Supplemental Information

NOTE 1: PCORNET DESCRIPTION, CDM, AND INSTITUTIONAL REVIEW BOARD DETERMINATIONS

PCORnet currently contains health information for >128 million patients across 13 demographically and geographically diverse clinical data research networks (CDRNs). A CDM is used in the network to organize and standardize EHRs across disparate network partners and source EHR systems; additional health care data, such as data from insurance claims and pharmacy dispensings, are incorporated for some of the network partners. The PCORnet CDM version 3.0, leveraged from the Food and Drug Administration's Sentinel System, has 15 domain tables and >100 different variables, including EHR-specific data (such as prescribing records and vital measures). In having network partners convert their source system data to comply with the CDM, PCORnet fosters data consistency and result aggregation across sites. This process also allows for certain privacy protections, such as the creation of deidentified patient identifications and, for some sites, date obfuscation.

Four CDRNs, including 11 of the health care institutions participating in the study, used a central institutional review board (IRB) for review and approval. Three CDRNs with 16 health care institutions used an IRB reliance model, with 1 institution serving as the CDRN's IRB of record for the study. The 3 remaining CDRNs with 8 institutions used a combination of IRB reliance and individual site IRB review. IRB determinations differed at participating institutions: 8 institutions deemed the study to be nonhuman subjects research, foregoing IRB oversight; 9 institutions deemed it to be exempt from IRB review because the data transferred was deidentified; 18 institutions reviewed the study and determined it to be of minimal risk. The IRB of the lead site, Harvard Pilgrim Health Care Institute, also reviewed and approved the study as human subjects research with minimal risk.

NOTE 2: PROCESS FOR DEVELOPING ANTIBIOTIC CODE LOOK-UP

To capture the appropriate list of antibiotics, we used the First Databank look-up tool (http://www.fdbhealth.com/) licensed by the Sentinel Network (https://clt.sentinelsystem.org/managecondition.jsf) to manually compile a list of National Drug Code values for antibiotics. We used First Databank's functional classification, which was translated into RxNorm concept unique identifiers by using the RxNorm crosswalk available from the NLM. Similarly, we queried RxNorm directly using the Anatomical Therapeutic Chemical class J01 (antibacterials for systemic use) to extract a set of concept unique identifiers for antibiotics and merged these additional codes with those obtained above. Because not all network partners had data available from inpatient settings and because outpatient oral and intramuscular medication usage are likely more modifiable than intravenous medications, we limited the set of antibiotics to oral and common intramuscular formulations. We further curated the set to exclude some medications initially captured that were not available for distribution in the United States or were antiprotozoal medications, topical preparations, or solely available as veterinary medications. Finally, we used the RxNorm hierarchy to expand the initial set to include semantic drug form codes that had information on medication name, dose, and route of administration as well as less-specific ingredient, multi-ingredient, precise-ingredient, or brand-name codes that only had information about the ingredients in medications. For corticosteroids, we followed a similar process, limiting our selection to dose forms and ingredients available as oral formulations.

NOTE 3: PCORNET PRIVACY PROTECTIONS AND VARIABLES NEEDED TO CALCULATE ANTIBIOTIC EPISODES

A core principle of PCORnet is the use of privacy-protecting methods to the maximum extent possible. In addition to limiting data to the minimum necessary and specific code-matched records needed for the study analyses, we also masked all dates to prevent potential reidentification of records and patients. However, to calculate antibiotic exposure episodes and link antibiotic episodes with relevant infection diagnoses, we needed some measure of time intervals. In the distributed program, the date variables from the various CDM tables were used to generate 3 new, date-masked variables.

We calculated age in months for encounters and prescriptions using the birth date variable compared against the record's relevant date variable in the given table (eg, prescription order date in the prescribing table). For individual patient records that occurred in the same age month, we used age order to indicate the relative order in which various health events occurred. Record(s) that occurred earliest within the given age month were assigned a value of 1, and subsequent records were assigned a value of 2, 3, 4, etc. Records occurring on the same day were assigned the same value for the age order variable. This variable was used to assemble a timeline of relevant health events for the cohort patients. Finally, to better understand the relative distance between encounters, link antibiotics prescribed during the same treatment episode, and connect infections to antibiotics, we calculated the variable days between records. For days between records, dates were subtracted between consecutive records. Calculations were all done relative to the previous record; the first days between records value for any given cohort patient was left unpopulated.

This data structure facilitated the creation of antibiotic episodes. We joined together all antibiotics prescribed within 10 days of a previous antibiotic. We assigned the antibiotic spectrum of the episode to the higher spectrum antibiotic prescribed during the episode. For example, a prescription written on day 1 for amoxicillin (narrow), day 7 for amoxicillin, and day 10 for azithromycin (broad) became a single prescription episode for a broad-spectrum antibiotic.

To inform the distributed SAS program that built the study cohort and pulled the relevant study data, we generated technical specifications that detailed the cohort formation flowchart, required CDM variables, non-CDM variables (eg, age order, days between records, and age in months), and code-list restrictions. Programmers used the technical specifications to translate the request into a distributed SAS program, which was extensively tested both internally by using simulated data and externally by using participating network partners as β testers.

NOTE 4: CAPTURE OF COMPLEX CHRONIC CONDITIONS AND CREATING EPISODES FOR INFECTIONS

Feudtner et al[36] subclassified complex chronic diseases into 9 categories. Among cohort participants classified as having a complex chronic condition in our study, the breakdown by category was cardiovascular (31%), other congenital of genetic defect (30%), neuromuscular (15%), respiratory (14%), renal (13%), hematologic or immunodeficiency (11%), metabolic (8%), malignant neoplasms (4%), and gastrointestinal (4%). We added an additional category of growth conditions, including hypothyroidism and pituitary disorders, which was present in 6% of children. These add up to >100% because some children had >1 chronic condition.

To accommodate those institutions that recorded diagnoses in the Systematized Nomenclature of Medicine (SNOMED), we translated the ICD-9-CM codes to SNOMED Clinical Terms codes using NLM's Unified Medical Language System mappings.[44] We only accounted for diagnoses that were available through September 30, 2015, the date mandated for health care systems to switch from using ICD-9-CM codes to *International Classification of Diseases, 10th Revision* codes. We defined a child as having a complex chronic condition if the child had at least 2 diagnostic codes for any of the conditions at <72 months of age. These complex chronic condition diagnoses included diagnostic codes found after the designated exposure period of <24 months of age because of the inherent difficulty in diagnosing many chronic diseases in early childhood.

For infections, we used the Fleming-Dutra et al[35] classification system. In this system, tier 1 infections are those that almost always require antibiotics, such as pneumonia and other bacterial infections. Tier 2 infections are those for which antibiotics might be discretionary, the most prevalent of which are suppurative otitis media, sinusitis, and pharyngitis. Tier 3 infections are those that typically do not require antibiotics, such as nonsuppurative otitis media and other skin, cutaneous, and mucosal conditions. If a child had >1 same-day infection, we used a hierarchy, giving priority to lower tier infections (eg, if tier 1 and tier 2 diagnostic codes were present on the same day, we assigned the encounter as a tier 1 infection). Accounting for the likelihood that some infections would require multiple clinical encounters and multiple diagnostic codes within a brief time interval, we created infection episodes by joining together infections within 14 days; we gave priority during this interval to the lowest tier infections. We derived infections as a categorical count of infection episodes. Because of the skewed nature of this variable, we log transformed it when including in models.

NOTE 5: INCORPORATION OF MATERNAL VARIABLES IN SUBSTUDY ANALYSES

Mother-child linkages are not routinely available in EHRs. To incorporate maternal variables, we relied on 7 institutions that could

make these linkages. Five of the sites were integrated delivery systems that have available insurance identifications shared within families. One of the sites has an institutional policy that links mothers to children at the time of birth; linkages were thus available for all children born in the health care system. One site used a variety of methods to link mothers to children, including available insurance identifications, matching geocoded addresses and telephone numbers, and free-text information on emergency contacts, among other data points.

Of 214 780 children in these 7 institutions with same-day child height and weight measurements at 0 to <12 months of age and 12 to <30 months of age and at least 1 measurement after 24 months of age, 137 815 children were able to be linked to mothers. Of these children, 73 475 had same-day height and weight measurements at 48 to <72 months of age, and 53 320 of the mothers had any vitals data during pregnancy. This was the sample size for the substudy analysis.

We defined pregnancy as the period from the index child's date of birth minus 9 months (273 days). We captured several potential confounders from mothers' records, including maternal age at delivery, prepregnancy BMI captured up to 1 year before the pregnancy, diagnoses of diabetes or gestational diabetes, whether the child was delivered via vaginal birth or cesarean delivery, and maternal smoking status during pregnancy. For the prepregnancy BMI, we chose the weight closest to 9 months before the child's birth date and incorporated any height available.

We defined a mother as having diabetes if she had ≥2 of the following criteria: glycosylated hemoglobin level of ≥6.5%, ICD-9-CM code for diabetes, or receipt of any diabetes prescription during the year before pregnancy. A diagnosis of gestational diabetes required an ICD-9-CM code for gestational diabetes mellitus and no diagnosis of diabetes per the criteria above. Smoking was available in the CDM, and we restricted the capture of this data to the pregnancy period; mothers were classified as never, former, or active smokers, with active smoker designated if defined as such at any point during pregnancy. Delivery method was available in the CDM by using diagnostic codes and procedural codes available as Healthcare Common Procedure Coding System and *Current Procedural Terminology* codes.

Because of a small sample size, we excluded children with complex chronic conditions from these analyses. For the 48 908 children without a complex chronic condition, the mean age of mothers at delivery was 29.5 (SD 5.9) and the prepregnancy BMI was 27 (SD 6.3); 6.1% of mothers smoked during pregnancy (16% had an unknown smoking status), 1.3% had diabetes, 11.7% had gestational diabetes, and 19.1% had a cesarean delivery (29.3% of mothers had missing data on delivery method). The mean birth weight in grams was 3351 g (SD 529). Results are in Supplemental Tables 14 and 15.

NOTE 6: SENSITIVITY ANALYSES

We conducted several sensitivity analyses to determine if results were robust to different restrictions on the data (Supplemental Table 13). In the first sensitivity analysis, we limited the analytic sample to children with any well-child visits at <72 months of age. We conducted this analysis because we believed that these children were receiving primary care at the institution providing data and, therefore, were more likely to get most of their care there. If a child received most of their care at a specific institution, we would better capture their antibiotic prescriptions.

Second, we limited the analytic sample to sites with a ≥40% antibiotic rate at <24 months of age. Some institutions with lower antibiotic prescribing rates might have missed a large portion of antibiotic prescriptions or had a different case mix of patients (eg, tertiary care versus primary care networks); thus, it was important to determine if the prescribing rate had an impact on results.

Third, we restricted the analytic sample to children with no antibiotics linked to tier 1 infections to assess associations only for antibiotics prescribed for indications that were either discretionary (eg, tier 2 suppurative otitis media) or not indicated (eg, tier 3 nonsuppurative otitis media). This allowed for us to assess whether we found similar associations for required antibiotics versus those that were possibly not required and thus modifiable. We linked antibiotics to infectious diagnoses within 7 days of the prescription to accommodate this analysis. If >1 infectious diagnosis was linked to an antibiotic prescription, we prioritized the more serious infection (tier 2 over tier 3).

In addition to these sensitivity analyses, we assessed whether parameter estimates were sensitive to the inclusion of asthma and infections as covariates in the model. The inclusion of these covariates did slightly attenuate results but not substantively (Supplemental Tables 10 and 12). In addition, we assessed whether infections were effect modifiers of the antibiotics to weight relationship, and we found some evidence for this (Supplemental Table 11).

NOTE 7: SENSITIVITY ANALYSIS ON UNMEASURED CONFOUNDING AND A NOTE ON MEASURED TIME-VARYING CONFOUNDERS AFFECTED BY PAST EXPOSURE

We assessed the possible role of unmeasured confounding by a binary unmeasured outcome risk factor *U* using a simple approach to sensitivity analyses proposed by Vanderweele and Arah.[45] In our analysis, an important example of *U* is an indicator of socioeconomic status, breastfeeding, or diet (not available for adjustment in our study).[46,47] This sensitivity analysis approach gives a formula for bias that is due to unmeasured confounding by *U* under the assumptions that (1) the association between the mean of the outcome (child BMI *z* score at 48–<72 months of age) and *U* does not vary by level of antibiotic exposure nor by level of the measured confounders (eg, race and corticosteroids) and (2) the association between the prevalence of *U* and exposure does not vary by level of the measured confounders. As we discuss further below, the validity of this approach, along with the validity of our main analysis results, also relies on the assumption that time-varying measured confounders (eg, corticosteroids and number of encounters) are not themselves affected by past antibiotic exposure. Under these simplifying assumptions, Vanderweele and Arah[45] show that bias due to unmeasured confounding by *U* is equal to the product of the associations in (1) and (2) above.

This approach can be useful for understanding what magnitude of the associations in (1) and (2) would need to be present to eliminate our observed exposure-outcome association. Specifically, suppose that the adjusted mean difference in the BMI *z* score at 48 to <72 months of age is 0.45 for some unmeasured confounder (yes versus no); in this case, lower income versus higher income or being breastfed exclusively for 6 months versus not, adjusted for covariates. This is the association in (1).[46] As reported in Table 2, we estimated that the adjusted mean difference in the BMI *z* score at 48 to <72 months of age was higher by 0.04 (95% CI 0.03 to 0.05) among children without a complex chronic condition with any antibiotic exposure versus none at <24 months of age. As the product of $0.09 \times 0.45 = 0.05$, the association in (2) of 0.09 would lead to a bias corrected estimate of 0.0 (95% CI −0.01 to 0.01), completely eliminating the association we found. This bias corrected estimate is simply the original estimate minus the measure of bias (0.09×0.45). Similarly, the bias corrected CIs are computed by the taking the upper and lower bounds of the original CIs and subtracting 0.09×0.45. None of the variables in our model had an association of ≥0.45 with the outcome of the mean BMI *z* score; the strongest association was −0.38 for preterm birth among children with a complex chronic condition.

Another source of bias in our effect estimates may be present because of the time-varying nature of our exposure of interest and possible confounders given the potential for feedback between them. In particular, any versus no antibiotic exposure or the number of antibiotic episodes over the first 2 years of life are functions of a time-changing indicator of exposure status over the course of those 2 years. In addition, any versus no diagnosis of asthma and the number of corticosteroids, along with other covariates we included in regression models or stratified on, over that same period are also functions of time-changing indicators in that period.

We included covariates, such as asthma and the count of corticosteroids, in our regression models because we assume they were needed to control confounding. Given this assumption, ignoring these covariates would result in residual confounding. However, inclusion of these covariates in our regression models (which corresponds to a form of conditioning on them) may also result in a biased effect estimate even if all covariates needed to control confounding are included in the model and even if the model is correctly specified.

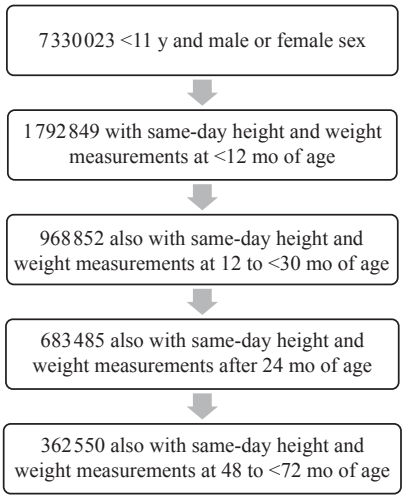
In particular, Robins[48] showed that a standard regression analysis that included (ie, conditions on) a function of a time-varying covariate L_t (with t indexing a particular time during the exposure period) would generally be biased for the causal effect of a time-varying exposure in that period if (1) L_t (eg, asthma status at t and any corticosteroid given at t) is a measured covariate needed to control confounding for the exposure effect at future times in that period and (2) L_t is itself affected by past exposure in that period. For example, this structure would hold in our study if the number of corticosteroids and/or asthma status by a time t in the first 2 years of life are needed to control confounding for the effect of future antibiotic exposure on childhood BMI and are also, themselves, affected (directly or indirectly) by previous antibiotic exposure during that first 2 years.

In this case, failure to include asthma and/or the number of corticosteroids in the model will result in residual confounding. However, including (conditioning on) these covariates may result in a particular form of selection bias if these covariates share a common cause with the outcome that is not accounted for in the analysis. Because it is particularly unreasonable to assume we have accounted for all such common causes, our conclusions in the main text rest on the additional assumption that corticosteroids and/or asthma and other time-varying covariates in our models are not affected by antibiotic exposure. We believe this to be a reasonable

assumption because we are not aware of any evidence that antibiotics are associated with the development of asthma or the subsequent use of corticosteroids; the exception would be an allergic reaction to an antibiotic requiring a corticosteroid; this would not be prevalent enough in our data to affect our results.

By the same arguments, our choice to stratify on chronic conditions is appropriate if these are unaffected by antibiotic exposure but, otherwise, may result in selection bias because of conditioning on an effect of exposure that likely shares unmeasured common causes with the outcome.[49] Again, we believe this decision is reasonable because of the nature of these chronic conditions, which are severe conditions.

Alternatives to standard regression, known collectively as "g-methods," can recover causal effects of time-varying exposures in the presence of time-varying confounders affected by previous exposure. These methods still rely on the assumptions of no unmeasured confounding and no measurement error. One relatively, computationally simple example of a g-method is an inverse probability–weighted estimation of marginal structural models. We will consider this approach in future work to ensure that we obtain similar conclusions to those reported in the main text.[50,51]



SUPPLEMENTAL FIGURE 2
Flow diagram of cohort participants.

SUPPLEMENTAL TABLE 5 PCORnet Network Partners Participating in the PCORnet Antibiotics and Childhood Growth Study

CDRN	Network Partners (Institutions Included in Network Partners if Centralized)
ADVANCE	ADVANCE (OCHIN and Health Choice Network of Florida)
CAPriCORN	NorthShore University Health System, University of Chicago Medicine, Rush University Medical Center, Lurie Children's Hospital, and Loyola Medicine
GPC	Medical College of Wisconsin, University of Iowa Health Care, Marshfield Clinic, and University of Texas Health Science Center at San Antonio
Mid-South Clinical Data Research Network	Vanderbilt University Medical Center, Greenway Health, and University of North Carolina at Chapel Hill
NYC-CDRN	New York Genome Center (Mount Sinai, Albert Einstein College of Medicine, and the Children's Hospital at Montefiore)
OneFlorida Clinical Data Research Network	OneFlorida (University of Florida Health and Tallahassee Memorial)
PEDSnet	PEDSnet centralized data mart (Children's Hospital of Philadelphia, Seattle Children's Hospital, Children's Hospital Colorado, Nemours Children's Hospital, and Nationwide Children's Hospital) and Cincinnati Children's Hospital Medical Center
Kaiser Permanente and Strategic Partners PORTAL	Kaiser Permanente Colorado, Denver Health, Kaiser Permanente Washington Health Research Institute, HealthPartners Research Foundation, Kaiser Permanente Mid-Atlantic States, and Kaiser Permanente Northwest
REACHnet	Tulane University, Ochsner Health System, and Baylor Scott and White Health North
ARCH	Boston Medical Center and Wake Forest Baptist Medical Center

ADVANCE, Accelerating Data Value Across a National Community Health Center Network; ARCH, Accessible Research Commons for Health; CAPriCORN, Chicago Area Patient Centered Outcomes Research Network; CDRN, clinical data research network; GPC, Greater Plains Collaborative; NYC-CDRN, New York City Clinical Data Research Network; PEDSnet, Pediatric Learning Health System; PORTAL, Kaiser Permanente & Strategic Partners Patient Outcomes Research To Advance Learning; REACHnet, Research Action for Health Network.

SUPPLEMENTAL TABLE 6 Demographic and Clinical Characteristics of the Study Population, Overall and Stratified by Chronic Condition Status

Characteristic	Total Study Population, *N* = 362 550	No Complex Chronic Condition, *N* = 310 947	With Complex Chronic Condition,[a] *N* = 51 603
Female sex, *n* (%)	173 908 (48)	150 549 (48)	23 359 (45)
Race, *n* (%)			
Asian American	14 513 (4)	12 972 (4)	1541 (3)
African American	97 801 (27)	85 204 (27)	12 597 (24)
White	190 812 (53)	161 814 (52)	28 998 (56)
Other	27 852 (8)	22 277 (7)	5575 (11)
Unknown	31 572 (8)	28 680 (9)	2892 (6)
Hispanic ethnicity, *n* (%)	64 019 (18)	56 255 (18)	7764 (15)
Preterm[b], *n* (%)	26 019 (7)	16 979 (5)	9040 (18)
Asthma[c], *n* (%)	47 596 (13)	38 346 (12)	9250 (18)
Systemic corticosteroid episodes[d] at <24 mo of age, *n* (%)			
0	314 395 (87)	271 298 (87)	43 097 (84)
1	32 214 (9)	27 432 (9)	4782 (9)
2	9047 (2)	7292 (2)	1755 (3)
3	3544 (1)	2689 (1)	855 (2)
4+	3350 (1)	2236 (1)	1114 (2)
Episodes for presumed infectious illnesses[e] at <24 mo of age, *n* (%)			
0	46 672 (13)	40 821 (13)	5851 (11)
1	27 986 (8)	24 351 (8)	3635 (7)
2	32 889 (9)	29 286 (9)	3603 (7)
3	34 598 (10)	30 990 (10)	3608 (7)
4+	220 405 (61)	185 499 (60)	34 906 (68)
No. encounters[f] at <24 mo of age, median (IQR)	16.0 (10.0 to 24.0)	15.0 (10.0 to 22.0)	23.0 (13.0 to 39.0)
Systemic antibiotic prescribing episodes[g] at <24 mo of age, *n* (%)			
0	153 366 (42)	130 208 (42)	23 158 (45)
1	77 250 (21)	67 285 (22)	9965 (19)
2	46 235 (13)	40 201 (13)	6034 (12)
3	29 005 (8)	25 202 (8)	3803 (7)
4+	56 694 (16)	48 051 (15)	8643 (17)
Systemic broad-spectrum antibiotic prescribing episodes[g] at <24 mo of age, *n* (%)			
0	235 024 (65)	203 728 (66)	31 296 (61)
1	62 430 (17)	53 513 (17)	8917 (17)
2	26 855 (7)	22 636 (7)	4219 (8)
3	14 582 (4)	12 115 (4)	2467 (5)
4+	23 659 (7)	18 955 (6)	4704 (9)
Systemic narrow-spectrum antibiotic prescribing episodes[g] at <24 mo of age, *n* (%)			
0	192 039 (53)	159 729 (51)	32 310 (63)
1	89 256 (25)	79 034 (25)	10 222 (20)
2	45 001 (12)	40 333 (13)	4668 (9)
3	21 152 (6)	18 903 (6)	2249 (4)
4+	15 102 (4)	12 948 (4)	2154 (4)
BMI category at 4–<6 y of age, *n* (%)			
Underweight (less than the fifth percentile)	16 310 (4)	12 860 (4)	3450 (7)
Normal wt (fifth to <85th percentile)	245 242 (68)	211 995 (68)	33 247 (64)
Overweight (85th to <95th percentile)	52 774 (15)	45 295 (15)	7479 (14)
Obese (≥95th percentile)	48 224 (13)	40 797 (13)	7427 (14)
Age, mo, mean (SD)	57.8 (5.3)	57.8 (5.4)	58.0 (4.9)
BMI *z* score, mean (SD)	0.40 (1.19)	0.41 (1.12)	0.35 (1.30)

IQR, interquartile range.

[a] Defined as ≥2 ICD-9-CM codes for a complex chronic condition at <72 months of age on the basis of a previously published code set.

[b] One or more ICD-9-CM codes for prematurity at <24 months of age.

[c] Two or more ICD-9-CM codes for asthma at <72 months of age.

[d] Multiple corticosteroids given on the same day or within 10 days of each other were considered a single prescribing episode.

[e] Defined by ICD-9-CM codes on the basis of Fleming-Dutra, et al.[35]

[f] Included all encounters in the inpatient, emergency department, urgent care, and outpatient settings.

[g] Multiple antibiotics given on the same day or within 10 days of each other were considered a single prescribing episode; 91.6% of episodes included a prescription written on a single day, with 99.6% of episodes spanning ≤30 days.

SUPPLEMENTAL TABLE 7 Multivariable Linear Regression Results for the Association of Antibiotics Episodes at <24 Months of Age With the BMI *z* Score at 48–<72 Months of Age, by Antibiotic Spectrum

Episodes[a]	No Complex Chronic Condition, *N* = 310 947		Complex Chronic Condition, *N* = 51 603	
	Model 1,[b] β (95% CI)	Model 2,[c] β (95% CI)	Model 1,[b] β (95% CI)	Model 2,[c] β (95% CI)
Any antibiotic				
0	.0 (reference)	.0 (reference)	.0 (reference)	.0 (reference)
1	.04 (0.03 to 0.05)	.02 (0.01 to 0.03)	.04 (0.01 to 0.07)	.03 (0.00 to 0.06)
2	.08 (0.07 to 0.09)	.04 (0.03 to 0.06)	.09 (0.06 to 0.13)	.07 (0.04 to 0.11)
3	.09 (0.07 to 0.11)	.05 (0.03 to 0.06)	.10 (0.06 to 0.15)	.07 (0.03 to 0.12)
4+	.12 (0.11 to 0.14)	.07 (0.06 to 0.08)	.14 (0.11 to 0.17)	.10 (0.07 to 0.14)
Broad spectrum				
0	.0 (reference)	.0 (reference)	.0 (reference)	.0 (reference)
1	.06 (0.05 to 0.07)	.03 (0.02 to 0.05)	.06 (0.03 to 0.09)	.04 (0.01 to 0.07)
2	.09 (0.07 to 0.10)	.05 (0.03 to 0.06)	.09 (0.05 to 0.13)	.07 (0.03 to 0.11)
3	.07 (0.05 to 0.10)	.03 (0.01 to 0.06)	.17 (0.12 to 0.22)	.15 (0.10 to 0.21)
4+	.12 (0.10 to 0.13)	.06 (0.05 to 0.08)	.13 (0.09 to 0.17)	.09 (0.05 to 0.14)
Narrow spectrum[d]				
0	.0 (reference)	.0 (reference)	.0 (reference)	.0 (reference)
1	.04 (0.02 to 0.05)	.02 (0.00 to 0.03)	.03 (−0.01 to 0.07)	.02 (−0.02 to 0.06)
2	.06 (0.05 to 0.08)	.03 (0.01 to 0.05)	.11 (0.05 to 0.17)	.08 (0.02 to 0.14)
3	.07 (0.04 to 0.10)	.03 (0.00 to 0.06)	.08 (−0.02 to 0.18)	.04 (−0.07 to 0.14)
4+	.11 (0.07 to 0.16)	.06 (0.02 to 0.10)	−.02 (−0.14 to 0.10)	−.06 (−0.18 to 0.06)

[a] Antibiotic episodes were defined as all antibiotics prescribed within a 10-day period of a previous antibiotic; if both narrow- and broad-spectrum antibiotics were prescribed during the episode, then the episode was a broad-spectrum antibiotic episode.
[b] Corrected for clustering by site.
[c] Corrected for clustering by site and adjusted for sex, race, ethnicity, preterm birth, asthma, corticosteroid episodes (continuous, 0–4+) at 0–<24 months of age, number of encounters (continuous, log transformed) at 0–<24 months of age, infection episodes (continuous, log transformed) at 0–<24 months of age, and age at outcome.
[d] For narrow-spectrum antibiotic exposures, analyses were limited to participants with no broad-spectrum antibiotics during the same time window as exposure or before.

SUPPLEMENTAL TABLE 8 Multivariable Linear Regression Results for the Association of Antibiotics Episodes at <24 Months of Age With the BMI *z* Score at 48–<72 Months of Age, by Broad-spectrum Antibiotic Class (Any of This Class of Antibiotics Versus None of This Class as a Reference)

	No Complex Chronic Condition, *N* = 310 947		Complex Chronic Condition, *N* = 51 603	
	Model 1,[a] β (95% CI)	Model 2,[b] β (95% CI)	Model 1,[a] β (95% CI)	Model 2,[b] β (95% CI)
Third generation cephalosporin[c]	.07 (0.05 to 0.08)	.03 (0.02 to 0.04)	.12 (0.09 to 0.16)	.09 (0.05 to 0.12)
Penicillin combination	.07 (0.06 to 0.08)	.04 (0.03 to 0.05)	.08 (0.05 to 0.11)	.04 (0.01 to 0.08)
Macrolide	.07 (0.06 to 0.08)	.02 (0.01 to 0.04)	.05 (0.02 to 0.09)	.01 (−0.02 to 0.05)
Sulfa	.11 (0.09 to 0.13)	.09 (0.07 to 0.11)	.12 (0.09 to 0.16)	.10 (0.06 to 0.14)
First or second generation cephalosporin	.06 (0.04 to 0.08)	.03 (0.01 to 0.05)	.09 (0.05 to 0.13)	.07 (0.03 to 0.11)

[a] Corrected for clustering by site, with the primary exposure defined as receiving a prescription for an antibiotic in the class versus not; these classes were not compared with one another. Results were similar when children who were prescribed other broad-spectrum antibiotics were excluded from each specific antibiotic class analysis (eg, children who were prescribed a sulfa drug were excluded from the analysis of third generation cephalosporins).
[b] Corrected for clustering by site and adjusted for sex, race, ethnicity, preterm birth, asthma, corticosteroid episodes (continuous, 0–4+) at 0–<24 months of age, number of encounters (continuous, log transformed) at 0–<24 mo of age, infection episodes (continuous, log transformed) at 0–<24 months of age, and age at outcome.
[c] Sample sizes for these analyses are listed In Supplemental Table 9; Numbers correspond to children coded as a "yes" for exposure to the specific antibiotic class.

SUPPLEMENTAL TABLE 9 Sample Sizes for Children Exposed to Specific Classes of Antibiotics

	No CCC, *N* with any at 0–<24 mo of age	CCC, *N* with any at 0–<24 mo of age
Third generation cephalosporin	42 968	7268
Penicillin combination	52 651	7715
Macrolide	37 673	5189
Sulfa	12 579	5623
First or second generation cephalosporin	19 166	3924

CCC, complex chronic condition.

SUPPLEMENTAL TABLE 10 Comparing Results of Models With Versus Without Including Infections as a Covariate; Multivariable Linear Regression Results for the Association of Any Exposure to Antibiotics at <24 Months of Age With the BMI *z* Score at 48–<72 Months of Age, by Timing of Antibiotic Prescription

Antibiotics	No Complex Chronic Condition, *N* = 310 947		Complex Chronic Condition, *N* = 51 603	
	Model 2 Without Infections,[a] β (95% CI)	Model 2 With Infections,[b] β (95% CI)	Model 2 Without Infections,[a] β (95% CI)	Model 2 With Infections,[b] β (95% CI)
Any, mo				
0–<24	.05 (0.04 to 0.06)	.04 (0.03 to 0.05)	.07 (0.05 to 0.10)	.06 (0.04 to 0.09)
0–<6[c,d]	.06 (0.05 to 0.08)	.05 (0.04 to 0.06)	.05 (0.02 to 0.08)	.05 (0.02 to 0.08)
6–<12[c,d]	.04 (0.03 to 0.05)	.03 (0.02 to 0.04)	.04 (0.02 to 0.07)	.04 (0.01 to 0.06)
12–<24[c,d]	.04 (0.03 to 0.05)	.02 (0.01 to 0.03)	.07 (0.04 to 0.10)	.06 (0.03 to 0.08)
Broad spectrum, mo				
0–<24	.05 (0.04 to 0.06)	.04 (0.03 to 0.05)	.08 (0.06 to 0.10)	.07 (0.05 to 0.10)
0–<6[c,d]	.06 (0.04 to 0.07)	.04 (0.02 to 0.06)	.06 (0.02 to 0.09)	.05 (0.01 to 0.09)
6–<12[c,d]	.05 (0.03 to 0.06)	.03 (0.02 to 0.05)	.05 (0.02 to 0.08)	.05 (0.01 to 0.08)
12–<24[c,d]	.04 (0.03 to 0.05)	.03 (0.02 to 0.04)	.08 (0.05 to 0.11)	.07 (0.04 to 0.10)
Narrow spectrum[e], mo				
0–<24	.03 (0.02 to 0.04)	.02 (0.01 to 0.03)	.04 (0.00 to 0.07)	.03 (−0.01 to 0.06)
0–<6[c,d]	.06 (0.05 to 0.08)	.05 (0.04 to 0.07)	.04 (0.00 to 0.09)	.04 (−0.01 to 0.08)
6–<12[c,d]	.04 (0.02 to 0.05)	.02 (0.01 to 0.04)	.02 (−0.02 to 0.06)	.01 (−0.03 to 0.05)
12–<24[c,d]	.02 (0.01 to 0.04)	.01 (0.00 to 0.02)	.04 (0.00 to 0.08)	.02 (−0.02 to 0.06)

[a] Corrected for clustering by site and adjusted for sex, race, ethnicity, preterm birth, asthma, corticosteroid episodes (continuous, 0–4+) at 0–<24 months of age, number of encounters (continuous, log transformed) at 0–<24 months of age, and age at outcome. Infection episodes are not included.

[b] Corrected for clustering by site and adjusted for sex, race, ethnicity, preterm birth, asthma, corticosteroid episodes (continuous, 0–4+) at 0–<24 months of age, number of encounters (continuous, log transformed) at 0–<24 months of age, infection episodes (continuous, log transformed) at 0–<24 months of age, and age at outcome.

[c] For exposure time windows, Model 2 was additionally adjusted for previous antibiotics: (1) antibiotics at 6–<12 months, adjusted for 0–<6 months antibiotics and (2) antibiotics at 12–<24 months, adjusted for 0–<12 months antibiotics.

[d] For exposure time windows, covariates were used during the same time window (infections, corticosteroids, and encounters): (1) antibiotics at 0–<6 months, covariates used for 0–<6 months; (2) antibiotics at 6–<12 months, covariates used for 6–<12 months; and (3) antibiotics 12–<24 months, covariates used for 12–<24 months.

[e] For narrow-spectrum antibiotic exposures, analyses were limited to participants with no broad-spectrum antibiotics during the same time window as exposure or before.

SUPPLEMENTAL TABLE 11 Multivariable Regression Results for the Association of Any Exposure to Antibiotics at <24 Months of Age With the BMI *z* Score at 48–<72 Months of Age, by Stratum of Number of Infections at <24 Months of Age

Any Antibiotics	No Complex Chronic Condition		Complex Chronic Condition	
	Model 1,[a] β (95% CI)	Model 2,[b] β (95% CI)	Model 1,[a] β (95% CI)	Model 2,[b] β (95% CI)
Stratum: 0–1 infections at <24 mo of age	.03 (0.01 to 0.05)	.02 (0.00 to 0.04)	.02 (−0.05 to 0.09)	.04 (−0.03 to 0.11)
Stratum: 2–3 infections at <24 mo of age	.02 (0.00 to 0.04)	.02 (0.00 to 0.04)	.03 (−0.04 to 0.09)	.01 (−0.06 to 0.07)
Stratum: 4+ infections at <24 mo of age	.07 (0.06 to 0.08)	.05 (0.04 to 0.07)	.11 (0.08 to 0.14)	.08 (0.04 to 0.11)
Data from Table 2 for any antibiotic at <24 mo of age without stratification	.08 (0.07 to 0.08)	.04 (0.03 to 0.05)	.09 (0.07 to 0.11)	.06 (0.04 to 0.09)

We statistically assessed whether infections were an effect modifier of the association between antibiotics and BMI *z* score. To Model 2, we added interaction terms for infections (coded as continuous and log transformed) and antibiotic use (yes versus no); interaction *P* values were <.0001 and .0009 for children without and with complex chronic conditions, respectively.

[a] Corrected for clustering by site.

[b] Corrected for clustering by site and adjusted for sex, race, ethnicity, preterm birth, asthma, corticosteroid episodes (continuous, 0–4+) at 0–<24 months of age, number of encounters (continuous, log transformed) at 0–<24 months of age, tier 1 infection episodes (continuous, log transformed) at 0–<24 months of age, and age at outcome. For the final row, this estimate is slightly different from what is found in Table 2 because this model has tier 1 infections included in it.

SUPPLEMENTAL TABLE 12 Comparing Results of Models With Versus Without Including Asthma as a Covariate (Multivariable Linear Regression Results for the Association of Any Exposure to Antibiotics at <24 Months of Age With the BMI *z* Score at 48–<72 Months of Age, by Timing of Antibiotic Prescription)

Antibiotics	No Complex Chronic Condition, *N* = 310 947		Complex Chronic Condition, *N* = 51 603	
	Model 2 Without Asthma,[a] β (95% CI)	Model 2 With Asthma,[b] β (95% CI)	Model 2 Without Asthma,[a] β (95% CI)	Model 2 With Asthma,[b] β (95% CI)
Any, mo				
0–<24	.04 (0.03 to 0.05)	.04 (0.03 to 0.05)	.07 (0.04 to 0.09)	.06 (0.04 to 0.09)
0–<6[c,d]	.06 (0.05 to 0.07)	.05 (0.04 to 0.06)	.05 (0.02 to 0.08)	.05 (0.02 to 0.08)
6–<12[c,d]	.03 (0.02 to 0.04)	.03 (0.02 to 0.04)	.04 (0.01 to 0.07)	.04 (0.01 to 0.06)
12–<24[c,d]	.02 (0.01 to 0.03)	.02 (0.01 to 0.03)	.06 (0.03 to 0.08)	.06 (0.03 to 0.08)
Broad spectrum, mo				
0–<24	.05 (0.04 to 0.05)	.04 (0.03 to 0.05)	.07 (0.05 to 0.10)	.07 (0.05 to 0.10)
0–<6[c,d]	.05 (0.03 to 0.07)	.04 (0.02 to 0.06)	.05 (0.01 to 0.09)	.05 (0.01 to 0.09)
6–<12[c,d]	.04 (0.03 to 0.05)	.03 (0.02 to 0.05)	.05 (0.02 to 0.08)	.05 (0.01 to 0.08)
12–<24[c,d]	.03 (0.02 to 0.04)	.03 (0.02 to 0.04)	.07 (0.04 to 0.10)	.07 (0.04 to 0.10)
Narrow spectrum[e], mo				
0–<24	.02 (0.01 to 0.03)	.02 (0.01 to 0.03)	.03 (0.00 to 0.07)	.03 (−0.01 to 0.06)
0–<6[c,d]	.06 (0.04 to 0.08)	.05 (0.04 to 0.07)	.04 (−0.01 to 0.09)	.04 (−0.01 to 0.08)
6–<12[c,d]	.02 (0.01 to 0.04)	.02 (0.01 to 0.04)	.02 (−0.02 to 0.06)	.01 (−0.03 to 0.05)
12–<24[c,d]	.01 (−0.01 to 0.02)	.01 (0.00 to 0.02)	.03 (−0.02 to 0.07)	.02 (−0.02 to 0.06)

[a] Corrected for clustering by site and adjusted for sex, race, ethnicity, preterm birth, corticosteroid episodes (continuous, 0–4+) at 0–<24 months of age, number of encounters (continuous, log transformed) at 0–<24 months of age, infection episodes (continuous, log transformed) at 0–<24 months of age, and age at outcome. Asthma is not included.

[b] Corrected for clustering by site and adjusted for sex, race, ethnicity, preterm birth, asthma, corticosteroid episodes (continuous, 0–4+) at 0–<24 months of age, number of encounters (continuous, log transformed) at 0–<24 months of age, infection episodes (continuous, log transformed) at 0–<24 months of age, and age at outcome.

[c] For exposure time windows, Model 2 was additionally adjusted for previous antibiotics: (1) antibiotics at 6–<12 months, adjusted for 0–<6 months antibiotics and (2) antibiotics at 12–<24 months, adjusted for 0–<12 months antibiotics.

[d] For exposure time windows, covariates were used during the same time window (infections, corticosteroids, and encounters): (1) antibiotics at 0–<6 months, covariates used for 0–<6 months; (2) antibiotics at 6–<12 months, covariates used for 6–<12 months; and (3) antibiotics at 12–<24 months, covariates used for 12–<24 months.

[e] For narrow-spectrum antibiotic exposures, analyses limited to participants with no broad during the same time window as exposure or before.

SUPPLEMENTAL TABLE 13 Multivariable Regression Results for the Association of Any Exposure to Antibiotics at <24 Months of Age With the BMI *z* Score at 48–<72 Months of Age, Sensitivity Analyses

Any Antibiotics	No Complex Chronic Condition		Complex Chronic Condition	
	Model 1,[a] β (95% CI)	Model 2,[b] β (95% CI)	Model 1,[a] β (95% CI)	Model 2,[b] β (95% CI)
Limited to participants with any well-child visits at <72 mo of age, *N* = 280 590; 28 220[c]	.08 (0.07 to 0.09)	.04 (0.03 to 0.05)	.10 (0.07 to 0.13)	.05 (0.02 to 0.08)
Limited to sites with a ≥40% antibiotic prescribing rate at <24 mo of age, *N* = 284 712; 47 496[c]	.07 (0.07 to 0.08)	.04 (0.03 to 0.05)	.09 (0.07 to 0.12)	.06 (0.04 to 0.09)
Limited to participants without an antibiotic prescription linked to a tier 1 diagnosis, *N* = 285 736; 44 382[c]	.07 (0.06 to 0.08)	.04 (0.03 to 0.05)	.08 (0.05 to 0.10)	.06 (0.03 to 0.08)

[a] Corrected for clustering by site.

[b] Corrected for clustering by site and adjusted for sex, race, ethnicity, preterm birth, asthma, corticosteroid episodes (continuous, 0–4+) at 0–<24 months of age, number of encounters (continuous, log transformed) at 0–<24 months of age, infection episodes (continuous, log transformed) at 0–<24 months of age, and age at outcome.

[c] The 2 values represent sample sizes for children without (larger number) and with complex chronic conditions.

SUPPLEMENTAL TABLE 14 Multivariable Linear Regression Results for the Association of Antibiotics Episodes at <24 Months of Age With the BMI *z* Score at 48–<72 Months of Age, by Antibiotic Spectrum, Incorporating Maternal Covariates for 7 Health Care Institutions When Available (Data Only for Children Without Complex Chronic Conditions)

Antibiotics	Model 1,[a] β (95% CI)	Model 2,[b] β (95% CI)	Model 3,[c] β (95% CI)	Model 4,[d] β (95% CI)
	N = 48 908	*N* = 48 908	*N* = 22 310	*N* = 12 698
Any	.05 (0.03 to 0.08)	.03 (0.00 to 0.05)	.02 (−0.01 to 0.06)	.04 (−0.01 to 0.08)
Broad spectrum	.06 (0.04 to 0.08)	.03 (0.01 to 0.06)	.01 (−0.02 to 0.04)	.04 (0.00 to 0.08)
Narrow spectrum[e]	.03 (0.01 to 0.06)	.02 (0.00 to 0.05)	.04 (0.00 to 0.07)	.03 (−0.02 to 0.08)
	N = 12 698	*N* = 12 698	*N* = 12 698	*N* = 12 698
Any	.08 (0.04 to 0.12)	.05 (0.00 to 0.09)	.05 (0.01 to 0.09)	.04 (−0.01 to 0.08)
Broad spectrum	.07 (0.03 to 0.10)	.04 (0.00 to 0.09)	.04 (0.00 to 0.08)	.04 (0.00 to 0.08)
Narrow spectrum[e]	.06 (0.01 to 0.11)	.04 (−0.01 to 0.10)	.05 (0.00 to 0.10)	.03 (−0.02 to 0.08)

[a] Corrected for clustering by site.

[b] Corrected for clustering by site and adjusted for sex, race, ethnicity, preterm birth, asthma, corticosteroid episodes (continuous, 0–4+) at 0–<24 months of age, number of encounters (continuous, log transformed) at 0–<24 months of age, infection episodes (continuous, log transformed) at 0–<24 months of age, and age at outcome.

[c] Model 2 was additionally adjusted for maternal age, prepregnancy BMI, total gestational wt gain, pregnancy smoking status, glucose status, and mode of delivery.

[d] Model 3 was additionally adjusted for child birth wt.

[e] For narrow-spectrum antibiotic exposures, analyses were limited to participants with no broad-spectrum antibiotics during the same time window as exposure or before.

SUPPLEMENTAL TABLE 15 Multivariable Linear Regression Results for the Association of Antibiotics Episodes at <24 Months of Age With the BMI *z* Score at 48–<72 Months of Age, by Antibiotic Spectrum and Number of Episodes, Incorporating Maternal Covariates for 7 Health Care Institutions When Available (Data Only for Children Without Complex Chronic Conditions)

Episodes	Model 1[a] (*N* = 48 908), β (95% CI)	Model 2[b] (*N* = 48 908), β (95% CI)	Model 3[c] (*N* = 22 310), β (95% CI)	Model 4[d] (*N* = 12 698), β (95% CI)
Overall				
0	.0 (reference)	.0 (reference)	.0 (reference)	.0 (reference)
1	.01 (−0.01 to 0.04)	.00 (−0.02 to 0.03)	.01 (−0.03 to 0.05)	.02 (−0.03 to 0.07)
2	.06 (0.03 to 0.09)	.03 (0.00 to 0.07)	.03 (−0.01 to 0.08)	.03 (−0.02 to 0.09)
3	.07 (0.04 to 0.11)	.05 (0.01 to 0.09)	.05 (−0.01 to 0.10)	.07 (0.00 to 0.14)
4+	.11 (0.08 to 0.14)	.07 (0.03 to 0.10)	.03 (−0.01 to 0.08)	.08 (0.01 to 0.14)
Broad spectrum				
0	.0 (reference)	.0 (reference)	.0 (reference)	.0 (reference)
1	.04 (0.02 to 0.07)	.03 (0.00 to 0.05)	.01 (−0.03 to 0.04)	.02 (−0.02 to 0.07)
2	.05 (0.01 to 0.09)	.02 (−0.02 to 0.06)	.01 (−0.04 to 0.07)	.02 (−0.05 to 0.09)
3	.10 (0.04 to 0.15)	.07 (0.01 to 0.12)	.06 (−0.02 to 0.13)	.12 (0.02 to 0.22)
4+	.11 (0.06 to 0.16)	.07 (0.02 to 0.12)	.02 (−0.05 to 0.08)	.07 (−0.01 to 0.16)
Narrow spectrum[e]				
0	.0 (reference)	.0 (reference)	.0 (reference)	.0 (reference)
1	.02 (−0.01 to 0.05)	.02 (−0.01 to 0.05)	.03 (−0.01 to 0.07)	.04 (−0.01 to 0.10)
2	.04 (0.00 to 0.09)	.03 (−0.01 to 0.08)	.04 (−0.02 to 0.10)	.01 (−0.07 to 0.08)
3	.05 (−0.02 to 0.12)	.03 (−0.04 to 0.10)	.07 (−0.02 to 0.16)	.04 (−0.08 to 0.16)
4+	.09 (−0.02 to 0.20)	.03 (−0.08 to 0.14)	.00 (−0.16 to 0.15)	−.06 (−0.26 to 0.13)

[a] Corrected for clustering by site.

[b] Corrected for clustering by site and adjusted for sex, race, ethnicity, preterm birth, asthma, corticosteroid episodes (continuous, 0–4+) at 0–<24 months of age, number of encounters (continuous, log transformed) at 0–<24 months of age, infection episodes (continuous, log transformed) at 0–<24 months of age, and age at outcome.

[c] Model 2 was additionally adjusted for maternal age, prepregnancy BMI, total gestational wt gain, pregnancy smoking status, glucose status, and mode of delivery.

[d] Model 3 was additionally adjusted for child birth wt.

[e] For narrow-spectrum antibiotic exposures, analyses were limited to participants with no broad-spectrum antibiotics during the same time window as exposure or before.

SUPPLEMENTAL TABLE 16 Multivariable Logistic Regression Results for the Association of Any Exposure to Antibiotics at <24 Months of Age and Risk Obesity (≥95th Percentile) at 48–<72 Months of Age, by Timing of Antibiotic Prescription (Comparison is to BMI in the <85th Percentile)

Antibiotics	No Complex Chronic Condition, *N* = 265 652[a]		Complex Chronic Condition, *N* = 44 124[a]	
	Model 1,[b] OR (95% CI)	Model 2,[c] OR (95% CI)	Model 1,[b] OR (95% CI)	Model 2,[c] OR (95% CI)
Any, mo				
0–<24	1.10 (1.08 to 1.12)	1.04 (1.01 to 1.06)	1.09 (1.04 to 1.15)	1.00 (0.94 to 1.06)
0–<6[d,e]	1.18 (1.14 to 1.21)	1.09 (1.06 to 1.13)	1.07 (1.00 to 1.14)	1.01 (0.94 to 1.08)
6–<12[d,e]	1.10 (1.08 to 1.13)	1.02 (1.00 to 1.05)	1.05 (1.00 to 1.11)	0.96 (0.90 to 1.02)
12–<24[d,e]	1.08 (1.06 to 1.11)	1.01 (0.99 to 1.04)	1.10 (1.04 to 1.15)	1.00 (0.94 to 1.06)
Broad spectrum, mo				
0–<24	1.11 (1.08 to 1.13)	1.06 (1.04 to 1.09)	1.10 (1.05 to 1.16)	1.03 (0.97 to 1.09)
0–<6[d,e]	1.17 (1.12 to 1.23)	1.08 (1.03 to 1.14)	1.05 (0.97 to 1.14)	1.00 (0.92 to 1.09)
6–<12[d,e]	1.10 (1.07 to 1.13)	1.03 (1.00 to 1.06)	1.06 (1.00 to 1.13)	0.99 (0.92 to 1.06)
12–<24[d,e]	1.10 (1.07 to 1.12)	1.05 (1.02 to 1.07)	1.12 (1.06 to 1.18)	1.04 (0.97 to 1.11)
Narrow spectrum,[f] mo				
0–<24	1.06 (1.03 to 1.08)	1.01 (0.98 to 1.04)	1.04 (0.97 to 1.12)	0.96 (0.89 to 1.04)
0–<6[d,e]	1.17 (1.12 to 1.22)	1.09 (1.04 to 1.14)	1.09 (0.98 to 1.20)	1.01 (0.91 to 1.12)
6–<12[d,e]	1.09 (1.06 to 1.12)	1.02 (0.99 to 1.05)	1.02 (0.94 to 1.11)	0.93 (0.85 to 1.02)
12–<24[d,e]	1.04 (1.01 to 1.07)	1.00 (0.96 to 1.03)	1.04 (0.95 to 1.13)	0.97 (0.89 to 1.07)

[a] The number is smaller here than in other models because children with a BMI from the 85th to <95th percentile were excluded from this model.

[b] Corrected for clustering by site.

[c] Corrected for clustering by site and adjusted for sex, race, ethnicity, preterm birth, asthma, corticosteroid episodes (continuous, 0–4+) at 0–<24 months of age, number of encounters (continuous, log transformed) at 0–<24 months of age, infection episodes (continuous, log transformed) at 0–<24 months of age, and age at outcome.

[d] For exposure time windows, Model 2 was additionally adjusted for previous antibiotics: (1) antibiotics at 6–<12 months, adjusted for 0–<6 months antibiotics and (2) antibiotics at 12–<24 months, adjusted for 0–<12 months antibiotics.

[e] For exposure time windows, covariates were used during the same time window (infections, corticosteroids, and encounters): (1) antibiotics at 0–<6 months, covariates used for 0–<6 months; (2) antibiotics at 6–<12 months, covariates used for 6–<12 months; and (3) antibiotics at 12–<24 months, covariates used for 12–<24 months.

[f] For narrow-spectrum antibiotic exposures, analyses were limited to participants with no broad-spectrum antibiotics during the same time window as exposure or before.

SUPPLEMENTAL TABLE 17 Associations of Covariates With the BMI z Score at 48–<72 Months of Age in Models With Infections Included

Covariates	No Complex Chronic Condition (*N* = 310 947), β (95% CI)	Complex Chronic Condition (*N* = 51 603), β (95% CI)
Any antibiotics at <24 mo	.04 (0.03 to 0.05)	.06 (0.04 to 0.09)
Female sex (yes versus no)	.01 (0.01 to 0.02)	.01 (-0.02 to 0.03)
Age at outcome (mo)	.01 (0.00 to 0.01)	.00 (0.00 to 0.01)
Preterm (yes versus no)	−.22 (−0.24 to −0.20)	−.38 (−0.41 to −0.35)
Asthma (yes versus no)	.15 (0.14 to 0.17)	.14 (0.10 to 0.17)
Corticosteroid episodes at <24 mo (continuous, 0–4+)	.06 (0.05 to 0.07)	.05 (0.03 to 0.06)
No. encounters at <24 mo (log transformed)	−.02 (−0.02 to −0.01)	−.03 (−0.04 to −0.01)
Infection episodes at <24 mo (log transformed)	.02 (0.02 to 0.02)	.01 (0.00 to 0.02)
Race		
Asian American	−.21 (−0.23 to −0.19)	−.32 (−0.38 to −0.25)
African American	.06 (0.05 to 0.07)	.05 (0.02 to 0.08)
Other	.03 (0.02 to 0.05)	.03 (−0.01 to 0.07)
Unknown	.03 (0.02 to 0.05)	.11 (0.05 to 0.16)
White	.0 (ref)	.0 (ref)
Hispanic (yes versus no)	.34 (0.33 to 0.35)	.24 (0.21 to 0.28)

The model was adjusted for all covariates at the same time. We also assessed for the possibility that antibiotics were mediating the relationship between infections and wt outcomes. To do so, we ran models without including antibiotics (and only including infections). These models had parameter estimates for log-transformed infections of 0.02 (95% CI 0.01 to 0.03) for children without and 0.02 (95% CI 0.02 to 0.03) for children with complex chronic conditions, revealing minimal difference.

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