

## SUPPLEMENTAL MATERIAL

**Association of childhood infections and perinatal factors with ankylosing spondylitis: a Swedish nationwide case-control and sibling study**Matilda Morin, MSc<sup>1</sup>, Karin Hellgren, MD, PhD<sup>1</sup>, Ulf Lindström, MD, PhD<sup>2</sup>, Thomas Frisell, PhD<sup>1</sup><sup>1</sup> Clinical Epidemiology Division, Department of Medicine, Solna, Karolinska Institutet, Stockholm, Sweden<sup>2</sup> Department of Rheumatology and Inflammation Research, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden**Supplemental table 1.** Sources and definitions of outcome, exposures, and covariates

|                                     | Source   | ATC and ICD-10 codes     | Details/Definition  |
|-------------------------------------|----------|--------------------------|---|
| <b>Outcome</b>                      |          |                          |   |
| Ankylosing spondylitis              | NPR      | ICD-10 M45.9, M08.1      | ≥1 visit at specialist clinic of internal medicine or rheumatology, with a recorded diagnosis of AS after 2001.   |
| <b>Exposures</b>                    |          |                          |   |
| Maternal age                        | MBR      |                          | In years. Modelled as second-degree polynomial.   |
| Maternal smoking                    | MBR      |                          | At first antenatal visit. Coded smoker/non-smoker.  |
| Maternal BMI                        | MBR      |                          | In kg/m <sup>2</sup> , at first antenatal visit. Modelled as second-degree polynomial, and in categories <18.5, 18.5-24.9, 25-29.9, ≥30.  |
| Gestational age                     | MBR      |                          | In weeks. Modelled as second-degree polynomial, and in categories very preterm (<32 weeks), preterm (32-36 weeks), term (37-40 weeks), post-term (≥41 weeks).   |
| Weight for gestational age          | MBR      |                          | In standard deviations from sex-specific mean weight per gestational age in growth curves by Marsál et al. Modelled as second-degree polynomial and in categories small for gestational age (SGA; >2 SD below), moderately small (1-2 SD below), normal (±1 SD), moderately large (1-2 SD above), and large for gestational age (LGA; >2 SD above). |
| Birth weight                        | MBR      |                          | Modelled as second-degree polynomial per 100 g, and in categories <2500 g, 2500-4299 g, ≥4300 g.  |
| Multiple birth                      | MBR      |                          | Coded singleton/multiple.   |
| Caesarean delivery                  | MBR      |                          | Including both elective and emergency Caesarean delivery.   |
| Maternal infection during pregnancy | NPR, MBR | See Supplemental table 2 | Hospitalisation with ICD code for infection during pregnancy, or infection recorded in MBR. Where data on gestational age was missing, it was assumed to be 40 weeks.   |
| Season of birth                     | MBR      |                          | Coded winter (December-February), spring (March-May), summer (June-August), autumn (September-November).  |
| Number of full siblings             | MGR      |                          | Coded 0, 1, ≥2.   |
| Number of older siblings            | MBR      |                          | Based on parity variable in MBR. Coded 0, 1, ≥2.  |
| Number of younger siblings          | MGR      |                          | Only including younger full siblings. Coded 0, 1, ≥2.   |
| Serious childhood infection         | NPR, MBR | See Supplemental table 2 | Infection recorded at birth (in MBR) or hospitalisation with ICD code for infection as main diagnosis between ages 0-15 (excluding index patients with AS diagnosis before age 16).   |

| Cont. from previous page                            | Source                              | ATC and ICD-10 codes  | Details/Definition  |
|---|-------------------------------------|---|---|
| Tonsillectomy                                       | NPR                                 | Procedure codes 2710, 2720, 2730 (1973-1996) or EMB10, EMB15, EMB20, EMB30 (1997-)  | Between ages 0-15 (excluding index patients with AS diagnosis before age 16).   |
| Appendectomy  | NPR                                 | Procedure codes 4510, 4511, 0058 (1973-1996) or JEA00, JEA01, JEA10 (1997-)   | Between ages 0-15 (excluding index patients with AS diagnosis before age 16).   |
| Appendicitis with appendectomy                      | NPR                                 | ICD-8 540-543<br>ICD-9 540-543<br>ICD-10 K35-38<br>plus procedure code for appendectomy (see above)   | Both appendicitis and appendectomy recorded in NPR between ages 0-15 (excluding index patients with AS diagnosis before age 16).  |
| <b>Other covariates</b>                             |                                     |   |   |
| Parental country of birth                           | Total Population Register           |   | Coded "Both born in Nordic country" vs. not   |
| Maternal disposable income                          | Population and housing census, LISA |   | In quintiles per year/census. For births 1973-1979, we used census data from 1975. For births 1980-1987, census data from 1985. Births 1988-1990, LISA from 1990. For births 1991 onwards, LISA from the year before childbirth.              |
| Maternal level of formal education                  | LISA                                |   | In year of childbirth, coded ≤9 years, 10-12 years, >12 years. Data only available from 1990, thus educational level in 1990 was used for those with earlier births.  |
| Maternal inflammatory disease (SpA, IBD, psoriasis) | NPR                                 | ICD-8 563.00, 563.10, 563.99, 569.02, 696, 712.40, 726.99<br>ICD-9 555, 556, 696, 713D, 720A, 720W, 720X, 713B, 711B, 711D-711F, 711X<br>ICD-10 K50, M09.1, K51, M09.2, M08.1, M45.9, M46.8, M46.9, M07.2, M07.4, M07.5, L40, M07.3, M09.0, M02.3, M02.8, M02.9 | Hospitalisation with any of the listed ICD codes before childbirth.   |
| <b>SpA manifestations</b>                           |                                     |   |   |
| Anterior uveitis                                    | NPR                                 | ICD-10 H20, H22.1   | ≥1 visit with a recorded diagnosis of anterior uveitis at a specialist clinic of ophthalmology 1997-2022.   |
| Psoriasis   | NPR, PDR                            | ICD-10 L40 (except L40.5)<br>ATC D05  | ≥1 visit with a recorded diagnosis of psoriasis at a specialist clinic of dermatology 1997-2022, or dispensed prescription of ATC D05 2005-2022.  |
| IBD   | NPR                                 | ICD-10 K50, M07.4, M09.1 K51, M07.5, M09.2  | ≥1 visit with a recorded diagnosis of IBD at a specialist clinic of internal medicine, rheumatology or gastroenterology 1997-2022.  |
| <b>SpA-free sibling</b>                             | MGR, MBR, NPR                       | ICD-8 563.00, 563.10, 563.99, 569.02, 696, 712.40, 726.99<br>ICD-9 555, 556, 696, 713D, 720A, 720W, 720X, 713B, 711B, 711D-711F, 711X<br>ICD-10 K50, M09.1, K51, M09.2, M08.1, M45.9, M46.8, M46.9, M07.2, M07.4, M07.5, L40, M07.3, M09.0, M02.3, M02.8, M02.9 | Any full sibling of an AS index case, whose birth is registered in MBR and who has NOT received a diagnosis of the listed ICD codes (of SpA, IBD, or psoriasis) in NPR at a specialist clinic of internal medicine or rheumatology 2001-2022. |

ATC, Anatomic Therapeutic Chemical; ICD, International Classification of Diseases; NPR, National Patient Register; MBR, Medical Birth Register; MGR, Multi-Generation Register; LISA, Longitudinal integrated database for health insurance and labour market studies; PDR, Prescribed Drug Register; AS, ankylosing spondylitis; SpA, spondyloarthritis; IBD, inflammatory bowel disease.

**Supplemental table 2.** ICD codes used to identify infections during pregnancy and childhood, according to the different ICD editions

| Years     | ICD version | Diagnostic codes  |
|-----------|-------------|---|
| -1986     | ICD-8       | 000-136, 320, 322, 360.00, 366.00, 369.00, 380-383, 420, 421, 422, 460-466, 470-474, 480-486, 490, 500.99, 501, 503, 508.00-508.02, 510, 511.10, 513.99, 522.40, 522.50, 522.70, 527.30, 540-543, 562, 566, 567.00-567.02, 569.00, 572.99, 590, 595.00, 595.09, 597.00, 599.02, 611.00-611.01, 612-614, 616.00-616.03, 620, 622.00, 622.19, 629.40, 630, 635, 636, 645.90-645.91, 680-686, 710, 720, 732.99, 761.00, 761.20-761.40, 763.00, 763.10, 998.50, 999.30  |
| 1987-1996 | ICD-9       | 001-139, 254B, 279K, 320, 321, 322, 324, 360A, 372A, 380B, 382, 383, 420X, 421, 422X, 460-466, 473, 474, 475, 480-487, 490, 510, 511B, 513, 522E, 522F, 522H, 526E, 527D, 540-543, 562, 566, 567B, 567C, 569F, 572A, 590B, 595A, 595X, 597A, 597W, 599A, 601C, 611A, 614A-F, 615A, 616, 639A, 646F, 646G, 647, 658E, 659D, 680-686, 711A, 728A, 730, 770A, 771, 996G, 998F, 999D  |
| 1997-     | ICD-10*     | A00-B99, E32.1, G00-02, G04.2, G05.0, G05-G07, H10.0, H13.0, H13.1, H44.0, H60.0-H60.3, H62.0-H62.3, H66, H67, H70, I30.1, I33.0, I40.0, J00-J22, J32, J34.0, J35, J36, J39.0, J39.1, J44.0, J85, J86, K04.4, K04.6, K04.7, K10.2, K11.3, K35-38, K57.0, K57.2, K57.4, K57.8, K61, K63.0, K65.0, K67, K75.0, L00-08, L30.3, M00-01, M46.2, M46.3, M46.5, M49.0-M49.3, M60.0, M65.0, M65.1, M71.0, M71.1, M72.6, M86, N10, N13.6, N15.1, N30.0, N30.9, N34.0, N34.1, N34.2, N39.0, N41.2, N61, N70, N71.0, N72, N73.0, N73.3, N75.1, N76.0, N76.2, N76.4, N76.8b, O07.0, O07.5, O08.0, O23, O41.1, O75.3, O98, P23, P35-37, T80.2, T81.4, T82.6, T82.7, T83.5, T83.6, T84.5-T84.7, T85.7, T88.0, Z21 |

\*Skåne county used ICD-9 until 1997

ICD, International Classification of Diseases.

**Supplemental table 3.** Number and proportion of subjects with missing data

|                                      | AS cases<br>(N=5612) | Population controls<br>(N=22,042) |
|--------------------------------------|----------------------|-----------------------------------|
| Maternal smoking                     | 2799 (49.9)          | 10884 (49.4)                      |
| Maternal smoking (births from 1982)* | 289 (9.3)            | 1105 (9.0)                        |
| Maternal BMI                         | 3551 (63.3)          | 14053 (63.8)                      |
| Maternal BMI (births from 1982)*     | 1041 (33.6)          | 4274 (34.9)                       |
| Birthweight                          | 17 (0.3)             | 50 (0.2)                          |
| Gestational age                      | 14 (0.2)             | 65 (0.3)                          |
| Weight for gestational age           | 30 (0.5)             | 114 (0.5)                         |
| Parental country of birth            | 33 (0.6)             | 142 (0.6)                         |
| Maternal disposable income           | 54 (1.0)             | 212 (1.0)                         |
| Maternal educational level           | 71 (1.3)             | 327 (1.5)                         |

Data are n (%). Only variables with missing data included.

\*Data on maternal smoking and maternal BMI was not available for births before 1982. Total number of births 1982-2004 (and denominators for these proportions) are 3102 in AS cases and 12263 in population controls. AS, ankylosing spondylitis; BMI, body-mass index.

**Supplemental table 4.** Odds ratios for AS from conditional logistic regression on 25 multiply imputed datasets

| Risk factor  | AS cases<br>(N=5612) | Population<br>controls<br>(N=22,042) | OR (95% CI)         | Adj. OR* (95% CI)   |
|--|----------------------|--------------------------------------|---------------------|---------------------|
| <b>Maternal age in years, mean (SD)</b>              | 27.4 (5.0)           | 27.5 (5.1)                           | 1.00 (0.99 to 1.00) | 1.00 (0.99 to 1.00) |
| <b>Maternal smoking†, n (%)</b>                      | 687 (24.4)           | 2774 (24.9)                          | 0.98 (0.89 to 1.08) | 0.99 (0.90 to 1.10) |
| <b>Maternal BMI† in kg/m<sup>2</sup>, mean (SD)¶</b> | 22.6 (3.4)           | 22.8 (3.6)                           | 0.99 (0.98 to 1.00) | 0.99 (0.98 to 1.01) |
| <18.5 kg/m <sup>2</sup> , n (%)                      | 102 (4.9)            | 496 (6.2)                            | 0.84 (0.68 to 1.04) | 0.85 (0.68 to 1.05) |
| 18.5-24.9 kg/m <sup>2</sup> , n (%)                  | 1570 (76.2)          | 5806 (72.7)                          | Reference           | Reference           |
| 25-29.9 kg/m <sup>2</sup> , n (%)                    | 324 (15.7)           | 1330 (16.6)                          | 0.93 (0.81 to 1.06) | 0.93 (0.82 to 1.07) |
| ≥30 kg/m <sup>2</sup> , n (%)                        | 65 (3.2)             | 357 (4.5)                            | 0.80 (0.62 to 1.03) | 0.80 (0.62 to 1.04) |
| <b>Gestational age, mean (SD)</b>                    | 40 (2)               | 40 (2)                               | 0.98 (0.97 to 1.00) | 0.99 (0.97 to 1.00) |
| Very preterm, n (%)                                  | 29 (0.5)             | 106 (0.5)                            | 1.08 (0.72 to 1.64) | 1.07 (0.71 to 1.63) |
| Preterm, n (%)                                       | 283 (5.1)            | 1084 (4.9)                           | 1.02 (0.89 to 1.17) | 1.00 (0.87 to 1.15) |
| Term, n (%)  | 3776 (67.5)          | 14572 (66.3)                         | Reference           | Reference           |
| Post-term, n (%)                                     | 1510 (27.0)          | 6215 (28.3)                          | 0.94 (0.88 to 1.00) | 0.94 (0.88 to 1.01) |
| <b>Weight for gestational age in SDs, mean (SD)</b>  | -0.10 (1.12)         | -0.10 (1.10)                         | 1.01 (0.98 to 1.03) | 1.01 (0.98 to 1.04) |
| SGA (>2 SD below mean), n (%)                        | 210 (3.8)            | 733 (3.3)                            | 1.12 (0.96 to 1.31) | 1.10 (0.94 to 1.30) |
| Moderately small (1-2 SD below), n (%)               | 885 (15.9)           | 3483 (15.9)                          | 1.00 (0.92 to 1.08) | 1.00 (0.92 to 1.08) |
| Normal (±1 SD), n (%)                                | 3691 (66.1)          | 14582 (66.5)                         | Reference           | Reference           |
| Moderately large (1-2 SD above), n (%)               | 652 (11.7)           | 2493 (11.4)                          | 1.04 (0.94 to 1.14) | 1.04 (0.95 to 1.14) |
| LGA (>2 SD above mean), n (%)                        | 144 (2.6)            | 637 (2.9)                            | 0.90 (0.75 to 1.08) | 0.91 (0.76 to 1.10) |
| <b>Birthweight in grams‡, mean (SD)</b>              | 3508 (563)           | 3513 (553)                           | 1.00 (0.99 to 1.00) | 1.00 (0.99 to 1.01) |
| <2500 g, n (%)                                       | 218 (3.9)            | 816 (3.7)                            | 1.05 (0.90 to 1.23) | 1.02 (0.87 to 1.20) |
| 2500-4299 g, n (%)                                   | 4990 (89.2)          | 19679 (89.5)                         | Reference           | Reference           |
| ≥4300 g, n (%)                                       | 387 (6.9)            | 1497 (6.8)                           | 1.03 (0.91 to 1.16) | 1.04 (0.92 to 1.17) |
| <b>Multiple birth, n (%)</b>                         | 130 (2.3)            | 423 (1.9)                            | 1.22 (1.00 to 1.49) | 1.23 (1.01 to 1.50) |
| <b>Caesarean section, n (%)</b>                      | 624 (11.1)           | 2313 (10.5)                          | 1.07 (0.98 to 1.18) | 1.07 (0.97 to 1.18) |
| <b>Maternal infection during pregnancy, n (%)</b>    | 134 (2.4)            | 477 (2.2)                            | 1.09 (0.90 to 1.33) | 1.08 (0.89 to 1.32) |
| <b>Season of birth, n (%)</b>                        |                      |                                      |                     |                     |
| Dec-Feb  | 1399 (24.9)          | 5170 (23.5)                          | Reference           | Reference           |
| March-May  | 1615 (28.8)          | 6128 (27.8)                          | 0.97 (0.90 to 1.05) | 0.97 (0.90 to 1.05) |
| June-Aug   | 1381 (24.6)          | 5584 (25.3)                          | 0.91 (0.84 to 0.99) | 0.91 (0.84 to 0.99) |
| Sep-Nov  | 1217 (21.7)          | 5160 (23.4)                          | 0.87 (0.79 to 0.94) | 0.87 (0.80 to 0.95) |
| <b>No. of full siblings in total, n (%)</b>          |                      |                                      |                     |                     |
| 0  | 881 (15.7)           | 3498 (15.9)                          | Reference           | Reference           |
| 1  | 2557 (45.6)          | 9982 (45.3)                          | 1.02 (0.94 to 1.12) | 1.01 (0.92 to 1.11) |
| 2 or more  | 2174 (38.7)          | 8562 (38.8)                          | 1.02 (0.93 to 1.11) | 1.01 (0.92 to 1.10) |
| <b>No. of older siblings, n (%)</b>                  |                      |                                      |                     |                     |
| 0  | 2164 (38.6)          | 9098 (41.3)                          | Reference           | Reference           |
| 1  | 2172 (38.7)          | 8081 (36.7)                          | 1.13 (1.06 to 1.21) | 1.12 (1.04 to 1.22) |
| 2 or more  | 1276 (22.7)          | 4863 (22.1)                          | 1.11 (1.03 to 1.20) | 1.15 (1.04 to 1.27) |
| <b>No. of younger siblings, n (%)</b>                |                      |                                      |                     |                     |
| 0  | 3470 (61.8)          | 13155 (59.7)                         | Reference           | Reference           |
| 1  | 1531 (27.3)          | 6245 (28.3)                          | 0.93 (0.87 to 1.00) | 0.97 (0.89 to 1.04) |
| 2 or more  | 611 (10.9)           | 2642 (12.0)                          | 0.88 (0.80 to 0.97) | 0.91 (0.81 to 1.02) |
| <b>Serious childhood infection§, n (%)</b>           | 1396 (24.9)          | 5006 (22.8)                          | 1.13 (1.05 to 1.21) | 1.13 (1.05 to 1.21) |
| <b>Tonsillectomy§, n (%)</b>                         | 279 (5.0)            | 855 (3.9)                            | 1.29 (1.12 to 1.49) | 1.30 (1.13 to 1.49) |
| <b>Appendectomy§, n (%)</b>                          | 126 (2.3)            | 573 (2.6)                            | 0.87 (0.71 to 1.06) | 0.87 (0.71 to 1.06) |

\*Adjusted for maternal age, maternal BMI, maternal smoking, parental country of birth, maternal disposable income, maternal educational level, maternal inflammatory disease (hospitalisation for SpA, IBD, psoriasis), and multiple birth, with the exception that no exposure was adjusted for itself. Number of older siblings additionally adjusted for number of younger siblings, and vice versa.

†Analyses for smoking and BMI restricted to birth years from 1982 onwards.

‡Analysed per 100 g.

§Until age 15. 16 cases and their 72 matched controls excluded due to AS diagnosis in index case before age 16. AS, ankylosing spondylitis; BMI, body-mass index; SpA, spondyloarthritis; IBD, inflammatory bowel disease.

**Supplemental table 5.** Odds ratios for AS from conditional logistic regression on AS cases and population controls with complete data on all variables

| Risk factor  | AS cases<br>(N=1824) | Population<br>controls<br>(N=5317) | OR (95% CI)         | Adj. OR* (95% CI)   |
|--|----------------------|------------------------------------|---------------------|---------------------|
| <b>Maternal age in years, mean (SD)</b>              | 28.2 (5.0)           | 28.2 (5.1)                         | 1.00 (0.99 to 1.01) | 1.00 (0.99 to 1.01) |
| <b>Maternal smoking†, n (%)</b>                      | 428 (23.4)           | 1297 (24.4)                        | 0.94 (0.82 to 1.07) | 0.94 (0.82 to 1.07) |
| <b>Maternal BMI† in kg/m<sup>2</sup>, mean (SD)¶</b> | 22.7 (3.4)           | 22.9 (3.6)                         | 0.99 (0.97 to 1.00) | 0.99 (0.97 to 1.00) |
| <18.5 kg/m <sup>2</sup> , n (%)                      | 87 (4.8)             | 312 (5.9)                          | 0.75 (0.58 to 0.96) | 0.75 (0.58 to 0.96) |
| 18.5-24.9 kg/m <sup>2</sup> , n (%)                  | 1392 (76.2)          | 3828 (72.0)                        | Reference           | Reference           |
| 25-29.9 kg/m <sup>2</sup> , n (%)                    | 287 (15.7)           | 925 (17.4)                         | 0.89 (0.76 to 1.03) | 0.89 (0.76 to 1.03) |
| ≥30 kg/m <sup>2</sup> , n (%)                        | 61 (3.3)             | 252 (4.7)                          | 0.70 (0.52 to 0.94) | 0.70 (0.52 to 0.94) |
| <b>Gestational age, mean (SD)</b>                    | 40 (2)               | 40 (2)                             | 1.01 (0.98 to 1.04) | 1.02 (0.99 to 1.05) |
| Very preterm, n (%)                                  | 5 (0.3)              | 19 (0.4)                           | 0.75 (0.28 to 2.04) | 0.70 (0.25 to 1.95) |
| Preterm, n (%)                                       | 85 (4.7)             | 287 (5.4)                          | 0.85 (0.66 to 1.10) | 0.81 (0.63 to 1.06) |
| Term, n (%)  | 1292 (70.7)          | 3699 (69.6)                        | Reference           | Reference           |
| Post-term, n (%)                                     | 445 (24.4)           | 1312 (24.7)                        | 0.98 (0.86 to 1.11) | 0.99 (0.87 to 1.12) |
| <b>Weight for gestational age in SDs, mean (SD)</b>  | 0.04 (1.04)          | -0.00 (1.06)                       | 1.05 (0.99 to 1.10) | 1.05 (1.00 to 1.11) |
| SGA (>2 SD below mean), n (%)                        | 44 (2.4)             | 132 (2.5)                          | 0.99 (0.70 to 1.42) | 0.99 (0.69 to 1.42) |
| Moderately small (1-2 SD below), n (%)               | 234 (12.8)           | 695 (13.1)                         | 0.98 (0.83 to 1.16) | 0.98 (0.83 to 1.16) |
| Normal (±1 SD), n (%)                                | 1242 (68.0)          | 3681 (69.2)                        | Reference           | Reference           |
| Moderately large (1-2 SD above), n (%)               | 254 (13.9)           | 622 (11.7)                         | 1.23 (1.04 to 1.45) | 1.24 (1.05 to 1.46) |
| LGA (>2 SD above mean), n (%)                        | 53 (2.9)             | 187 (3.5)                          | 0.79 (0.57 to 1.09) | 0.81 (0.59 to 1.13) |
| <b>Birthweight in grams‡, mean (SD)</b>              | 3556 (540)           | 3531 (549)                         | 1.01 (1.00 to 1.02) | 1.01 (1.00 to 1.02) |
| <2500 g, n (%)                                       | 56 (3.1)             | 190 (3.6)                          | 0.87 (0.64 to 1.19) | 0.81 (0.59 to 1.13) |
| 2500-4299 g, n (%)                                   | 1627 (89.1)          | 4752 (89.4)                        | Reference           | Reference           |
| ≥4300 g, n (%)                                       | 144 (7.9)            | 375 (7.1)                          | 1.14 (0.93 to 1.39) | 1.16 (0.94 to 1.43) |
| <b>Multiple birth, n (%)</b>                         | 43 (2.4)             | 97 (1.8)                           | 1.31 (0.90 to 1.89) | 1.32 (0.91 to 1.91) |
| <b>Caesarean section, n (%)</b>                      | 217 (11.9)           | 583 (11.0)                         | 1.09 (0.92 to 1.30) | 1.08 (0.90 to 1.28) |
| <b>Maternal infection during pregnancy, n (%)</b>    | 50 (2.7)             | 151 (2.8)                          | 0.93 (0.67 to 1.29) | 0.92 (0.66 to 1.29) |
| <b>Season of birth, n (%)</b>                        |                      |                                    |                     |                     |
| Dec-Feb  | 478 (26.2)           | 1217 (22.9)                        | Reference           | Reference           |
| March-May  | 516 (28.2)           | 1480 (27.8)                        | 0.90 (0.77 to 1.04) | 0.90 (0.77 to 1.04) |
| June-Aug   | 453 (24.8)           | 1384 (26.0)                        | 0.84 (0.72 to 0.98) | 0.83 (0.71 to 0.97) |
| Sep-Nov  | 380 (20.8)           | 1236 (23.2)                        | 0.77 (0.65 to 0.90) | 0.77 (0.65 to 0.90) |
| <b>No. of full siblings in total, n (%)</b>          |                      |                                    |                     |                     |
| 0  | 252 (13.8)           | 799 (15.0)                         | Reference           | Reference           |
| 1  | 875 (47.9)           | 2466 (46.4)                        | 1.13 (0.96 to 1.33) | 1.12 (0.95 to 1.33) |
| 2 or more  | 700 (38.3)           | 2052 (38.6)                        | 1.06 (0.89 to 1.25) | 1.04 (0.87 to 1.25) |
| <b>No. of older siblings, n (%)</b>                  |                      |                                    |                     |                     |
| 0  | 715 (39.1)           | 2214 (41.6)                        | Reference           | Reference           |
| 1  | 672 (36.8)           | 1929 (36.3)                        | 1.09 (0.96 to 1.24) | 1.12 (0.96 to 1.31) |
| 2 or more  | 440 (24.1)           | 1174 (22.1)                        | 1.17 (1.01 to 1.35) | 1.24 (1.03 to 1.49) |
| <b>No. of younger siblings, n (%)</b>                |                      |                                    |                     |                     |
| 0  | 1090 (59.7)          | 3136 (59.0)                        | Reference           | Reference           |
| 1  | 536 (29.3)           | 1556 (29.3)                        | 0.98 (0.87 to 1.11) | 1.05 (0.91 to 1.21) |
| 2 or more  | 201 (11.0)           | 625 (11.8)                         | 0.90 (0.75 to 1.07) | 0.96 (0.78 to 1.18) |
| <b>Serious childhood infection§, n (%)</b>           | 518 (28.5)           | 1370 (25.9)                        | 1.15 (1.02 to 1.30) | 1.16 (1.02 to 1.31) |
| <b>Tonsillectomy§, n (%)</b>                         | 104 (5.7)            | 261 (4.9)                          | 1.15 (0.91 to 1.47) | 1.17 (0.92 to 1.49) |
| <b>Appendectomy§, n (%)</b>                          | 40 (2.2)             | 111 (2.1)                          | 1.12 (0.77 to 1.62) | 1.12 (0.77 to 1.63) |

\*Adjusted for maternal age, maternal BMI, maternal smoking, parental country of birth, maternal disposable income, maternal educational level, maternal inflammatory disease (hospitalisation for SpA, IBD, psoriasis), and multiple birth, with the exception that no exposure was adjusted for itself. Number of older siblings additionally adjusted for number of younger siblings, and vice versa.

†Analysed per 100 g.

‡Until age 15. 16 cases and their 72 matched controls excluded due to AS diagnosis in index case before age 16. AS, ankylosing spondylitis; BMI, body-mass index; SpA, spondyloarthritis; IBD, inflammatory bowel disease.

**Supplemental table 6.** Odds ratios for AS in men and females separately, in relation to childhood infections and perinatal factors, with p-values for significance of interaction by sex

| Risk factor  | Females<br>cases/controls | Females<br>OR (95% CI) | Female<br>Adj. OR* (95% CI) | Males<br>cases/controls   | Males<br>OR (95% CI) | Males<br>Adj. OR* (95% CI) | p-value for<br>interaction |
|--|---------------------------|------------------------|-----------------------------|---------------------------|----------------------|----------------------------|----------------------------|
| <b>Maternal age in years, mean (SD)</b>              | 27.3 (5.1)/27.4 (5.1)     | 1.00 (0.99 to 1.00)    | 1.00 (0.99 to 1.00)         | 27.5 (5.0)/27.5 (5.1)     | 1.00 (0.99 to 1.01)  | 1.00 (0.99 to 1.01)        | 0.8212                     |
| <b>Maternal smoking†, n (%)</b>                      | 326 (27.2)/1158 (24.3)    | 1.15 (1.00 to 1.33)    | <b>1.13 (0.97 to 1.32)</b>  | 361 (22.4)/1616 (25.3)    | 0.87 (0.76 to 0.99)  | <b>0.89 (0.78 to 1.02)</b> | <b>0.0226</b>              |
| <b>Maternal BMI† in kg/m<sup>2</sup>, mean (SD)¶</b> | 22.7 (3.4)/22.8 (3.6)     | 0.99 (0.97 to 1.01)    | 0.99 (0.97 to 1.01)         | 22.6 (3.4)/22.8 (3.6)     | 0.99 (0.97 to 1.01)  | 0.99 (0.97 to 1.01)        | 0.8196                     |
| <18.5 kg/m <sup>2</sup> , n (%)                      | 42 (4.9)/237 (6.9)        | 0.78 (0.55 to 1.10)    | 0.78 (0.55 to 1.10)         | 60 (5.0)/259 (5.7)        | 0.89 (0.68 to 1.18)  | 0.90 (0.68 to 1.19)        | 0.5145                     |
| 18.5-24.9 kg/m <sup>2</sup> , n (%)                  | 657 (76.2)/2495 (72.7)    | Reference              | Reference                   | 913 (76.1)/3311 (72.7)    | Reference            | Reference                  |                            |
| 25-29.9 kg/m <sup>2</sup> , n (%)                    | 135 (15.7)/550 (16.0)     | 0.95 (0.77 to 1.16)    | 0.95 (0.78 to 1.16)         | 189 (15.8)/780 (17.1)     | 0.91 (0.77 to 1.08)  | 0.92 (0.78 to 1.10)        | 0.8402                     |
| ≥30 kg/m <sup>2</sup> , n (%)                        | 28 (3.2)/152 (4.4)        | 0.79 (0.53 to 1.17)    | 0.79 (0.53 to 1.17)         | 37 (3.1)/205 (4.5)        | 0.80 (0.57 to 1.11)  | 0.81 (0.58 to 1.13)        | 0.9255                     |
| <b>Gestational age, mean (SD)</b>                    | 40 (2)/40 (2)             | 0.98 (0.96 to 1.00)    | 0.98 (0.96 to 1.01)         | 40 (2)/40 (2)             | 0.99 (0.97 to 1.01)  | 0.99 (0.97 to 1.01)        | 0.6835                     |
| Very preterm, n (%)                                  | 11 (0.5)/52 (0.6)         | 0.84 (0.43 to 1.61)    | 0.82 (0.42 to 1.59)         | 18 (0.6)/54 (0.4)         | 1.32 (0.77 to 2.25)  | 1.34 (0.78 to 2.30)        | 0.2619                     |
| Preterm, n (%)                                       | 112 (4.7)/432 (4.6)       | 0.98 (0.79 to 1.21)    | 0.95 (0.76 to 1.19)         | 171 (5.4)/652 (5.2)       | 1.05 (0.88 to 1.25)  | 1.03 (0.87 to 1.24)        | 0.5764                     |
| Term, n (%)  | 1660 (68.9)/6272 (66.5)   | Reference              | Reference                   | 2116 (66.3)/8300 (66.1)   | Reference            | Reference                  |                            |
| Post-term, n (%)                                     | 625 (26.0)/2673 (28.3)    | 0.88 (0.80 to 0.98)    | 0.88 (0.80 to 0.98)         | 885 (27.7)/3542 (28.2)    | 0.98 (0.90 to 1.07)  | 0.98 (0.90 to 1.08)        | 0.1241                     |
| <b>Weight for gestational age in SDs, mean (SD)</b>  | -0.16 (1.07)/-0.13 (1.08) | 0.97 (0.93 to 1.01)    | <b>0.98 (0.94 to 1.02)</b>  | -0.05 (1.09)/-0.08 (1.07) | 1.03 (1.00 to 1.07)  | <b>1.04 (1.00 to 1.08)</b> | <b>0.0341</b>              |
| SGA (>2 SD below mean), n (%)                        | 97 (4.0)/326 (3.5)        | 1.15 (0.91 to 1.45)    | 1.12 (0.88 to 1.42)         | 113 (3.6)/407 (3.2)       | 1.09 (0.88 to 1.36)  | 1.09 (0.88 to 1.36)        | 0.8635                     |
| Moderately small (1-2 SD below), n (%)               | 405 (16.9)/1526 (16.2)    | 1.03 (0.91 to 1.17)    | 1.03 (0.91 to 1.17)         | 480 (15.1)/1957 (15.6)    | 0.97 (0.87 to 1.08)  | 0.97 (0.87 to 1.09)        | 0.4936                     |
| Normal (±1 SD), n (%)                                | 1596 (66.5)/6268 (66.7)   | Reference              | Reference                   | 2095 (65.8)/8314 (66.4)   | Reference            | Reference                  |                            |
| Moderately large (1-2 SD above), n (%)               | 252 (10.5)/1014 (10.8)    | 0.98 (0.85 to 1.14)    | 0.99 (0.85 to 1.15)         | 400 (12.6)/1479 (11.8)    | 1.07 (0.95 to 1.21)  | 1.08 (0.95 to 1.22)        | 0.3831                     |
| LGA (>2 SD above mean), n (%)                        | 49 (2.0)/268 (2.9)        | 0.73 (0.53 to 0.99)    | 0.73 (0.54 to 1.00)         | 95 (3.0)/369 (2.9)        | 1.03 (0.82 to 1.30)  | 1.04 (0.83 to 1.31)        | 0.0760                     |
| <b>Birthweight in gramst, mean (SD)</b>              | 3422 (542)/3441 (539)     | 0.99 (0.98 to 1.00)    | 0.99 (0.99 to 1.00)         | 3573 (570)/3566 (558)     | 1.00 (1.00 to 1.01)  | 1.00 (1.00 to 1.01)        | 0.1257                     |
| <2500 g, n (%)                                       | 112 (4.7)/385 (4.1)       | 1.13 (0.91 to 1.41)    | 1.10 (0.87 to 1.37)         | 106 (3.3)/431 (3.4)       | 0.98 (0.79 to 1.22)  | 0.95 (0.76 to 1.20)        | 0.3958                     |
| 2500-4299 g, n (%)                                   | 2184 (90.9)/8584 (91.1)   | Reference              | Reference                   | 2806 (87.9)/11095 (88.3)  | Reference            | Reference                  |                            |
| ≥4300 g, n (%)                                       | 106 (4.4)/454 (4.8)       | 0.91 (0.73 to 1.13)    | 0.92 (0.74 to 1.15)         | 281 (8.8)/1043 (8.3)      | 1.08 (0.94 to 1.24)  | 1.09 (0.95 to 1.25)        | 0.2078                     |
| <b>Multiple birth, n (%)</b>                         | 57 (2.4)/195 (2.1)        | 1.17 (0.87 to 1.58)    | 1.18 (0.87 to 1.59)         | 73 (2.3)/228 (1.8)        | 1.27 (0.97 to 1.66)  | 1.28 (0.98 to 1.67)        | 0.6830                     |



| Risk factor cont.                          | Females<br>cases/controls | Females<br>OR (95% CI) | Female<br>Adj. OR* (95% CI) | Males<br>cases/controls | Males<br>OR (95% CI) | Males<br>Adj. OR* (95% CI) | p-value for<br>interaction |
|--|---------------------------|------------------------|-----------------------------|-------------------------|----------------------|----------------------------|----------------------------|
| Caesarean section, n (%)                   | 277 (11.5)/972 (10.3)     | 1.13 (0.98 to 1.31)    | 1.13 (0.98 to 1.31)         | 347 (10.8)/1341 (10.6)  | 1.03 (0.91 to 1.17)  | 1.02 (0.90 to 1.16)        | 0.2862                     |
| Maternal infection during pregnancy, n (%) | 57 (2.4)/198 (2.1)        | 1.15 (0.85 to 1.55)    | 1.13 (0.83 to 1.52)         | 77 (2.4)/279 (2.2)      | 1.05 (0.81 to 1.36)  | 1.05 (0.81 to 1.36)        | 0.7302                     |
| Season of birth, n (%)                     |                           |                        |                             |                         |                      |                            |                            |
| Dec-Feb                                    | 587 (24.3)/2184 (23.1)    | Reference              | Reference                   | 812 (25.4)/2986 (23.7)  | Reference            | Reference                  |                            |
| March-May                                  | 711 (29.5)/2626 (27.8)    | 1.00 (0.89 to 1.14)    | 1.00 (0.88 to 1.14)         | 904 (28.2)/3502 (27.8)  | 0.95 (0.85 to 1.06)  | 0.95 (0.85 to 1.05)        | 0.5022                     |
| June-Aug                                   | 584 (24.2)/2453 (26.0)    | 0.88 (0.77 to 1.00)    | 0.88 (0.77 to 1.00)         | 797 (24.9)/3131 (24.9)  | 0.93 (0.84 to 1.04)  | 0.93 (0.83 to 1.04)        | 0.5046                     |
| Sep-Nov                                    | 529 (21.9)/2187 (23.1)    | 0.89 (0.78 to 1.02)    | 0.89 (0.78 to 1.02)         | 688 (21.5)/2973 (23.6)  | 0.85 (0.76 to 0.95)  | 0.85 (0.76 to 0.95)        | 0.5817                     |
| No. of full siblings in total, n (%)       |                           |                        |                             |                         |                      |                            |                            |
| 0  | 414 (17.2)/1496 (15.8)    | Reference              | Reference                   | 467 (14.6)/2002 (15.9)  | Reference            | Reference                  |                            |
| 1  | 1059 (43.9)/4329 (45.8)   | 0.89 (0.78 to 1.01)    | <b>0.90 (0.78 to 1.03)</b>  | 1498 (46.8)/5653 (44.9) | 1.15 (1.02 to 1.29)  | <b>1.11 (0.98 to 1.25)</b> | <b>0.0222</b>              |
| 2 or more                                  | 938 (38.9)/3625 (38.4)    | 0.94 (0.82 to 1.07)    | 0.96 (0.84 to 1.10)         | 1236 (38.6)/4937 (39.2) | 1.09 (0.97 to 1.23)  | 1.05 (0.92 to 1.19)        | 0.3629                     |
| No. of older siblings, n (%)               |                           |                        |                             |                         |                      |                            |                            |
| 0  | 925 (38.4)/3967 (42.0)    | Reference              | Reference                   | 1239 (38.7)/5131 (40.7) | Reference            | Reference                  |                            |
| 1  | 908 (37.7)/3407 (36.1)    | 1.14 (1.02 to 1.26)    | 1.13 (0.99 to 1.27)         | 1264 (39.5)/4674 (37.1) | 1.12 (1.03 to 1.23)  | 1.12 (1.01 to 1.25)        | 0.9782                     |
| 2 or more                                  | 578 (24.0)/2076 (22.0)    | 1.19 (1.06 to 1.34)    | 1.24 (1.07 to 1.44)         | 698 (21.8)/2787 (22.1)  | 1.05 (0.95 to 1.17)  | 1.09 (0.95 to 1.25)        | 0.2064                     |
| No. of younger siblings, n (%)             |                           |                        |                             |                         |                      |                            |                            |
| 0  | 1524 (63.2)/5605 (59.3)   | Reference              | Reference                   | 1946 (60.8)/7550 (60.0) | Reference            | Reference                  |                            |
| 1  | 639 (26.5)/2710 (28.7)    | 0.88 (0.79 to 0.97)    | 0.91 (0.80 to 1.03)         | 892 (27.9)/3535 (28.1)  | 0.98 (0.89 to 1.07)  | 1.01 (0.91 to 1.12)        | 0.2097                     |
| 2 or more                                  | 248 (10.3)/1135 (12.0)    | 0.81 (0.70 to 0.94)    | 0.84 (0.71 to 1.00)         | 363 (11.3)/1507 (12.0)  | 0.93 (0.82 to 1.05)  | 0.96 (0.83 to 1.11)        | 0.2275                     |
| Serious childhood infection‡, n (%)        | 590 (24.5)/1935 (20.5)    | 1.27 (1.14 to 1.41)    | <b>1.26 (1.13 to 1.40)</b>  | 806 (25.3)/3071 (24.5)  | 1.03 (0.94 to 1.13)  | <b>1.04 (0.95 to 1.14)</b> | <b>0.0078</b>              |
| Tonsillectomy§, n (%)                      | 121 (5.0)/356 (3.8)       | 1.34 (1.08 to 1.66)    | 1.32 (1.06 to 1.64)         | 158 (5.0)/499 (4.0)     | 1.26 (1.05 to 1.52)  | 1.27 (1.06 to 1.54)        | 0.8094                     |
| Appendectomy§, n (%)                       | 65 (2.7)/238 (2.5)        | 1.08 (0.82 to 1.43)    | <b>1.08 (0.81 to 1.43)</b>  | 61 (1.9)/335 (2.7)      | 0.72 (0.55 to 0.95)  | <b>0.72 (0.55 to 0.95)</b> | <b>0.0453</b>              |

Odds ratios from conditional logistic regression on 25 multiply imputed datasets, in AS cases and population controls stratified by sex.

\*Adjusted for maternal age, maternal BMI, maternal smoking, parental country of birth, maternal disposable income, maternal educational level, maternal inflammatory disease (hospitalisation for SpA, IBD, psoriasis), and multiple birth, with the exception that no exposure was adjusted for itself. Number of older siblings additionally adjusted for number of younger siblings, and vice versa.

†Analyses for smoking and BMI restricted to birth years 1982-2004.

‡Analysed per 100 g.

§Until age 15.

AS, ankylosing spondylitis; BMI, body-mass index; SpA, spondyloarthritis; IBD, inflammatory bowel disease.

**Supplemental table 7.** Odds ratios for AS from sibling comparison analysis, only including individuals who reached age 35 during follow-up

| Risk factor                                | AS cases<br>(N=2317) | SpA-free<br>siblings<br>(N=3193) | OR (95% CI)         | Adj. OR* (95% CI)   |
|--|----------------------|----------------------------------|---------------------|---------------------|
| <b>Multiple birth, n (%)</b>               | 80 (3.5)             | 110 (3.4)                        | 1.46 (0.86 to 2.50) | 1.36 (0.79 to 2.33) |
| <b>Season of birth, n (%)</b>              |                      |                                  |                     |                     |
| Dec-Feb                                    | 585 (25.2)           | 779 (24.4)                       | Reference           | Reference           |
| March-May                                  | 656 (28.3)           | 917 (28.7)                       | 0.96 (0.82 to 1.11) | 0.97 (0.83 to 1.13) |
| June-Aug                                   | 565 (24.4)           | 792 (24.8)                       | 0.97 (0.83 to 1.14) | 0.96 (0.82 to 1.13) |
| Sep-Nov                                    | 511 (22.1)           | 705 (22.1)                       | 1.00 (0.85 to 1.17) | 1.00 (0.83 to 1.19) |
| <b>No. of older siblings, n (%)</b>        |                      |                                  |                     |                     |
| 0  | 782 (33.8)           | 1071 (33.5)                      | Reference           | Reference           |
| 1  | 981 (42.3)           | 1145 (35.9)                      | 1.09 (0.99 to 1.20) | 1.35 (1.16 to 1.57) |
| 2 or more                                  | 554 (23.9)           | 977 (30.6)                       | 1.06 (0.91 to 1.22) | 1.75 (1.31 to 2.34) |
| <b>Serious childhood infection†, n (%)</b> | 536 (23.2)           | 692 (21.7)                       | 1.08 (0.94 to 1.24) | 1.07 (0.93 to 1.24) |
| <b>Tonsillectomy†, n (%)</b>               | 99 (4.3)             | 101 (3.2)                        | 1.41 (1.04 to 1.92) | 1.44 (1.06 to 1.96) |

Odds ratios from conditional logistic regression.

\*Adjusted for maternal age, year of birth, sex of child, and parity (except when exposure is number of older siblings).

†Until age 15. 3 cases and their 4 SpA-free siblings excluded due to AS diagnosis in index case before age 16. AS, ankylosing spondylitis; SpA, spondyloarthritis.

**Supplemental table 8.** Odds ratios for AS only including cases and population controls who reached age 35 during follow-up

| Risk factor                                | AS cases<br>(N=3836) | Population<br>controls<br>(N=14,791) | OR (95% CI)         | Adj. OR* (95% CI)   |
|--|----------------------|--------------------------------------|---------------------|---------------------|
| <b>Multiple birth, n (%)</b>               | 95 (2.5)             | 247 (1.7)                            | 1.50 (1.18 to 1.90) | 1.51 (1.18 to 1.92) |
| <b>Season of birth, n (%)</b>              |                      |                                      |                     |                     |
| Dec-Feb                                    | 947 (24.7)           | 3405 (23.0)                          | Reference           | Reference           |
| March-May                                  | 1105 (28.8)          | 4171 (28.2)                          | 0.95 (0.86 to 1.05) | 0.96 (0.87 to 1.06) |
| June-Aug                                   | 940 (24.5)           | 3718 (25.1)                          | 0.91 (0.82 to 1.00) | 0.91 (0.82 to 1.01) |
| Sep-Nov                                    | 844 (22.0)           | 3497 (23.6)                          | 0.86 (0.78 to 0.96) | 0.87 (0.78 to 0.96) |
| <b>No. of older siblings, n (%)</b>        |                      |                                      |                     |                     |
| 0  | 1470 (38.3)          | 6134 (41.5)                          | Reference           | Reference           |
| 1  | 1503 (39.2)          | 5486 (37.1)                          | 1.14 (1.05 to 1.24) | 1.13 (1.03 to 1.25) |
| 2 or more                                  | 863 (22.5)           | 3171 (21.4)                          | 1.14 (1.04 to 1.26) | 1.18 (1.05 to 1.34) |
| <b>Serious childhood infection†, n (%)</b> | 899 (23.5)           | 3227 (21.8)                          | 1.09 (1.00 to 1.19) | 1.09 (1.00 to 1.18) |
| <b>Tonsillectomy†, n (%)</b>               | 170 (4.4)            | 536 (3.6)                            | 1.21 (1.01 to 1.45) | 1.21 (1.01 to 1.45) |

Odds ratios from conditional logistic regression on 25 multiply imputed datasets.

\*Adjusted for maternal age, maternal BMI, maternal smoking, parental country of birth, maternal disposable income, maternal educational level, maternal inflammatory disease (hospitalisation for SpA, IBD, psoriasis), and multiple birth, with the exception that no exposure was adjusted for itself. Number of older siblings additionally adjusted for number of younger siblings.

†Until age 15. 3 cases and their 13 matched controls excluded due to AS diagnosis before age 16. AS, ankylosing spondylitis.

**Supplemental table 9.** Odds ratios for AS in cases and population controls with at least one sibling

| Risk factor                                | AS cases<br>(N=4704) | Population controls<br>(N=15,667) | OR (95% CI)         | Adj. OR* (95% CI)   |
|--|----------------------|-----------------------------------|---------------------|---------------------|
| <b>Multiple birth, n (%)</b>               | 129 (2.7)            | 364 (2.3)                         | 1.20 (0.98 to 1.47) | 1.21 (0.98 to 1.48) |
| <b>Season of birth, n (%)</b>              |                      |                                   |                     |                     |
| Dec-Feb                                    | 1161 (24.7)          | 3596 (23.0)                       | Reference           | Reference           |
| March-May                                  | 1373 (29.2)          | 4397 (28.1)                       | 0.96 (0.87 to 1.05) | 0.95 (0.87 to 1.04) |
| June-Aug                                   | 1158 (24.6)          | 3996 (25.5)                       | 0.89 (0.81 to 0.98) | 0.89 (0.81 to 0.98) |
| Sep-Nov                                    | 1012 (21.5)          | 3678 (23.5)                       | 0.85 (0.77 to 0.93) | 0.85 (0.77 to 0.94) |
| <b>No. of older siblings, n (%)</b>        |                      |                                   |                     |                     |
| 0  | 1564 (33.2)          | 5687 (36.3)                       | Reference           | Reference           |
| 1  | 1997 (42.5)          | 6295 (40.2)                       | 1.15 (1.07 to 1.24) | 1.15 (1.03 to 1.29) |
| 2 or more                                  | 1143 (24.3)          | 3685 (23.5)                       | 1.13 (1.03 to 1.23) | 1.18 (1.03 to 1.35) |
| <b>Serious childhood infection†, n (%)</b> | 1159 (24.7)          | 3469 (22.2)                       | 1.15 (1.06 to 1.24) | 1.15 (1.06 to 1.24) |
| <b>Tonsillectomy†, n (%)</b>               | 236 (5.0)            | 611 (3.9)                         | 1.31 (1.12 to 1.53) | 1.32 (1.12 to 1.54) |

Odds ratios from conditional logistic regression on 25 multiply imputed datasets.

\*Adjusted for maternal age, maternal BMI, maternal smoking, parental country of birth, maternal disposable income, maternal educational level, maternal inflammatory disease (hospitalisation for SpA, IBD, psoriasis), and multiple birth, with the exception that no exposure was adjusted for itself. Number of older siblings additionally adjusted for number of younger siblings.

†Until age 15. 14 cases and their 51 matched controls excluded due to AS diagnosis in index case before age 16. AS, ankylosing spondylitis.

**Supplemental table 10.** Odds ratios for AS in cases and population controls by timing of infection or procedure

|   | AS cases<br>(N=5612) | Population controls<br>(N=22,042) | OR (95% CI)         |
|---|----------------------|-----------------------------------|---------------------|
| <b>Serious infection during first year of life, n (%)</b> | 471 (8.4)            | 1721 (7.8)                        | 1.08 (0.97 to 1.21) |
| <b>Tonsillectomy*, n (%)</b>                              |                      |                                   |                     |
| No  | 5317 (95.0)          | 21115 (96.1)                      | Reference           |
| <5 years of age   | 83 (1.5)             | 278 (1.3)                         | 1.18 (0.92 to 1.51) |
| 5-9 years   | 128 (2.3)            | 361 (1.6)                         | 1.42 (1.15 to 1.74) |
| 10-15 years   | 68 (1.2)             | 216 (1.0)                         | 1.23 (0.93 to 1.63) |
| <b>Appendectomy*, n (%)</b>                               |                      |                                   |                     |
| No  | 5470 (97.7)          | 21397 (97.4)                      | Reference           |
| <5 years of age   | 6 (0.1)              | 32 (0.1)                          | 0.70 (0.29 to 1.69) |
| 5-9 years   | 30 (0.5)             | 185 (0.8)                         | 0.62 (0.42 to 0.92) |
| 10-15 years   | 90 (1.6)             | 356 (1.6)                         | 1.02 (0.81 to 1.29) |

Odds ratios from conditional logistic regression on 25 multiply imputed datasets.

\*Until age 15. 16 cases and their 72 matched controls excluded due to AS diagnosis in index case before age 16. AS, ankylosing spondylitis.