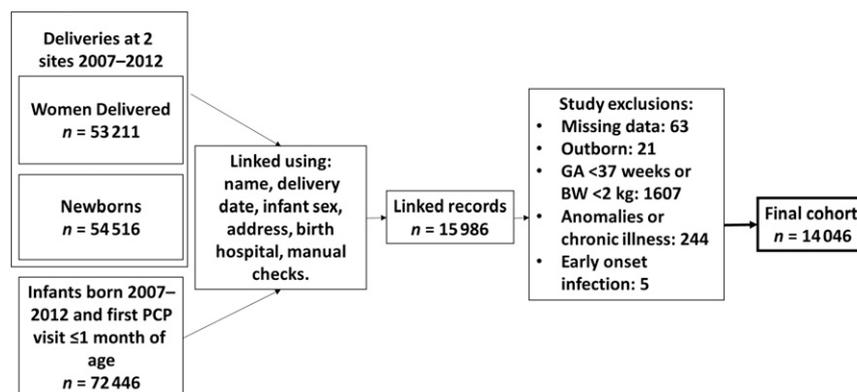


Supplemental Information

POWER CALCULATION

Power calculation before analysis was based on an estimated sample size of 12 000 with 40% ($n = 4800$) retention at 5 years. On the basis of previous work, we assumed that the event rate of atopy diagnosis will be 8% and the exposure rate will be ~25%. Under these assumptions and a type 1 error rate of 0.05, the described cohort would provide a power of 0.99 to detect an HR of 1.10 between infants exposed and unexposed to perinatal antibiotics. Poststratification for an exposure rate of 13% and a type 1 error rate of 0.05, we would have a power of >0.80 to detect an HR of 1.10 for a sample size of 9000 and 1.15 for a sample size of 4000. For logistic regression, restricting the cohort to only infants who remained in the study for 5 years, we would expect a sample size of 4800. Assuming a baseline prevalence of atopic diseases at 8%, we can detect

a relative risk of 1.30 with a power of 0.80 and a type 1 error rate of 0.05.



SUPPLEMENTAL FIGURE 1

Study cohort derivation. BW, birth weight; GA, gestational age; PCP, primary care physician.

SUPPLEMENTAL TABLE 5 Definition of Outcomes

Criteria	ICD-9 and ICD-10 Codes	Medications
Asthma^{a,b}		
1. ICD-9/10 diagnosis code for asthma used after 1 y of age.	ICD-9 codes: 493.00–493.02, 493.10–493.12, 493.22, 493.82, 493.90–493.92.	Albuterol, beclomethasone dipropionate, budesonide, budesonide-formoterol fumarate, ciclesonide, fluticasone furoate, fluticasone propionate, fluticasone-salmeterol, levalbuterol, mometasone furoate, mometasone furoate/formoterol fumarate, montelukast sodium
2. ICD-9/10 diagnosis code for asthma used at least twice at 2 separate visits, at least 6 mo apart.	ICD-10 codes: J45.20-J45.22, J45.30-J45.32, J45.40-J45.42, J45.50-J45.52, J45.901, J45.902, J45.909.	
3. Asthma medication prescribed at any time.		
All 3 criteria must be present to meet study definition of asthma.		
Eczema^b		
1. ICD-9/10 diagnosis code for eczema used at least twice at 2 separate visits, at least 6 mo apart.	ICD-9 codes: 691.8. ICD-10 codes: L20.82-L20.84, L20.89, L20.9.	Alclometasone dipropionate, betamethasone dipropionate, betamethasone valerate, clobetasol propionate, desonide, desoximetasone, flucinolone acetone, flucinonide, hydrocortisone preparation, mometasone furoate, pimecrolimus, tacrolimus, triamcinolone acetone
2. Eczema medications prescribed at any time.		
Both criteria must be present to meet study definition of eczema.		
Food allergy		
1. Food allergy noted in the electronic health record's allergy module and manually verified.	ICD-9 codes: 995.6, 995.61–995.69, 995.7, V15.01-V15.05.	Epinephrine auto injector prescription
2. ICD-9/10 diagnosis code for food allergy used at any visit.	ICD-10 Codes: T78.00XA-T78.09XA, T78.1XXA, Z91.010-Z91.013, Z91.018.	
3. Prescription of “epinephrine injector” at any time.		
Criteria 1 and 3, or 2 and 3 must be present to meet study definition of food allergy.		
Allergic rhinitis		
1. ICD-9/10 diagnosis code for allergic rhinitis used at least twice at 2 separate visits, at least 6 mo apart.	ICD-9 codes: 477.0–477.2, 477.8, 477.9. ICD-10 Codes: H10.10, H10.12, H10.13, J30.0-J30.2, J30.5, J30.81, J30.89, J30.9, L23.81.	Not applicable ^c

^a We excluded ICD-9 and ICD-10 diagnosis codes when the associated description mentioned viral, reactive airway disease, or exercise induced asthma.

^b Medications only list those identified in our cohort. Asthma medications are identified on the basis of previous work.²⁹ We used the list of prescription topical medication from the National Eczema Association⁵⁰ and matched them to topical medications in our cohort to identify eczema medications.

^c Diagnosis-specific prescribed medications were not available consistently for allergic rhinitis, and thus, allergic rhinitis was not included in the definition of primary composite outcome.

SUPPLEMENTAL TABLE 6 Definition of Covariates

Variable	Source	Definition and Variable Characteristic in the Model
Maternal intrapartum antibiotics	Maternal medical record and pharmacy data	All intravenous and intramuscular antibiotics administered to the mother during the hospital admission leading to delivery (upper margin 5 d before delivery) and categorized into “GBS IAP” or “other” on the basis of antibiotic type and duration of first dose from delivery.
Maternal race and ethnicity	Maternal medical record and infant’s birth certificate	Reported value at the time of admission leading to delivery. Categorical variable as white and non-Hispanic, Black and non-Hispanic, Asian, Hispanic, and other or unknown.
Maternal BMI	Calculated from maternal wt and height	Maternal wt and height from maternal medical chart as reported at admission for delivery or from infant’s birth certificate used to calculate BMI. Continuous variable.
Parity	Labor room delivery summary	Recorded after delivery of infant. Categorical variable as 1 and 2 or more.
GBS status	Labor room delivery summary	Recorded status as known at the time of delivery. Categorical variable as positive, negative, or unknown.
Chorioamnionitis	Labor room delivery summary, maternal and infant admission diagnostic codes	Maternal ICD-9 diagnosis codes 658.41, 658.43, 658.4 or infant ICD-9 diagnosis code 762.7, or text extraction from labor room summary notable for maternal chorioamnionitis or fever. Binary variable.
Maternal asthma	Labor room delivery summary, maternal admission diagnostic codes	Maternal ICD-9 diagnosis codes 493, 493.02, 493.2, 493.22, 493.81, 493.9, 493.91, 493.92, or labor room summary mentioning history of asthma. Binary variable.
Maternal allergy	Maternal admission diagnostic codes with manual verification of each description	Maternal ICD-9 diagnosis codes 372.14, 477, 477.1, 477.2, 477.8, 477.9, 692.4, 692.6, 692.89, 692.9, 693, 708, 995.27, 995.3, 995.7, V14.0–14.9, V15.01–15.09 with a description that, on manual review, was considered to be a true allergy.
Variables related to residence	American Community Survey 2009–2012	By using the Federal Information Processing Series codes associated with the child’s earliest residential address documented in the pediatric record, children were linked to the ACS tract-level data.
Proportion with <high school education		Percent of population from tract-level census data whose level of education was less than high school. Continuous variable.
Median household income quartile		Median household income (\$) from tract-level census data divided into quartiles. Categorical variable as $\leq 27\,800$, 27 801 to $\leq 39\,610$, 39 611 to $\leq 62\,315$, and $\geq 62\,316$.
Birth wt z scores	www.peditools.com	Z scores obtained by using sex, birth wt, and gestational age obtained from labor room delivery summary. ⁵¹ Continuous variable.
Neonatal antibiotics	Neonatal medical record and pharmacy data	Any intravenous or intramuscular antibiotic administered to the neonate within first 72 h of age. Binary variable.
Breastfeeding, 3 mo	Pediatric medical records	Text string following “Diet” field in all pediatric progress notes were extracted and manually reviewed for presence of breastfeeding. Review started at the progress note closest to the 6-mo visit. No breastfeeding was assigned when no note between 0 and 6 mo mentioned breastfeeding. Breastfeeding duration was determined at the age of the progress note that last mentioned any breastfeeding. Breastfeeding at 3 mo was then derived as a binary variable from the data.

SUPPLEMENTAL TABLE 7 Antibiotic Composition and Duration Among Women With GBS IAP Exposure by Delivery Mode

	Vaginal Cohort, GBS IAP (<i>n</i> = 1919)	Cesarean Cohort, GBS IAP (<i>n</i> = 573)	<i>P</i>
Type of GBS-specific antibiotic, ^a <i>n</i> (% GBS antibiotic exposed)			
Ampicillin	335 (17.5)	130 (22.7)	.005
Cefazolin	24 (1.3)	14 (2.4)	.04
Clindamycin	51 (2.7)	23 (4.0)	.09
Penicillin	1452 (75.7)	395 (68.9)	.001
Vancomycin	84 (4.4)	27 (4.7)	.73
Hours from first GBS-specific antibiotic dose to delivery, median (IQR)	9.20 (6.58–13.47)	13.12 (8.53–19.88)	<.001
Number of doses of GBS-specific antibiotic, median (IQR)	2 (2–3)	3 (2–5)	<.001
Exposure to other antibiotic (not GBS-specific) before delivery, <i>n</i> (%)	119 (6.2)	83 (14.5)	<.001
Exposure to other antibiotic type, <i>n</i> (%) of other antibiotic exposed)			
Ampicillin an sulbactam	57 (47.9)	42 (50.6)	.71
Gentamicin	54 (45.4)	32 (38.6)	.34
Metronidazole	8 (6.7)	8 (9.6)	.45
Azithromycin or erythromycin	2 (1.7)	1 (1.2)	>.99
Ceftriaxone or cefepime	4 (3.4)	0	.15
Hours from first dose of other antibiotic to delivery, median (IQR)	3.50 (1.48–6.57)	3.45 (1.52–6.40)	.99
No. doses of other antibiotic, median (IQR)	1 (1–1)	1 (1–1)	.35

IQR, interquartile range.

^a A woman may be administered >1 type of antibiotic.

SUPPLEMENTAL TABLE 8 Distribution of Age at First Diagnosis Among Infants With Asthma, Eczema, Food Allergy and Allergic Rhinitis

Age Range (in mo) at First Diagnosis, <i>n</i> (%)	Any of the 4 Outcomes, <i>n</i> = 4390	Asthma, <i>n</i> = 2488	Eczema, <i>n</i> = 1551	Food Allergy, <i>n</i> = 862	Allergic Rhinitis, <i>n</i> = 1525
0–5	809 (18.4)	0	777 (50.1)	178 (20.6)	1 (0.1)
6–11	510 (11.6)	0	352 (22.7)	183 (21.2)	68 (4.5)
12–17	958 (21.8)	820 (33.0)	188 (12.1)	211 (24.5)	177 (11.6)
18–23	584 (13.3)	497 (20.0)	89 (5.7)	95 (11.0)	204 (13.4)
24–29	432 (9.8)	334 (13.4)	46 (3.0)	57 (6.6)	232 (15.2)
30–35	322 (7.3)	250 (10.0)	42 (2.7)	33 (3.8)	196 (12.9)
36–41	269 (6.1)	198 (8.0)	24 (1.5)	30 (3.5)	217 (14.2)
41–47	186 (4.2)	145 (5.8)	19 (1.2)	23 (2.7)	170 (11.1)
48–53	162 (3.7)	135 (5.4)	12 (0.8)	14 (1.6)	156 (10.2)
54–59	97 (2.2)	78 (3.1)	2 (0.1)	12 (1.4)	80 (5.2)
60–65	52 (1.2)	29 (1.2)	0	19 (2.2)	24 (1.6)
66–72	9 (0.2)	2 (0.1)	0	7 (0.8)	0

SUPPLEMENTAL TABLE 9 Sensitivity Analyses for the Primary Composite Outcome

	Vaginal Cohort			Cesarean Cohort		
	HR	95% CI	<i>n</i>	HR	95% CI	<i>n</i>
Effect of including only penicillin and ampicillin as GBS IAP ^a			9718			4328
No GBS IAP	Reference	Reference		N/A	N/A	
GBS IAP (penicillin and ampicillin only)	1.15	0.97–1.36		1.10	0.90–1.35	
Other antibiotics	0.95	0.78–1.14		Reference	Reference	
Effect of health care received outside of CHOP network: Restricted to 4 pediatrics care sites where 80% to 90% of health care is obtained within network ^a			7637			3129
No GBS IAP	Reference	Reference		N/A	N/A	
GBS IAP	1.09	0.91–1.30		1.18	0.94–1.48	
Other antibiotics	0.94	0.77–1.15		Reference	Reference	
Effect of GBS colonization: Restricted to women with known GBS colonization ^b			2770			1157
No GBS IAP	Reference	Reference		N/A	N/A	
GBS IAP	1.21	0.98–1.49		1.18	0.92–1.52	
Other antibiotics	1.07	0.83–1.38		Reference	Reference	
Effect of chorioamnionitis: Restricted to dyads without chorioamnionitis ^c			9307			3958
No GBS IAP	Reference	Reference		N/A	N/A	
GBS IAP	1.15	0.97–1.37		1.05	0.84–1.31	
Other antibiotics	0.96	0.80, 1.19		Reference	Reference	

N/A, not applicable.

^a Adjusted for maternal age, maternal race and ethnicity, maternal BMI, parity, GBS colonization status, chorioamnionitis, maternal asthma, maternal allergy, proportion of residents with less than high school education, median household income quartile, infant's sex, birth wt-for-gestation z score, neonatal antibiotics, and breastfeeding at 3 mo.

^b Adjusted for all above except GBS colonization status.

^c Adjusted for all above except chorioamnionitis.

SUPPLEMENTAL REFERENCES

50. National Eczema Association. What are topicals? Available at: <https://>

nationaleczema.org/eczema/treatment/topicals/. Accessed May 22, 2020