³ | 0.0 (Reference) | 3.1 (-34.7,62.7) | 10.9 (-22.8,59.2) | 58.1 (-9.4,175.9) | 0.07 |
| AST:ALT Ratio ³ | 0.0 (Reference) | 2.8 (-34.6,61.5) | -2.5 (-33.4,42.8) | -10.2 (-51.7,66.9) | 0.58 |
| Liver Fat Percent ^{3,4} | 0.0 (Reference) | 0.0 (-61.8,162.0) | 62.5 (-25.0,252.0) | 60.5 (-41.7,341.7) | 0.27 |
| GGT ³ | 0.0 (Reference) | 87.2 (-20.3,339.5) | 49.4 (-25.3,198.6) | 153.0 (0.3,538.0) | 0.11 |
| Bilirubin ³ | 0.0 (Reference) | -15.0 (-57.9,71.6) | 23.3 (-21.2,92.9) | -7.4 (-60.7,118.4) | 0.95 |
| Binary Outcomes ^{2,5} | | | | | |
| (2012-2014) | | | | | |
| Hyperglycemia | | | | | |
| Type 2 Diabetes | 1.00 (Reference) | 0.60 (0.12,2.95) | 1.83 (0.47,7.15) | 0.89 (0.19,4.09) | 0.72 |
| Hypertriglyceridemia | | | | | |
| Obesity | 1.00 (Reference) | 1.24 (0.46,3.38) | 1.19 (0.45,3.11) | 1.48 (0.49,4.45) | 0.49 |
| Elevated ALT ³ | 1.00 (Reference) | 0.59 (0.15,2.28) | 1.31 (0.49,3.49) | 1.67 (0.54,5.17) | 0.19 |
| Elevated AST:ALT | ```´`´ | | | | |
| Ratio ³ | | | | | |
| Elevated Liver Fat | | | | | |
| Score ^{3,6} | | | | | |

Supplementary Table 8. Consumption of artificially sweetened beverages during pregnancy and adjusted associations with cardiometabolic outcomes 9-16 years later among women with a history of gestational diabetes who consumed < 1 serving of sugar sweetened beverages during pregnancy (n=82).

Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase; BMI, body mass index; HDL, high-density lipoprotein; HOMA-IR, Homeostatic model assessment for insulin resistance; HOMA-B, Homeostatic model assessment for β-cell function; LDL, low-density lipoprotein.

¹Continuous outcomes were log-transformed. Results are presented as the percent difference (95% confidence interval) calculated as the exponentiated beta coefficient from the adjusted model, subtracting 1 and multiplying by 100.

² Analyses adjusted for current characteristics including maternal age, parity, education, smoking, moderate/vigorous physical activity, alternative healthy eating index-2010, intake of tea, and intake of coffee, and pre-pregnancy chronic diseases at the index pregnancy. Multiple imputation with 20 replicates was used for missing exposure and covariate data. Boldfaced indicates estimates that are significant at P<0.05.

³ Outcomes related to liver function exclude women with habitual alcohol intake > 24 g/d, approximately equivalent to 2 standard drinks/d.

⁴ Calculated liver fat percent = $10^{(-0.805+0.282 * \text{metabolic syndrome (yes=1; no=0)} + 0.078 * T2DM (yes=2; no=0) + 0.525 * log(fs-insulin[mU/L]) + 0.521 * log(fs-AST[U/L]) - 0.454 * log(AST/ALT))$

⁵ Binary outcomes are presented as the relative risk (95% confidence interval). The following definitions were used for the Binary outcomes: elevated ALT, \geq 19.0 U/L; elevated AST:ALT ratio, ratio \geq 2; Liver fat score, > -0.640; hypertriglyceridemia, triglycerides \geq 200 mg/dL; hyperglycemia, fasting glucose \geq 7.0 mmol/l; type 2 diabetes, HbA_{1C} \geq 6.5%, fasting glucose \geq 7.0 mmol/l, or 2-hour oral glucose tolerance test glucose \geq 11.1 mmol/l or self-report of physician diagnosis; obesity, BMI \geq 30.0 kg/m². ⁶ Liver Fat Score=-2.89 +1.18*metabolic syndrome(yes=1/no=0) +0.45*T2DM(yes=1/no=0) +insulin(mU/L) +0.04*AST(U/L) -0.94*AST/ALT.

| Habitual Artificially Sweetened Beverage Intake at Follow Up (2012-2014) | | | | | |
|--|------------------|--------------------|-------------------|----------------------|-------|
| Continuous Outcomes | | • | | • • | Р- |
| (2012-2014) ^{1, 2} | < 1 serving / mo | 1-4 serving / mo | 2-6 serving / wk | \geq 1 serving / d | Trend |
| HbA _{1C} | 0.0 (Reference) | 0.7 (-4.4,6.0) | 3.8 (0.3,7.4) | 4.9 (-0.4,10.5) | 0.16 |
| Fasting Glucose | 0.0 (Reference) | 4.5 (-2.2,11.7) | 6.9 (1.2,12.9) | 3.6 (-4.0,11.9) | 0.89 |
| Fasting Insulin | 0.0 (Reference) | 9.6 (-14.8,41.1) | -1.7 (-18.9,19.2) | 5.8 (-19.1,38.3) | 0.69 |
| C-Peptide | 0.0 (Reference) | 7.5 (-8.6,26.3) | -4.6 (-15.3,7.5) | -10.1 (-24.4,7.0) | 0.20 |
| HOMA-IR | 0.0 (Reference) | 13.2 (-13.9,48.8) | 4.6 (-14.4,28.0) | 10.3 (-15.5,43.9) | 0.60 |
| HOMA-B | 0.0 (Reference) | 0.7 (-22.1,30.1) | -14.7 (-31.2,5.7) | -1.8 (-29.2,36.3) | 0.80 |
| Triglycerides | 0.0 (Reference) | -9.1 (-22.4,6.6) | 7.6 (-4.3,21.0) | -2.9 (-16.4,12.9) | 0.54 |
| HDL | 0.0 (Reference) | 0.4 (-8.5,10.2) | 0.4 (-6.1,7.4) | -0.4 (-8.7,8.7) | 0.88 |
| LDL | 0.0 (Reference) | -13.5 (-23.1,-2.6) | -6.4 (-14.2,2.0) | -7.3 (-16.9,3.5) | 0.56 |
| BMI | 0.0 (Reference) | 3.4 (-1.9,9.0) | 2.0 (-2.1,6.4) | 4.1 (-3.3,12.0) | 0.42 |
| Waist Circumference | 0.0 (Reference) | 3.3 (-0.8,7.5) | 1.6 (-1.1,4.4) | 1.6 (-2.0,5.4) | 0.73 |
| Visceral Adipose | | | | | |
| Tissue | 0.0 (Reference) | 18.4 (-28.4,95.7) | -3.8 (-33.0,38.1) | -26.3 (-54.3,18.9) | 0.16 |
| Mean Arterial Pressure | 0.0 (Reference) | 0.3 (-3.9,4.6) | -1.2 (-4.1,1.8) | 0.7 (-3.3,4.8) | 0.57 |
| CRP | 0.0 (Reference) | -32.6 (-60.3,14.7) | 1.3 (-26.4,39.5) | -10.9 (-39.3,30.9) | 0.74 |
| ALT ³ | 0.0 (Reference) | 4.9 (-17.2,32.9) | 3.3 (-13.0,22.6) | -9.3 (-25.3,10.1) | 0.11 |
| AST ³ | 0.0 (Reference) | -8.3 (-24.4,11.3) | -1.7 (-13.0,11.2) | -8.8 (-21.3,5.8) | 0.26 |
| AST:ALT Ratio ³ | 0.0 (Reference) | -12.8 (-26.1,2.9) | -4.3 (-14.8,7.4) | 0.2 (-12.6,14.9) | 0.45 |
| Liver Fat Percent ^{3,4} | 0.0 (Reference) | -1.1 (-29.0,37.8) | 14.4 (-11.7,48.1) | -5.2 (-31.4,30.9) | 0.44 |
| GGT ³ | 0.0 (Reference) | 53.2 (-2.6,141.0) | 4.3 (-17.3,31.4) | 6.7 (-18.2,39.2) | 0.80 |
| Bilirubin ³ | 0.0 (Reference) | 18.1 (-10.2,55.4) | 9.2 (-7.1,28.3) | -3.2 (-19.0,15.8) | 0.18 |
| Binary Outcomes ^{2,5} | . , | | | | |
| (2012-2014) | | | | | |
| Hyperglycemia | | 2.47 (0.75,8.18) | 2.09 (0.79,5.54) | 1.55 (0.51,4.70) | 0.79 |
| Type 2 Diabetes | 1.00 (Reference) | 1.12 (0.55,2.27) | 1.58 (1.00,2.50) | 1.06 (0.62, 1.80) | 0.42 |
| Hypertriglyceridemia | | 0.63 (0.06,6.82) | 2.36 (0.83,6.70) | 1.37 (0.39,4.85) | 0.90 |
| Obesity | 1.00 (Reference) | 1.26 (0.74,2.17) | 1.54 (1.03,2.29) | 1.59 (1.02,2.47) | 0.12 |
| Elevated ALT ³ | 1.00 (Reference) | 0.86 (0.50, 1.47) | 1.12 (0.81,1.56) | 0.84 (0.55,1.27) | 0.21 |
| Elevated AST:ALT | | | . , | . , | |
| Ratio ³ | | | | | |
| Elevated Liver Fat | | | | | |
| Score ^{3,6} | | 1.04 (0.54,2.02) | 1.50 (0.89,2.53) | 1.18 (0.67,2.10) | 0.83 |

Supplementary Table 9. Consumption of artificially sweetened beverages during the past year and adjusted associations with cardiometabolic outcomes among women with a history of gestational diabetes who consumed < 1 serving of sugar sweetened beverages during the past year (n=319).

Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase; BMI, body mass index; HDL, high-density lipoprotein; HOMA-IR, Homeostatic model assessment for insulin resistance; HOMA-B, Homeostatic model assessment for β-cell function; LDL, low-density lipoprotein.

¹Continuous outcomes were log-transformed. Results are presented as the percent difference (95% confidence interval) calculated as the exponentiated beta coefficient from the adjusted model, subtracting 1 and multiplying by 100.

² Analyses adjusted for current characteristics including maternal age, parity, education, smoking, moderate/vigorous physical activity, alternative healthy eating index-2010, intake of tea, and intake of coffee, and pre-pregnancy chronic diseases at the index pregnancy. Multiple imputation with 20 replicates was used for missing exposure and covariate data. Boldfaced indicates estimates that are significant at P<0.05.

³ Outcomes related to liver function exclude women with habitual alcohol intake > 24 g/d, approximately equivalent to 2 standard drinks/d.

⁴ Calculated liver fat percent = $10^{(-0.805+0.282 * \text{metabolic syndrome (yes=1; no=0)} + 0.078 * T2DM (yes=2; no=0) + 0.525 * log(fs-insulin[mU/L]) + 0.521 * log(fs-AST[U/L]) - 0.454 * log(AST/ALT))$

⁵ Binary outcomes are presented as the relative risk (95% confidence interval). The following definitions were used for the Binary outcomes: elevated ALT, \geq 19.0 U/L; elevated AST:ALT ratio, ratio \geq 2; Liver fat score, > -0.640; hypertriglyceridemia, triglycerides \geq 200 mg/dL; hyperglycemia, fasting glucose \geq 7.0 mmol/l; type 2 diabetes, HbA_{1C} \geq 6.5%, fasting glucose \geq 7.0 mmol/l, or 2-hour oral glucose tolerance test glucose \geq 11.1 mmol/l or self-report of physician diagnosis; obesity, BMI \geq 30.0 kg/m². ⁶ Liver Fat Score=-2.89 +1.18*metabolic syndrome(yes=1/no=0) +0.45*T2DM(yes=1/no=0)

+insulin(mU/L) +0.04*AST(U/L) -0.94*AST/ALT.