

**Antibiotic Use in Children and Youth with Asthma:
A Population-Based Case-Control Study**

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Online Supplementary Material

Table S1. International Classification of Diseases, 10th Revision (ICD-10), Ontario Health Insurance Plan (OHIP), and Canadian Classification of Health Interventions (CCI) codes for common infections and allergic conditions.

Condition	ICD-10 Code	OHIP Code	CCI Code
Asthma	J45, J46	493	
Bronchitis	J20, J22, J40	466	
Influenza	J10-J18	487	
Pneumonia	J10-J18	480	
Allergic Rhinitis	J30	477	
Eczema	L20	691	
Tonsillitis & Adenoiditis	J03, J35	463, 474	1.FR.87, 1.FR.89
Ear Infection	H60, H65, H66	380-382	1.DK.52
Appendicitis	K35-K37	540	1.NV.89

Table S2. International Classification of Diseases, 10th Revision (ICD-10) codes for complex chronic conditions.

Condition	ICD-10 Code
Anencephaly and similar malformations	Q00
Spina bifida	Q05
Encephalocele, unspecified	Q01.9
Microcephaly	Q02
Congenital hydrocephalus, unspecified	Q03.9
Other reduction deformities of brain	Q04.3
Other specified congenital malformations of brain	Q04.8
Diastematomyelia	Q06.2
Hydromyelia	Q06.4
Other specified congenital malformations of spinal cord	Q06.8
Other specified congenital malformations of nervous system	Q07.8
Congenital malformation of nervous system, unspecified	Q07.9
Parkinson's	G20
Other degenerative diseases of basal ganglia	G23
Drug-induced dystonia	G24.0
Idiopathic familial dystonia	G24.1
Idiopathic nonfamilial dystonia	G24.2
Other dystonia	G24.8
Essential tremor	G25.0
Drug-induced tremor	G25.1
Other specified forms of tremor	G25.2
Myoclonus	G25.3
Drug-induced chorea	G25.4
Other chorea	G25.5
Drug-induced tics and other tics of organic origin	G25.6
Other specified degenerative diseases of nervous system	G31.8
Multi-system degeneration	G90.3
Huntington's disease	G10
Dyskinetic cerebral palsy	G80.3
Hereditary Ataxias	G11
SMA and related syndromes	G12
Communicating hydrocephalus	G91.0
Obstructive hydrocephalus	G91.1
Normal-pressure hydrocephalus	G91.2

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Table S2. (continued).

Condition	ICD-10 Code
Post-traumatic hydrocephalus, unspecified	G91.3
Other hydrocephalus	G91.8
Hydrocephalus, unspecified	G91.9
Hydrocephalus in neoplastic disease	G94.1
Hydrocephalus in other diseases classified elsewhere	G94.2
Other diseases of spinal cord	G95
Autonomic dysreflexias	G90.4
Peripheral neuropathies in other disorders	G99
Malformations of aqueduct of Sylvius	Q03.0
Atresia of foramina of Magendie and Luschka	Q03.1
Other congenital hydrocephalus	Q03.8
Epilepsy	G40
Status epilepticus	G41
Cerebral palsy	G80
Hemiplegia	G81
Paraplegia and tetraplegia	G82
Mild mental retardation, significant impairment of behaviour requiring attention or treatment	F70.1
Mild mental retardation, other impairments of behaviour	F70.8
Moderate mental retardation	F71
Severe mental retardation	F72
Profound mental retardation	F73
Other mental retardation	F78
Unspecified mental retardation	F79
Primary disorders of muscles	G71
Other myopathies	G72
Congenital malformations of cardiac chambers and connections	Q20
Congenital malformations of cardiac septa	Q21
Congenital malformations of pulmonary and tricuspid valves	Q22
Congenital malformations of aortic and mitral valves	Q23
Other congenital malformations of heart	Q24
Congenital malformations of great arteries	Q25
Congenital malformations of great veins	Q26
Cardiomyopathy	I42
Myocardial degeneration	I51.5

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Table S2. (continued).

Condition	ICD-10 Code
Atrioventricular and left bundle-branch block	I44
Other conduction disorders	I45
Paroxysmal tachycardia	I47
Atrial fibrillation and flutter	I48
Other cardiac arrhythmias	I49
Congenital malformations of nose	Q30
Congenital malformations of larynx	Q31
Congenital malformations of trachea and bronchus	Q32
Congenital malformations of lung	Q33
Other congenital malformations of respiratory system	Q34
Chronic respiratory disease originating in the perinatal period	P27
Cystic fibrosis	E84
Renal agenesis and other reduction defects of kidney	Q60
Cystic kidney disease	Q61
Congenital obstructive defects of renal pelvis and congenital malformations of ureter	Q62
Other congenital malformations of kidney	Q63
Other congenital malformations of urinary system	Q64
Chronic kidney disease	N18
Congenital malformations of oesophagus	Q39
Congenital absence, atresia and stenosis of small intestine	Q41
Congenital absence, atresia and stenosis of large intestine	Q42
Hirschsprung's disease	Q43.1
Duplication of intestine	Q43.4
Persistent cloaca	Q43.7
Congenital malformations of gallbladder, bile ducts and liver	Q44
Other congenital malformations of digestive system	Q45
Chronic hepatitis, not elsewhere classified	K73
Fibrosis and cirrhosis of liver	K74
Autoimmune hepatitis	K75.4
Other specified inflammatory liver diseases	K75.8
Inflammatory liver disease, unspecified	K75.9
Fatty (change of) liver, not elsewhere classified	K76.0
Crohn's disease [regional enteritis]	K50
Ulcerative colitis	K51

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Table S2. (continued).

Condition	ICD-10 Code
Sickle-cell disorders	D57
Anaemia due to enzyme disorders	D55
Beta thalassaemia	D56.1
Delta-beta thalassaemia	D56.2
Hereditary persistence of fetal haemoglobin [HPFH]	D56.4
Other thalassaemias	D56.8
Other hereditary haemolytic anaemias	D58
Immunodeficiency with predominantly antibody defects	D80
Combined immunodeficiencies	D81
Immunodeficiency associated with other major defects	D82
Common variable immunodeficiency	D83
Other immunodeficiencies	D84
Other specified disorders involving the immune mechanism, not elsewhere classified	D89.8
Disorder involving the immune mechanism, unspecified	D89.9
Human immunodeficiency virus [HIV] disease	B24
Disorders of aromatic amino-acid metabolism	E70
Maple-syrup-urine disease	E71.0
Other disorders of branched-chain amino-acid metabolism	E71.1
Disorder of branched-chain amino-acid metabolism, unspecified	E71.2
Other disorders of amino-acid metabolism	E72
Congenital lactase deficiency	E73.0
Other disorders of carbohydrate metabolism	E74
Disorders of sphingolipid metabolism and other lipid storage disorders	E75
Disorders of glycoprotein metabolism	E77
Disorders of lipoprotein metabolism and other lipidaemias	E78
Lipodystrophy, not elsewhere classified	E88.1
Lipomatosis, not elsewhere classified	E88.2
Disorders of glycosaminoglycan metabolism	E76
Amyloidosis	E85
Disorders of fatty-acid metabolism	E71.3
Disorders of purine and pyrimidine metabolism	E79
Defects of catalase and peroxidase	E80.3
Gilbert's syndrome	E80.4
Crigler-Najjar syndrome	E80.5

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Table S2. (continued).

Condition	ICD-10 Code
Other disorders of bilirubin metabolism	E80.6
Disorder of bilirubin metabolism, unspecified	E80.7
Disorders of mineral metabolism	E83
Other specified metabolic disorders	E88.8
Metabolic disorder, unspecified	E88.9
Down's syndrome	Q90
Edwards' syndrome and Patau's syndrome	Q91
Monosomies and deletions from the autosomes, not elsewhere classified	Q93
Balanced autosomal rearrangement in abnormal individual	Q95.2
Balanced sex/autosomal rearrangement in abnormal individual	Q95.3
Turner's syndrome	Q96
Klinefelter's syndrome, male with more than two X chromosomes	Q98.1
Klinefelter's syndrome, male with 46,XX karyotype	Q98.2
Klinefelter's syndrome, unspecified	Q98.4
Chromosomal abnormality, unspecified	Q99.9
Short stature, not elsewhere classified	E34.3
Scoliosis	M41
Other congenital malformations of skull and face bones	Q75
Congenital malformations of spine and bony thorax	Q76
Osteochondrodysplasia with defects of growth of tubular bones and spine	Q77
Other osteochondrodysplasias	Q78
Malignant neoplasms	C00-C97
In situ neoplasms	D00-D09
Benign neoplasms	D10-D36
Neoplasms of uncertain or unknown behaviour	D37-D48

Table S3. Characteristics of the study population by type of antibiotic received (N=1,174,424).

Characteristic	No. or Mean (% or SD)				Standardized Difference *
	No Antibiotics (n=858,790)	Respiratory Antibiotics Only (n=243,887)	Non-Respiratory Antibiotics Only (n=45,884)	Respiratory and Non-Respiratory Antibiotics (n=25,863)	
Age Group at Baseline (years)					
5-9	155,487 (18.1)	65,852 (27.0)	5,005 (10.9)	4,034 (15.6)	0.214
10-14	228,315 (26.6)	54,564 (22.4)	8,700 (19.0)	3,895 (15.1)	0.098
15-19	246,935 (28.8)	68,967 (28.3)	17,230 (37.6)	9,580 (37.0)	0.011
20-24	228,053 (26.6)	54,504 (22.3)	14,949 (32.6)	8,354 (32.3)	0.098
Sex					
Female	340,094 (39.6)	112,850 (46.3)	20,994 (45.8)	14,000 (54.1)	0.135
Male	518,696 (60.4)	131,037 (53.7)	24,890 (54.2)	11,863 (45.9)	0.135
Asthma Duration Among Individuals with Asthma (years)					
Mean (SD)	11.9 (5.9)	5.9 (10.6)	10.6 (6.1)	6.1 (12.9)	0.031
Ontario Marginalization Index:					
Deprivation Quintile					
1 (lowest)	194,237 (22.6)	54,326 (22.3)	10,729 (23.4)	5,689 (22.0)	0.008
2	185,259 (21.6)	54,148 (22.2)	10,057 (21.9)	5,598 (21.6)	0.015
3	162,594 (18.9)	46,864 (19.2)	8,650 (18.9)	4,999 (19.3)	0.007
4	150,587 (17.5)	42,452 (17.4)	8,035 (17.5)	4,571 (17.7)	0.003
5 (highest)	166,113 (19.3)	46,097 (18.9)	8,413 (18.3)	5,006 (19.4)	0.011
Dependency Quintile					
1 (lowest)	280,726 (32.7)	84,488 (34.6)	14,195 (30.9)	8,394 (32.5)	0.041
2	188,495 (21.9)	53,166 (21.8)	10,014 (21.8)	5,582 (21.6)	0.004
3	147,837 (17.2)	40,709 (16.7)	7,963 (17.4)	4,426 (17.1)	0.014
4	131,046 (15.3)	36,019 (14.8)	7,347 (16.0)	3,997 (15.5)	0.014
5 (highest)	110,686 (12.9)	29,505 (12.1)	6,365 (13.9)	3,464 (13.4)	0.024

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Table S3. (continued).

Characteristic	No. or Mean (% or SD)				Standardized Difference *
	No Antibiotics (n=858,790)	Respiratory Antibiotics Only (n=243,887)	Non-Respiratory Antibiotics Only (n=45,884)	Respiratory and Non-Respiratory Antibiotics (n=25,863)	
Ethnic Concentration Quintile					
1 (lowest)	100,699 (11.7)	25,113 (10.3)	6,105 (13.3)	3,118 (12.1)	0.046
2	121,805 (14.2)	32,532 (13.3)	7,254 (15.8)	3,795 (14.7)	0.025
3	145,034 (16.9)	40,812 (16.7)	8,320 (18.1)	4,707 (18.2)	0.004
4	189,651 (22.1)	54,859 (22.5)	10,046 (21.9)	5,729 (22.2)	0.010
5 (highest)	301,601 (35.1)	90,571 (37.1)	14,159 (30.9)	8,514 (32.9)	0.042
Residential Instability Quintile					
1 (lowest)	239,385 (27.9)	74,992 (30.7)	12,840 (28.0)	7,584 (29.3)	0.063
2	170,628 (19.9)	48,245 (19.8)	9,221 (20.1)	5,066 (19.6)	0.002
3	148,298 (17.3)	41,397 (17.0)	8,240 (18.0)	4,426 (17.1)	0.008
4	144,668 (16.8)	39,518 (16.2)	7,766 (16.9)	4,400 (17.0)	0.017
5 (highest)	155,811 (18.1)	39,735 (16.3)	7,817 (17.0)	4,387 (17.0)	0.049
Rurality					
Urban	790,066 (92.0)	228,446 (93.7)	41,777 (91.0)	24,013 (92.8)	0.065
Rural	68,724 (8.0)	15,441 (6.3)	4,107 (9.0)	1,850 (7.2)	0.065
Presence of Common Infections and Allergic Conditions					
Bronchitis	10,273 (1.2)	33,565 (13.8)	847 (1.8)	3,621 (14.0)	0.492
Influenza	7,397 (0.9)	5,419 (2.2)	578 (1.3)	658 (2.5)	0.111
Pneumonia	1,818 (0.2)	10,010 (4.1)	209 (0.5)	1,069 (4.1)	0.270
Allergic Rhinitis	28,787 (3.4)	15,494 (6.4)	2,083 (4.5)	1,845 (7.1)	0.140
Eczema	43,742 (5.1)	19,422 (8.0)	5,619 (12.2)	3,519 (13.6)	0.116
Tonsillitis and Adenoiditis	8,138 (0.9)	25,252 (10.4)	886 (1.9)	3,116 (12.0)	0.416
Ear Infection	21,634 (2.5)	40,856 (16.8)	1,937 (4.2)	3,967 (15.3)	0.497
Appendicitis	1,796 (0.2)	1,101 (0.5)	198 (0.4)	224 (0.9)	0.042

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Table S3. (continued).

Characteristic	No. or Mean (% or SD)				Standardized Difference *
	No Antibiotics (n=858,790)	Respiratory Antibiotics Only (n=243,887)	Non-Respiratory Antibiotics Only (n=45,884)	Respiratory and Non-Respiratory Antibiotics (n=25,863)	
Presence of Any Complex Chronic Condition					
Yes	1,332 (0.2)	726 (0.3)	175 (0.4)	156 (0.6)	0.030
No	857,458 (99.8)	243,161 (99.7)	45,709 (99.6)	25,707 (99.4)	0.030

Abbreviation: SD, standard deviation.

* Standardized difference of >0.1 generally considered different (shown in bold).

Table S4. Number of individuals with asthma who filled at least 1 antibiotic prescription by asthma duration (N=587,212).

Antibiotic Prescriptions by Asthma Duration	No. Filled At Least 1 Antibiotic Prescription (%)				Standardized Difference *
	Asthma Duration <Q1 <6.76 y (n=146,729)	Asthma Duration Q1-Q2 6.76-11.52 y (n=146,892)	Asthma Duration Q2-Q3 11.53-16.54 y (n=146,760)	Asthma Duration ≥Q3 ≥16.55 y (n=146,831)	
All Antibiotics	54,115 (36.9)	42,131 (28.7)	42,234 (28.8)	41,457 (28.2)	0.175
Antibiotics Commonly Prescribed for Respiratory Infections	49,545 (33.8)	37,051 (25.2)	34,819 (23.7)	33,795 (23.0)	0.188
Cephalosporins	5,468 (3.7)	3,483 (2.4)	2,760 (1.9)	2,523 (1.7)	0.079
Macrolides	15,759 (10.7)	12,776 (8.7)	12,892 (8.8)	12,955 (8.8)	0.069
Penicillins	37,242 (25.4)	26,009 (17.7)	23,883 (16.3)	22,788 (15.5)	0.188

Abbreviations: Q, quartile. y, years.

* Standardized difference of >0.1 generally considered different (shown in bold).

Table S5. Unadjusted and adjusted odds of having filled at least 1 antibiotic prescription for children and youth with asthma vs. without asthma from conditional logistic regression for age and sex subgroups (N=1,174,424).

Antibiotic Prescriptions by Age Group and Sex	Unadjusted OR (95% CI)	P-Value *	Adjusted OR (95% CI)	P-Value *
All Antibiotics				
5-9	1.66 (1.63, 1.69)	<0.0001	1.45 (1.41, 1.48)	<0.0001
10-14	1.55 (1.53, 1.58)	<0.0001	1.40 (1.37, 1.43)	<0.0001
15-19	1.42 (1.40, 1.44)	<0.0001	1.31 (1.28, 1.33)	<0.0001
20-24	1.35 (1.33, 1.37)	<0.0001	1.25 (1.23, 1.28)	<0.0001
Female	1.51 (1.49, 1.53)	<0.0001	1.36 (1.34, 1.38)	<0.0001
Male	1.46 (1.44, 1.48)	<0.0001	1.32 (1.30, 1.34)	<0.0001
Antibiotics Commonly Prescribed for Respiratory Infections				
5-9	1.66 (1.63, 1.69)	<0.0001	1.45 (1.42, 1.49)	<0.0001
10-14	1.58 (1.55, 1.61)	<0.0001	1.43 (1.39, 1.46)	<0.0001
15-19	1.44 (1.42, 1.46)	<0.0001	1.32 (1.29, 1.34)	<0.0001
20-24	1.35 (1.32, 1.37)	<0.0001	1.24 (1.22, 1.27)	<0.0001
Female	1.51 (1.49, 1.53)	<0.0001	1.36 (1.34, 1.38)	<0.0001
Male	1.48 (1.46, 1.50)	<0.0001	1.34 (1.32, 1.35)	<0.0001
Cephalosporins				
5-9	1.65 (1.58, 1.73)	<0.0001	1.38 (1.30, 1.46)	<0.0001
10-14	1.68 (1.59, 1.78)	<0.0001	1.49 (1.39, 1.59)	<0.0001
15-19	1.50 (1.42, 1.58)	<0.0001	1.36 (1.27, 1.44)	<0.0001
20-24	1.43 (1.35, 1.52)	<0.0001	1.28 (1.19, 1.37)	<0.0001
Female	1.55 (1.49, 1.61)	<0.0001	1.35 (1.29, 1.42)	<0.0001
Male	1.60 (1.54, 1.66)	<0.0001	1.39 (1.33, 1.45)	<0.0001
Macrolides				
5-9	1.80 (1.74, 1.85)	<0.0001	1.52 (1.47, 1.58)	<0.0001
10-14	1.77 (1.71, 1.82)	<0.0001	1.59 (1.53, 1.65)	<0.0001
15-19	1.59 (1.55, 1.63)	<0.0001	1.46 (1.41, 1.50)	<0.0001
20-24	1.46 (1.42, 1.50)	<0.0001	1.34 (1.29, 1.38)	<0.0001
Female	1.64 (1.61, 1.68)	<0.0001	1.45 (1.42, 1.49)	<0.0001
Male	1.62 (1.59, 1.65)	<0.0001	1.46 (1.43, 1.50)	<0.0001

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Table S5. (continued).

Antibiotic Prescriptions by Age Group and Sex	Unadjusted OR (95% CI)	P-Value *	Adjusted OR (95% CI)	P-Value *
Penicillins				
5-9	1.53 (1.50, 1.56)	<0.0001	1.35 (1.31, 1.38)	<0.0001
10-14	1.44 (1.41, 1.47)	<0.0001	1.30 (1.27, 1.34)	<0.0001
15-19	1.32 (1.29, 1.34)	<0.0001	1.22 (1.20, 1.25)	<0.0001
20-24	1.24 (1.21, 1.26)	<0.0001	1.16 (1.14, 1.19)	<0.0001
Female	1.39 (1.37, 1.41)	<0.0001	1.26 (1.24, 1.28)	<0.0001
Male	1.37 (1.35, 1.39)	<0.0001	1.24 (1.23, 1.26)	<0.0001

Abbreviations: OR, odds ratio. CI, confidence interval.

The conditional logistic regression models were adjusted for Ontario Marginalization Index, rurality, bronchitis, influenza, pneumonia, allergic rhinitis, eczema, tonsillitis, ear infection, appendicitis, and complex chronic conditions.

* A p-value of <0.05 was used to determine statistical significance.