**Supplementary Tables**

Supplementary Table 1: Comparison of participant demographics and covariates between included and excluded participants.

|  |  |  |  |
| --- | --- | --- | --- |
|  | Included1 | Excluded1 | *p* value2 |
|  | 1905 (66.42) | 963 (33.58) |  |
| Maternal smoking in pregnancy |  |  |  |
| None | 1477 (77.53) | 428 (66.46) | *p* < .001 |
| 1-10 cigarettes daily | 224 (11.76) | 101 (15.68) |  |
| 11 + cigarettes daily | 204 (10.71) | 115 (17.86) |  |
| Maternal alcohol intake in pregnancy |  |  |  |
| None | 1139 (59.79) | 429 (44.55) | *p* = .42 |
| Once a week or less | 645 (33.86) | 177 (18.38) |  |
| Several times a week or more | 105 (5.51) | 29 (3.01) |  |
| Offspring sex |  |  |  |
| Female | 921 (48.35) | 493 (51.19) | *p* = .16 |
| Male | 984 (51.65) | 470 (48.81) |  |
| Mother’s age at delivery |  |  |  |
| Mean (SD) | 28.06 (5.86) | 26.51 (5.97) | *p* < .001 |

AAAE, Atopy/Allergy/Asthma/Eczema; SD, standard deviation.

1Data presented as N (%) or mean (SD) as appropriate.

2*p* values are for Chi-squared or t-test comparisons as appropriate.

Supplementary Table 2: Comparison of participant demographics and covariates between AAAE and infection groups.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | All AAAE1 | AAAE  and Comparison  (*p* value)2 | All Infection1 | Infection and Comparison  (*p* value)2 |
|  | 1267 (66.51) |  | 1082 (56.80) |  |
| Maternal smoking in pregnancy |  |  |  |  |
| None | 990 (78.14) | *p* = .32 | 829 (76.62) | *p* = .002 |
| 1-10 cigarettes daily | 139 (10.97) |  | 115 (10.63) |  |
| 11 + cigarettes daily | 138 (10.89) |  | 138 (12.75) |  |
| Maternal alcohol intake in pregnancy |  |  |  |  |
| None | 759 (59.91) | *p* = .91 | 660 (61.00) | *p* = .31 |
| Once a week or less | 438 (34.57) |  | 364 (33.64) |  |
| Several times a week or more | 70 (5.52) |  | 58 (5.36) |  |
| Offspring sex |  |  |  |  |
| Female | 611 (48.22) | *p* = .92 | 520 (48.06) | *p* = .81 |
| Male | 656 (51.78) |  | 562 (51.94) |  |
| Mother’s age at delivery |  |  |  |  |
| Mean (SD) | 28.33 (5.70) | *p* = .15 | 28.70 (5.81) | *p* < .001 |

AAAE, Atopy/Allergy/Asthma/Eczema; SD, standard deviation.

1Data presented as N (%) or mean (SD) as appropriate.

2*p* values are for Chi-squared or t-test comparisons as appropriate.

Supplementary Table 3: Percentage of behavioral and emotional morbidity (CBCL T score ≥ 60) for males at each follow-up for the AAAE and infection groups in comparison with the remainder of the sample.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | All AAAE | | All Infection | | Comparison Group | |
|  | *N1* | *n* (%)2 | *N1* | *n* (%)2 | *N1* | *n* (%)2 |
| CBCL year 5 morbidity |  |  |  |  |  |  |
| Total | 600 | 154 (25.67) | 526 | 139 (26.43) | 152 | 32 (21.05) |
| Externalizing |  | 145 (24.17) |  | 127 (24.14) |  | 36 (23.68) |
| Internalizing |  | 140 (23.33) |  | 127 (24.14) |  | 28 (18.42) |
| CBCL year 8 morbidity |  |  |  |  |  |  |
| Total | 544 | 124 (22.79) | 477 | 100 (20.96) | 138 | 20 (14.49) |
| Externalizing |  | 122 (22.43) |  | 102 (21.38) |  | 24 (17.39) |
| Internalizing |  | 135 (24.82) |  | 114 (23.90) |  | 32 (23.19) |
| CBCL year 10 morbidity |  |  |  |  |  |  |
| Total | 549 | 97 (17.67) | 469 | 89 (18.98) | 136 | 20 (14.71) |
| Externalizing |  | 86 (15.66) |  | 79 (16.84) |  | 18 (13.24) |
| Internalizing |  | 112 (20.40) |  | 96 (20.47) |  | 22 (16.18) |
| CBCL year 14 morbidity |  |  |  |  |  |  |
| Total | 474 | 73 (15.40) | 411 | 69 (16.79) | 115 | 14 (12.17) |
| Externalizing |  | 88 (18.57) |  | 84 (20.44) |  | 19 (16.52) |
| Internalizing |  | 53 (11.18) |  | 42 (10.22) |  | 10 (8.70) |
| CBCL year 17 morbidity |  |  |  |  |  |  |
| Total | 367 | 36 (9.81) | 321 | 30 (9.35) | 94 | 5 (5.32) |
| Externalizing |  | 35 (9.54) |  | 31 (9.66) |  | 7 (7.45) |
| Internalizing |  | 36 (9.81) |  | 32 (9.97) |  | 5. (5.32) |

AAAE, Asthma/Allergy/Atopy/Eczema; CBCL, Child Behavior Checklist.

1Number of mothers who completed the CBCL at each follow-up time point.

2CBCL scores are presented as the number and percentage of participants in each group with a T score above 60.

Supplementary Table 4: Percentage of behavioral and emotional morbidity (CBCL T score ≥ 60) for females at each follow-up for the AAAE and infection groups in comparison with the remainder of the sample.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | All AAAE | | All Infection | | Comparison Group | |
|  | *N1* | *n* (%)2 | *N1* | *n* (%)2 | *N1* | *n* (%)2 |
| CBCL year 5 morbidity |  |  |  |  |  |  |
| Total | 553 | 123 (22.24) | 475 | 96 (20.21) | 146 | 17 (11.64) |
| Externalizing |  | 115 (20.80) |  | 92 (19.37) |  | 19 (13.01) |
| Internalizing |  | 88 (15.91) |  | 72 (15.16) |  | 12 (8.22) |
| CBCL year 8 morbidity |  |  |  |  |  |  |
| Total | 505 | 98 (19.41) | 430 | 82 (19.07) | 141 | 20 (14.18) |
| Externalizing |  | 84 (16.63) |  | 72 (16.74) |  | 16 (11.35) |
| Internalizing |  | 96 (19.01) |  | 71 (16.51) |  | 16 (11.35) |
| CBCL year 10 morbidity |  |  |  |  |  |  |
| Total | 490 | 71 (14.49) | 427 | 58 (13.58) | 125 | 10 (8.00) |
| Externalizing |  | 58 (11.84) |  | 52 (12.18) |  | 10 (8.00) |
| Internalizing |  | 88 (17.96) |  | 76 (17.80) |  | 12 (9.60) |
| CBCL year 14 morbidity |  |  |  |  |  |  |
| Total | 438 | 64 (14.61) | 396 | 52 (13.13) | 109 | 7 (6.42) |
| Externalizing |  | 59 (13.47) |  | 52 (13.13) |  | 12 (11.01) |
| Internalizing |  | 75 (17.12) |  | 57 (14.39) |  | 9 (8.26) |
| CBCL year 17 morbidity |  |  |  |  |  |  |
| Total | 348 | 37 (10.63) | 310 | 24 (7.74) | 94 | 10 (10.64) |
| Externalizing |  | 40 (11.49) |  | 33 (10.65) |  | 12 (12.77) |
| Internalizing |  | 47 (13.51) |  | 26 (8.39) |  | 8 (8.51) |

AAAE, Asthma/Allergy/Atopy/Eczema; CBCL, Child Behavior Checklist.

1Number of mothers who completed the CBCL at each follow-up time point.

2CBCL scores are presented as the number and percentage of participants in each group with a T score above 60.

Supplementary Table 5: Generalized estimating equation (GEE) models showing relationships between AAAE and infection conditions and offspring CBCL scores at 5-, 8-, 10-, 14-, and 17-years of age.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | GEE1,3  β Coefficient  95% Confidence Interval  *p* value | | | GEE2,3  Odds Ratio  95% Confidence Interval  *p* value | | |
|  | Total Score | Externalizing Score | Internalizing Score | Total Score > 60 | Externalizing Score > 60 | Internalizing Score > 60 |
| AAAE | | | | | | |
| Asthma | 2.29  (1.58, 2.99)  *p* < .001 | 1.53  (0.86, 2.20)  *p* < .001 | 1.78  (1.12, 2.45)  *p* < .001 | 1.44  (1.23, 1.69)  *p* < .001 | 1.28  (1.09, 1.51)  *p* = .003 | 1.38  (1.17, 1.62)  *p* < .001 |
| Allergies | 2.08  (1.57, 2.58)  *p* < .001 | 1.23  (0.75, 1.71)  *p* < .001 | 1.97  (1.50, 2.45)  *p* < .001 | 1.47  (1.29, 1.67)  *p* < .001 | 1.26  (1.11, 1.44)  *p* < .001 | 1.53  (1.35, 1.74)  *p* < .001 |
| Hay fever | 1.82  (1.29, 2.35)  *p* < .001 | 1.16  (0.65, 1.67)  *p* < .001 | 1.46  (0.95, 1.96)  *p* < .001 | 1.34  (1.17, 1.53)  *p* < .001 | 1.20  (1.05, 1.38)  *p* = .008 | 1.28  (1.12, 1.47)  *p* < .001 |
| Eczema | 2.20  (1.61, 2.79)  *p* < .001 | 1.63  (1.06, 2.19)  *p* < .001 | 1.92  (1.35, 2.50)  *p* < .001 | 1.35  (1.17, 1.57)  *p* < .001 | 1.28  (1.10, 1.48)  *p* = .001 | 1.49  (1.30, 1.72)  *p* < .001 |
| Infection | | | | | | |
| UTI | 1.48  (0.45, 2.50)  *p* = .005 | 0.74  (, 0.24, 1.73)  *p* = 0.14 | 1.25  (0.26, 2.23)  *p* = .01 | 1.39  (1.10, 1.74)  *p* = .005 | 1.08  (0.85, 1.38)  *p* = .52 | 1.35  (1.07, 1.70)  *p* = .01 |
| Cold/flu | 1.53  (1.03, 2.02)  *p* < .001 | 1.55  (1.07, 2.02)  *p* < .001 | 0.90  (0.42, 1.37)  *p* < .001 | 1.28  (1.13, 1.46)  *p* < .001 | 1.25  (1.10, 1.42)  *p* < .001 | 1.24  (1.09, 1.41)  *p* < .001 |
| Chest infection | 2.99  (1.86, 4.12)  *p* < .001 | 2.58  (1.51, 3.65)  *p* < .001 | 2.62  (1.57, 3.68)  *p* < .001 | 1.93  (1.53, 2.43)  *p* < .001 | 1.77  (1.40, 2.24)  *p* < .001 | 1.76  (1.39, 2.24)  *p* < .001 |
| Herpes | 0.32  (-0.66, 1.29)  *p* = .52 | 0.26  (-0.66, 1.18)  *p* = .58 | 0.19  (-0.75, 1.13)  *p* = .70 | 1.29  (1.03, 1.61)  *p* = .03 | 1.10  (0.87, 1.39)  *p* = .43 | 1.28  (1.03, 1.61)  *p* = .03 |
| Other infection | 1.70  (0.77, 2.63)  *p* < .001 | 2.16  (1.24, 3.08)  *p* < .001 | 1.05  (0.16, 1.94)  *p* = .02 | 1.22  (0.97, 1.52)  *p* = .09 | 1.51  (1.22, 1.87)  *p* < .001 | 1.14  (0.91, 1.44)  *p* = .25 |
| Other viral infection | 1.61  (0.35, 2.87)  *p* = .01 | 1.06  (, 0.16, 2.29)  *p* = .09 | 2.20  (1.00, 3.40)  *p* < .001 | 1.39  (1.05, 1.84)  *p* < .001 | 1.31  (0.99, 1.74)  *p* = .06 | 1.50  (1.13, 1.99)  *p* = .005 |

AAAE, Asthma/Allergy/Atopy/Eczema; CBCL, Child Behavior Checklist; GEE, generalized estimating equation; UTI, urinary tract infection.

1GEE (normal distribution) to assess continuous CBCL scores, generating β coefficients, 95% confidence intervals, and *p* values. β coefficients above 0 indicate an increase in scores compared to the comparison group.

2GEE (binomial, logit link) to assess CBCL morbidity, generating odds ratios, 95% confidence intervals, and *p* values. Odds ratios above 1 indicate an increase in scores compared to the comparison group.

3GEE models adjusted for maternal age, smoking and alcohol intake during pregnancy, and offspring sex.

Supplementary Table 6: Generalized estimating equation (GEE) models showing relationships between AAAE and infection combination groups and male offspring CBCL scores at 5-, 8-, 10-, 14-, and 17-years of age.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | GEE1,3  β Coefficient  95% Confidence Interval  *p* value | | | GEE2,3  Odds Ratio  95% Confidence Interval  *p* value | | |
|  | Total Score | Externalizing Score | Internalizing Score | Total Score > 60 | Externalizing Score > 60 | Internalizing Score > 60 |
| All AAAE | 2.21  (1.50, 2.92)  *p* < .001 | 1.58  (0.89, 2.28)  *p* < .001 | 1.64  (0.96, 2.31)  *p* < .001 | 1.53  (1.27, 1.85)  *p* < .001 | 1.37  (1.14, 1.66)  *p* = .001 | 1.34  (1.11, 1.61)  *p* = .002 |
| 1 AAAE condition | 1.86  (1.00, 2.71)  *p* < .001 | 1.39  (0.56, 2.21)  *p* = .001 | 1.47  (0.66, 2.29)  *p* < .001 | 1.51  (1.22, 1.88)  *p* < .001 | 1.36  (1.09, 1.69)  *p* = .006 | 1.33  (1.08, 1.65)  *p* = .009 |
| 2+ AAAE conditions | 2.52  (1.71, 3.32)  *p* < .001 | 1.76  (0.96, 2.55)  *p* < .001 | 1.77  (1.00, 2.54)  *p* < .001 | 1.55  (1.25, 1.91)  *p* < .001 | 1.38  (1.12, 1.71)  *p* = .002 | 1.34  (1.09, 1.65)  *p* = .005 |
| All infection | 1.04  (0.35, 1.74)  *p* = .003 | 1.14  (0.47, 1.82)  *p* < .001 | 0.61  (-0.06, 1.27)  *p* = .07 | 1.31  (1.10, 1.57)  *p* = .003 | 1.22  (1.02, 1.46)  *p* = .03 | 1.16  (0.97, 1.38)  *p* = .10 |
| 1 infection condition | 0.17  (-0.56, 0.90)  *p* = .65 | 0.46  (-0.25, 1.18)  *p* = .21 | -0.19  (-0.88, 0.51)  *p* = .60 | 1.03  (0.84, 1.26)  *p* = .77 | 1.05  (0.86, 1.27)  *p* = .65 | 0.96  (0.79, 1.17)  *p* = .70 |
| 2+ infection conditions | 3.59  (2.50, 4.68)  *p* < .001 | 3.13  (2.08, 4.19)  *p* < .001 | 2.93  (1.88, 3.97)  *p* < .001 | 2.26  (1.79, 2.86)  *p* < .001 | 1.77  (1.40, 2.24)  *p* < .001 | 1.80  (1.42, 2.28)  *p* < .001 |
| Either AAAE or infection | 0.78  (-0.14, 1.70)  *p* = .10 | 0.30  (-0.61, 1.20)  *p* = .52 | 0.92  (0.05, 1.80)  *p* = .04 | 1.18  (0.92, 1.51)  *p* = .18 | 0.95  (0.75, 1.20)  *p* = .68 | 1.16  (0.91, 1.48)  *p* = .22 |
| Both AAAE and infection | 2.75  (2.04, 3.46)  *p* < .001 | 2.53  (1.83, 3.22)  *p* < .001 | 1.67  (0.99, 2.35)  *p* < .001 | 1.74  (1.47, 2.07)  *p* < .001 | 1.66  (1.40, 1.97)  *p* < .001 | 1.39  (1.17, 1.65)  *p* < .001 |

AAAE, Asthma/Allergy/Atopy/Eczema; CBCL, Child Behavior Checklist; GEE, generalized estimating equation.

1GEE (normal distribution) to assess continuous CBCL scores, generating β coefficients, 95% confidence intervals, and *p* values. β coefficients above 0 indicate an increase in scores compared to the comparison group.

2GEE (binomial, logit link) to assess CBCL morbidity, generating odds ratios, 95% confidence intervals, and *p* values. Odds ratios above 1 indicate an increase in scores compared to the comparison group.

3GEE models adjusted for maternal age, smoking and alcohol intake during pregnancy.

Supplementary Table 7: Generalized estimating equation (GEE) models showing relationships between AAAE and infection combination groups and female offspring CBCL scores at 5-, 8-, 10-, 14-, and 17-years of age.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | GEE1,3  β Coefficient  95% Confidence Interval  *P* value | | | GEE2,3  Odds Ratio  95% Confidence Interval  *P* value | | |
|  | Total Score | Externalizing Score | Internalizing Score | Total Score > 60 | Externalizing Score > 60 | Internalizing Score > 60 |
| All AAAE | 2.82  (2.08, 3.56)  *p* < .001 | 1.52  (0.83, 2.20)  *p* < .001 | 2.95  (2.27, 3.63)  *p* < .001 | 1.60  (1.30, 1.98)  *p* < .001 | 1.30  (1.06, 1.61)  *p* = .01 | 1.97  (1.58, 2.45)  *p* < .001 |
| 1 AAAE condition | 2.21  (1.33, 3.09)  *p* < .001 | 1.04  (0.23, 1.85)  *p* = .01 | 2.66  (1.86, 3.47)  *p* < .001 | 1.57  (1.23, 1.99)  *p* < .001 | 1.29  (1.02, 1.64)  *p* = .04 | 1.71  (1.33, 2.20)  *p* < .001 |
| 2+ AAAE conditions | 3.40  (2.55, 4.25)  *p* < .001 | 1.97  (1.18, 2.76)  *p* < .001 | 3.23  (2.43, 4.03)  *p* < .001 | 1.64  (1.29, 2.08)  *p* < .001 | 1.31  (1.04, 1.67)  *p* = .02 | 2.22  (1.75, 2.83)  *p* < .001 |
| All infection | 1.42  (0.69, 2.16)  *p* < .001 | 1.13  (0.46, 1.81)  *p* = .001 | 0.78  (0.09, 1.46)  *p* = .03 | 1.04  (0.86, 1.26)  *p* = .71 | 1.09  (0.90, 1.33)  *p* = .38 | 1.06  (0.87, 1.28)  *p* = .57 |
| 1 infection condition | 1.21  (0.43, 2.00)  *p* = .003 | 0.84  (0.12, 1.56)  *p* = .02 | 0.56  (-0.17, 1.28)  *p* = .13 | 0.98  (0.79, 1.20)  *p* = .81 | 1.02  (0.82, 1.27)  *p* = .85 | 0.92  (0.75, 1.14)  *p* = .46 |
| 2+ infection conditions | 1.98  (0.90, 3.05)  *p* < .001 | 1.91  (0.91, 2.90)  *p* < .001 | 1.36  (0.32, 2.40)  *p* = .01 | 1.21  (0.92, 1.58)  *p* = .16 | 1.29  (0.98, 1.70)  *p* = .06 | 1.45  (1.11, 1.88)  *p* = .006 |
| Either AAAE or infection | 3.15  (2.19, 4.10)  *p* < .001 | 2.18  (1.30, 3.07)  *p* < .001 | 2.59  (1.73, 3.46)  *p* < .001 | 1.54  (1.16, 2.05)  *p* = .003 | 1.33  (1.00, 1.76)  *p* = .05 | 1.73  (1.29, 2.34)  *p* < .001 |
| Both AAAE and infection | 2.39  (1.64, 3.13)  *p* < .001 | 1.37  (0.68, 2.06)  *p* < .001 | 2.18  (1.48, 2.87)  *p* < .001 | 1.29  (1.06, 1.56)  *p* =.01 | 1.21  (0.99, 1.48)  *p* = .06 | 1.47  (1.21, 1.78)  *p* < .001 |

AAAE, Asthma/Allergy/Atopy/Eczema; CBCL, Child Behavior Checklist; GEE, generalised estimating equation.

1GEE (normal distribution) to assess continuous CBCL scores, generating β coefficients, 95% confidence intervals, and *p* values. β coefficients above 0 indicate an increase in scores compared to the comparison group.

2GEE (binomial, logit link) to assess CBCL morbidity, generating odds ratios, 95% confidence intervals, and *p* values. Odds ratios above 1 indicate an increase in scores compared to the comparison group.

3GEE models adjusted for maternal age, smoking and alcohol intake during pregnancy.

Supplementary Table 8: Generalized estimating equation (GEE) models showing a sensitivity analysis of CBCL scores from 301 participants whose mothers reported either AAAE or infection with 301 participants in the comparison group.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | GEE1,3  β Coefficient  95% Confidence Interval  *p* value | | | GEE2,3  Odds Ratio  95% Confidence Interval  *p* value | | |
|  | Total Score | Externalizing Score | Internalizing Score | Total Score > 60 | Externalizing Score > 60 | Internalizing Score > 60 |
| Full Cohort4 | 1.96  (1.30, 2.63)  *p* < .001 | 1.23  (0.60, 1.87)  *p* < .001 | 1.78  (1.16, 2.39)  *p* < .001 | 1.34  (1.11, 1.61)  *p* = .002 | 1.10  (0.92, 1.31)  *p* = .30 | 1.39  (1.15, 1.67)  *p* < .001 |
| Matched Cohort5 | 1.26  (0.39, 2.13)  *p* = .005 | 0.79  (-0.05, 1.63)  *p* = .07 | 1.15  (0.36, 1.94)  *p* = .005 | 1.20  (0.95, 1.52)  *p* = .13 | 1.05  (0.83, 1.32)  *p* = .70 | 1.19  (0.94, 1.15)  *p* = .16 |

AAAE, Asthma/Allergy/Atopy/Eczema; CBCL, Child Behavior Checklist; GEE, generalized estimating equation

1GEE (normal distribution) to assess continuous CBCL scores, generating β coefficients, 95% confidence intervals, and *p* values. β coefficients above 0 indicate an increase in scores compared to the comparison group.

2GEE (binomial, logit link) to assess CBCL morbidity, generating odds ratios, 95% confidence intervals, and *p* values. Odds ratios above 1 indicate an increase in scores compared to the comparison group.

3GEE models adjusted for maternal age, smoking and alcohol intake during pregnancy, and offspring sex.

4Full cohort included in the study. *N* (either AAAE or infection) = 1604; *N* (comparison group) = 301.

5Matched cohort for sensitivity analysis. *N* (either AAAE or infection) = 301; *N* (comparison group) = 301.