**Supplemental material**

**STable 1 Description of study population enrolled during week 8-13 (N=754) and week 4-19 (N=905)**

**STable 2 Association between reported APAP use during pregnancy and language delay at 30 months of age (N=754 and 905)**

**STable 3 Association between creatinine-adjusted APAP in prenatal urine at enrollment and language delay at 30 months of age (N=111 and 127)**

**STable 4 Maternal characteristics and medical use at enrollment in relation to children´s LD at 30 months and prenatal use of APAP (N=754)**

**STable 1**

|  |  |
| --- | --- |
| **Study variables** | **Study population** |
| *Continuous variables, Mean (SD)* | N=754 | N=905 |
| Age at enrollment (years) | 31.3 (4.67) | 31.3 (4.70) |
| Weight at enrollment (kg) | 69.7 (13.3) | 69.9 (13.7) |
| Median gestational week at enrollment (range) | 10 (8-13) | 10 (4-19) |
|  |  |  |
| *Categorical variables N (%)* |  |  |
| Sex of child |  |  |
| Girls | 366 (48.5) | 432 (47.7) |
| Boys | 388 (51.5) | 473 (52.3) |
| Mother completed university | 493 (65.4) | 585 (64.6) |
| Mother smoking during 1st trimester | 22 (2.9) | 25 (2.8) |
| Mother’s use of APAP during 1st trimester |  |  |
| 0 pills | 308 (40.8) | 3890 (42.0) |
| 1-3 pills | 176 (23.4) | 209 (23.1) |
| 4-6 pills | 137 (18.2) | 159 (17.6) |
| > 6 pills | 133 (17.6) | 157 (17.3) |
| Number of words used at 30 months |  |  |
| <25 words | 16 (2.1) | 23 (2.5) |
| 25-50 words | 48 (6.4) | 65 (7.2) |
| >50 words | 690 (91.5) | 817 (90.3) |
| Girls |  |  |
| <25 words | 2 (0.5) | 5 (1.2) |
| 25-50 words | 13 (3.6) | 20 (4.6) |
| >50 words | 351 (95.9) | 407 (94.2) |
| Boys |  |  |
| <25 words | 14 (3.6) | 18 (3.8) |
| 25-50 words | 35 (9.0) | 45 (9.5) |
| >50 words | 339 (87.4) | 410 (86.7) |

**STable 2**

|  |  |
| --- | --- |
| **APAP use** | **Adjusted Odds Ratio1) (95% CI)** |
| Enrollment week 8-13 (N=754) |
|  | Girls(N=366) | Boys(N=388) |
| Any pills |
| Any vs. no pills | 4.64(1.02-21.05) | 0.89(0.47-1.66) |
| Number of pills |
| 0  | REF | REF |
| 1-3  | 4.62(0.87-24.64) | 1.10(0.51-2.36) |
| 4-6  | 3.45(0.56-21.42) | 0.84(0.35-2.06) |
| >6  | 5.92(1.10-31.94) | 0.68(0.27-1.72) |
| Enrollment week 4-19 (N=905) |
|  | Girls(N=432) | Boys(N=473) |
| Any pills |
| Any vs. no pills | 2.31(0.88-6.04) | 0.95(0.55-1.64) |
| Number of pills |
| 0  | REF | REF |
| 1-3  | 1.78(0.54-5.85) | 1.07(0.54-2.12) |
| 4-6  | 2.05(0.59-7.14) | 1.14(0.54-2.38) |
| >6  | 3.32(1.07-10.32) | 0.64(0.28-1.49) |

1. Adjusted for mother’s education (complete university vs. less education), mother’s weight at enrollment (kg), mother´s smoking at enrollment, and week of enrollment.

**STable 3**

|  |  |
| --- | --- |
| **Urinary APAP** | **Adjusted Odds Ratio1) (95% CI)** |
| Enrollment week 8-13 (N=111) |
|  | Girls(N=48) | Boys(N=63) |
| Continuous urinary APAP  |
| Log(APAP) | 1.50(0.95-2.34) | 0.94(0.60-1.48) |
| Urinary APAP in quartiles |
| 1st  | REF | REF |
| 2nd | 3.57(0.54-23.80) | 0.32(0.06-1.69) |
| 3rd | 2.99(0.39-23.21) | 0.46(0.09-2.33) |
| 4th | 10.34(1.37-77.86) | 0.54(0.11-2.68) |
| Enrollment week 4-19 (N=127) |
|  | Girls(N=53) | Boys(N=74) |
| Continuous urinary APAP  |
| Log(APAP) | 1.37(0.91-2.06) | 0.92(0.61-1.40) |
| Urinary APAP in quartiles |
| 1st  | REF | REF |
| 2nd | 2.78(0.48-15.93) | 0.41(0.09-1.80) |
| 3rd  | 2.84(0.43-18.91) | 0.55(0.13-2.35) |
| 4th | 6.71(1.10-40.77) | 0.56(0.12-2.57) |

1. Adjusted for mother’s education (complete university vs. less education), mother’s weight at enrollment (kg), mother´s smoking at enrollment, and enrollment week.

**STable 4**

|  |  |  |
| --- | --- | --- |
| **Maternal characteristics and medical use** | **Frequency** **(%)** | **Chi-square test****(p-value)** |
| Number of words used at 30 months |
|  | >50 words (N=690) | <=50 words(N=64) |  |
| Mother enrolled after week 10 (%) | 33.0 | 34.4 | 0.892 |
| Mothers age at enrollment (year; mean) | 31.2 | 31.8 | 0.2801 |
| Mothers weight at enrollment (kg; mean) | 69.2 | 74.6 | 0.0021 |
| Mother completed university (%) | 66.5 | 53.1 | 0.031 |
| Mother´s smoking in pregnancy (%) | 2.9 | 3.1 | 0.918 |
| Mother having more than 3 colds the last year (%) | 28.3 | 37.5 | 0.091 |
| Prescribed antibiotics during pregnancy (%) | 4.9 | 7.8 | 0.323 |
| Prescribed pain killers during pregnancy (%) | 16.6 | 21.9 | 0.288 |
| Prescribed asthma medicine during pregnancy (%) | 6.1 | 7.8 | 0.594 |
| Use of non-prescribed aspirin or ibuprofen during pregnancy (%) | 9.6 | 7.9 | 0.670 |
| Prematurity (born before week 37) (%) | 4.5 | 6.3 | 0.525 |
| Mother´s use of APAP during 1st trimester |
|  | No use(N=308) | Use(N=446) |  |
| Mother enrolled after week 10 (%) | 30.8 | 34.8 | 0.262 |
| Mothers age at enrollment (year; mean) | 31.0 | 31.4 | 0.1861 |
| Mothers weight at enrollment (kg; mean) | 68.0 | 70.8 | 0.0041 |
| Mother completed university (%) | 64.0 | 66.4 | 0.495 |
| Mother´s smoking in pregnancy (%) | 2.9 | 2.9 | 0.995 |
| Mother having more than 3 colds the last year (%) | 27.1 | 30.5 | 0.251 |
| Prescribed antibiotics during pregnancy (%) | 2.3 | 7.2 | 0.003 |
| Prescribed pain killers during pregnancy (%) | 4.6 | 25.7 | <0.001 |
| Prescribed asthma medicine during pregnancy (%) | 4.9 | 7.2 | 0.200 |
| Use of non-prescribed aspirin or ibuprofen during pregnancy (%) | 10.1 | 9.0 | 0.621 |
| Prematurity (born before week 37) (%) | 4.9 | 4.5 | 0.810 |

1 t-test