

Table S1. Demographic characteristics of individuals in the population-based cohort and sibling cohort. Figures are numbers (%).

Characteristics	Population-based cohort (N=407,804)	Sibling cohort (N=83,066)
Maternal age at delivery (years)		
<25	48,701 (11.9)	10,267 (12.4)
25–34	280,495 (68.8)	60,530 (72.9)
≥35	78,608 (19.3)	12,269 (14.8)
Parity		
1	183,117 (44.9)	31,834 (38.3)
≥2	224,687 (55.1)	51,232 (61.7)
Maternal smoking during pregnancy		
Yes	56,889 (14.0)	10,408 (12.5)
No	342,666 (84.0)	71,013 (85.5)
Unknown	8249 (2.0)	1645 (2.0)
Maternal cohabiting status		
Married or cohabiting	354,734 (87.0)	74,341 (89.5)
Single, divorced, or widowed	48,938 (12.0)	8179 (9.8)
Unknown	4132 (1.0)	546 (0.7)
Maternal highest education attained at delivery		
Elementary school	68,242 (16.7)	13,670 (16.5)
Above elementary school	324,505 (79.6)	67,299 (81.0)
Unknown	15,057 (3.7)	2097 (2.5)
Maternal diabetes during pregnancy	9981 (2.4)	1923 (2.3)
Premature rupture of membranes	25,294 (6.2)	4562 (5.5)
Cesarean section	68,947 (16.9)	12,825 (15.4)
Maternal atopic disposition	21,126 (5.2)	4483 (5.4)
Paternal atopic disposition	18,048 (4.4)	3801 (4.6)
Paternal antibiotic use during the index pregnancy	75,720 (18.6)	16,434 (19.8)
Preterm birth	20,114 (4.9)	3633 (4.4)
Calendar year of birth		
2005–2006	119,281 (29.2)	22,513 (27.1)
2007–2008	119,092 (29.2)	26,437 (31.8)
2009–2011	169,431 (41.5)	34,116 (41.1)

Table S2. Crude hazard ratio of childhood asthma by timing, number, duration, and combination treatment of maternal antibiotic use during pregnancy in the population-based analysis and sibling design

Antibiotic use during pregnancy	Population-based cohort analysis	Sibling analysis
	Crude HRs (95% CI)	Crude HRs (95% CI)
No antibiotic use during pregnancy	1 (Ref)	1 (Ref)
Any antibiotic use during pregnancy	1.24 (1.21 - 1.28)	0.94 (0.88 - 1.00)
Timing of antibiotics use		
First trimester only	1.15 (1.10 - 1.20)	0.92 (0.82 - 1.03)
Second trimester only	1.21 (1.15 - 1.26)	0.94 (0.85 - 1.05)
Third trimester only	1.18 (1.13 - 1.22)	0.97 (0.89 - 1.07)
More than more trimester	1.44 (1.39 - 1.50)	0.91 (0.82 - 1.00)
Number of antibiotic prescriptions		
One prescription	1.15 (1.12 - 1.19)	0.96 (0.90 - 1.03)
Two prescriptions	1.27 (1.21 - 1.32)	0.87 (0.79 - 0.97)
Three or more prescriptions	1.58 (1.51 - 1.65)	0.94 (0.84 - 1.07)
Duration of antibiotic use (days)		
<30	1.22 (1.18 - 1.25)	0.94 (0.88 - 1.00)
30-60	1.62 (1.52 - 1.74)	0.99 (0.83 - 1.18)
>60	1.64 (1.38 - 1.95)	0.75 (0.49 - 1.15)
Combination treatment		
One type of antibiotics only	1.17 (1.14 - 1.21)	0.95 (0.89 - 1.02)
Two types of antibiotics	1.37 (1.31 - 1.43)	0.89 (0.80 - 0.99)
Three or more types of antibiotics	1.67 (1.56 - 1.79)	0.92 (0.77 - 1.10)

Abbreviations: HR, hazard ratio; CI, confidence interval.

Table S3. Crude hazard ratio of childhood asthma by types of antibiotics in the population-based analysis and sibling design

Antibiotic use during pregnancy	Population-based cohort analysis	Sibling analysis
	Crude HRs (95% CI)	Crude HRs (95% CI)
Generic names of antibiotics		
Penicillins (yes versus no)	1.21 (1.18 - 1.24)	0.98 (0.92 - 1.05)
Cephalosporins (yes versus no)	1.19 (0.83 - 1.72)	0.77 (0.34 - 1.74)
Sulfonamides (yes versus no)	1.15 (1.10 - 1.21)	0.93 (0.82 - 1.05)
Macrolides (yes versus no)	1.31 (1.23 - 1.40)	0.78 (0.66 - 0.92)
Other antibiotics	1.21 (1.11 - 1.30)	0.97 (0.79 - 1.19)
Indications for antibiotic treatment		
Urinary tract antibiotics (yes versus no)	1.18 (1.14 - 1.21)	0.96 (0.89 - 1.03)
Airway antibiotics (yes versus no)	1.23 (1.19 - 1.26)	0.91 (0.85 - 0.98)
Skin and soft tissue antibiotics (yes versus no)	1.06 (0.82 - 1.38)	0.86 (0.47 - 1.55)
Antibiotics for other disorders (yes versus no)	1.22 (1.14 - 1.30)	1.06 (0.91 - 1.24)

Abbreviations: HR, hazard ratio; CI, confidence interval.

Table S4. Adjusted hazard ratio of childhood asthma by timing, number, duration, and combination treatment of maternal antibiotic use during pregnancy in the population-based analysis and sibling design with or without further adjustment for premature rupture of membranes and cesarean section

Antibiotic use during pregnancy	Population-based cohort analysis		Sibling analysis	
	Adjusted HRs (95% CI) ^a	Adjusted HRs (95% CI) ^b	Adjusted HRs (95% CI) ^a	Adjusted HRs (95% CI) ^b
No antibiotic use during pregnancy	1 (Ref)	1 (Ref)	1 (Ref)	1 (Ref)
Any antibiotic use during pregnancy	1.21 (1.18 - 1.24)	1.21 (1.18 - 1.24)	0.96 (0.90 - 1.03)	0.97 (0.91 - 1.03)
Timing of antibiotics use				
First trimester only	1.12 (1.07 - 1.17)	1.11 (1.06 - 1.17)	0.94 (0.84 - 1.05)	0.94 (0.84 - 1.05)
Second trimester only	1.18 (1.13 - 1.23)	1.17 (1.12 - 1.23)	0.96 (0.87 - 1.07)	0.96 (0.87 - 1.07)
Third trimester only	1.16 (1.12 - 1.21)	1.16 (1.12 - 1.21)	1.00 (0.91 - 1.10)	1.00 (0.91 - 1.10)
More than more trimester	1.38 (1.33 - 1.44)	1.38 (1.33 - 1.43)	0.94 (0.85 - 1.04)	0.94 (0.85 - 1.05)
Number of antibiotic prescriptions				
One prescription	1.13 (1.10 - 1.17)	1.13 (1.10 - 1.16)	0.98 (0.92 - 1.06)	0.99 (0.92 - 1.06)
Two prescriptions	1.23 (1.18 - 1.28)	1.22 (1.17 - 1.28)	0.90 (0.81 - 1.00)	0.90 (0.91 - 1.00)
Three or more prescriptions	1.51 (1.44 - 1.58)	1.50 (1.43 - 1.57)	0.98 (0.87 - 1.11)	0.99 (0.87 - 1.12)
Duration of antibiotic use (days)				
<30	1.19 (1.16 - 1.22)	1.18 (1.15 - 1.21)	0.96 (0.91 - 1.03)	0.96 (0.90 - 1.03)
30-60	1.55 (1.45 - 1.66)	1.54 (1.44 - 1.65)	1.05 (0.88 - 1.26)	1.05 (0.88 - 1.26)
>60	1.55 (1.30 - 1.84)	1.53 (1.29 - 1.81)	0.79 (0.51 - 1.22)	0.80 (0.52 - 1.24)
Combination treatment				
One type of antibiotics only	1.15 (1.12 - 1.18)	1.15 (1.12 - 1.18)	0.98 (0.91 - 1.05)	0.98 (0.91 - 1.05)
Two types of antibiotics	1.32 (1.27 - 1.38)	1.32 (1.26 - 1.38)	0.92 (0.82 - 1.02)	0.92 (0.82 - 1.02)
Three or more types of antibiotics	1.56 (1.46 - 1.67)	1.55 (1.45 - 1.66)	0.95 (0.79 - 1.13)	0.95 (0.79 - 1.14)

Abbreviations: HR, hazard ratio; CI, confidence interval.

^a Models for adjusted HRs include maternal age at delivery, parity, maternal smoking during pregnancy, maternal cohabiting status, maternal education status at delivery, maternal diabetes during pregnancy, maternal atopic disposition, paternal atopic disposition, paternal antibiotic use during the index pregnancy, and calendar year of birth.

^b Further adjusted for premature rupture of membranes and cesarean section.

Table S5. Adjusted hazard ratio of childhood asthma by types of antibiotics in the population-based analysis and sibling design with or without further adjustment for premature rupture of membranes and cesarean section

Antibiotic use during pregnancy	Population-based cohort analysis		Sibling analysis	
	Adjusted HRs (95% CI) ^c	Adjusted HRs (95% CI) ^d	Adjusted HRs (95% CI) ^c	Adjusted HRs (95% CI) ^d
Generic names of antibiotics^a				
Penicillins (yes versus no)	1.19 (1.16 - 1.22)	1.19 (1.16 - 1.22)	1.03 (0.96 - 1.10)	1.03 (0.96 - 1.10)
Cephalosporins (yes versus no)	1.12 (0.78 - 1.62)	1.11 (0.77 - 1.60)	0.77 (0.34 - 1.76)	0.77 (0.34 - 1.75)
Sulfonamides (yes versus no)	1.11 (1.06 - 1.17)	1.11 (1.06 - 1.17)	0.87 (0.77 - 0.99)	0.87 (0.77 - 0.99)
Macrolides (yes versus no)	1.24 (1.16 - 1.33)	1.24 (1.16 - 1.32)	0.79 (0.67 - 0.93)	0.79 (0.67 - 0.93)
Other antibiotics	1.17 (1.08 - 1.26)	1.16 (1.08 - 1.26)	0.94 (0.77 - 1.16)	0.95 (0.77 - 1.17)
Indications for antibiotic treatment^b				
Urinary tract antibiotics (yes versus no)	1.15 (1.12 - 1.19)	1.15 (1.12 - 1.18)	0.95 (0.88 - 1.03)	0.95 (0.88 - 1.03)
Airway antibiotics (yes versus no)	1.20 (1.16 - 1.23)	1.19 (1.16 - 1.23)	0.95 (0.88 - 1.02)	0.95 (0.88 - 1.02)
Skin and soft tissue antibiotics (yes versus no)	1.05 (0.81 - 1.35)	1.04 (0.80 - 1.34)	0.84 (0.46 - 1.52)	0.84 (0.47 - 1.53)
Antibiotics for other disorders (yes versus no)	1.21 (1.13 - 1.30)	1.21 (1.13 - 1.29)	1.14 (0.98 - 1.33)	1.15 (0.98 - 1.34)

Abbreviations: HR, hazard ratio; CI, confidence interval.

^a The types of antibiotics were mutually adjusted for in the models.

^b The indications for antibiotic treatment were mutually adjusted for in the models.

^c Models for adjusted HRs include maternal age at delivery, parity, maternal smoking during pregnancy, maternal cohabiting status, maternal education status at delivery, maternal diabetes during pregnancy, maternal atopic disposition, paternal atopic disposition, paternal antibiotic use during the index pregnancy, and calendar year of birth.

^d Further adjusted for premature rupture of membranes and cesarean section.