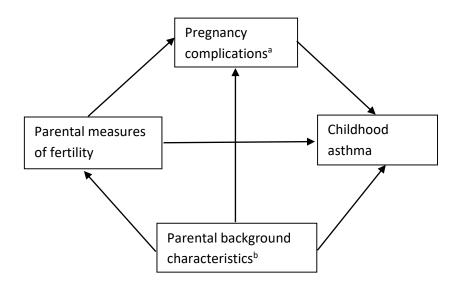
Supplementary Figure S1. Illustration of the underlying theoretical framework



^a Pregnancy complications evaluated as potential mediators included preterm birth, low birth weight, pre-eclampsia and delivery by caesarean section.

^b Parental background characteristic evaluated as potential confounders included maternal age, parity, education, smoking during pregnancy, pre-pregnancy body-mass index and asthma.

Supplementary Table S1. Comparing the distribution of background characteristics among children who were included and excluded from the registry-based analysis due to missing exposure information

| Background characteristics | Excluded (N=129,174) | Included (N=474,402) |
|----------------------------------------------------|----------------------|-----------------------|
| Maternal age at delivery, years N (%) | | |
| <25 | 24,873 (19.3) | 79,803 (16.8) |
| 25-29 | 45,427 (35.2) | 155,866 (32.9) |
| 30-34 | 40,413 (31.3) | 159,001 (33.5) |
| 35 and older | 18,461 (14.3) | 79,732 (16.8) |
| Maternal parity, N (%) | | |
| 0 | 53,538 (41.5) | 193,503 (40.8) |
| 1 | 45,311 (35.1) | 170,737 (36.0) |
| 2 | 21,684 (16.8) | 78,163 (16.5) |
| 3+ | 8,641 (6.7) | 31,999 (6.8) |
| Maternal smoking during pregnancy, N (%) | | |
| No | 56,162 (78.5) | 317,226 (80.5) |
| Only at the beginning of pregnancy | 6,098 (8.5) | 27,929 (7.1) |
| Still smoking at the end of pregnancy | 9,294 (13.0) | 48,855 (12.4) |
| Missing | 57,620 | 80,392 |
| Maternal current asthma, N (%) | | |
| No | 124,586 (96.5) | 454,114 (95.7) |
| Yes | 4,588 (3.6) | 20,288 (4.3) |
| Maternal pre-eclampsia, N (%) | | |
| No | 124,414 (96.3) | 456,100 (96.1) |
| Yes | 4,760 (3.7) | 18,302 (3.9) |
| Child sex, N (%) | | |
| Male | 66,203 (51.3) | 243,413 (51.3) |
| Female | 62,971 (48.7) | 230,989 (48.7) |
| Child preterm birth (<37 gestational weeks), N (%) | | |
| No | 122,563 (94.9) | 449,218 (94.7) |
| Yes | 6,611 (5.1) | 25,184 (5.3) |
| Child low birthweight (<2500 grams), N (%) | | |
| No | 125,047 (96.8) | 458,572 (96.7) |
| Yes | 4,127 (3.2) | 15,830 (3.3) |
| Missing | | |
| Child delivery by caesarean section, N(%) | | |
| No | 112,292 (86.9) | 404,328 (85.2) |
| Yes | 16,882 (13.1) | 70,074 (14.8) |
| Child asthma at 7 years, N(%) | | |
| No | 123,875 (95.9) | 454,213 (95.7) |
| Yes | 5,299 (4.1) | 20,189 (4.3) |

Supplementary Table S2. Distribution of background characteristics according to time to conception and use of assisted reproductive technologies in the Norwegian Mother and Child Cohort Study (**N**= **75,797**)

| Background characteristic | Time to concep 12 months | tion more than | Conceived by a reproductive te | |
|-----------------------------------------------|--------------------------------|------------------|--------------------------------|------------------|
| | No (N = 69,916) | Yes (N=5,881) | No (N=74,406) | Yes (N=1,391) |
| Maternal age at delivery, Mean(SD) | 29.9 (4.6) | 31.6 (4.4) | 30.0 (4.6) | 32.9 (3.8) |
| Maternal parity, N (%) | | | | |
| 0 | 29,741 (42.5) | 3,318 (56.4) | 32,118 (43.2) | 941 (67.7) |
| 1 | 25,496 (36.5) | 1,795 (30.5) | 26,917 (36.2) | 374 (26.9) |
| 2 | 11,412 (16.3) | 597 (10.2) | 11,946 (16.1) | 63 (4.5) |
| 3+ | 3,267 (4.7) | 171 (2.9) | 3,425 (4.6) | 13 (0.9) |
| Maternal education, N (%) | , , , | , , | , , , | , |
| Less than high school | 6,171 (8.8) | 527 (9.0) | 6,607 (8.9) | 91 (6.5) |
| High school | 21,532 (30.8) | 1,953 (33.2) | 23,084 (31.0) | 401 (28.8) |
| Up to four years of college | 27,955 (40.0) | 2,268 (38.6) | 29,641 (39.8) | 582 (41.8) |
| More than four years of college | 13,901 (19.9) | 1,117 (19.0) | 14,707 (19.8) | 311 (22.4) |
| Missing | 357 (0.5) | 16 (0.3) | 367 (0.5) | 6 (0.4) |
| Maternal pre-pregnancy body-mass index, N (%) | | | , , | |
| <18.5 | 2,132 (3.1) | 181 (3.1) | 2,283 (3.1) | 30 (2.2) |
| 18.5-24.9 | 44,498 (63.6) | 3,270 (55.6) | 46,896 (63.0) | 872 (62.7) |
| 25-29.9 | 14,955 (21.4) | 1,436 (24.4) | 16,066 (21.6) | 325 (23.4) |
| 30 or higher | 6,233 (8.9) | 889 (15.1) | 6,985 (9.4) | 137 (9.9) |
| Missing | 2,098 (3.0) | 105 (1.8) | 2,176 (2.9) | 27 (1.9) |
| Maternal folic acid supplement intake | , , , | | | |
| No | 15,053 (21.5) | 967 (16.4) | 15,927 (21.4) | 93 (6.7) |
| Started before pregnancy | 27,944 (40.0) | 2,891 (49.2) | 29,718 (39.9) | 1,117 (80.3) |
| Started during pregnancy | 26,919 (38.5) | 2,023 (34.4) | 28,761 (38.7) | 181 (13.0) |
| Maternal smoking during pregnancy, N (%) | | | | |
| No | 52,213 (74.7) | 4,351 (74.0) | 55,358 (74.4) | 1,206 (86.7) |
| Quit by 18 weeks | 9,973 (14.3) | 838 (14.3) | 10,725 (14.4) | 86 (6.2) |
| Smoked after 18 weeks | 7,390 (10.6) | 667 (11.3) | 7,964 (10.7) | 93 (6.7) |
| Missing | 340 (0.5) | 25 (0.4) | 359 (0.5) | 6 (0.4) |
| Maternal current asthma, N (%) | | | | |
| No | 64,658 (92.5) | 5,425 (92.3) | 71,859 (96.6) | 1,361 (97.8) |
| Yes | 5,258 (7.5) | 456 (7.8) | 2,547 (3.4) | 30 (2.2) |
| Maternal pre-eclampsia, N (%) | | | | |
| No | 67,333 (96.3) | 5,581 (94.9) | 71,590 (96.2) | 1,324 (95.2) |
| Yes | 2,583 (3.7) | 300 (5.1) | 2,816 (3.8) | 67 (4.8) |

| Child sex, N (%) | | | | |
|----------------------------------------------------|---------------|--------------|---------------|--------------|
| Male | 35,784 (51.2) | 3,027 (51.5) | 38,089 (51.2) | 722 (51.9) |
| Female | 34,132 (48.8) | 2,854 (48.5) | 36,317 (48.8) | 669 (48.1) |
| Child preterm birth (<37 gestational weeks), N (%) | | | | |
| No | 66,413 (95.0) | 5,436 (92.4) | 70,606 (94.9) | 1,243 (89.4) |
| Yes | 3,254 (4.7) | 392 (6.7) | 3,528 (4.7) | 118 (8.5) |
| Missing | 249 (0.4) | 53 (0.9) | 272 (0.4) | 30 (2.2) |
| Child low birthweight (<2500 grams), N (%) | | | | |
| No | 67,966 (97.2) | 5,645 (96.0) | 72,294 (97.2) | 1,317 (94.7) |
| Yes | 1,914 (2.7) | 232 (3.9) | 2,073 (2.8) | 73 (5.3) |
| Missing | 36 (0.1) | 4 (0.1) | 39 (0.1) | 1 (0.1) |
| Child delivery by caesarean section, N(%) | | | | |
| No | 60,529 (86.6) | 4,759 (80.9) | 64,185 (86.3) | 1,103 (79.3) |
| Yes | 9,387 (13.4) | 1,122 (19.1) | 10,221 (13.7) | 288 (20.7) |

Supplementary Table S3. Examining the direct association between assisted reproductive technologies and childhood asthma at 7 years not mediated by adverse pregnancy outcomes (low birth weight, preterm birth, pre-eclampsia and delivery by caesarean section)

| Study population | Conceived by assisted reproductive | Total association OR (95% CI) ^a | Direct association OR (95% CI) ^a | Indirect association OR (95% CI) ^a |
|-----------------------|------------------------------------|--------------------------------------------|------------------------------------------------|-----------------------------------------------|
| | technologies | | | |
| Register-based cohort | No | 1 | 1 | 1 |
| | Yes (total) | 1.24 (1.12, 1.36) | 1.19 (1.08, 1.31) | 1.040 (1.034, 1.045) |
| | Yes (IVF) | 1.24 (1.11, 1.38) | 1.19 (1.06, 1.33) | 1.039 (1.033, 1.045) |
| | Yes (ICSI) | 1.27 (0.80, 2.02) | 1.20 (0.75, 1.92) | 1.052 (1.029, 1.076) |
| | Yes (Other/ | 1.20 (0.81, 1.78) | 1.15 (0.77, 1.72) | 1.037 (1.019, 1.057) |
| | unspecified) | | | |
| MoBa | No | 1 | 1 | 1 |
| | Yes | 1.49 (1.19, 1.87) | 1.43 (1.14, 1.80) | 1.04 (1.02, 1.05) |

^a The analysis of the register-based cohort was adjusted for maternal age, parity, maternal current asthma and child sex. The analysis of MoBa was adjusted for maternal age, parity, education, smoking during pregnancy, pre-pregnancy BMI, maternal current asthma and child sex.

Supplementary Table S4. Examining the direct associations of parental history of treatment for childlessness and time to conception with childhood asthma at 7 years not mediated by adverse pregnancy outcomes (low birth weight, preterm birth, pre-eclampsia and delivery by caesarean section)

| Exposure | Exposure group | Total association OR (95% CI) ^a | Direct association OR (95% CI) ^a | Indirect association OR (95% CI) ^a |
|------------------------|---------------------|--------------------------------------------|---------------------------------------------|-----------------------------------------------|
| Previously treated for | No | 1 | 1 | 1 |
| unwanted childlessness | Yes | 1.31 (1.14, 1.51) | 1.28 (1.11, 1.48) | 1.03 (1.02, 1.03) |
| Time to conception | <6 months | 1 | 1 | 1 |
| | 6-12 months | 0.97 (0.88, 1.08) | 0.97 (0.87, 1.08) | 1.00 (0.99, 1.01) |
| | More than 12 months | 1.23 (1.08, 1.39) | 1.19 (1.05, 1.35) | 1.03 (1.02, 1.04) |

^a Adjusted for maternal age, parity, education, smoking during pregnancy, pre-pregnancy BMI, maternal current asthma and child sex.

Supplementary Table S5. Examining the direct association between maternal history of miscarriages and childhood asthma at 7 years not mediated by adverse pregnancy outcomes (low birth weight, preterm birth, pre-eclampsia and delivery by caesarean section)

| Study population | Exposure | Exposure group | Total association OR (95% CI) ^a | Direct association OR (95% CI) ^a | Indirect association OR (95% CI) ^a |
|-----------------------|-----------------------------------|----------------|--------------------------------------------|---------------------------------------------|-----------------------------------------------|
| Register-based cohort | Number of miscarriages within the | None | 1 | 1 | 1 |
| | first 12 gestational weeks | 1 | 1.07 (1.03, 1.11) | 1.06 (1.02, 1.11) | 1.004 (1.003, 1.006) |
| | | 2 | 1.20 (1.11, 1.28) | 1.18 (1.10, 1.27) | 1.012 (1.009, 1.016) |
| | | 3 or more | 1.26 (1.14, 1.39) | 1.21 (1.10, 1.34) | 1.037 (1.032, 1.043) |
| | Number of miscarriages between | None | 1 | 1 | 1 |
| | 12 and 23 gestational weeks | 1 | 1.21 (1.11, 1.31) | 1.18 (1.09, 1.28) | 1.022 (1.016, 1.027) |
| | | 2 | 1.03 (0.79, 1.33) | 0.99 (0.76, 1.28) | 1.042 (1.025, 1.058) |
| | | 3 or more | 1.08 (0.60, 1.94) | 1.00 (0.55, 1.80) | 1.077 (1.051, 1.104) |
| MoBa | Number of miscarriages within the | None | 1 | 1 | 1 |
| | first 22 gestational weeks | 1 | 1.06 (0.97, 1.16) | 1.06 (0.97, 1.16) | 1.00 (0.99, 1.01) |
| | | 2 | 1.18 (0.98, 1.42) | 1.17 (0.98, 1.41) | 1.01 (0.99, 1.01) |
| | | 3 or more | 1.12 (0.75, 1.68) | 1.10 (0.73, 1.65) | 1.02 (1.01, 1.03) |

^a The analysis of the register-based cohort was adjusted for maternal age, parity, maternal current asthma and child sex. The analysis of MoBa was adjusted for maternal age, parity, education, smoking during pregnancy, pre-pregnancy BMI, maternal current asthma and child sex.

Supplementary Table S6. Association between different measures of maternal fertility and childhood asthma at 7 years defined based on maternal report in the Norwegian Mother and Child Cohort Study

| Exposure | Exposure group | N | N cases (%) | Unadjusted | Adjusted ^a | Adjusted ^b |
|---------------------------|---------------------|--------|-------------|-------------------|-----------------------|-----------------------|
| | | | | RR 95% CI | RR 95% CI | RR 95% CI |
| Number of miscarriages | None | 31,550 | 1,744 (5.5) | 1 | 1 | 1 |
| within 22 completed | 1 | 6,015 | 339 (5.6) | 1.02 (0.91, 1.14) | 1.04 (0.92, 1.17) | 1.04 (0.93, 1.17) |
| gestational weeks | 2 | 1,345 | 79 (5.9) | 1.06 (0.85, 1.33) | 1.08 (0.86, 1.35) | 1.07 (0.85, 1.34) |
| | 3 or more | 463 | 28 (6.1) | 1.09 (0.76, 1.57) | 1.07 (0.75, 1.55) | 1.04 (0.73, 1.49) |
| Previously treated for | No | 35,224 | 1,931 (5.5) | 1 | 1 | 1 |
| unwanted childlessness | Yes | 3,293 | 214 (6.5) | 1.19 (1.03, 1.36) | 1.22 (1.06, 1.41) | 1.22 (1.06, 1.41) |
| Time to conception | <6 months | 31,112 | 1,679 (5.4) | 1 | 1 | 1 |
| | 6-12 months | 5,046 | 303 (6.0) | 1.11 (0.99, 1.25) | 1.11 (0.99, 1.25) | 1.11 (0.98, 1.25) |
| | More than 12 months | 3,215 | 208 (6.5) | 1.20 (1.04, 1.38) | 1.20 (1.03, 1.38) | 1.17 (1.01, 1.35) |
| Conceived by assisted | No | 38,590 | 2,141 (5.6) | 1 | 1 | 1 |
| reproductive technologies | Yes | 783 | 49 (6.3) | 1.13 (0.86, 1.48) | 1.23 (0.93, 1.62) | 1.20 (0.91, 1.59) |

^a Adjusted for maternal age, parity, education, smoking during pregnancy, pre-pregnancy BMI and maternal current asthma.

^b Adjusted for maternal age, parity, education, smoking during pregnancy, pre-pregnancy BMI, maternal current asthma, in addition to child sex, low birthweight, preterm birth, pre-eclampsia and delivery by caesarean sections.

Supplementary Table S7. Association between conception by assisted reproductive technologies and childhood asthma at 7 years stratified by maternal current asthma

| Study | Conceived | No materr | nal current asth | ma | | Maternal | current asthma | | | |
|--------------|--------------|-----------|------------------|-------------------|-----------------------|----------|----------------|-------------------|-----------------------|---------------|
| population | by assisted | N | N cases | Unadjusted | Adjusted ^a | N | N cases (%) | Unadjusted | Adjusted ^a | p-value |
| | reproductive | | (%) | RR 95% CI | RR 95% CI | | | RR 95% CI | RR 95% CI | from test for |
| | technologies | | | | | | | | | interaction |
| Register- | No | 446,064 | 17,616 | 1 | 1 | 19,970 | 2,144 (10.7) | 1 | 1 | 0.11 |
| based cohort | | | (4.0) | | | | | | | |
| | Yes (total) | 8,050 | 397 (4.9) | 1.25 (1.13, 1.38) | 1.23 (1.12, 1.36) | 318 | 32 (10.1) | 0.94 (0.67, 1.30) | 0.90 (0.65, 1.26) | |
| | Yes (IVF) | 7,066 | 353 (5.0) | 1.27 (1.14, 1.40) | 1.25 (1.12, 1.39) | 273 | 24 (8.8) | 0.82 (0.56, 1.20) | 0.78 (0.54, 1.16) | 0.07 |
| | Yes (ICSI) | 462 | 20 (4.3) | 1.10 (0.71, 1.68) | 1.08 (0.70, 1.66) | 21 | 5 (23.8) | 2.22 (1.06, 4.65) | 2.10 (0.99, 4.45) | |
| | Yes (Other/ | 522 | 24 (4.6) | 1.16 (0.79, 1.72) | 1.15 (0.78, 1.70) | 24 | 3 (12.5) | 1.16 (0.40, 3.38) | 1.12 (0.38, 3.27) | |
| | unspecified) | | | | | | | | | |
| MoBa | No | 71,859 | 2,831 (3.9) | 1 | 1 | 2,547 | 313 (12.3) | 1 | 1 | 0.52 |
| | Yes | 1,361 | 80 (5.9) | 1.49 (1.20, 1.85) | 1.45 (1.16, 1.81) | 30 | 5 (16.7) | 1.36 (0.61, 3.04) | 1.00 (0.39, 2.54) | |

^a The analysis of the register-based cohort was adjusted for maternal age, parity, and maternal current asthma. The analysis of MoBa was adjusted for maternal age, parity, education, smoking during pregnancy, pre-pregnancy BMI and maternal current asthma.

Supplementary Table S8. Association between measures of parental fertility and childhood asthma at 7 years in the Norwegian Mother and Child Cohort Study stratified by maternal current asthma

| Exposure | Exposure group | No maternal current asthma | | | | | Maternal current asthma | | | |
|------------------------------------------|---------------------|----------------------------|-------------|-------------------------|------------------------------------|-------|-------------------------|-------------------------|------------------------------------|-----------------------------------------|
| | | N | N cases (%) | Unadjusted RR 95% CI | Adjusted ^a RR 95% CI | N | N cases (%) | Unadjusted RR 95% CI | Adjusted ^a RR 95% CI | p-value from test for interaction |
| Previously | No | 65,683 | 2,545 (3.9) | 1 | 1 | 2,328 | 282 (12.1) | 1 | 1 | 0.46 |
| treated for unwanted childlessness | Yes | 5,825 | 299 (5.1) | 1.32 (1.18, 1.49) | 1.29 (1.14, 1.46) | 193 | 26 (13.5) | 1.11 (0.76, 1.63) | 1.04 (0.71, 1.53) | |
| Time to | <6 months | 58,409 | 2,272 (3.9) | 1 | 1 | 2,076 | 253 (12.2) | 1 | 1 | 0.28 |
| conception | 6-12 months | 9,136 | 346 (3.8) | 0.97 (0.87, 1.09) | 0.97 (0.86, 1.08) | 295 | 40 (13.6) | 1.11 (0.81, 1.52) | 1.06 (0.78, 1.46) | |
| | More than 12 months | 5,675 | 293 (5.2) | 1.33 (1.18, 1.49) | 1.23 (1.09, 1.39) | 206 | 25 (12.1) | 1.00 (0.68, 1.46) | 0.86 (0.57, 1.30) | |

^a Adjusted for maternal age, parity, education, smoking during pregnancy, pre-pregnancy BMI and maternal current asthma.

Supplementary Table S9. Association between maternal history of miscarriages and childhood asthma at 7 years stratified by maternal current asthma

| Study | Exposure | Exposure | No matern | al current ast | hma | | Maternal | current asthma | | | |
|--------------------|---------------------------------|-----------|-----------|-----------------|-------------------------|------------------------------------|----------|-----------------|-------------------------|------------------------------------|-----------------------------------------|
| population | | group | N | N cases (%) | Unadjusted RR 95% CI | Adjusted ^a RR 95% CI | N | N cases (%) | Unadjusted RR 95% CI | Adjusted ^a RR 95% CI | p-value from test for interaction |
| Register- based | Number of miscarriages | None | 359,367 | 13,971 (3.9) | 1 | 1 | 15,499 | 1,657 (10.7) | 1 | 1 | 0.48 |
| cohort | within the first 12 gestational | 1 | 69,864 | 2,895 (4.1) | 1.07 (1.02, 1.11) | 1.08 (1.04, 1.12) | 3,459 | 361 (10.4) | 0.98 (0.87, 1.09) | 0.96 (0.86, 1.08) | |
| | weeks | 2 | 17,506 | 798 (4.6) | 1.17 (1.09, 1.26) | 1.20 (1.12, 1.29) | 909 | 104 (11.4) | 1.07 (0.89, 1.29) | 1.04 (0.86, 1.26) | |
| | | 3 or more | 7,377 | 349 (4.7) | 1.22 (1.10, 1.35) | 1.25 (1.12, 1.39) | 421 | 54 (12.8) | 1.20 (0.93 (1.55) | 1.16 (0.89, 1.50) | |
| | Number of miscarriages | None | 429,158 | 16,941 (4.0) | 1 | 1 | 19,040 | 2,038 (10.7) | 1 | 1 | 0.66 |
| | between 12 and | 1 | 10,595 | 484 (4.6) | 1.16 (1.06, 1.27) | 1.22 (1.11, 1.33) | 491 | 62 (12.6) | 1.18 (0.92, 1.51) | 1.15 (0.90, 1.48) | |
| | 23 gestational | 2 | 1,224 | 50 (4.1) | 1.03 (0.78, 1.36) | 1.10 (0.83, 1.46) | 49 | 3 (6.1) | 0.57 (0.19, 1.72) | 0.54 (0.18, 1.65) | |
| | weeks | 3 or more | 396 | 15 (3.8) | 0.96 (0.58, 1.58) | 1.01 (0.61, 1.67) | 22 | 3 (13.6) | 1.27 (0.44, 3.68) | 1.19 (0.41, 3.47) | |
| MoBa | Number of miscarriages | None | 58,901 | 2,314 (3.9) | 1 | 1 | 2,081 | 250 (12.0) | 1 | 1 | 0.50 |
| | within the first | 1 | 11,008 | 456 (4.1) | 1.05 (0.96, 1.16) | 1.06 (0.96, 1.18) | 356 | 43 (12.1) | 1.01 (0.74, 1.36) | 1.01 (0.74, 1.37) | |
| | 22 gestational | 2 | 2,454 | 105 (4.3) | 1.09 (0.90, 1.32) | 1.14 (0.94, 1.38) | 101 | 18 (17.8) | 1.48 (0.94, 2.34) | 1.45 (0.92, 2.30) | |
| | weeks | 3 or more | 857 | 36 (4.2) | 1.07 (0.77, 1.48) | 1.09 (0.79, 1.51) | 39 | 7 (18.0) | 1.49 (0.77, 2.90) | 1.42 (0.69, 2.92) | |

^a The analysis of the register-based cohort was adjusted for maternal age, parity, and maternal current asthma. The analysis of MoBa was adjusted for maternal age, parity, education, smoking during pregnancy, pre-pregnancy BMI and maternal current asthma.

^b Additional adjustment child sex, low birthweight, preterm birth, pre-eclampsia and delivery by caesarean section.

Supplementary Table S10. Association between conception by assisted reproductive technologies and childhood asthma at 7 years stratified by preterm birth

| Study | Conceived by | Term | | | | Preterm | | | | |
|------------|------------------------------------------|---------|--------------|-------------------------|------------------------------------|---------|-------------|-------------------------|------------------------------------|-----------------------------------------|
| population | assisted reproductive technologies | N | N cases (%) | Unadjusted RR 95% CI | Adjusted ^a RR 95% CI | N | N cases (%) | Unadjusted RR 95% CI | Adjusted ^a RR 95% CI | p-value from test for interaction |
| Register- | No | 441,516 | 18,041 (4.1) | 1 | 1 | 24,518 | 1,719 (7.0) | 1 | 1 | 0.68 |
| based | Yes (total) | 7,702 | 372 (4.8) | 1.18 (1.07, 1.31) | 1.17 (1.06, 1.30) | 666 | 57 (8.6) | 1.22 (0.95, 1.57) | 1.22 (0.94, 1.58) | |
| cohort | Yes (IVF) | 6,753 | 325 (4.8) | 1.18 (1.06, 1.31) | 1.17 (1.05, 1.30) | 586 | 52 (8.9) | 1.27 (0.97, 1.65) | 1.27 (0.97, 1.66) | 0.39 |
| | Yes (ICSI) | 445 | 24 (5.4) | 1.32 (0.89, 1.95) | 1.31 (0.89, 1.92) | 38 | 1 (2.6) | 0.37 (0.05, 2.60) | 0.39 (0.06, 2.49) | |
| | Yes (Other/ unspecified) | 504 | 23 (4.6) | 1.12 (0.75, 1.67) | 1.11 (0.74, 1.65) | 42 | 4 (9.5) | 1.36 (0.53, 3.45) | 1.27 (0.49, 3.30) | |
| MoBa | No | 70,606 | 2,904 (4.1) | 1 | 1 | 3,528 | 233 (6.6) | 1 | 1 | 0.34 |
| | Yes | 1,243 | 71 (5.7) | 1.39 (1.11, 1.74) | 1.35 (1.07, 1.70) | 118 | 13 (11.0) | 1.67 (0.98, 2.83) | 1.77 (1.03, 3.06) | |

^a The analysis of the register-based cohort was adjusted for maternal age, parity, and maternal current asthma. The analysis of MoBa was adjusted for maternal age, parity, education, smoking during pregnancy, pre-pregnancy BMI and maternal current asthma.

Supplementary Table S11. Association between measures of parental fertility and childhood asthma at 7 years in the Norwegian Mother and Child Cohort Study stratified by preterm birth

| Exposure | Exposure group | Term | | | | | | | | |
|------------------------------------------|---------------------|--------|-------------|-------------------------|------------------------------------|-------|-------------|-------------------------|------------------------------------|--------------------------------------------|
| | | N | N cases (%) | Unadjusted RR 95% CI | Adjusted ^a RR 95% CI | N | N cases (%) | Unadjusted RR 95% CI | Adjusted ^a RR 95% CI | p-value from test for interaction |
| Previously | No | 64,598 | 2,614 (4.1) | 1 | 1 | 3,173 | 206 (6.5) | 1 | 1 | 0.88 |
| treated for unwanted childlessness | Yes | 5,575 | 290 (5.2) | 1.29 (1.14, 1.45) | 1.26 (1.11, 1.42) | 390 | 34 (8.7) | 1.34 (0.94, 1.91) | 1.28 (0.87, 1.86) | |
| Time to | <6 months | 57,466 | 2,339 (4.1) | 1 | 1 | 2,804 | 182 (6.5) | 1 | 1 | 0.77 |
| conception | 6-12 months | 8,947 | 355 (4.0) | 0.97 (0.87, 1.09) | 0.97 (0.87, 1.08) | 450 | 29 (6.4) | 0.99 (0.68, 1.45) | 1.02 (0.70, 1.50) | |
| | More than 12 months | 5,436 | 281 (5.2) | 1.27 (1.13, 1.43) | 1.16 (1.03, 1.32) | 392 | 35 (8.9) | 1.38 (0.98, 1.94) | 1.31 (0.91, 1.90) | |

^a Adjusted for maternal age, parity, education, smoking during pregnancy, pre-pregnancy BMI and maternal current asthma.

Supplementary Table S12. Association between maternal history of miscarriages and childhood asthma at 7 years stratified by preterm birth

| Study | Exposure | Exposure | Term | | | | Preterm | | | | |
|--------------------|-------------------------|-----------|---------|--------------|-------------------------|------------------------------------|---------|-------------|-------------------------|------------------------------------|--------------------------------------------|
| population | | group | N | N cases (%) | Unadjusted RR 95% CI | Adjusted ^a RR 95% CI | N | N cases (%) | Unadjusted RR 95% CI | Adjusted ^a RR 95% CI | p-value from test for interaction |
| Register- based | Number of | None | 355,532 | 14,328 (4.0) | 1 | 1 | 19,334 | 1,300 (6.7) | 1 | 1 | 0.27 |
| | miscarriages | 1 | 69,280 | 2,938 (4.2) | 1.05 (1.01, 1.09) | 1.05 (1.01, 1.10) | 4,043 | 318 (7.9) | 1.17 (1.04, 1.32) | 1.15 (1.02, 1.29) | |
| cohort | within the first | 2 | 17,272 | 805 (4.7) | 1.16 (1.08, 1.24) | 1.16 (1.08, 1.25) | 1,143 | 97 (8.5) | 1.26 (1.04, 1.54) | 1.24 (1.02, 1.51) | |
| | 12 gestational weeks | 3 or more | 7,134 | 342 (4.8) | 1.19 (1.07, 1.32) | 1.19 (1.07, 1.33) | 664 | 61 (9.2) | 1.37 (1.06, 1.75) | 1.32 (1.02, 1.70) | |
| | Number of | None | 424,857 | 17,352 (4.1) | 1 | 1 | 23,341 | 1,627 (7.0) | 1 | 1 | 0.44 |
| | miscarriages | 1 | 10,227 | 471 (4.6) | 1.13 (1.03, 1.24) | 1.18 (1.07, 1.29) | 859 | 75 (8.7) | 1.25 (1.00, 1.56) | 1.21 (0.96, 1.52) | |
| | between 12 and | 2 | 1,152 | 48 (4.2) | 1.02 (0.77, 1.35) | 1.09 (0.83, 1.45) | 121 | 5 (4.1) | 0.60 (0.25, 1.40) | 0.55 (0.24, 1.30) | |
| | 23 gestational weeks | 3 or more | 364 | 15 (4.1) | 1.01 (0.61, 1.66) | 1.06 (0.64, 1.75) | 54 | 3 (5.6) | 0.80 (0.26, 2.40) | 0.71 (0.25, 2.06) | |
| MoBa | Number of | None | 57,867 | 2,379 (4.1) | 1 | 1 | 2,869 | 179 (6.2) | 1 | 1 | 0.13 |
| | miscarriages | 1 | 10,748 | 449 (4.2) | 1.02 (0.92, 1.12) | 1.03 (0.93, 1.14) | 575 | 49 (8.5) | 1.37 (1.00, 1.86) | 1.47 (1.06, 2.04) | |
| | within the first | 2 | 2,401 | 111 (4.6) | 1.12 (0.93, 1.36) | 1.16 (0.96, 1.40) | 143 | 11 (7.7) | 1.23 (0.69, 2.21) | 1.27 (0.69, 2.34) | |
| | 22 gestational weeks | 3 or more | 833 | 36 (4.3) | 1.05 (0.76, 1.45) | 1.06 (0.77, 1.47) | 59 | 7 (11.9) | 1.90 (0.95, 3.81) | 1.90 (1.08, 3.36) | |

^a The analysis of the register-based cohort was adjusted for maternal age, parity, and maternal current asthma. The analysis of MoBa was adjusted for maternal age, parity, education, smoking during pregnancy, pre-pregnancy BMI and maternal current asthma.

^b Additional adjustment child sex, low birthweight, preterm birth, pre-eclampsia and delivery by caesarean section.

Supplementary Table S13. Exploring the additional adjustment for use of assisted reproductive technologies for the association between maternal history of miscarriages and childhood asthma at 7 years

| Study population | Exposure | Exposure group | N | N cases (%) | Unadjusted RR 95% CI | Adjusted ^a RR 95% CI | Adjusted ^b RR 95% CI |
|-----------------------|------------------------------------------------------------------|----------------|---------|--------------|-------------------------|------------------------------------|------------------------------------|
| Register-based cohort | Number of miscarriages | None | 374,866 | 15,628 (4.2) | 1 | 1 | 1 |
| | within the first 12 gestational weeks | 1 | 73,323 | 3,256 (4.4) | 1.07 (1.03, 1.11) | 1.07 (1.03, 1.11) | 1.07 (1.03, 1.11) |
| | | 2 | 18,415 | 902 (4.9) | 1.17 (1.10, 1.26) | 1.18 (1.10, 1.26) | 1.18 (1.10, 1.26) |
| | | 3 or more | 7,798 | 403 (5.2) | 1.24 (1.12, 1.37) | 1.24 (1.12, 1.37) | 1.24 (1.12, 1.36) |
| | Number of miscarriages between 12 and 23 gestational weeks | None | 448,198 | 18,979 (4.2) | 1 | 1 | 1 |
| | | 1 | 11,086 | 546 (4.9) | 1.16 (1.07, 1.27) | 1.21 (1.11, 1.32) | 1.20 (1.10, 1.31) |
| | | 2 | 1,273 | 53 (4.2) | 0.98 (0.75, 1.29) | 1.04 (0.79, 1.36) | 1.03 (0.79, 1.35) |
| | | 3 or more | 418 | 18 (4.3) | 1.02 (0.65, 1.60) | 1.04 (0.66, 1.65) | 1.04 (0.66, 1.64) |
| MoBa | Number of miscarriages | None | 60,982 | 2,564 (4.2) | 1 | 1 | 1 |
| | within the first 22 | 1 | 11,364 | 499 (4.4) | 1.04 (0.95, 1.15) | 1.06 (0.96, 1.16) | 1.06 (0.96, 1.16) |
| | gestational weeks | 2 | 2,555 | 123 (4.8) | 1.14 (0.96, 1.37) | 1.18 (0.98, 1.41) | 1.18 (0.98, 1.41) |
| | | 3 or more | 896 | 43 (4.8) | 1.14 (0.85, 1.53) | 1.14 (0.85, 1.53) | 1.13 (0.84, 1.51) |

^a The analysis of the register-based cohort was adjusted for maternal age, parity, and maternal current asthma. The analysis of MoBa was adjusted for maternal age, parity, education, smoking during pregnancy, pre-pregnancy BMI and maternal current asthma.

^b Additional adjustment for use of assisted reproductive technologies.