**Supplemental Tables 1a:** Unadjusted and adjusted associations between concurrent L:M and cholesterol profiles

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **TC (mmol/L)** | | **LDL-c (mmol/L)** | | **vLDL (mmol/L)** | | **HDL-c (mmol/L)** | | **TC/HDL** | |
|  | **unadjusted** | **adjusted** | **unadjusted** | **adjusted** | **unadjusted** | **adjusted** | **unadjusted** | **adjusted** | **unadjusted** | **adjusted** |
| **per SD L:M** | -0.06 (-0.15, 0.02)  (p=0.134) | -0.07 (-0.15, 0.01)  (p=0.096) | -0.05 (-0.13, 0.02)  (p=0.142) | -0.06 (-0.13, 0.01)  (p=0.113) | 0.02 (-0.01, 0.06)  (p=0.240) | 0.02 (-0.01, 0.06)  (p=0.240) | -0.03 (-0.07, 0.00)  (p=0.071) | -0.03 (-0.06, 0.01)  (p=0.143) | 0.05 (-0.06, 0.16)  (p=0.363) | 0.05 (-0.06, 0.16)  (p=0.363) |
| **sex=girls (boys=reference)** | - | 0.17 (0.00, 0.34)  (p=0.044) | - | 0.19 (0.05, 0.34)  (p=0.010) | - | - | - | - | - | - |
| **age (in months)** | - | - | - | - | - | - | - | 0.01 (0.00, 0.01)  (p=0.027) | - | - |
| **WHZ** | - | - | - | - | - | - | - | - | - | - |
| **breastfeeding** | - | 0.04 (-0.01, 0.09)  (p=0.090) | - | - | - | - | - | - | - | - |
| **WAMI** | - | 0.68 (0.03, 1.33)  (p=0.040) | - | 0.44 (-0.12, 0.99)  (p=0.122) | - | - | - | - | - | - |
| **per SD % Lactulose excretion** | -0.04 (-0.12, 0.04)  (p=0.322) | -0.04 (-0.13, 0.04)  (p=0.309) | -0.03 (-0.100, 0.04)  (p=0.407) | -0.03 (-0.10, 0.04)  (p=0.423) | -0.03 (-0.07, -0.00)  (p=0.045) | -0.03 (-0.07, -0.00)  (p=0.045) | 0.02 (-0.02, 0.06)  (p=0.275) | 0.02 (-0.02, 0.05)  (p=0.293) | -0.09 (-0.20, 0.01)  (p=0.076) | -0.09 (-0.20, 0.01)  (p=0.076) |
| **sex=girls (boys=reference)** | - | 0.18 (0.01, 0.35)  (p=0.038) | - | 0.20 (0.05, 0.34)  (p=0.008) | - | - | - | - | - | - |
| **age (in months)** | - | - | - | - | - | - | - | 0.01 (0.00, 0.01)  (p=0.015) | - | - |
| **WHZ** | - | - | - | - | - | - | - | - | - | - |
| **breastfeeding** | - | 0.04 (-0.01, 0.09)  (p=0.119) | - | - | - | - | - | - | - | - |
| **WAMI** | - | 0.70 (0.04, 1.36)  (p=0.036) | - | 0.45 (-0.11, 1.02)  (p=0.114) | - | - | - | - | - | - |
| **per SD % Mannitol excretion** | 0.02 (-0.02, 0.05)  (p=0.293) | 0.01 (-0.07, 0.10)  (p=0.789) | 0.01 (-0.06, 0.08)  (p=0.783) | 0.01 (-0.06, 0.09)  (0.698) | -0.04 (-0.08, -0.01)  (p=0.017) | -0.04 (-0.08, -0.01)  (p=0.017) | 0.04 (0.00, 0.08)  (p=0.040) | 0.03 (-0.00, 0.07)  (p=0.072) | -0.11 (-0.22, -0.00)  (p=0.043) | -0.11 (-0.22, -0.00)  (p=0.043) |
| **sex=girls (boys=reference)** | - | 0.18 (0.01, 0.35)  (p=0.039) | - | 0.20 (0.05, 0.34)  (p=0.009) | - | - | - | - | - | - |
| **age (in months)** | - | - | - | - | - | - | - | 0.01 (0.00, 0.010)  (p=0.025) | - | - |
| **WHZ** | - | - | - | - | - | - | - | - | - | - |
| **breastfeeding** | - | 0.04 (-0.01, 0.09)  (p=0.096) | - | - | - | - | - | - | - | - |
| **WAMI** | - | 2.83 (2.29, 3.37)  (p=0.049) | - | 0.42 (-0.14, 0.98)  (p=0.145) | - | - | - | - | - | - |

**Supplemental Tables 1b:** Unadjusted and adjusted associations between concurrent L:M and apolipoprotein profiles

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | **Apo AI (g/L)** | | **Apo B (g/L)** | | **Apo B/A\*1000** | |
|  | **unadjusted** | **adjusted** | **unadjusted** | **adjusted** | **unadjusted** | **adjusted** |
| **per SD L:M** | -0.05 (-0.15, 0.05)  (p=0.340) | -0.05 (-0.15, 0.05)  (p=0.365) | -0.00 (-0.01, 0.01)  (p=0.534) | -0.00 (-0.01, 0.01)  (p=0.503) | 4.26 (-2.10, 10.61)  (p=0.189) | 2.91 (-3.38, 9.19)  (p=0.365) |
| **sex=girls (boys=reference)** | - | - | - | 0.01 (-0.00, 0.03)  (p=0.089) | - | - |
| **age (in months)** | - | - | - | - | - | -1.17 (-1.99, -0.35)  (p=0.005) |
| **WHZ** | - | - | - | - | - | - |
| **breastfeeding** | - | - | - | - | - | - |
| **WAMI** | - | 0.68 (-0.10, 1.46)  (p=0.087) | - | 0.05 (-0.01, 0.10)  (p=0.101) | - | - |
| **per SD % Lactulose excretion** | 0.15 (0.05, 0.24)  (p=0.002) | 0.15 (0.05, 0.24)  (p=0.002) | 0.01 (0.00, 0.02)  (p=0.002) | 0.01 (0.00, 0.02)  (p=0.001) | -8.86 (-14.96, -2.76)  (p=0.004) | -8.64 (-14.59, -2.69)  (p=0.004) |
| **sex** | - | - | - | 0.02 (0.00, 0.03)  (p=0.029) | - | - |
| **age** | - | 0.01 (-0.00, 0.02)  (p=0.070) | - | - | - | -1.19 (-1.99, -0.40)  (p=0.003) |
| **WHZ** | - | - | - | - | - | - |
| **breastfeeding** | - | - | - | - | - | - |
| **WAMI** | - | - | - | - | - | - |
| **per SD % Mannitol**  **excretion** | 0.15 (0.06, 0.25)  (p=0.002) | 0.15 (0.05, 0.25)  (p=0.003) | 0.01 (0.00, 0.02)  (p=0.004) | 0.01 (0.00, 0.02)  (p=0.004) | -9.99 (-16.18, -3.80)  (p=0.002) | -9.02 (-15.12, -2.91)  (p=0.004) |
| **sex** | - | - | - | 0.01 (-0.00, 0.03)  (p=0.089) | - | - |
| **age** | - | - | - | - | - | -1.09 (-1.88, -0.29)  (p=0.007) |
| **WHZ** | - | - | - | - | - | - |
| **breastfeeding** | - | - | - | - | - | - |
| **WAMI** | - | 0.58 (-0.18, 1.34)  (p=0.136) | - | 0.04 (-0.02, 0.10)  (p=0.153) | - | - |

**Supplemental Tables 1c:** Unadjusted and adjusted associations between concurrent L:M and glucose, HOMA-IR, and plasma triglycerides

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | **Glucose (mmol/L)** | | **Homeostatic model assessment-insulin resistance** | | **Triglycerides (mmol/L)** | |
|  | **unadjusted** | **adjusted** | **unadjusted** | **adjusted** | **unadjusted** | **adjusted** |
| **per SD L:M** | -0.04 (-0.11, 0.03)  (p=0.265) | -0.05 (-0.11, 0.02)  (p=0.157) | 0.01 (-0.08, 0.09)  (p=0.903) | 0.01 (-0.07, 0.10)  (p=0.765) | 0.00 (-0.06, 0.07)  (p=0.880) | 0.00 (-0.06, 0.06)  (p=0.977) |
| **sex=girls (boys=reference)** | - | -0.10 (-0.23, 0.04)  (p=0.157) | - | - | - | 0.10 (-0.03, 0.22)  (p=0.139) |
| **age (in months)** | - | - | - | - | - | - |
| **WHZ** | - | - | - | 0.14 (0.07, 0.21)  (p<0.001) | - | 0.47 (-0.02, 0.96)  (p=0.058) |
| **breastfeeding** | - | - | - | 0.06 (0.01, 0.10)  (p=0.016) | - | - |
| **WAMI** | - | -0.43 (-0.95, 0.08)  (p=0.100) | - | - | - | - |
| **per SD % Lactulose excretion** | 0.03 (-0.04, 0.10)  (p=0.368) | 0.03 (-0.04, 0.09)  (p=0.480) | -0.06 (-0.14, 0.03)  (p=0.212) | -0.4 (-0.12, 0.05)  (p=0.394) | -0.01 (-0.07, 0.05)  (p=0.842) | -0.01 (-0.07, 0.05)  (p=0.733) |
| **sex** | - | - | - | - | - | 0.09 (-0.03, 0.22)  (p=0.147) |
| **age** | - | - | - | - | - | 0.01 (-0.00, 0.01)  (p=0.124) |
| **WHZ** | - | - | - | 0.14 (0.07, 0.21)  (p<0.001) | - | - |
| **breastfeeding** | - | - | - | 0.06 (0.01, 0.10)  (p=0.022) | - | - |
| **WAMI** | - | 4.89 (4.55, 5.23)  (p<0.001) | - | - | - | 0.49 (0.00, 0.98)  (p=0.049) |
| **per SD % Mannitol**  **excretion** | 0.05 (-0.02, 0.12)  (p=0.149) | 0.05 (-0.01, 0.12)  (p=0.123) | -0.05 (-0.14, 0.04)  (p=0.281) | -0.04 (-0.12, 0.05)  (p=0.378) | -0.01 (-0.07, 0.05)  (p=0.797) | 0.01 (-0.08, 0.05)  (p=0.660) |
| **Sex** | - | -0.09 (-0.23, 0.04)  (p=0.181) | - | - | - | 0.09 (-0.03, 0.22)  (p=0.144) |
| **Age** | - | - | - | - | - | 0.01 (-0.00, 0.02)  (p=0.116) |
| **WHZ** | - | 0.04 (-0.02, 0.10)  (p=0.192) | - | 0.14 (0.07, 0.21)  (p<0.001) | - | - |
| **breastfeeding** | - | - | - | 0.06 (0.01, 0.10)  (p=0.021) | - | - |
| **WAMI** | - | 0.54 (-1.06, -0.02)  (p=0.044) | - | - | - | 0.49 (0.00, 0.98)  (p=0.049) |

|  |  |  |
| --- | --- | --- |
|  | **High Blood Pressure** | |
|  | **unadjusted** | **adjusted** |
| **ln (L:M) 3 months** | 0.93 (0.45, 1.92)  (p=0.854) | 0.90 (0.42, 1.94)  (p=0.791) |
| **ln (L:M) 6 months** | 1.37 (0.70, 2.67)  (p=0.362) | 1.26 (0.63, 2.54)  (p=0.509) |
| **ln (L:M) 9 months** | 0.80 (0.41, 1.55)  (p=0.502) | 1.01 (0.50, 2.04)  (p=0.976) |
| **ln (L:M) 15 months** | 1.22 (0.70, 2.13)  (p=0.475) | 1.27 (0.70, 2.31)  (p=0.435) |
| **ln (L:M) concurrent** | 1.76 (1.10, 2.80)  (p=0.018) | 1.88 (1.14, 3.11)  (p=0.014) |
| **sex=girls (boys=reference)** | - | 0.45 (0.16, 1.23)  (p=0.120) |
| **age (in months)** | - | - |
| **WHZ** | - | 1.87 (1.26, 2.79)  (p=0.002) |
| **breastfeeding** | - | - |
| **WAMI** | - | - |
| **ln (percent lactulose) 3 months** | 0.71 (0.44, 1.15)  (p=0.164) | 0.73 (0.43, 1.23)  (p=0.239) |
| **ln (percent lactulose) 6 months** | 0.94 (0.59, 1.50)  (p=0.790) | 0.98 (0.61, 1.59)  (p=0.940) |
| **ln (percent lactulose) 9 months** | 0.65 (0.36, 1.15)  (p=0.139) | 0.57 (0.30, 1.10)  (p=0.096) |
| **ln (percent lactulose) 15 months** | 1.67 (0.96, 2.90)  (p=0.068) | 1.54 (0.85, 2.77)  (p=0.153) |
| **ln (percent lactulose) concurrent** | 0.82 (0.55, 1.23)  (p=0.338) | 0.80 (0.52, 1.25)  (p=0.336) |
| **sex** | - | 0.38 (0.13, 1.07)  (p=0.068) |
| **age** | - | - |
| **WHZ** | - | 1.73 (1.16, 2.58)  (p=0.007) |
| **breastfeeding** | - | - |
| **WAMI** | - | - |
| **ln (percent mannitol) 3 months** | 0.88 (0.60, 1.28)  (p=0.499) | 0.91 (0.61, 1.37)  (p=0.650) |
| **ln (percent mannitol) 6 months** | 0.86 (0.59, 1.27)  (p=0.453) | 0.92 (0.61, 1.41)  (p=0.714) |
| **ln (percent mannitol) 9 months** | 0.92 (0.62, 1.37)  (p=0.686) | 0.81 (0.53, 1.24)  (p=0.327) |
| **ln (percent mannitol) 15 months** | 1.20 (0.80, 1.80)  (p=0.372) | 1.14 (0.74, 1.74)  (p=0.562) |
| **ln (percent mannitol) concurrent** | 0.72 (0.52, 0.98) | 0.68 (0.48, 0.97)  (p=0.031) |
| **sex** | - | 0.35 (0.13, 1.00)  (p=0.050) |
| **age** | - | - |
| **WHZ** | - | 1.80 (1.20, 2.70)  (p=0.004) |
| **breastfeeding** | - | - |
| **WAMI** | - | - |

**Supplemental Table 2:** Unadjusted and adjusted associations between relatively elevated blood pressure and lactulose:mannitol ratios in infancy.

|  |  |  |
| --- | --- | --- |
|  | **High Blood Pressure** | |
|  | **Unadjusted Models**  **Odds Ratio (95% CI)** | **Adjusted Models**  **Odds Ratio (95% CI)** |
| **log(CRP at 7 months)** | 1.38 (1.00, 1.90)  (p=0.048) | 1.46 (1.02, 2.09)  (p=0.039) |
| **log(CRP at 15 months)** | 1.06 (0.80, 1.39)  (p=0.700) | 1.25 (0.92, 1.69)  (p=0.154) |
| **log(CRP at 24 months)** | 1.02 (0.79, 1.33)  (p=0.869) | 1.07 (0.77, 1.48)  (p=0.696) |
| **sex=girls (boys=reference)** | - | - |
| **age (in months)** | - | -0.09 (-0.16, -0.01)  (p=0.028) |
| **WHZ** | - | 0.57 (0.12, 1.03)  (p=0.012) |
| **breastfeeding** | - | - |
| **WAMI** | - | - |
| **AGP at 7 months (g/L)\*** | 2.88 (1.09, 7.60)  (p=0.033) | 2.20 (0.64, 7.58)  (p=0.211) |
| **AGP at 15 months**  **(g/L)\*** | 0.83 (0.28, 2.52)  (p=0.747) | 1.39 (0.32, 6.09)  (p=0.665) |
| **AGP at 24 months**  **(g/L)\*** | 0.68 (0.17, 2.79)  (p=0.597) | 2.71 (0.49, 14.9)  (p=0.252) |
| **sex=girls (boys=reference)** | - | 0.28 (0.08, 0.98)  (p=0.046) |
| **age (in months)** | - | 0.93 (0.85, 1.00)  (p=0.059) |
| **WHZ** | - | 2.36 (1.38, 4.05)  (p=0.002) |
| **breastfeeding** | - | - |
| **WAMI** | - | - |

**Supplemental Table 3:** Unadjusted and adjusted associations between relatively elevated blood pressure and inflammation in infancy.

\*In the adjusted AGP model the N is= 105 (due to multiple children without AGP results available at every time point) while in unadjusted models and in Figure 4, 7, 15, and 24 month comparisons have a sample size of N=141, 140, and 121, respectively).

Abbreviations used: C-reactive protein; AGP= alpha-1-acid glycoprotein.

**Supplemental Table 4:** Mediation analysis average direct and mediation effects with and without interaction between mannitol excretion (below versus above the median) and apolipoprotein AI.

|  |  |  |  |
| --- | --- | --- | --- |
|  | Product of coefficients | | |
|  |  | With interaction | |
|  | No interaction | Low mannitol | High mannitol |
| Average Causal Mediation Effect | 0.10 (0.02, 0.23) | 0.03 (-0.04, 0.37) | 0.18 (0.04, 0.37) |
| Average Direct Effect | 0.25 (-0.04, 0.57) | 0.17 (-0.13, 0.51) | 0.33 (0.03, 0.66) |
| % of Total Effect Mediated | 29% (14%, 140%) | 8% (4%, 37%) | 51% (24%, 242%) |