## *Epidemiology and Infection*

## Childhood infections and common carotid intima media thickness in adolescence

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### Supplementary Material

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| **Supplementary Table 1** |
| **ICPC code** | **Diagnosis** |
| A03 | Fever |
| A71 | Measles |
| A72 | Chickenpox |
| A74 | Rubella |
| A76 | Viral exanthem other |
| A76/A771 | Viral disease other [with exanthem] |
| A77 | Viral disease other/NOS |
| A78 | Infectious disease other/NOS |
| B70 | Lymphadenitis acute |
| D70 | Gastrointestinal infection |
| D70/D731 | Gastrointestinal [presumed] infection |
| D71 | Mumps |
| D73 | Gastroenteritis presumed infection |
| H71 | Acute otitis media/myringitis |
| H71/H721 | Otitis media |
| H72 | Serous otitis media |
| H74 | Chronic otitis media/ear infection other |
| L70 | Infections musculoskeletal system |
| N07 | Convulsion/seizure (including fever-) |
| N71 | Meningitis/encephalitis |
| R71 | Whooping cough |
| R72 | Strep throat/scarlet fever |
| R72/R761 | Strep throat/scarlet fever/tonsillitis acute |
| R74 | Upper respiratory infection acute |
| R75 | Sinusitis acute/chronic |
| R76 | Tonsillitis acute/peritonsillar abscess |
| R77 | Laryngitis/tracheitis acute |
| R78 | Acute bronchitis/bronchiolitis |
| R78/R80/R811 | Acute bronchitis/bronchiolitis/influenza/pneumonia |
| R80 | Influenza [ex. R81] |
| R81 | Pneumonia |
| R82 | Pleurisy/pleural effusion |
| R83 | Respiratory infection other |
| S70 | Herpes zoster |
| S71 | Herpes simplex [ex. F85,X90,Y72] |
| S84 | Impetigo/impetiginization |
| U70 | Acute pyelonephritis/pyelitis |
| U71 | Cystitis/urinary infection |
| Y74 | Orchitis/epididymitis |
|  | Viral infection NOS2 |
| ICPC: International Classification of Primary Care; NOS: Not otherwise specified. 1 For the convenience of the participating GP some infectious disease diagnoses were combined on the questionnaires. 2 The diagnosis viral infection not otherwise specified (NOS) was added to the questionnaire as a potential diagnosis. |

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| **Supplementary Table 2.** Characteristics of participants invited for the common carotid intima media thickness (CIMT) measurement at age 16. |
|  | Eligible study population |
|  | % | N |
| Complete parent-reported data on the first 4 years of life | 93.6 | 1153 |
| Complete GP data on the first 4 years of life | 25.2 | 310 |
| **Sex** |  | 1232 |
|  Male | 53.7 |  |
|  Female | 46.3 |  |
| **Overweight mother before pregnancy** |  | 1146 |
|  No | 83.2 |  |
|  Yes | 16.8 |  |
| **Parental education** |  | 1219 |
|  Low | 41.9 |  |
|  High | 58.1 |  |
| **Allergic mother** |  | 1232 |
|  No | 73.9 |  |
|  Yes | 26.1 |  |
| **Exposure to any smoking indoors first four years of life** |  | 1190 |
|  No | 65.9 |  |
|  Yes | 34.1 |  |
| **Breastfeeding** |  | 1213 |
|  No breastfeeding | 14.7 |  |
|  ≤16 weeks of breastfeeding | 48.9 |  |
|  >16 weeks of breastfeeding | 36.4 |  |
|  | Mean | SE (N) |
| Birth weight gram | 3533 | 15.2 (1228) |
| CIMT in μm age 16 years | 467 | 1.90 (420) |
| Total cholesterol mmol/L age 16 years | 3.85 | 0.03 (447) |
| HDL cholesterol mmol/L age 16 years | 1.35 | 0.02 (447) |
| GP: general practitioner; IMT: intima media thickness of common carotid artery; MI: multiple imputation; SE: standard error.  |

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| **Supplementary Table 3.** Difference in common carotid intima media thickness (CIMT) at age 16 years between exposed and reference group after multiple imputation and with total and HDL cholesterol in the model. |
| **Determinant** | **∆ CIMT μm (95% CI)** |
| GP diagnosed infections |  |  |
|  0-1 infection | Ref. |
|  2-3 infections | 4.4 (-9.7-18.6) |
|  4-6 infections | -1.9 (-16.7-12.9) |
|  ≥7 infections | 5.4 (-9.8-20.6) |
| Antibiotic prescriptions |  |  |
|  0 prescriptions | Ref. |
|  1 prescription | -7.8 (-21.1-5.4) |
|  2 prescriptions | 7.4 (-9.3-24.1) |
|  ≥3 prescriptions | 8.6 (-5.0-22.2) |
| Parent-reported infections |  |  |
|  0-2.5 infections | Ref. |
|  3-5 infections | -9.7 (-22.8-3.3) |
|  6-7 infections | 0.5 (-13.3-14.3) |
|  ≥8 infections | 10.9 (-2.1-23.8) |
| Models adjusted for gender, education of parents, birthweight, overweight of the mother before pregnancy, breastfeeding, allergy of the mother, indoor smoke exposure, high-density lipoprotein (HDL) and total cholesterol. GP: general practitioner; IMT: intima media thickness; MI: multiple imputation. |

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| **Supplementary table 4.** Mean p-values of interaction terms of the 10 multiple imputation datasets |
| Exposure variable | Confounder | p-value |
| GP diagnosed infections | Gender | 0.60 |
|  | **Parental education** | **0.08** |
|  | Breastfeeding | 0.23 |
|  | Maternal overweight | 0.67 |
|  | Birth weight | 0.46 |
|  | Allergic mother | 0.58 |
|  | Smoke exposure | 0.54 |
| Antibiotic prescriptions | Gender | 0.69 |
|  | **Parental education** | **0.02** |
|  | Breastfeeding | 0.62 |
|  | Maternal overweight | 0.36 |
|  | **Birth weight** | **0.04** |
|  | **Allergic mother** | **0.001** |
|  | Smoke exposure | 0.45 |
| Parent reported infections | Gender | 0.52 |
|  | Parental education | 0.53 |
|  | Breastfeeding | 0.31 |
|  | Maternal overweight | 0.23 |
|  | Birth weight | 0.14 |
|  | Allergic mother | 0.19 |
|  | Smoke exposure | 0.62 |
| GP: general practitioner; Bold indicates p-values below 0.10. |

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| **Supplementary Figure 1.** Directed acyclic graph (DAG) of the confounders for the association between infections in early childhood and IMT in adolescence. |
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| Confounders were selected based on previous studies investigating the association between infections and common intima media thickness (CIMT). The primary exposure and outcome are in red. The dashed line indicates (potential) effect modification. |