

SUPPLEMENT

Association of Infant Antibiotic Exposure With Childhood Health Outcomes

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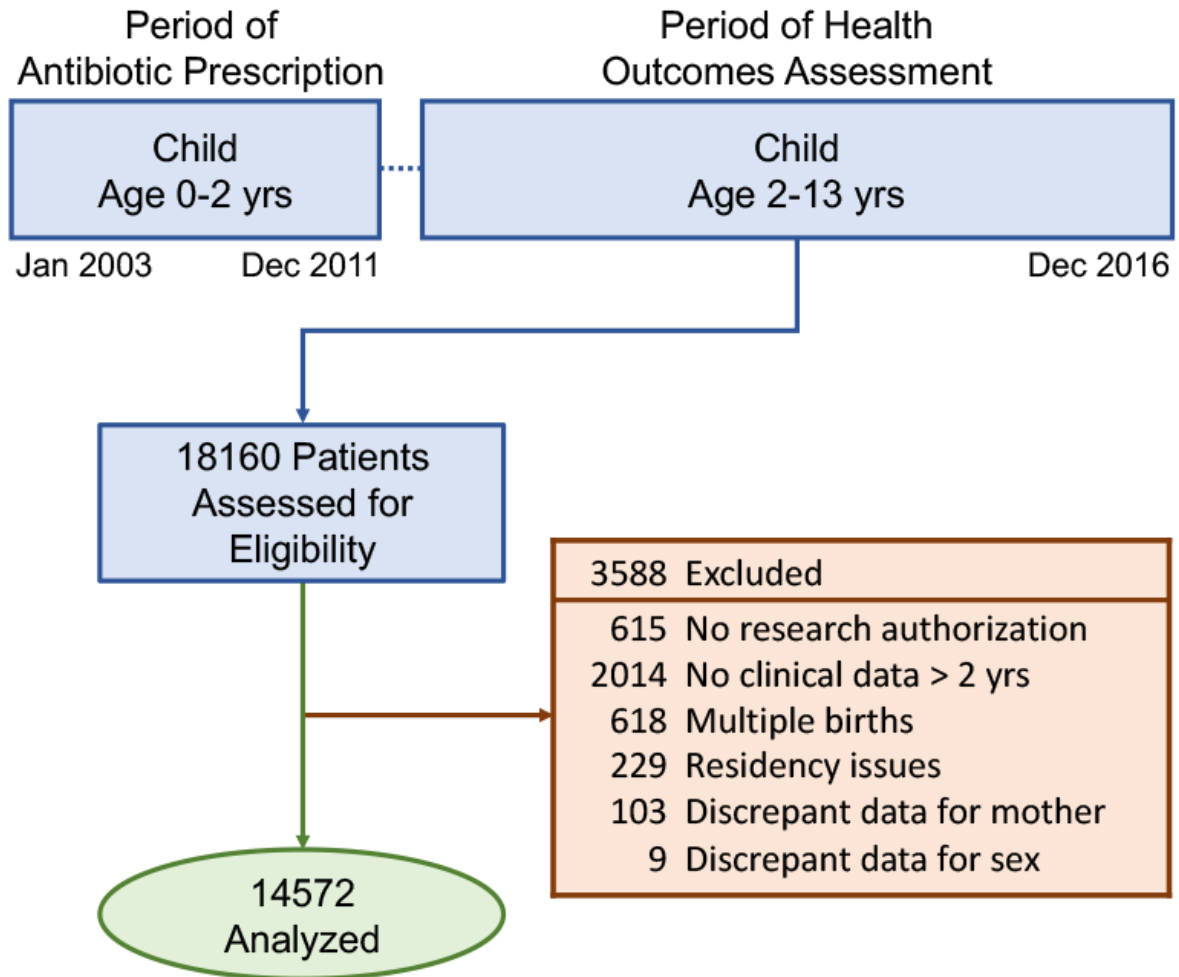
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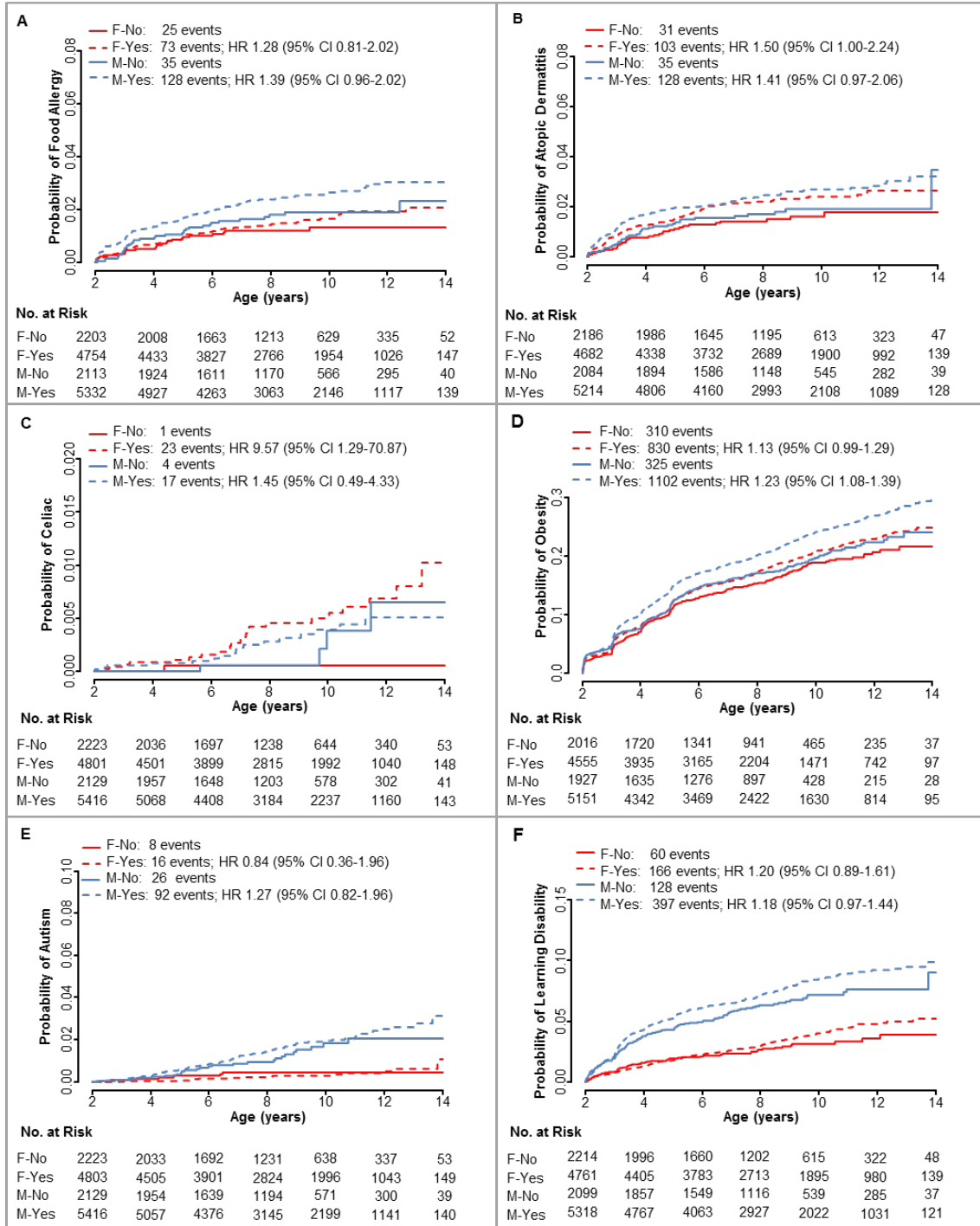
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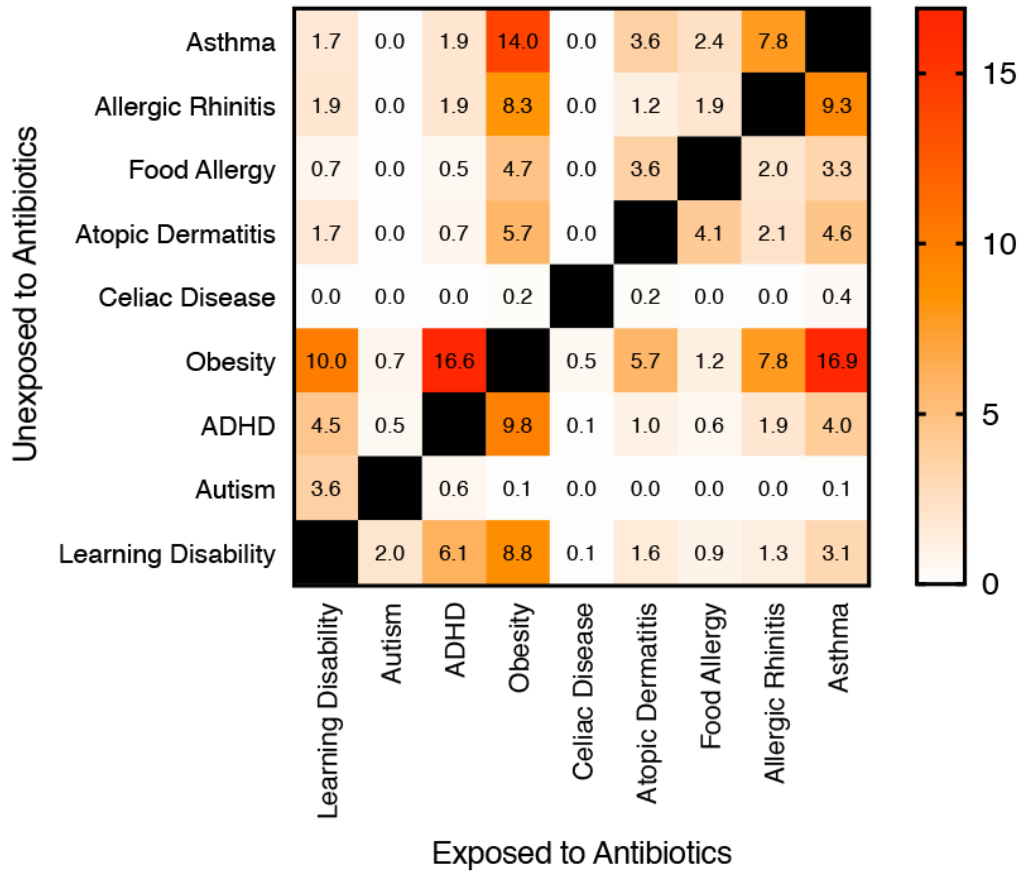
Supplemental Figure 1. Study Design and Participant Inclusion and Exclusion Flow Chart.



Supplemental Figure 2: Kaplan-Meier Curves of Time to Event for Health Conditions with Childhood Onset Stratified by Sex and Antibiotic Exposure in the First 24 Months of Life. The numbers (No.) of females unexposed (F-No), females exposed (F-Yes), males unexposed (M-No), and males exposed (M-Yes) to antibiotics and at risk for (A) food allergy, (B) atopic dermatitis, (C) celiac disease, (D) obesity, (E) autism, and (F) learning disability are reported below the x-axis for the specified ages. The total numbers of events for each group are reported in the legend for each condition.



Supplemental Figure 3. Heat Map of the Frequency of Health Condition Dyads among Children Unexposed to Antibiotics and among Children Exposed to Antibiotics. Data expressed as the percentage of children unexposed to antibiotics with at least 2 conditions (upper left, n = 422) or the percentage of children exposed to antibiotics with at least two conditions (lower right, n = 1,595).



Supplemental Table 1. Diagnostic Codes of Specified Health Conditions with Childhood Onset.

Outcome	Code type	Code	Description
Asthma	ICD-10	J44.1	Chronic obstructive pulmonary disease with (acute) exacerbation
	ICD-10	J44.9	Chronic obstructive pulmonary disease, unspecified
	ICD-10	J45.20	Mild intermittent asthma, uncomplicated
	ICD-10	J45.21	Mild intermittent asthma with (acute) exacerbation
	ICD-10	J45.22	Mild intermittent asthma with status asthmaticus
	ICD-10	J45.30	Mild persistent asthma, uncomplicated
	ICD-10	J45.31	Mild persistent asthma with (acute) exacerbation
	ICD-10	J45.32	Mild persistent asthma with status asthmaticus
	ICD-10	J45.40	Moderate persistent asthma, uncomplicated
	ICD-10	J45.41	Moderate persistent asthma with (acute) exacerbation
	ICD-10	J45.42	Moderate persistent asthma with status asthmaticus
	ICD-10	J45.50	Severe persistent asthma, uncomplicated
	ICD-10	J45.51	Severe persistent asthma with (acute) exacerbation
	ICD-10	J45.52	Severe persistent asthma with status asthmaticus
	ICD-10	J45.901	Unspecified asthma with (acute) exacerbation
	ICD-10	J45.902	Unspecified asthma with status asthmaticus
	ICD-10	J45.909	Unspecified asthma, uncomplicated
	ICD-10	J45.990	Exercise induced bronchospasm
	ICD-10	J45.991	Cough variant asthma
	ICD-10	J45.998	Other asthma
	ICD-10	Z87.09	Personal history of other diseases of the respiratory system
	ICD-9	493	Extrinsic asthma, unspecified
	ICD-9	493.01	Extrinsic asthma with status asthmaticus
	ICD-9	493.02	Extrinsic asthma with acute exacerbation
	ICD-9	493.1	Intrinsic asthma, unspecified
	ICD-9	493.11	Intrinsic asthma with status asthmaticus
	ICD-9	493.12	Intrinsic asthma with acute exacerbation
	ICD-9	493.2	Chronic obstructive asthma, unspecified
	ICD-9	493.21	Chronic obstructive asthma, with status asthmaticus
	ICD-9	493.22	Chronic obstructive asthma, with acute exacerbation
	ICD-9	493.81	Exercise induced bronchospasm
	ICD-9	493.82	Cough variant asthma
	ICD-9	493.9	Asthma, unspecified
ICD-9	493.91	Asthma, unspecified type, with status asthmaticus	
ICD-9	493.92	Asthma, unspecified, with acute exacerbation	
Allergic rhinitis	ICD-10	J30.1	Allergic rhinitis due to pollen
	ICD-10	J30.2	Other seasonal allergic rhinitis
	ICD-10	J30.5	Allergic rhinitis due to food
	ICD-10	J30.81	Allergic rhinitis due to animal (cat) (dog) hair and dander
	ICD-10	J30.89	Other allergic rhinitis
	ICD-10	J30.9	Allergic rhinitis, unspecified
	ICD-9	477	Allergic rhinitis due to pollen
	ICD-9	477.1	Allergic rhinitis, due to food
	ICD-9	477.2	Allergic rhinitis, due to animal (cat) (dog) hair and dander
	ICD-9	477.8	Allergic rhinitis due to other allergen
	ICD-9	477.9	Allergic rhinitis nos
	ICD-9	477.9	Allergic rhinitis, cause unspecified

Outcome	Code type	Code	Description
Food allergy	ICD-10	T78.00XA	Anaphylactic reaction due to unspecified food, initial encounter
	ICD-10	T78.01XA	Anaphylactic reaction due to peanuts, initial encounter
	ICD-10	T78.05XA	Anaphylactic reaction due to tree nuts and seeds, initial encounter
	ICD-10	T78.06XA	Anaphylactic reaction due to food additives, initial encounter
	ICD-10	T78.07XA	Anaphylactic reaction due to milk and dairy products, initial encounter
	ICD-10	T78.08XA	Anaphylactic reaction due to eggs, initial encounter
	ICD-10	T78.09XA	Anaphylactic reaction due to other food products, initial encounter
	ICD-10	T78.1XXA	Other adverse food reactions, not elsewhere classified, initial encounter
	ICD-10	T78.1XXD	Other adverse food reactions, not elsewhere classified, subsequent encounter
	ICD-10	Z91.010	Allergy to peanuts
	ICD-10	Z91.011	Allergy to milk products
	ICD-10	Z91.012	Allergy to eggs
	ICD-10	Z91.013	Allergy to seafood
	ICD-10	Z91.018	Allergy to other foods
	ICD-9	477.1	allergic rhinitis, due to food
	ICD-9	692.5	Contact dermatitis and other eczema due to food in contact with skin
	ICD-9	693.1	Dermatitis due to food taken internally
	ICD-9	995.6	Anaphylactic shock due to unspecified food
	ICD-9	995.61	Anaphylactic shock due to peanuts
	ICD-9	995.63	Anaphylactic shock due to fruits and vegetables
	ICD-9	995.64	Anaphylactic shock due to tree nuts and seeds
	ICD-9	995.65	Anaphylactic shock due to fish
	ICD-9	995.67	Anaphylactic shock due to milk products
	ICD-9	995.68	Anaphylactic shock due to eggs
	ICD-9	995.69	Anaphylactic shock due to other specified food
	ICD-9	995.7	Other adverse food reactions, not elsewhere classified
	ICD-9	V15.01	Allergy to peanuts
	ICD-9	V15.02	Allergy to dairy prods.
	ICD-9	V15.03	Allergy to eggs
	ICD-9	V15.04	Allergy to seafood
	ICD-9	V15.05	Allergy to other food
	Atopic dermatitis	ICD-10	L20.82
ICD-10		L20.84	Intrinsic (allergic) eczema
ICD-10		L20.89	Other atopic dermatitis
ICD-9		691.8	Other atopic dermatitis and related conditions
Celiac disease	ICD-10	K90.0	Celiac disease
	ICD-9	579	Celiac disease
ADHD	ICD-10	F90.0	Attention-deficit hyperactivity disorder, predominantly inattentive type
	ICD-10	F90.1	Attention-deficit hyperactivity disorder, predominantly hyperactive type
	ICD-10	F90.2	Attention-deficit hyperactivity disorder, combined type
	ICD-10	F90.8	Attention-deficit hyperactivity disorder, other type
	ICD-10	F90.9	Attention-deficit hyperactivity disorder, unspecified type
	ICD-9	314	Attention deficit disorder of childhood without mention of hyperactivity
	ICD-9	314.01	Attention deficit disorder of childhood with hyperactivity
	ICD-9	314.1	Hyperkinesis of childhood with developmental delay
	ICD-9	314.9	Unspecified hyperkinetic syndrome of childhood

Outcome	Code type	Code	Description
Autism	ICD-10	F84.0	Autistic disorder
	ICD-10	F84.5	Asperger's syndrome
	ICD-10	F84.8	Other pervasive developmental disorders
	ICD-10	F84.9	Pervasive developmental disorder, unspecified
	ICD-9	299	Infantile autism, current or active state
	ICD-9	299.01	Infantile autism, residual state
	ICD-9	299.1	Disintegrative psychosis, current or active state
	ICD-9	299.8	Other specified early childhood psychoses, current or active state
	ICD-9	299.9	Unspecified childhood psychosis, current or active state
Learning disability	ICD-10	F48.9	Nonpsychotic mental disorder, unspecified
	ICD-10	F80.0	Phonological disorder
	ICD-10	F80.1	Expressive language disorder
	ICD-10	F80.2	Mixed receptive-expressive language disorder
	ICD-10	F80.4	Speech and language development delay due to hearing loss
	ICD-10	F80.81	Childhood onset fluency disorder
	ICD-10	F80.82	Social pragmatic communication disorder
	ICD-10	F80.89	Other developmental disorders of speech and language
	ICD-10	F80.9	Developmental disorder of speech and language, unspecified
	ICD-10	F81.0	Specific reading disorder
	ICD-10	F81.2	Mathematics disorder
	ICD-10	F81.81	Disorder of written expression
	ICD-10	F81.89	Other developmental disorders of scholastic skills
	ICD-10	F81.9	Developmental disorder of scholastic skills, unspecified
	ICD-10	F82	Specific developmental disorder of motor function
	ICD-10	F88	Other disorders of psychological development
	ICD-9	315	Developmental reading disorder, unspecified
	ICD-9	315.02	Developmental dyslexia
	ICD-9	315.09	Other specific developmental reading disorder
	ICD-9	315.1	Developmental arithmetical disorder
	ICD-9	315.2	Other specific developmental learning difficulties
	ICD-9	315.31	Developmental language disorder
	ICD-9	315.32	Receptive language disorder (mixed)
	ICD-9	315.34	Speech and language developmental delay due to hearing loss
	ICD-9	315.35	Childhood onset fluency disorder
	ICD-9	315.39	Other developmental speech disorder
	ICD-9	315.4	Developmental coordination disorder
	ICD-9	315.5	Mixed development disorder
	ICD-9	315.8	Other specified delays in development
	ICD-9	315.9	Unspecified delay in development

Supplemental Table 2. Description of the Antibiotic Prescriptions Examined in this Study.

Antibiotic classes (NDF-RT classification)	Antibacterial agents (RxNorm description)
Penicillins	Amoxicillin Amoxicillin / Clavulanate Ampicillin Clavulanate Dicloxacillin Oxacillin Penicillin G Penicillin G benzathine / Penicillin G procaine Penicillin V
Cephalosporins	Cefaclor Cefadroxil Cefazolin Cefdinir Cefepime Cefixime Cefpodoxime Cefprozil Ceftazidime Ceftriaxone Cefuroxime Cephalexin
Sulfonamides	Sulfamethoxazole / Trimethoprim Sulfisoxazole Trimethoprim
Macrolides	Azithromycin Clarithromycin Erythromycin base
Lincomycins ^a	Clindamycin
Nitrofurans	Nitrofurantoin
Quinolones	Ciprofloxacin ophthalmic preparation (product) Levofloxacin
Aminoglycosides	Gentamicin sulfate (usp)
Antituberculars	Isoniazid Rifampin
Chloramphenicol	Chloramphenicol
Beta-lactams antimicrobials, other	Loracarbef
Anti-invectives, other	Colistin Erythromycin / sulfisoxazole Linezolid Metronidazole Vancomycin

^aLincomycins were included in the macrolides class in the statistical analysis.

Supplemental Table 3. Number of Children Without (no) and With (yes) Diagnosis of Specified Health Conditions by 2 Years of Age.

Condition	Females (n=7026)	Males (n=7546)	All (n=14572)
Asthma			
No	6940 (98.8%)	7359 (97.5%)	14299 (98.1%)
Yes	86 (1.2%)	187 (2.5%)	273 (1.9%)
Allergic rhinitis			
No	7017 (99.9%)	7528 (99.8%)	14545 (99.8%)
Yes	9 (0.1%)	18 (0.2%)	27 (0.2%)
Food allergy			
No	6957 (99.0%)	7445 (98.7%)	14402 (98.8%)
Yes	69 (1.0%)	101 (1.3%)	170 (1.2%)
Atopic dermatitis			
No	6868 (97.8%)	7298 (96.7%)	14166 (97.2%)
Yes	158 (2.2%)	248 (3.3%)	406 (2.8%)
Celiac disease			
No	7024 (100.0%)	7545 (100.0%)	14569 (100.0%)
Yes	2 (0.0%)	1 (0.0%)	3 (0.0%)
Overweight ^a			
No	6208 (88.4%)	6665 (88.3%)	12873 (88.3%)
Yes	818 (11.6%)	881 (11.7%)	1699 (11.7%)
Obesity ^a			
No	6571 (93.5%)	7078 (93.8%)	13649 (93.7%)
Yes	455 (6.5%)	468 (6.2%)	923 (6.3%)
ADHD			
No	7026 (100.0%)	7546 (100.0%)	14572 (100.0%)
Yes	0 (0.0%)	0 (0.0%)	0 (0.0%)
Autism			
No	7026 (100.0%)	7545 (100.0%)	14571 (100.0%)
Yes	0 (0.0%)	1 (0.0%)	1 (0.0%)
Learning disability			
No	6975 (99.3%)	7417 (98.3%)	14392 (98.8%)
Yes	51 (0.7%)	129 (1.7%)	180 (1.2%)

^aThe presence of overweight and obesity at age 2 years was determined by using the latest measurement prior to age 2 years.

Supplemental Table 4. The Prevalence of Common Diagnoses in Children during the First 2 Years of Life Stratified by the Number of Antibiotic Courses Prescribed.

Diagnosis (Dx)		No. of Antibiotic Exposures				Total (n=14572)
		0 (n=4352)	1-2 (n=4560)	3-4 (n=2434)	5+ (n=3226)	
Acute upper respiratory infections of multiple and unspecified sites	None	1931 (44.4%)	1264 (27.7%)	351 (14.4%)	242 (7.5%)	3788 (26.0%)
	≥1 Dx	2421 (55.6%)	3296 (72.3%)	2083 (85.6%)	2984 (92.5%)	10784 (74.0%)
Suppurative and unspecified otitis media	None	3402 (78.2%)	1203 (26.4%)	187 (7.7%)	103 (3.2%)	4895 (33.6%)
	≥1 Dx	950 (21.8%)	3357 (73.6%)	2247 (92.3%)	3123 (96.8%)	9677 (66.4%)
Other ear and sense organ disorders	None	1850 (42.5%)	1549 (34.0%)	751 (30.9%)	892 (27.7%)	5042 (34.6%)
	≥1 Dx	2502 (57.5%)	3011 (66.0%)	1683 (69.1%)	2334 (72.3%)	9530 (65.4%)
Other and unspecified perinatal conditions	None	1835 (42.2%)	1823 (40.0%)	816 (33.5%)	780 (24.2%)	5254 (36.1%)
	≥1 Dx	2517 (57.8%)	2737 (60.0%)	1618 (66.5%)	2446 (75.8%)	9318 (63.9%)
Other and unspecified lower respiratory disease	None	3055 (70.2%)	2595 (56.9%)	1064 (43.7%)	995 (30.8%)	7709 (52.9%)
	≥1 Dx	1297 (29.8%)	1965 (43.1%)	1370 (56.3%)	2231 (69.2%)	6863 (47.1%)
Fever of unknown origin	None	2981 (68.5%)	2587 (56.7%)	1100 (45.2%)	1067 (33.1%)	7735 (53.1%)
	≥1 Dx	1371 (31.5%)	1973 (43.3%)	1334 (54.8%)	2159 (66.9%)	6837 (46.9%)
Allergic reactions	None	2825 (64.9%)	2658 (58.3%)	1235 (50.7%)	1424 (44.1%)	8142 (55.9%)
	≥1 Dx	1527 (35.1%)	1902 (41.7%)	1199 (49.3%)	1802 (55.9%)	6430 (44.1%)
Other and unspecified viral infection	None	3349 (77.0%)	3133 (68.7%)	1443 (59.3%)	1642 (50.9%)	9567 (65.7%)
	>1 Dx	1003 (23.0%)	1427 (31.3%)	991 (40.7%)	1584 (49.1%)	5005 (34.3%)
Inflammation; infection of eye (except that caused by TB)	None	3410 (78.4%)	3307 (72.5%)	1511 (62.1%)	1637 (50.7%)	9865 (67.7%)
	≥1 Dx	942 (21.6%)	1253 (27.5%)	923 (37.9%)	1589 (49.3%)	4707 (32.3%)
Other skin disorders	None	3266 (75.0%)	3145 (69.0%)	1587 (65.2%)	1889 (58.6%)	9887 (67.8%)
	≥1 Dx	1086 (25.0%)	1415 (31.0%)	847 (34.8%)	1337 (41.4%)	4685 (32.2%)
Hemolytic jaundice and perinatal jaundice	None	3081 (70.8%)	3225 (70.7%)	1691 (69.5%)	2280 (70.7%)	10277 (70.5%)
	≥1 Dx	1271 (29.2%)	1335 (29.3%)	743 (30.5%)	946 (29.3%)	4295 (29.5%)
Other upper respiratory disease	None	3692 (84.8%)	3688 (80.9%)	1671 (68.7%)	1884 (58.4%)	10935(75.0%)
	≥1 Dx	660 (15.2%)	872 (19.1%)	763 (31.3%)	1342 (41.6%)	3637 (25.0%)

Diagnosis (Dx)		No. of Antibiotic Exposures				
		0 (n=4352)	1-2 (n=4560)	3-4 (n=2434)	5+ (n=3226)	Total (n=14572)
Other and unspecified upper respiratory infections	None	3743 (86.0%)	3672 (80.5%)	1720 (70.7%)	1877 (58.2%)	11012 (75.6%)
	≥1 Dx	609 (14.0%)	888 (19.5%)	714 (29.3%)	1349 (41.8%)	3560 (24.4%)
Other and unspecified gastrointestinal disorders	None	3606 (82.9%)	3592 (78.8%)	1785 (73.3%)	2086 (64.7%)	11069 (76.0%)
	≥1 Dx	746 (17.1%)	968 (21.2%)	649 (26.7%)	1140 (35.3%)	3503 (24.0%)
Other otitis media and related conditions	None	4039 (92.8%)	4018 (88.1%)	1893 (77.8%)	1608 (49.8%)	11558 (79.3%)
	≥1 Dx	313 (7.2%)	542 (11.9%)	541 (22.2%)	1618 (50.2%)	3014 (20.7%)
Other male genital disorders	None	3617 (83.1%)	3634 (79.7%)	1870 (76.8%)	2463 (76.3%)	11584 (79.5%)
	≥1 Dx	735 (16.9%)	926 (20.3%)	564 (23.2%)	763 (23.7%)	2988 (20.5%)
Non-infectious gastroenteritis	None	3759 (86.4%)	3690 (80.9%)	1842 (75.7%)	2298 (71.2%)	11589 (79.5%)
	≥1 Dx	593 (13.6%)	870 (19.1%)	592 (24.3%)	928 (28.8%)	2983 (20.5%)
Nausea and vomiting	None	3737 (85.9%)	3752 (82.3%)	1864 (76.6%)	2288 (70.9%)	11641 (79.9%)
	≥1 Dx	615 (14.1%)	808 (17.7%)	570 (23.4%)	938 (29.1%)	2931 (20.1%)

Supplemental Table 5. Association between Timing of Antibiotic Prescriptions and Risk of Several Common Health Conditions with Childhood Onset.

Condition	Timing (months)	Females HR (95% CI)	P-value	Males HR (95% CI)	P-value
Asthma	0-6	1.53 (1.24-1.89)	<.001	1.06 (0.89-1.27)	.494
	6-12	1.27 (1.05-1.54)	.013	1.21 (1.03-1.41)	.020
	12-24	1.63 (1.33-2.00)	<.001	1.67 (1.41-1.98)	<.001
Allergic rhinitis	0-6	1.59 (1.25-2.01)	<.001	0.99 (0.81-1.20)	.887
	6-12	1.25 (1.01-1.55)	.044	1.19 (1.00-1.42)	.045
	12-24	1.18 (0.95-1.47)	.141	1.47 (1.22-1.76)	<.001
Food allergy	0-6	1.59 (0.99-2.56)	.055	1.50 (1.05-2.13)	.025
	6-12	0.94 (0.61-1.44)	.784	0.96 (0.69-1.34)	.825
	12-24	1.24 (0.81-1.90)	.324	1.27 (0.90-1.79)	.169
Atopic dermatitis	0-6	1.52 (1.01-2.29)	.046	1.50 (1.05-2.14)	.024
	6-12	1.15 (0.80-1.66)	.448	1.14 (0.82-1.59)	.437
	12-24	1.08 (0.75-1.55)	.692	1.12 (0.80-1.58)	.496
Celiac disease	0-6	1.18 (0.45-3.08)	.730	1.19 (0.45-3.16)	.727
	6-12	1.20 (0.52-2.81)	.667	1.20 (0.48-2.99)	.699
	12-24	2.67 (0.97-7.41)	.059	1.90 (0.67-5.45)	.230
Overweight	0-6	1.25 (1.12-1.38)	<.001	1.18 (1.07-1.30)	.001
	6-12	1.13 (1.03-1.23)	.007	1.09 (1.00-1.18)	.042
	12-24	1.09 (1.00-1.19)	.049	1.15 (1.05-1.25)	.002
Obesity	0-6	1.17 (1.01-1.36)	.035	1.09 (0.96-1.23)	.202
	6-12	1.15 (1.01-1.30)	.031	1.24 (1.11-1.38)	<.001
	12-24	1.06 (0.94-1.20)	.332	1.09 (0.97-1.22)	.140
ADHD	0-6	1.46 (1.11-1.91)	.006	1.19 (1.01-1.41)	.039
	6-12	1.03 (0.81-1.32)	.792	1.07 (0.92-1.24)	.381
	12-24	1.29 (1.01-1.66)	.044	1.11 (0.95-1.30)	.176
Autism	0-6	2.08 (0.82-5.25)	.123	0.79 (0.49-1.26)	.316
	6-12	0.85 (0.36-2.04)	.719	1.42 (0.96-2.09)	.078
	12-24	0.84 (0.36-1.97)	.697	1.08 (0.73-1.61)	.694
Learning disability	0-6	1.11 (0.79-1.55)	.556	1.07 (0.87-1.32)	.516
	6-12	1.02 (0.77-1.34)	.914	1.12 (0.94-1.35)	.209
	12-24	1.24 (0.94-1.64)	.134	1.06 (0.88-1.27)	.559

Supplemental Table 6. Associations between Child and Maternal Factors and Several Common Health Conditions with Childhood Onset. Data are reported as hazard ratio (95% confidence interval), P-value.

	Asthma	Allergic rhinitis	Food allergy	Atopic dermatitis	Celiac disease
Male sex	1.39 (1.24-1.56), <.001	1.48 (1.30-1.68), <.001	1.56 (1.21-2.00), <.001	1.15 (0.91-1.44), .242	0.81 (0.45-1.46), .489
Birth weight	0.84 (0.74-0.95), .004	1.05 (0.90-1.22), .528	1.18 (0.91-1.54), .212	0.94 (0.75-1.19), .619	2.30 (1.17-4.54), .016
Ethnicity					
Black	1.55 (1.29-1.85), <.001	1.46 (1.19-1.78), <.001	1.24 (0.82-1.85), .305	1.67 (1.17-2.37), .004	0.66 (0.20-2.13), .489
Asian	0.96 (0.75-1.23), .765	0.82 (0.62-1.09), .166	1.47 (0.96-2.25), .077	1.56 (1.04-2.35), .033	-
Hawaiian/Pac. Islander	0.50 (0.12-2.00), .326	1.36 (0.57-3.28), .491	-	-	-
American Indian	2.45 (1.17-5.16), .018	3.03 (1.44-6.37), .004	-	5.54 (2.06-14.92), <.001	-
Other/unknown	1.16 (0.97-1.38), .109	0.86 (0.69-1.07), .179	0.87 (0.58-1.32), .517	1.15 (0.81-1.64), .443	-
Cesarean section	1.12 (0.98-1.28), .085	1.33 (1.16-1.53), <.001	1.31 (1.00-1.71), .051	1.57 (1.23-2.00), <.001	0.82 (0.39-1.69), .583
Mom age	0.85 (0.76-0.94), .002	1.21 (1.08-1.36), <.001	1.35 (1.08-1.68), .007	1.04 (0.85-1.28), .710	1.23 (0.73-2.08), .437
Mom education					
High school or less	1.20 (1.04-1.40), .013	0.93 (0.78-1.12), .445	0.52 (0.35-0.78), .002	0.79 (0.57-1.10), .159	0.94 (0.41-2.11), .872
Some college/4 years	0.84 (0.72-0.98), .028	1.03 (0.85-1.24), .754	1.65 (1.08-2.52), .021	1.22 (0.86-1.71), .264	0.99 (0.42-2.34), .977
Post graduate	0.81 (0.68-0.97), .020	1.15 (0.94-1.40), .185	2.41 (1.56-3.72), <.001	1.36 (0.94-1.96), .102	1.21 (0.49-3.01), .677
Mom smoking	1.39 (1.18-1.63), <.001	0.90 (0.73-1.11), .324	0.29 (0.15-0.56), <.001	0.64 (0.42-0.99), .045	0.39 (0.10-1.63), .199
Mom antibiotics during pregnancy	1.29 (1.15-1.44), <.001	1.34 (1.18-1.52), <.001	1.10 (0.86-1.41), .457	0.83 (0.65-1.05), .122	0.91 (0.49-1.68), .761

	Overweight	Obesity	ADHD	Autism	Learning Disability
Male sex	1.06 (1.00-1.12), .042	1.18 (1.09-1.28), <.001	2.56 (2.24-2.92), <.001	4.61 (2.97-7.15), <.001	2.24 (1.91-2.61), <.001
Birth weight	1.52 (1.43-1.63), <.001	1.38 (1.26-1.51), <.001	0.89 (0.78-1.01), .070	0.97 (0.68-1.38), .852	0.81 (0.70-0.93), .004
Ethnicity					
Black	1.25 (1.13-1.38), <.001	1.57 (1.38-1.78), <.001	0.76 (0.60-0.97), .029	1.10 (0.60-2.00), .764	1.08 (0.83-1.39), .566
Asian	0.78 (0.68-0.89), <.001	0.80 (0.66-0.96), .016	0.19 (0.12-0.32), <.001	1.16 (0.61-2.22), .653	0.99 (0.73-1.34), .959
Hawaiian/Pac. Islander	1.80 (1.18-2.73), .006	2.16 (1.32-3.54), .002	0.89 (0.33-2.37), .814	-	0.78 (0.20-3.14), .730
American Indian	1.10 (0.65-1.86), .722	0.78 (0.33-1.88), .586	4.06 (2.17-7.57), <.001	8.76 (2.77-27.65), <.001	1.47 (0.47-4.57), .507
Other/unknown	1.36 (1.25-1.47), <.001	1.72 (1.54-1.91), <.001	0.99 (0.82-1.20), .921	1.16 (0.70-1.95), .561	1.39 (1.14-1.71), .001
Cesarean section	1.14 (1.07-1.22), <.001	1.32 (1.21-1.44), <.001	1.21 (1.06-1.39), .005	1.29 (0.89-1.85), .179	1.15 (0.98-1.35), .094
Mom age	0.88 (0.83-0.92), <.001	0.83 (0.77-0.89), <.001	0.61 (0.55-0.68), <.001	1.58 (1.18-2.12), .002	1.01 (0.88-1.15), .924
Mom education					
High school or less	1.39 (1.30-1.50), <.001	1.80 (1.63-1.97), <.001	1.34 (1.16-1.56), <.001	0.89 (0.56-1.42), .620	1.46 (1.23-1.74), <.001
Some college/4 years	0.77 (0.71-0.83), <.001	0.63 (0.57-0.69), <.001	0.83 (0.71-0.97), .019	1.28 (0.79-2.07), .317	0.70 (0.58-0.84), <.001
Post graduate	0.63 (0.58-0.69), <.001	0.44 (0.39-0.50), <.001	0.60 (0.49-0.72), <.001	0.85 (0.49-1.50), .580	0.66 (0.53-0.81), <.001
Mom smoking	1.32 (1.21-1.43), <.001	1.45 (1.30-1.62), <.001	2.33 (2.01-2.70), <.001	1.22 (0.74-1.99), .438	1.38 (1.12-1.69), .002
Mom antibiotics during pregnancy	1.21 (1.14-1.28), <.001	1.26 (1.16-1.36), <.001	1.53 (1.36-1.72), <.001	1.10 (0.78-1.53), .592	1.20 (1.04-1.39), .013

Supplemental Table 7. Associations between Antibiotic Prescriptions in The First Two Years of Life and Risk of Common Health Conditions with Childhood Onset, after Adjustment for Child Confounders (birth weight, ethnicity, and cesarean section) and Maternal Confounders (age, education, smoking, and antibiotic use during pregnancy), in Females and Males, Separately.

Condition	Females		Males	
	HR (95% CI)	P-value	HR (95% CI)	P-value
Asthma	2.06 (1.63-2.60)	<.001	1.79 (1.47-2.17)	<.001
Allergic rhinitis	1.34 (1.05-1.69)	.017	1.38 (1.13-1.68)	.002
Food allergy	1.26 (0.80-1.99)	.313	1.37 (0.94-2.00)	.098
Atopic dermatitis	1.52 (1.01-2.27)	.042	1.43 (0.98-2.08)	.060
Celiac disease	9.04 (1.22-67.04)	.031	1.39 (0.47-4.14)	.556
Overweight	1.20 (1.09-1.32)	<.001	1.23 (1.12-1.35)	<.001
Obesity	1.15 (1.01-1.31)	.033	1.25 (1.10-1.41)	<.001
ADHD	1.53 (1.16-2.02)	.003	1.25 (1.06-1.48)	.008
Autism	0.85 (0.36-1.98)	.700	1.29 (0.83-2.00)	.256
Learning disability	1.22 (0.91-1.64)	.182	1.21 (0.99-1.48)	.062

Supplemental Table 8. The Number (No.) and Percentage (%) of Children with the Most Common Disease Dyads and Triads Stratified by Exposure to Antibiotics in the First 24 Months of Life.

Dyad Combinations	Not exposed No. (%)	Exposed No. (%)
Obesity - asthma	59 (14.0)	269 (16.9)
Obesity - ADHD	70 (16.6)	157 (9.8)
Asthma - allergic rhinitis	33 (7.8)	148 (9.3)
Obesity - learning disability	42 (10.0)	141 (8.8)
Obesity - allergic rhinitis	35 (8.3)	125 (7.8)
Learning disability - ADHD	19 (4.5)	97 (6.1)
Obesity - atopic dermatitis	24 (5.7)	91 (5.7)
Asthma - atopic dermatitis	15 (3.6)	73 (4.6)
Food allergy - atopic dermatitis	15 (3.6)	66 (4.1)
Asthma - ADHD	8 (1.9)	64 (4.0)
Asthma - food allergy	10 (2.4)	52 (3.3)
Asthma - learning disability	7 (1.7)	49 (3.1)
Learning disability - autism	15 (3.6)	32 (2.0)
Obesity – food allergy	20 (4.7)	19 (1.2)
Triad combinations	Not exposed No. (%)	Exposed No. (%)
Obesity - asthma - allergic rhinitis	16 (14.2)	68 (13.1)
Obesity - asthma - ADHD	5 (4.4)	39 (7.5)
Obesity - ADHD - learning disability	9 (8.0)	35 (6.8)
Obesity – asthma – atopic dermatitis	1 (0.9)	32 (6.2)
Asthma - food allergy - allergic rhinitis	7 (6.2)	29 (5.6)
Asthma - food allergy - atopic dermatitis	4 (3.5)	24 (4.6)
Asthma - obesity - learning disability	4 (3.5)	21 (4.1)
Asthma - allergic rhinitis - ADHD	3 (2.7)	21 (4.1)
Obesity - allergic rhinitis - ADHD	4 (3.5)	18 (3.5)
Asthma - allergic rhinitis - atopic dermatitis	6 (5.3)	17 (3.3)
Obesity – learning disability – autism	4 (3.5)	17 (3.3)
Food allergy - atopic dermatitis– allergic rhinitis	3 (2.7)	17 (3.3)
Obesity – atopic dermatitis – allergic rhinitis	5 (4.4)	8 (1.5)

Data expressed as No. (%) of children with at least 2 conditions for dyads (not exposed, n=422; exposed, n=1,595) and of children with at least 3 conditions for triads (not exposed, n=113; exposed, n=518).