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Predicting Risk of Hospitalization in a Pediatric Population

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Ethical approval: This study was conducted under the auspices of regulation of privacy of the Emilia-Romagna Region N.3 of 24 April 2006 (title: Processing of sensitive data) of act N.1 of 30 May 2014 still in force. In addition, this study was approved by the Institutional Review Board (IRB) of Thomas Jefferson University as an expedited retrospective database/record review. The IRB granted a waiver of informed consent.

ABSTRACT (294 words)

Objectives Develop predictive models for a pediatric population that provide information for pediatricians and health authorities to identify children at risk of hospitalisation for conditions that may be impacted through improved patient care.

Design Retrospective healthcare utilisation analysis with multivariate logistic regression models.

Data Demographic information linked with utilisation of health services in the years 2006–2014 was used to predict risk of hospitalisation or death in 2015 using a longitudinal administrative database of 527,458 children aged 1 to 13 residing in the Regione Emilia-Romagna (RER), Italy in 2014.

Outcome measures Models designed to predict risk of hospitalisation or death in 2015 for problems that are potentially avoidable were developed and evaluated using the C-statistic, for calibration to assess performance across levels of predicted risk, and in terms of their sensitivity, specificity and positive predictive value.

Results Of the 527,458 children residing in RER in 2014, 6,391 children (1.21%) were hospitalized for selected conditions or died in 2015. 49,486 children (9.4%) of the population were classified in the "At Higher Risk" group using a threshold of predicted risk >2.5%. The observed risk of hospitalization (5%) for the "At Higher Risk" group was more than 4 times higher than the overall population. We observed a C-statistic of 0.78 indicating good model performance. The model was well calibrated across categories of predicted risk.

Conclusions It is feasible to develop a population-based model using a longitudinal administrative database that identifies the risk of hospitalisation for a pediatric population.

The results of this model, along with profiles of children identified as high risk are being provided to the pediatricians and other healthcare professionals providing care to this population to aid in planning for care management and interventions that may reduce their patients' likelihood of a preventable, high-cost hospitalisation.

Strengths and limitations of this study

- This study included the entire pediatric population of the Emilia-Romagna Region of Italy, 527,458 children ages 1-13.
- The study used an existing longitudinal administrative healthcare database with both the advantage of much lower cost than new data collection and the disadvantage of gaps and potential errors in administrative data.
- The results of the study are being used to assist pediatricians and health authorities manage high risk children.

INTRODUCTION

Healthcare systems have been moving from a passive approach of waiting for and reacting to patients' problems to a more active model that includes identification of patients at risk, taking the initiative in offering care and actively seeking to avoid recurrence or progression of medical problems. With the aging of populations worldwide, and high prevalence of chronic diseases, it is not surprising that these efforts have often focused on the elderly. Less attention has been paid to the pediatric population. However, despite the relatively low prevalence of chronic disease in children, there is evidence that children experience preventable hospitalizations. (1) For example, a study of pediatric inpatient claims in the United States estimated that pediatric "ambulatory care sensitive" conditions accounted for $4.05 billion (USD) in hospital charges and over 1 million hospitalization days in a one year period. (2)

Predictive risk modeling is a tool that can be used to estimate the risk of an outcome within the context of pre-specified variables and uncertainty. Predictive risk modeling may offer an opportunity to better understand individuals who may be at higher risk for an undesirable outcome. (3) A number of predictive risk modeling studies have been conducted in pediatrics; however, many of these studies have focused on children with specific medical problems or use data that is not routinely available in administrative databases. (4), (5), (6), (7), (8), (9)

Under the auspices of the Italian National Health Service (NHS), the 21 regional governments are responsible for delivering health care through a network of geographically defined Local Health Authorities. Primary care physicians, including pediatricians, work for the Local Health Authorities as independent contractors. Every Italian is expected to enroll with a primary care physician (a pediatrician for those under age 14) who serve as the 'gatekeepers" for delivering primary care and coordinating specialty services for their enrolled patients. (10) This focus on primary care is ideal for the development and implementation of a proactive model of health care.

To further encourage coordinated care, the Regione Emilia-Romagna (RER) has established Patient-Centered Medical Homes. The identification of patients who would most benefit from outreach efforts is fundamental to achieving the goals of promoting population health and practicing proactive medicine. The RER has therefore developed and implemented a population-based model to predict risk of hospitalization or death for adult residents in the region. (11) The results of the model are presented to physicians in Patient-Centered Medical Homes as patient profiles to support care management and the identification of patients who may benefit from additional outreach such as home health care, disease management, or case management.

Current risk models used in RER focus on the adult population. This paper describes the development of predictive risk models for the pediatric population using the RER's regional longitudinal administrative healthcare database to help identify children who are at risk of hospitalization for conditions that may be affected through improved patient care.

METHODS

Data Source

The RER is a region of northern Italy that lies between the River Po and Apennine Mountains with approximately 4.5 million inhabitants. RER maintains a longitudinal healthcare database for all its residents. The RER database contains patient-level demographic data (age, gender, birth and death dates, location of residence, primary care physician/pediatrician) and utilization data for inpatient (hospital discharge abstract data with ICD-9-CM diagnosis and procedure codes, and admission/discharge dates), outpatient (laboratory, diagnoses, and physician services, pharmacy claims including WHO ATC/DDD system codes), (12). specialty (therapeutic procedures, rehabilitation, and specialist visits), and emergency room visits. Inpatient medications are not captured. Patients with disabilities or low family income are eligible for exemption of service copayment for specialty visits and outpatient prescriptions, which provide some socioeconomic information. Each resident is assigned an anonymous identifier so that utilization can be tracked over time while maintaining patient privacy. (13)

Study Cohort

In Italy, children age 14 years old are required to switch from a pediatrician to a primary care physician; therefore, we limited the study population to children 1-13 years old on December 31st, 2014. The study population also was narrowed to whom met the following criteria: (i) resident of the RER for the entire year 2014, (ii) have valid

information on age, gender, local health authority, district or geographic location in 2014, (iii) alive at the beginning of 2015. The study population was stratified into three age groups: 1-2 years old (on December 31, 2014); 3-5 years old; 6-13 years old. Children less than one year old on December 31, 2014 were not included in the study population due to insufficient data for prediction of outcomes.

Dependent Variable

The outcome was defined as the occurrence of hospitalization that could have potentially been prevented or delayed with appropriate patient care or death by any cause. (11) We developed a list of hospitalizations that are potentially preventable with appropriate patient care using a three step process. First, we conducted a literature search to evaluate pediatric studies that defined potentially avoidable disease in pediatrics that could require hospitalization. (14), (15), (16) We began with the listing of ICD-9-CM codes for "pediatric ambulatory care sensitive conditions" identified in Shi et al. (15) All hospitalizations in 2013 of children in the target age groups were classified using both ICD-9-CM codes and Disease Staging categories. (17), (18) The results were reviewed by the authors of this paper and compared to the Shi et al list. A number of changes were made for this project. For example, the list of immunization preventable conditions to be included in the dependent variable was expanded to include currently available vaccines. We included additional conditions, such as acute cystitis (ICD-9-CM code of 595.0) and hypoglycemic coma (ICD-9-CM code of 251.0). Advanced stages of selected medical problems were added where Stage 1 may not be avoidable but advanced stages can

potentially be delayed or prevented through timely intervention, e.g. Stage 2 or 3 appendicitis, Stage 2 or 3 sinusitis. While certainly not always preventable, we believed that inclusion of hospitalizations for certain types of trauma and toxicities (e.g., acetaminophen toxicity, adverse drug reactions, burns) was appropriate especially for a pediatric population. These changes are summarized in Appendix, Table 1.

Finally, we used disease staging categories for inclusion of relevant hospitalizations that would have been missed using solely primary ICD-9-CM codes. For example, if a child was hospitalized with a primary diagnosis of respiratory failure with asthma (ICD-9-CM code of 493) as the secondary diagnosis, then the disease staging category of Asthma would include that admission that might have been missed by including only primary ICD-9-CM codes. This is summarized in Appendix, Table 2.

Children hospitalized for these selected conditions or who died from any cause in 2015 were counted as being positive for the outcome.

Independent Variables

A list of predictor variables was developed utilizing the RER administrative data from 2006-2014. Independent variables included information such as: demographics, socioeconomic factors, diseases/conditions grouped by etiology or body systems, mother's medical history and pregnancy/birthing information, emergency-room visits, potentially inappropriate prescriptions and antibiotic usage.

Demographic variables included: age on December 31st, 2014, gender, and citizenship (Italian or non-Italian). Children from low-income families or with disabilities

are exempt from copayments for prescriptions and specialty visits. This information was used as a potential predictor variable.

We mapped diseases defined primarily by the affected body system with the exceptions of cancer, genetic conditions, and trauma which were based on etiology (Louis, 2014) using 2014 hospital discharge data, outpatient prescription information, and specialty visit claims. A total of 24 groups were defined. Disease Staging diagnostic categories was used to map hospital admissions to the 24 body system/etiology groups. (17) (see first column of Table 1) Patients with cardiovascular diseases, chronic respiratory diseases, diabetes mellitus, epilepsy, and disorders of the thyroid were identified using the Anatomical Therapeutic Chemical (ATC) Classification System codes from outpatient prescriptions. (19) Specialty visit records were also used for identifying medical conditions of some body systems. For example, if a child was admitted to the hospital for type 1 diabetes mellitus, or visited an endocrinologist, or had filled a prescription for insulin injection(s) (ATC code of A10AB), this patient would be identified as having an endocrine diagnosis in 2014.

Severity level codes (critical (C), acute (A), urgent but deferred (U), and not urgent (N)) are assigned to individuals upon discharge from the emergency department. We excluded ER visits that resulted in a hospital admission because diagnosis information was captured by hospital discharge data with more accurate information. We believe more frequent or severe ER visits may indicate a poor outcome, therefore, number of emergency room visits by severity level was calculated for each patient.

There is evidence that the risks outweigh the benefits for certain medication usage in the pediatric population. (20) For example, certain mood-altering medications such as,

citalopram, sertraline, fluvoxamine, and any tricyclic antidepressants are not recommended in children of any age. Some medications can be harmful within specified ages. For example, loperamide is not indicated for children under three years old. For children who filled an outpatient prescription in 2014, we calculated their age at dispensation date and amount of medications they had filled, in order to identify patients with potentially inappropriate prescriptions in 2014. The number of antibiotic prescriptions utilized in 2014 was estimated since high utilization of antibiotics has been linked to decreased gut microflora, decreased immune function, and resistant strains of bacteria. (21)

For children ages 1-5 the models considered problems identified at birth as potential predictors using hospital discharge abstract data. About 86% of the newborns were healthy, with no serious medical problems noted on their birth records. Infants with diagnostic categories of premature birth with low birth weight, full-term infants with abnormal birth weight, premature with very low birth weight, or extremely low birth weight, were classified as abnormal birth weight; all other conditions were considered as a group. The mothers' delivery information, such as age at delivery, C-section, and parity, were identified based on the mothers' hospitalization records, and linked to children. Information about deliveries that occurred outside hospitals could not be captured.

Children ages 1-5 years old were also linked with information regarding their mothers' medical history and drug use during pregnancy. There is evidence on the association between pre-natal (up-to 270 days before delivery) exposure to antibiotics and the development of asthma. (22) We estimated the total exposure to any antibiotics during the pre-natal period using the mother outpatient prescription claims. We included two

categories of mother's potentially inappropriate drug use, class D (potential risks outweigh the benefits) and X (contraindicated during pregnancy), since these drugs may be linked to harm to children. Mothers' 3 year medical history before delivery was retrieved for identifying certain conditions such as abortion, diabetes and psychological condition. For about 22% of children we were not able to establish the mother-baby linkage.

We developed history variables with up to five years of data (pharmacy, specialty, hospital admission, and emergency room visit) for children in age strata 3-5 years old and 6-13 years old. Children who had conditions in any year from 2009 to 2013 were flagged as having a utilization history.

Modeling

Logistic regressions were used to estimate predicted probability for the occurrence of an inpatient hospital stay for the selected conditions, or death from any cause, for the individual patients. Since age and gender may be strongly correlated with children's' risk, we fit a total of six multivariate logistic regression models: female and male by age groups (1-2, 3-5, and 6-13 years old). All models were developed using SAS 9.3 statistical software (SAS Institute, Cary, NC, U.S.A.).

Model Validation

The predicted accuracy of the modeling was evaluated using C-statistics (the area under the receiver operating characteristics curve), comparing the results of the 'predicted' to the 'observed' outcomes in 2015. We stratified patients into risk strata based on the predicted risk of hospitalization or death. "At higher risk" was defined as children with a

predicted risk greater than 2.5%. "Higher than average" was defined as children with a predicted risk of hospitalization or death between the mean rate and 2.5%. The rest of population was grouped into "Lower than average". Calibration of the model across these risk groups was assessed by comparing observed to predicted rates among the risk groups. We also report the sensitivity, specificity and positive predictive value (PPV) for the defined risk group cutoffs.

RESULTS

Characterization of Risk Groups

A total of 527,458 children resided in RER in 2014; of those, 6,391 children (1.21%) were hospitalized for selected conditions or died in 2015. Table 1 displays the distribution of gender, age category, presence of selected chronic conditions, ER visits, selected prescription drug usage, co-pay exemption for income or disability and specialty visits for the eligible RER residents as of December 31 2014.

Table 1 also compares the characteristics of the total selected pediatric population to the subgroups of the population classified by risk categories based on the model results. Forty nine thousand four hundred and eighty-six children (9.4%) of the population were classified in the "At Higher Risk" group using a threshold of predicted risk >2.5%. The children predicted to be At Higher Risk were more likely to be male (58.9%) compared to 51.5% in the total population. The two youngest age strata (1-2 and 3-5 years) had much higher proportions of children identified in the At Higher Risk group than the 6-13 year old

children. For example, 18,112 (23%) of the children age 1-2 years were identified in the At Higher Risk Group. This age category includes 36% of the At Higher Risk children although it represents 15% of the total pediatric population. Children in the "At Higher Risk" category were more likely to have each of the selected conditions. When looking at the highest prevalence conditions, 43.8% of children in the "At Higher Risk" category had an ear, nose, or throat problem, compared to 6.1% in the overall population; 5.5% had a gastrointestinal problem compared to 1.4% in the overall population; 4.3% had a neurological problem compared to 0.7% in the overall population; 14.7% had a respiratory problem compared to 3.9% in the overall population; and 11.7% had a skin problem compared to 7.5% in the overall population.

Children identified as being "At Higher Risk" were much more likely to have a history of emergency room visits and were more likely to have a history of 2, 3, or more antibiotic prescriptions. Overall, 14.6% of children had 3 or more antibiotic prescriptions; in the "At Higher Risk" category 51.7% had a history of 3 or more antibiotic prescriptions. Children with exemptions from co-payments due to either family income or disability were more likely to be identified as being At Higher Risk as were children with a history of medical or surgical specialty visits.

Table 2 displays information about the delivery (for the children age 1-5) and medical history of the mother for those children where we were able to match to their mother's record. First children, children who were delivered by caesarean section and children where an abnormal birth weight or other problems were noted at birth were more likely to be classified in the "At Higher Risk" category. If the mother was prescribed a potentially

inappropriate drug or an antibiotic during pregnancy, the child was more likely to be classified in the "At Higher Risk" category. When examining a 3 year medical history of the mother, the mother's asthma, cardiovascular disease, diabetes mellitus, or mental health problems, or the record of a previous abortion, were all relatively frequent and more prevalent in the mothers of children predicted to be in the "At Higher Risk" category.

Calibration

The population was divided into three risk groups based on predicted probability of hospitalization as defined above. We observed good calibration; each stratum's predicted risks were similar to observed prevalence of hospitalizations or deaths. (Figure 1) Individuals, who fell in the "At Higher Risk" group, with predicted risk greater than 2.5%, had 2,683 predicted events based on the model results, and 2,737 observed events. While the overall rate of hospitalization or death for children ages 1-13 was 1.21% the predicted and observed risk of the "At Higher Risk" group was over 5%.

Model Performance among Risk Groups

We observed a c-statistic of 0.78 indicating good model performance (Table 3). The sensitivity (proportion predicted to be At Higher Risk of those who had an event in 2015) was 0.43 and 0.70 for predicted risk categories of "at higher risk" and "higher than average", respectively. In other words, among those whom were hospitalized or deceased in 2015, 43% were predicted to have risk greater than 2.5% of hospitalization or death,

and 70% have risk higher than average. The specificity (proportion predicted to be at a "lower" risk of those who did not have an event) was 0.91 and 0.72 for the predicted 'higher' and "higher than average" risk categories; among those who were not hospitalized and did not die in 2015, 91% were not predicted to be "at higher risk". The positive predictive value (proportion with an event of those who were predicted to be at an elevated risk) was 0.06 and 0.03 for the "higher" and "higher than average" predicted risk categories. In other words, of those individuals who were estimated to have a >2.5% risk of hospitalization or death approximately 6% had an event in 2015.

DISCUSSION

We have developed a population-based model that identifies risk of hospitalization for potentially preventable problems in a pediatric population including all children under the age of 14 living in the RER of Italy. The C-statistic of 0.78 indicates that the model performs well. By comparison, in a study predicting high-cost pediatric patients, Leininger et al reported a C-statistic of 0.73. (9)

We believe that the definition of the dependent variable used in our models increases the likelihood that they are identifying patients whose risk may be reduced through proactive care. We have updated previously published criteria to include hospitalizations that may have been prevented by currently available vaccines. And we have used the logic of disease staging to include relevant hospitalizations that would have been missed using solely primary ICD-9-CM codes. Specifics of the selection criteria are available in the supplemental material.

The richness of the administrative data available in the RER allowed for a robust definition of the predictive variables. The RER data allow for the linkage of patients' use of diverse in and out-patient health care services over multiple years. In addition, the ability to link child and mother's information allows the models to consider some of the mother's medical history such as the presence of chronic disease and use of prescription drugs in the years prior to birth as well as complications that may have arisen at birth.

There are limitations to our models. The models were developed with administrative data which lack some of the clinical specificity which would be useful in assessing patient risk. Children who have not had the types of encounters included in the RER database would have potentially missing information. The RER database does not have encounter level diagnostic data available documenting visits with the primary care pediatrician. The administrative data have very limited information available about the patient and family socio economic status. Our models use prior utilization among the predictor variables. With the administrative date, we cannot distinguish appropriate from inappropriate prior utilization which may bias our results. Despite their limitations administrative data have many advantages for a project such as ours. They are relatively inexpensive to analyze and in the case of the RER include a large population over multiple years.

While the evidence was mixed, a systematic review suggests that hospitalizations can be prevented in children with medical complexity. (1) The Local Health Authority of Parma has begun working with the primary care pediatricians caring for the patients identified by the models to develop individual "profiles" of children identified as being at

higher risk. Data in the profiles, along with the more detailed information available in the medical record, can be used by the pediatricians to assess what additional intervention, if any, may help to manage the child's risk. For example, review of the profiles of higher risk children can help identify children whose parents might be contacted for a visit if they have not been seen recently. Summaries of prescriptions that have been filled from the profiles can be reviewed for potential over use, under use, or inappropriate use of mediation. High risk children with chronic illness might be referred to a specialist or home health care provided.

The RER healthcare system offers several advantages in the goal of reducing potentially preventable hospitalization. Every child is enrolled with a primary care pediatrician. The population is quite stable allowing for continuity of care. Through the Italian National Health Service every child is entitled to health care with little or no cost at the point of service. While the primary care pediatricians are paid on a per capita basis the RER can negotiate incentive payments and monitor improvements in care that may help to reduce avoidable hospitalizations. If successful, the results of the models can be applied by other Local Health Authorities in the Regione Emilia-Romagna, other Italian regions, and other countries with similar data availability.

Contributors: DZL, VM, ML, and JSG were responsible for the conceptualization of this project. MR and ML were responsible for creation of the datasets used in this project. DZL, CAC, VM, MR, and JSG were responsible for the definition of analytical variables. MR and ML were responsible for modeling and statistical analysis. DZL managed the research team. CAC, VM, ML, and JSG advised on the analyses and results. All authors contributed to the preparation of the manuscript.

Competing interests: DZL and JSG declare personal fees from Truven Health Analytics. CAC, MR, ML, JM, ML, and VM declare no conflict of interests.

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Table 1: Study Population 2014

	Total Population		At Higher Risk		Higher than average		Lower than average	
			Risk >2.5%		Risk 1.2-2.5%		Risk <1.2%	
	527,458		49,486		99,714		378,258	
	Number	%	Number	%	Number	%	Number	%
Gender								
Female	255,875	48.5%	20,315	41.1%	43,030	43.2%	192,530	50.9%
Male	271,583	51.5%	29,171	58.9%	56,684	56.8%	185,728	49.1%
Age Group								
1 to 2 years	78,051	14.8%	18,112	36.6%	44,084	44.2%	15,855	4.2%
3 to 5 years	125,459	23.8%	20,180	40.8%	35,543	35.6%	69,736	18.4%
6 to 13 years	323,948	61.4%	11,194	22.6%	20,087	20.1%	292,667	77.4%
Selected condition/body system								
Cancer	1,138	0.2%	477	1.0%	252	0.3%	409	0.1%
Cardiovascular	1,624	0.3%	653	1.3%	211	0.2%	760	0.2%
Dental Conditions	442	0.1%	138	0.3%	109	0.1%	195	0.1%
Endocrine	6,458	1.2%	1,276	2.6%	1,074	1.1%	4,108	1.1%
Ear, Nose, Throat	31,919	6.1%	21,664	43.8%	7,376	7.4%	2,879	0.8%
Eye	821	0.2%	165	0.3%	145	0.1%	511	0.1%
Genetic Conditions	274	0.1%	188	0.4%	29	0.0%	57	0.0%
Gastrointestinal	7,380	1.4%	2,724	5.5%	1,578	1.6%	3,078	0.8%
Genitourinary	3,389	0.6%	987	2.0%	836	0.8%	1,566	0.4%
OB/GYN	128	0.0%	17	0.0%	19	0.0%	92	0.0%
Hematological	1,114	0.2%	596	1.2%	247	0.2%	271	0.1%
Hepatobiliary	245	0.0%	82	0.2%	39	0.0%	124	0.0%
Immunologic Disease	199	0.0%	80	0.2%	45	0.0%	74	0.0%
Infectious Disease	869	0.2%	596	1.2%	160	0.2%	113	0.0%
Male Genital	1,329	0.3%	179	0.4%	209	0.2%	941	0.2%
Musculoskeletal	3,817	0.7%	664	1.3%	453	0.5%	2,700	0.7%
Neurologic Diseases	3,738	0.7%	2,123	4.3%	912	0.9%	703	0.2%
Nutrition	924	0.2%	446	0.9%	201	0.2%	277	0.1%
Other Conditions	1,703	0.3%	1,150	2.3%	247	0.2%	306	0.1%
Neonatal Conditions	186	0.0%	111	0.2%	50	0.1%	25	0.0%
Psychological	854	0.2%	388	0.8%	141	0.1%	325	0.1%
Respiratory	20,450	3.9%	7,285	14.7%	5,886	5.9%	7,279	1.9%
Skin	39,344	7.5%	5,809	11.7%	7,461	7.5%	26,074	6.9%
Trauma	737	0.1%	177	0.4%	167	0.2%	393	0.1%
ER visits based on severity level								
Critical	182	0.0%	117	0.2%	35	0.0%	30	0.0%

Acute	15,029	2.8%	5,219	10.5%	3,915	3.9%	5,895	1.6%
Urgent but could be deferred	118,372	22.4%	26,945	54.5%	33,241	33.3%	58,186	15.4%
Not Urgent	45,336	8.6%	11,216	22.7%	13,080	13.1%	21,040	5.6%
Inappropriate Rx*	8,077	1.5%	2,376	4.8%	3,090	3.1%	2,611	0.7%
Antibiotic use								
1	114,421	21.7%	8,248	16.7%	24,544	24.6%	81,629	21.6%
2	63,151	12.0%	9,359	18.9%	19,035	19.1%	34,757	9.2%
3+	76,878	14.6%	25,587	51.7%	29,144	29.2%	22,147	5.9%
Non-Italian citizen	90,760	17.2%	8,975	18.1%	18,390	18.4%	63,395	16.8%
Copay exempted based on family income/employment status	244,911	46.4%	37,502	75.8%	64,776	65.0%	142,633	37.7%
Copay exempted based on disabled status	6,173	1.2%	2,029	4.1%	1,321	1.3%	2,823	0.7%
Specialty visits in pediatrics								
Medical	12,642	2.4%	3,987	8.1%	2,735	2.7%	5,920	1.6%
Surgical	8,982	1.7%	2,060	4.2%	2,294	2.3%	4,628	1.2%

Table 2: Birthing and Medical History of Mother*

	Total Population		At Higher Risk		Higher than average		Lower than average	
			Risk >2.5%		Risk 1.2-2.5%		Risk <1.2%	
	203,510		38,292		79,627		85,591	
	Number	%	Number	%	Number	%	Number	%
Birthing								
Age at delivery**								
24 and less	12,728	6.3%	3,275	8.6%	5,651	7.1%	3,802	4.4%
25-34	88,370	43.4%	18,227	47.6%	35,681	44.8%	34,462	40.3%
35-39	45,575	22.4%	8,170	21.3%	17,679	22.2%	19,726	23.0%
40 and over	12,529	6.2%	2,344	6.1%	4,528	5.7%	5,657	6.6%
First delivery	99,190	48.7%	23,336	60.9%	42,662	53.6%	33,192	38.8%
C-section	48,282	23.7%	11,370	29.7%	19,480	24.5%	17,432	20.4%
Baby's birth condition								
Normal Newborns	172,497	84.8%	30,214	78.9%	67,522	84.8%	74,761	87.3%
Abnormal Birth Weight	20,128	9.9%	4,757	12.4%	7,756	9.7%	7,615	8.9%
Other Abnormal Birth Condition	10,885	5.3%	3,321	8.7%	4,349	5.5%	3,215	3.8%
Medical History								
Number of ordinary hospitalization 1 year before delivery								
1	16,145	7.9%	4,578	12.0%	6,856	8.6%	4,711	5.5%
2+	3,920	1.9%	1,670	4.4%	1,500	1.9%	750	0.9%
Inappropriate prescription during pregnancy								
Class D	10,594	5.2%	2,970	7.8%	3,886	4.9%	3,738	4.4%
Class X	4,874	2.4%	1,086	2.8%	1,811	2.3%	1,977	2.3%
Antibiotic use during pregnancy	60,679	29.8%	14,422	37.7%	25,757	32.3%	20,500	24.0%
3-year history before delivery								
Abortion	19,919	9.8%	4,970	13.0%	8,165	10.3%	6,784	7.9%
Asthma	35,590	17.5%	9,026	23.6%	14,894	18.7%	11,670	13.6%
Bacterial pneumonia	188	0.1%	36	0.1%	14	0.0%	138	0.2%
Cardiovascular disease	18,756	9.2%	5,068	13.2%	7,742	9.7%	5,946	6.9%
Diabetes	2,602	1.3%	1,003	2.6%	1,106	1.4%	493	0.6%
Hypertension	140	0.1%	51	0.1%	39	0.0%	50	0.1%
Infection	935	0.5%	283	0.7%	325	0.4%	327	0.4%
Psychological condition	9,215	4.5%	2,701	7.1%	3,709	4.7%	2,805	3.3%

*Information about the delivery was considered only for children 1-5 years old.
** For 22% of children we were not able to establish the mother-baby linkage.

Table 3: Observed and Predicted Events by Risk Group

Risk groups (predicted risk range)	N	Average predicted risk	Observed prevalence	Expected frequency based on predicted risk	Number of observed events
Lower than average (<=1.2%)	378,258	0.5%	0.5%	2,018	1,896
Higher than average (1.2-2.5%)	99,714	1.7%	1.8%	1,690	1,758
At higher risk (>2.5%)	49,486	5.4%	5.5%	2,683	2,737
TOTAL	527,458		1.2%	6,391	6,391

Table 4: C-statistic, Sensitivity, Specificity, and PPV

	C-statistic (overall model) = 0.78	
	Cut-off points for comparison	
	"At higher risk"[1] score	"At higher risk"[1] + "Higher than average"[2] score
Sensitivity[3]	0.43	0.70
Specificity[4]	0.91	0.72
Positive Predictive Value[5]	0.06	0.03
True Positives[6]	2,737	4,495

[1]"At higher risk" is defined as patients with a predicted risk of hospitalization of > 2.5%.

[2]"At higher risk"[1] + "Higher than average", is defined as patients with a predicted risk of hospitalization of > 1.2%.

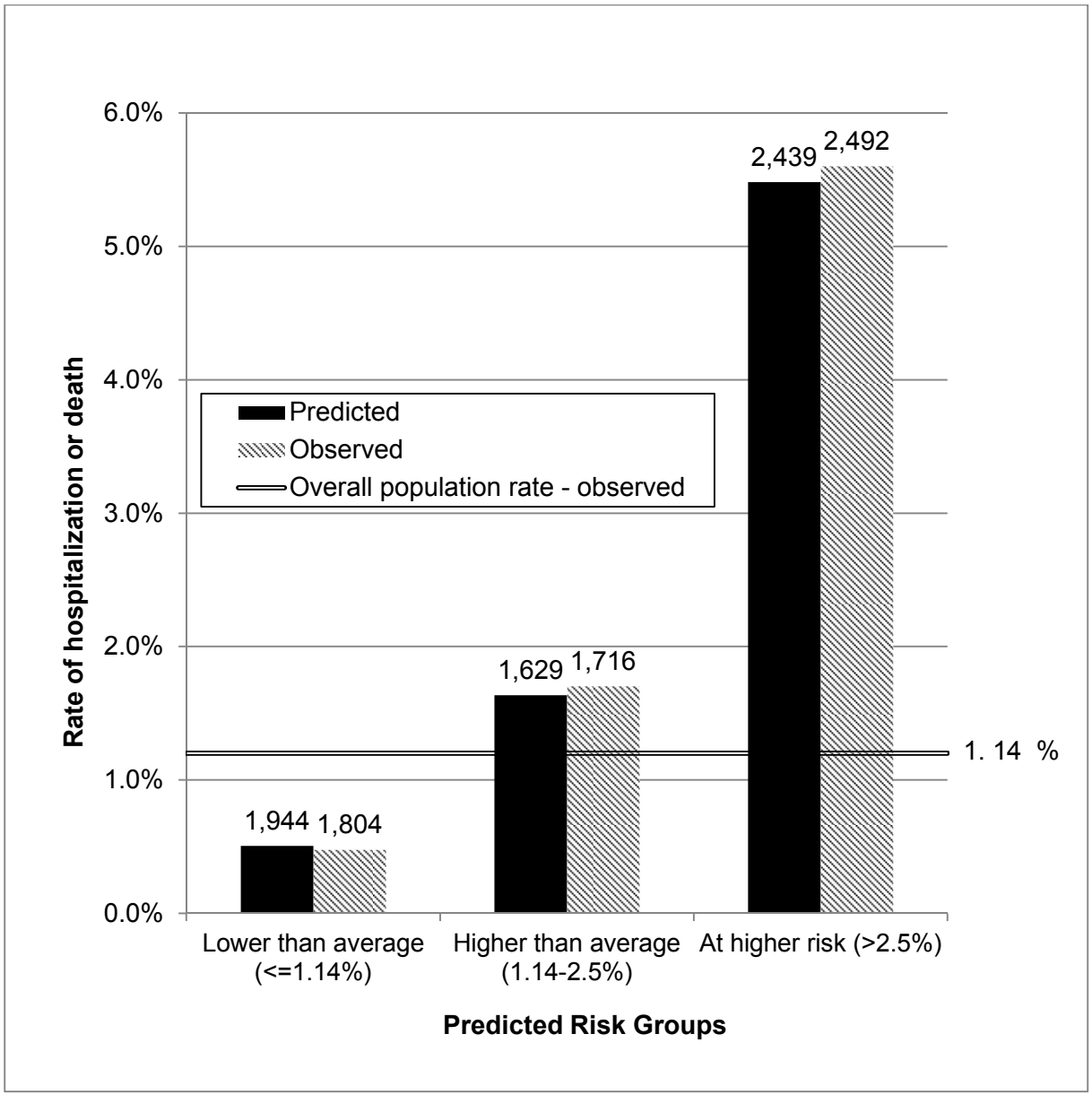
[3] Sensitivity is defined as the proportion of those hospitalized who were predicted to be hospitalized (true positive rate).

[4] Specificity is the proportion of those not hospitalized who were not predicted to be hospitalized (true negative rate).

[5] Positive Predictive Value is the proportion of those predicted to be hospitalized who were actually hospitalized.

[6] Positive Predictives are the number of residents who were predicted to be at risk of hospitalization at the predicted risk threshold and were actually hospitalized

Figure 1: Model calibration: predicted and observed prevalence of hospitalization or death in 2015 by risk category



STROBE 2007 (v4) checklist of items to be included in reports of observational studies in epidemiology*

Checklist for cohort, case-control, and cross-sectional studies (combined)

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2-3
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4-5
Objectives	3	State specific objectives, including any pre-specified hypotheses	5
Methods			
Study design	4	Present key elements of study design early in the paper	6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	6
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	7
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	7-11
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	*7-11*
Bias	9	Describe any efforts to address potential sources of bias	7-11
Study size	10	Explain how the study size was arrived at	7
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	7-11
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	11-12
		(*b*) Describe any methods used to examine subgroups and interactions	
		(*c*) Explain how missing data were addressed	
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed	

		Cross-sectional study—If applicable, describe analytical methods taking account of sampling strategy	
		(*e*) Describe any sensitivity analyses	
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	12
		(b) Give reasons for non-participation at each stage	
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	12-14, Table 1 and 2
		(b) Indicate number of participants with missing data for each variable of interest	
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	12-14, Table 3
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	
		Cross-sectional study—Report numbers of outcome events or summary measures	
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	14-15, Table 4, Fig. 1
		(*b*) Report category boundaries when continuous variables were categorized	
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	
Discussion			
Key results	18	Summarise key results with reference to study objectives	15
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	16
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	17
Generalisability	21	Discuss the generalisability (external validity) of the study results	17
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	18

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.
Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Predicting Risk of Hospitalization: A retrospective population-based analysis in a Pediatric Population in Emilia-Romagna, Italy

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Predicting Risk of Hospitalization: A retrospective population-based analysis in a Pediatric Population in Emilia-Romagna, Italy

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Ethical approval: This study was conducted under the auspices of regulation of privacy of the Emilia-Romagna Region N.3 of 24 April 2006 (title: Processing of sensitive data) of act N.1 of 30 May 2014 still in force. In addition, this study was approved by the Institutional Review Board (IRB) of Thomas Jefferson University as an expedited retrospective database/record review. The IRB granted a waiver of informed consent.

ABSTRACT (294 words)

Objectives Develop predictive models for a pediatric population that provide information for pediatricians and health authorities to identify children at risk of hospitalisation for conditions that may be impacted through improved patient care.

Design Retrospective healthcare utilisation analysis with multivariable logistic regression models.

Data Demographic information linked with utilisation of health services in the years 2006–2014 was used to predict risk of hospitalisation or death in 2015 using a longitudinal administrative database of 527,458 children aged 1 to 13 residing in the Regione Emilia-Romagna (RER), Italy in 2014.

Outcome measures Models designed to predict risk of hospitalisation or death in 2015 for problems that are potentially avoidable were developed and evaluated using the C-statistic, for calibration to assess performance across levels of predicted risk, and in terms of their sensitivity, specificity and positive predictive value.

Results Of the 527,458 children residing in RER in 2014, 6,391 children (1.21%) were hospitalized for selected conditions or died in 2015. 49,486 children (9.4%) of the population were classified in the "At Higher Risk" group using a threshold of predicted risk >2.5%. The observed risk of hospitalization (5%) for the "At Higher Risk" group was more than 4 times higher than the overall population. We observed a C-statistic of 0.78 indicating good model performance. The model was well calibrated across categories of predicted risk.

Conclusions It is feasible to develop a population-based model using a longitudinal administrative database that identifies the risk of hospitalisation for a pediatric population.

The results of this model, along with profiles of children identified as high risk are being provided to the pediatricians and other healthcare professionals providing care to this population to aid in planning for care management and interventions that may reduce their patients' likelihood of a preventable, high-cost hospitalisation.

Strengths and limitations of this study

- This study included the entire pediatric population of the Emilia-Romagna Region of Italy, 527,458 children ages 1-13.
- The study used an existing longitudinal administrative healthcare database with both the advantage of much lower cost than new data collection and the disadvantage of gaps and potential errors in administrative data.
- The results of the study are being used to assist pediatricians and health authorities manage high risk children.

INTRODUCTION

Healthcare systems have been moving from a passive approach of waiting for and reacting to patients' problems to a more active model that includes identification of patients at risk, taking the initiative in offering care and actively seeking to avoid recurrence or progression of medical problems. With the aging of populations worldwide, and high prevalence of chronic diseases, it is not surprising that these efforts have often focused on the elderly. Less attention has been paid to the pediatric population. However, despite the relatively low prevalence of chronic disease in children, there is evidence that children experience preventable hospitalizations. (1) For example, a study of pediatric inpatient claims in the United States estimated that pediatric "ambulatory care sensitive" conditions accounted for $4.05 billion (USD) in hospital charges and over 1 million hospitalization days in a one year period. (2)

Predictive risk modeling is a tool that can be used to estimate the risk of an outcome within the context of pre-specified variables and uncertainty. Predictive risk modeling may offer an opportunity to better understand individuals who may be at higher risk for an undesirable outcome. (3) A number of predictive risk modeling studies have been conducted in pediatrics; however, many of these studies have focused on children with specific medical problems or use data that is not routinely available in administrative databases. (4), (5), (6), (7), (8), (9)

Under the auspices of the Italian National Health Service (NHS), the 21 regional governments are responsible for delivering health care through a network of geographically defined Local Health Authorities. Primary care physicians, including pediatricians, work for the Local Health Authorities as independent contractors. Every Italian is expected to enroll with a primary care physician (a pediatrician for those under age 14) who serve as the 'gatekeepers" for delivering primary care and coordinating specialty services for their enrolled patients. (10) This focus on primary care is ideal for the development and implementation of a proactive model of health care.

To further encourage coordinated care, the Regione Emilia-Romagna (RER) has established Patient-Centered Medical Homes. The identification of patients who would most benefit from outreach efforts is fundamental to achieving the goals of promoting population health and practicing proactive medicine. The RER has therefore developed and implemented a population-based model to predict risk of hospitalization or death for adult residents in the region. (11) The results of the model are presented to physicians in Patient-Centered Medical Homes as patient profiles to support care management and the identification of patients who may benefit from additional outreach such as home health care, disease management, or case management.

Current risk models used in RER focus on the adult population. This paper describes the development of predictive risk models for the pediatric population using the RER's regional longitudinal administrative healthcare database to help identify children who are at risk of hospitalization for conditions that may be affected through improved patient care.

METHODS

Data Source

The RER is a region of northern Italy that lies between the River Po and Apennine Mountains with approximately 4.5 million inhabitants. RER maintains a longitudinal healthcare database for all its residents. The RER database contains patient-level demographic data (age, gender, birth and death dates, location of residence, primary care physician/pediatrician) and utilization data for inpatient (hospital discharge abstract data with ICD-9-CM diagnosis and procedure codes, and admission/discharge dates), outpatient (laboratory, diagnoses, and physician services, pharmacy claims including WHO ATC/DDD system codes), (12). specialty (therapeutic procedures, rehabilitation, and specialist visits), and emergency room visits. Inpatient medications are not captured. Patients with disabilities or low family income are eligible for exemption of service copayment for specialty visits and outpatient prescriptions, which provide some socioeconomic information. Each resident is assigned an anonymous identifier so that utilization can be tracked over time while maintaining patient privacy. (13)

Study Cohort

In Italy, children age 14 years old are required to switch from a pediatrician to a primary care physician; therefore, we limited the study population to children 1-13 years old on December 31st, 2014. The study population also was narrowed to exclude children who did not reside in RER for the entire year 2014. The study population was stratified

into three age groups: 1-2 years old (on December 31, 2014); 3-5 years old; 6-13 years old. Children less than one year old on December 31, 2014 were not included in the study population due to insufficient data for prediction of outcomes.

Dependent Variable

The outcome was defined as the occurrence of hospitalization that could have potentially been prevented or delayed with appropriate patient care or death by any cause. (11) We developed a list of hospitalizations that are potentially preventable with appropriate patient care using a three step process. First, we conducted a literature search to evaluate pediatric studies that defined potentially avoidable disease in pediatrics that could require hospitalization. (14), (15), (16) We began with the listing of ICD-9-CM codes for "pediatric ambulatory care sensitive conditions" identified in Shi et al. (15) All hospitalizations in 2013 of children in the target age groups were classified using both ICD-9-CM codes and Disease Staging categories. (17), (18) The results were reviewed by the authors of this paper and compared to the Shi et al list. A number of changes were made for this project. For example, the list of immunization preventable conditions to be included in the dependent variable was expanded to include currently available vaccines. We included additional conditions, such as acute cystitis (ICD-9-CM code of 595.0) and hypoglycemic coma (ICD-9-CM code of 251.0). Advanced stages of selected medical problems were added where Stage 1 may not be avoidable but advanced stages can potentially be delayed or prevented through timely intervention, e.g. Stage 2 or 3 appendicitis, Stage 2 or 3 sinusitis. While certainly not always preventable, we believed

that inclusion of hospitalizations for certain types of trauma and toxicities (e.g., acetaminophen toxicity, adverse drug reactions, burns) was appropriate especially for a pediatric population. These changes are summarized in Appendix 1.

Finally, we used disease staging categories for inclusion of relevant hospitalizations that would have been missed using solely primary ICD-9-CM codes. For example, if a child was hospitalized with a primary diagnosis of respiratory failure with asthma (ICD-9-CM code of 493) as the secondary diagnosis, then the disease staging category of Asthma would include that admission that might have been missed by including only primary ICD-9-CM codes. This is summarized in Appendix 2.

Children hospitalized for these selected conditions or who died from any cause in 2015 were counted as being positive for the outcome.

Independent Variables

A list of predictor variables was developed utilizing the RER administrative data from 2006-2014. Independent variables included information such as: demographics, socioeconomic factors, diseases/conditions grouped by etiology or body systems, mother's medical history and pregnancy/birthing information, emergency-room visits, potentially inappropriate prescriptions and antibiotic usage.

Demographic variables included age on December 31st, 2014, gender, and citizenship (Italian or non-Italian). Children from low-income families or with disabilities are exempt from copayments for prescriptions and specialty visits. This information was used as a potential predictor variable.

We mapped diseases defined primarily by the affected body system with the exceptions of cancer, genetic conditions, and trauma which were based on etiology (11) using 2014 hospital discharge data, outpatient prescription information, and specialty visit claims. A total of 24 groups were defined. Disease Staging diagnostic categories was used to map hospital admissions to the 24 body system/etiology groups. (17) (see first column of Table 1) Patients with cardiovascular diseases, chronic respiratory diseases, diabetes mellitus, epilepsy, and disorders of the thyroid were identified using the Anatomical Therapeutic Chemical (ATC) Classification System codes from outpatient prescriptions. (19) Specialty visit records were also used for identifying medical conditions of some body systems. For example, if a child was admitted to the hospital for type 1 diabetes mellitus, or visited an endocrinologist, or had filled a prescription for insulin injection(s) (ATC code of A10AB), this patient would be identified as having an endocrine diagnosis in 2014.

Severity level codes (critical (C), acute (A), urgent but deferred (U), and not urgent (N)) are assigned to individuals upon discharge from the emergency department. We excluded ER visits that resulted in a hospital admission because diagnosis information was captured by hospital discharge data with more accurate information. We believe more frequent or severe ER visits may indicate a poor outcome, therefore, number of emergency room visits by severity level was calculated for each patient.

There is evidence that the risks outweigh the benefits for certain medication usage in the pediatric population. (20) For example, certain mood-altering medications such as, citalopram, sertraline, fluvoxamine, and any tricyclic antidepressants are not recommended in children of any age. Some medications can be harmful within specified ages. For example, loperamide is not indicated for children under three years old. For

children who filled an outpatient prescription in 2014, we calculated their age at dispensation date and amount of medications they had filled, in order to identify patients with potentially inappropriate prescriptions in 2014. The number of antibiotic prescriptions utilized in 2014 was estimated since high utilization of antibiotics has been linked to decreased gut microflora, decreased immune function, and resistant strains of bacteria. (21)

For children ages 1-5 the models considered problems identified at birth as potential predictors using hospital discharge abstract data. About 86% of the newborns were healthy, with no serious medical problems noted on their birth records. Infants with diagnostic categories of premature birth with low birth weight, full-term infants with abnormal birth weight, premature with very low birth weight, or extremely low birth weight, were classified as abnormal birth weight; all other conditions were considered as a group. The mothers' delivery information, such as age at delivery, C-section, and parity, were identified based on the mothers' hospitalization records, and linked to children. Information about deliveries that occurred outside hospitals could not be captured.

Children ages 1-5 years old were also linked with information regarding their mothers' medical history and drug use during pregnancy. There is evidence on the association between pre-natal (up-to 270 days before delivery) exposure to antibiotics and the development of asthma. (22) We estimated the total exposure to any antibiotics during the pre-natal period using the mother outpatient prescription claims. We included two categories of mother's potentially inappropriate drug use, class D (potential risks outweigh the benefits) and X (contraindicated during pregnancy), since these drugs may be linked to harm to children. Mothers' 3 year medical history before delivery was retrieved for

identifying certain conditions such as abortion, diabetes and psychological condition. For about 22% of children we were not able to establish the mother-baby linkage.

We developed history variables with up to five years of data (pharmacy, specialty, hospital admission, and emergency room visit) for children in age strata 3-5 years old and 6-13 years old. Children who had conditions in any year from 2009 to 2013 were flagged as having a utilization history.

Modeling

Logistic regression was used to estimate predicted probabilities for the occurrence of an inpatient hospital stay for the selected conditions, or death from any cause, for the individual patients. Since age and gender may be strongly correlated with children's' risk, we fit a total of six multivariable logistic regression models: female and male by age groups (1-2, 3-5, and 6-13 years old). All models were developed using SAS 9.3 statistical software (SAS Institute, Cary, NC, U.S.A.).

Model Validation

The predicted accuracy of the modeling was evaluated using C-statistics (the area under the receiver operating characteristics curve), comparing the results of the 'predicted' to the 'observed' outcomes in 2015. We stratified patients into risk strata based on the predicted risk of hospitalization or death. "At higher risk" was defined as children with a predicted risk greater than 2.5%. "Higher than average" was defined as children with a predicted risk of hospitalization or death between the mean rate and 2.5%. The rest of population was grouped into "Lower than average". These risk strata were defined to yield

a manageable number of patients to review for the typical pediatric panel of approximately 800 patients. Calibration of the model across these risk groups was assessed by comparing observed to predicted rates among the risk groups. We also report the sensitivity, specificity and positive predictive value (PPV) for the defined risk group cutoffs.

RESULTS

Characterization of Risk Groups

A total of 568,117 children ages 1 through 13 resided in RER in 2014. We excluded from our anlysis 40,659 children (7.2%) who did not reside in RER for the entire year resulting in a population of 527,458 children. Of those, 6,391 children (1.21%) were hospitalized for selected conditions or died in 2015. Table 1 displays the distribution of gender, age category, presence of selected chronic conditions, ER visits, selected prescription drug usage, co-pay exemption for income or disability and specialty visits for the eligible RER residents as of December 31 2014.

Table 1 also compares the characteristics of the total selected pediatric population to the subgroups of the population classified by risk categories based on the model results. Forty nine thousand four hundred and eighty-six children (9.4%) of the population were classified in the "At Higher Risk" group using a threshold of predicted risk >2.5%. The children predicted to be At Higher Risk were more likely to be male (58.9%) compared to 51.5% in the total population. The two youngest age strata (1-2 and 3-5 years) had much higher proportions of children identified in the At Higher Risk group than the 6-13 year old

children. For example, 18,112 (23%) of the children age 1-2 years were identified in the At Higher Risk Group. This age category includes 36% of the At Higher Risk children although it represents 15% of the total pediatric population. Children in the "At Higher Risk" category were more likely to have each of the selected conditions. When looking at the highest prevalence conditions, 43.8% of children in the "At Higher Risk" category had an ear, nose, or throat problem, compared to 6.1% in the overall population; 5.5% had a gastrointestinal problem compared to 1.4% in the overall population; 4.3% had a neurological problem compared to 0.7% in the overall population; 14.7% had a respiratory problem compared to 3.9% in the overall population; and 11.7% had a skin problem compared to 7.5% in the overall population.

Children identified as being "At Higher Risk" were much more likely to have a history of emergency room visits and were more likely to have a history of 2, 3, or more antibiotic prescriptions. Overall, 14.6% of children had 3 or more antibiotic prescriptions; in the "At Higher Risk" category 51.7% had a history of 3 or more antibiotic prescriptions. Children with exemptions from co-payments due to either family income or disability were more likely to be identified as being At Higher Risk as were children with a history of medical or surgical specialty visits.

Table 2 displays information about the delivery (for the children age 1-5) and medical history of the mother for those children where we were able to match to their mother's record. First children, children who were delivered by caesarean section and children where an abnormal birth weight or other problems were noted at birth were more likely to be classified in the "At Higher Risk" category. If the mother was prescribed a potentially

inappropriate drug or an antibiotic during pregnancy, the child was more likely to be classified in the "At Higher Risk" category. When examining a 3 year medical history of the mother, the mother's asthma, cardiovascular disease, diabetes mellitus, or mental health problems, or the record of a previous abortion, were all relatively frequent and more prevalent in the mothers of children predicted to be in the "At Higher Risk" category.

Calibration

The population was divided into three risk groups based on predicted probability of hospitalization as defined above. We observed good calibration; each stratum's predicted risks were similar to observed prevalence of hospitalizations or deaths. (Figure 1) Individuals, who fell in the "At Higher Risk" group, with predicted risk greater than 2.5%, had 2,683 predicted events based on the model results, and 2,737 observed events. While the overall rate of hospitalization or death for children ages 1-13 was 1.21% the predicted and observed risk of the "At Higher Risk" group was over 5%.

Model Performance among Risk Groups

We observed a c-statistic of 0.78 indicating good model performance (Table 3). The sensitivity (proportion predicted to be At Higher Risk of those who had an event in 2015) was 0.43 and 0.70 for predicted risk categories of "at higher risk" and "higher than average", respectively (Table 4). In other words, among those whom were hospitalized or deceased in 2015, 43% were predicted to have risk greater than 2.5% of hospitalization or

death, and 70% have risk higher than average. The specificity (proportion predicted to be at a "lower" risk of those who did not have an event) was 0.91 and 0.72 for the predicted 'higher' and "higher than average" risk categories; among those who were not hospitalized and did not die in 2015, 91% were not predicted to be "at higher risk". The positive predictive value (proportion with an event of those who were predicted to be at an elevated risk) was 0.06 and 0.03 for the "higher" and "higher than average" predicted risk categories. In other words, of those individuals who were estimated to have a >2.5% risk of hospitalization or death approximately 6% had an event in 2015. (Regression coefficients and significance levels of independent variables for multivariable logistic regression models for each the 6 age and gender strata are included in Appendix 3).

DISCUSSION

We have developed a population-based model that identifies risk of hospitalization for potentially preventable problems in a pediatric population including all children under the age of 14 living in the RER of Italy. The C-statistic of 0.78 indicates that the model performs well. By comparison, in a study predicting high-cost pediatric patients, Leininger et al reported a C-statistic of 0.73. (9) In their work in predictive risk modeling in the UK, Billings et al reported a C-statistics of .685 (23) and C-statistics ranging from .731 to .780. (24) However, neither of these papers focused on a pediatric population. In a project also conducted in the Emilia-Romagna region of Italy but focused on the adult population, Louis et al (11) reported a C-statistic of .856. Given the similar organization of the health care system and the similar database used for the adult and pediatric analyses, we believe that

the somewhat lower C-staitstic in the pediatric study results form the fact that hospitalization is less frequent in children.

We believe that the definition of the dependent variable used in our models increases the likelihood that they are identifying patients whose risk may be reduced through proactive care. We have updated previously published criteria to include hospitalizations that may have been prevented by currently available vaccines. And we have used the logic of disease staging to include relevant hospitalizations that would have been missed using solely primary ICD-9-CM codes. Specifics of the selection criteria are available in the supplemental material.

The richness of the administrative data available in the RER allowed for a robust definition of the predictive variables. The RER data allow for the linkage of patients' use of diverse in and out-patient health care services over multiple years. In addition, the ability to link child and mother's information allows the models to consider some of the mother's medical history such as the presence of chronic disease and use of prescription drugs in the years prior to birth as well as complications that may have arisen at birth.

There are limitations to our models. The models were developed with administrative data which lack some of the clinical specificity which would be useful in assessing patient risk. Children who have not had the types of encounters included in the RER database would have potentially missing information. The RER database does not have encounter level diagnostic data available documenting visits with the primary care pediatrician. The administrative data have very limited information available about the patient and family socio economic status. Our models use prior utilization among the

predictor variables. With the administrative date, we cannot distinguish appropriate from inappropriate prior utilization which may bias our results. Despite their limitations administrative data have many advantages for a project such as ours. They are relatively inexpensive to analyze and in the case of the RER include a large population over multiple years.

While the evidence was mixed, a systematic review suggests that hospitalizations can be prevented in children with medical complexity. (1) The Local Health Authority of Parma has begun working with the primary care pediatricians caring for the patients identified by the models to develop individual "profiles" of children identified as being at higher risk. Data in the profiles, along with the more detailed information available in the medical record, can be used by the pediatricians to assess what additional intervention, if any, may help to manage the child's risk. For example, review of the profiles of higher risk children can help identify children whose parents might be contacted for a visit if they have not been seen recently. Summaries of prescriptions that have been filled from the profiles can be reviewed for potential over use, under use, or inappropriate use of mediation. High risk children with chronic illness might be referred to a specialist or home health care provided.

The RER healthcare system offers several advantages in the goal of reducing potentially preventable hospitalization. Every child is enrolled with a primary care pediatrician. The population is quite stable allowing for continuity of care. Through the Italian National Health Service every child is entitled to health care with little or no cost at the point of service. While the primary care pediatricians are paid on a per capita basis the

RER can negotiate incentive payments and monitor improvements in care that may help to reduce avoidable hospitalizations. If successful, the results of the models can be applied by other Local Health Authorities in the Regione Emilia-Romagna, other Italian regions, and other countries with similar data availability.

Contributors: DZL, VM, ML, and JSG were responsible for the conceptualization of this project. MR and ML were responsible for creation of the datasets used in this project. DZL, CAC, VM, MR, and JSG were responsible for the definition of analytical variables. MR and ML were responsible for modeling and statistical analysis. DZL managed the research team. CAC, VM, ML, JM, and JSG advised on the analyses and results. All authors contributed to the preparation of the manuscript.

Competing interests: DZL and JSG declare personal fees from Truven Health Analytics. CAC, MR, ML, JM, ML, and VM declare no conflict of interests.

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Table 1: Study Population 2014

	Total Population		At Higher Risk		Higher than average		Lower than average	
			Risk >2.5%		Risk >1.2-2.5%		Risk ≤1.2%	
	527,458		49,486		99,714		378,258	
	Number	%	Number	%	Number	%	Number	%
Gender								
Female	255,875	48.5%	20,315	41.1%	43,030	43.2%	192,530	50.9%
Male	271,583	51.5%	29,171	58.9%	56,684	56.8%	185,728	49.1%
Age Group								
1 to 2 years	78,051	14.8%	18,112	36.6%	44,084	44.2%	15,855	4.2%
3 to 5 years	125,459	23.8%	20,180	40.8%	35,543	35.6%	69,736	18.4%
6 to 13 years	323,948	61.4%	11,194	22.6%	20,087	20.1%	292,667	77.4%
Selected condition/body system								
Cancer	1,138	0.2%	477	1.0%	252	0.3%	409	0.1%
Cardiovascular	1,624	0.3%	653	1.3%	211	0.2%	760	0.2%
Dental Conditions	442	0.1%	138	0.3%	109	0.1%	195	0.1%
Endocrine	6,458	1.2%	1,276	2.6%	1,074	1.1%	4,108	1.1%
Ear, Nose, Throat	31,919	6.1%	21,664	43.8%	7,376	7.4%	2,879	0.8%
Eye	821	0.2%	165	0.3%	145	0.1%	511	0.1%
Genetic Conditions	274	0.1%	188	0.4%	29	0.0%	57	0.0%
Gastrointestinal	7,380	1.4%	2,724	5.5%	1,578	1.6%	3,078	0.8%
Genitourinary	3,389	0.6%	987	2.0%	836	0.8%	1,566	0.4%
OB/GYN	128	0.0%	17	0.0%	19	0.0%	92	0.0%
Hematological	1,114	0.2%	596	1.2%	247	0.2%	271	0.1%
Hepatobiliary	245	0.0%	82	0.2%	39	0.0%	124	0.0%
Immunologic Disease	199	0.0%	80	0.2%	45	0.0%	74	0.0%
Infectious Disease	869	0.2%	596	1.2%	160	0.2%	113	0.0%
Male Genital	1,329	0.3%	179	0.4%	209	0.2%	941	0.2%
Musculoskeletal	3,817	0.7%	664	1.3%	453	0.5%	2,700	0.7%
Neurologic Diseases	3,738	0.7%	2,123	4.3%	912	0.9%	703	0.2%
Nutrition	924	0.2%	446	0.9%	201	0.2%	277	0.1%
Other Conditions	1,703	0.3%	1,150	2.3%	247	0.2%	306	0.1%
Neonatal Conditions	186	0.0%	111	0.2%	50	0.1%	25	0.0%
Psychological	854	0.2%	388	0.8%	141	0.1%	325	0.1%
Respiratory	20,450	3.9%	7,285	14.7%	5,886	5.9%	7,279	1.9%
Skin	39,344	7.5%	5,809	11.7%	7,461	7.5%	26,074	6.9%
Trauma	737	0.1%	177	0.4%	167	0.2%	393	0.1%
ER visits based on severity level								
Critical	182	0.0%	117	0.2%	35	0.0%	30	0.0%
Acute	15,029	2.8%	5,219	10.5%	3,915	3.9%	5,895	1.6%

Urgent but could be deferred	118,372	22.4%	26,945	54.5%	33,241	33.3%	58,186	15.4%
Not Urgent	45,336	8.6%	11,216	22.7%	13,080	13.1%	21,040	5.6%
Inappropriate Rx*	8,077	1.5%	2,376	4.8%	3,090	3.1%	2,611	0.7%
Antibiotic use								
1	114,421	21.7%	8,248	16.7%	24,544	24.6%	81,629	21.6%
2	63,151	12.0%	9,359	18.9%	19,035	19.1%	34,757	9.2%
3+	76,878	14.6%	25,587	51.7%	29,144	29.2%	22,147	5.9%
Non-Italian citizen	90,760	17.2%	8,975	18.1%	18,390	18.4%	63,395	16.8%
Copay exempted based on family income/employment status	244,911	46.4%	37,502	75.8%	64,776	65.0%	142,633	37.7%
Copay exempted based on disabled status	6,173	1.2%	2,029	4.1%	1,321	1.3%	2,823	0.7%
Specialty visits in pediatrics								
Medical	12,642	2.4%	3,987	8.1%	2,735	2.7%	5,920	1.6%
Surgical	8,982	1.7%	2,060	4.2%	2,294	2.3%	4,628	1.2%

Table 2: Birthing and Medical History of Mother*

	Total Population		At Higher Risk		Higher than average		Lower than average	
			Risk >2.5%		Risk >1.2-2.5%		Risk ≤1.2%	
	203,510		38,292		79,627		85,591	
	Number	%	Number	%	Number	%	Number	%
Birthing								
Age at delivery**								
24 and less	12,728	6.3%	3,275	8.6%	5,651	7.1%	3,802	4.4%
25-34	88,370	43.4%	18,227	47.6%	35,681	44.8%	34,462	40.3%
35-39	45,575	22.4%	8,170	21.3%	17,679	22.2%	19,726	23.0%
40 and over	12,529	6.2%	2,344	6.1%	4,528	5.7%	5,657	6.6%
First delivery	99,190	48.7%	23,336	60.9%	42,662	53.6%	33,192	38.8%
C-section	48,282	23.7%	11,370	29.7%	19,480	24.5%	17,432	20.4%
Baby's birth condition								
Normal Newborns	172,497	84.8%	30,214	78.9%	67,522	84.8%	74,761	87.3%
Abnormal Birth Weight	20,128	9.9%	4,757	12.4%	7,756	9.7%	7,615	8.9%
Other Abnormal Birth Condition	10,885	5.3%	3,321	8.7%	4,349	5.5%	3,215	3.8%
Medical History								
Number of ordinary hospitalization 1 year before delivery								
1	16,145	7.9%	4,578	12.0%	6,856	8.6%	4,711	5.5%
2+	3,920	1.9%	1,670	4.4%	1,500	1.9%	750	0.9%
Inappropriate prescription during pregnancy								
Class D	10,594	5.2%	2,970	7.8%	3,886	4.9%	3,738	4.4%
Class X	4,874	2.4%	1,086	2.8%	1,811	2.3%	1,977	2.3%
Antibiotic use during pregnancy	60,679	29.8%	14,422	37.7%	25,757	32.3%	20,500	24.0%
3-year history before delivery								
Abortion	19,919	9.8%	4,970	13.0%	8,165	10.3%	6,784	7.9%
Asthma	35,590	17.5%	9,026	23.6%	14,894	18.7%	11,670	13.6%
Bacterial pneumonia	188	0.1%	36	0.1%	14	0.0%	138	0.2%
Cardiovascular disease	18,756	9.2%	5,068	13.2%	7,742	9.7%	5,946	6.9%
Diabetes	2,602	1.3%	1,003	2.6%	1,106	1.4%	493	0.6%
Hypertension	140	0.1%	51	0.1%	39	0.0%	50	0.1%
Infection	935	0.5%	283	0.7%	325	0.4%	327	0.4%
Psychological condition	9,215	4.5%	2,701	7.1%	3,709	4.7%	2,805	3.3%

*Information about the delivery was considered only for children 1-5 years old.
** For 22% of children we were not able to establish the mother-baby linkage.

Table 3: Observed and Predicted Events by Risk Group

Risk groups (predicted risk range)	N	Average predicted risk	Observed prevalence	Expected frequency based on predicted risk	Number of observed events
Lower than average (≤1.2%)	378,258	0.5%	0.5%	2,018	1,896
Higher than average (>1.2-2.5%)	99,714	1.7%	1.8%	1,690	1,758
At higher risk (>2.5%)	49,486	5.4%	5.5%	2,683	2,737
TOTAL	527,458		1.2%	6,391	6,391

Table 4: C-statistic, Sensitivity, Specificity, and PPV

	C-statistic (overall model) = 0.78	
	Cut-off points for comparison	
	"At higher risk"[1] score	"At higher risk"[1] + "Higher than average"[2] score
Sensitivity[3]	0.43	0.70
Specificity[4]	0.91	0.72
Positive Predictive Value[5]	0.06	0.03
True Positives[6]	2,737	4,495

[1]"At higher risk" is defined as patients with a predicted risk of hospitalization of > 2.5%.

[2]"At higher risk"[1] + "Higher than average", is defined as patients with a predicted risk of hospitalization of >1.2%.

[3] Sensitivity is defined as the proportion of those hospitalized who were predicted to be hospitalized (true positive rate).

[4] Specificity is the proportion of those not hospitalized who were not predicted to be hospitalized (true negative rate).

[5] Positive Predictive Value is the proportion of those predicted to be hospitalized who were actually hospitalized.

[6] Positive Predictives are the number of residents who were predicted to be at risk of hospitalization at the predicted risk threshold and were actually hospitalized

Figure 1: Model calibration: predicted and observed prevalence of hospitalization or death in 2015 by risk category

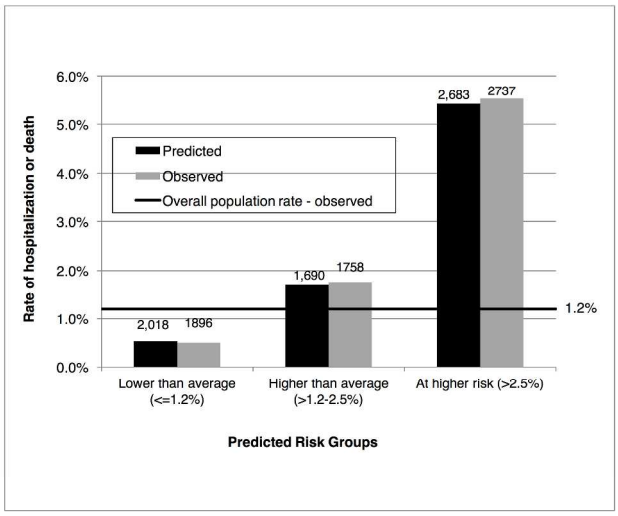

Figure 1. Model calibration: predicted and observed prevalence of hospitalization or death in 2015 by risk category

279x215mm (300 x 300 DPI)

Appendix 1: Hospitalization that could have potentially been prevented or delayed with appropriate patient care

Condition Category		Added Conditions	
	ICD-9-CM Code+	**ICD-9-CM Code**	**Disease Staging Category**
Immunization preventable conditions	033 Whooping cough	052 Chickenpox	NEU14(Meningitis: Bacterial)*
	~~390 Rheumatic fever without mention of heart involvement~~	055 Measles	RES11 (Influenza)**
	~~391 Rheumatic fever with heart involvement~~	056 Rubella	RES23(Respiratory Syncytial Virus Infections 1.06 above)**
	037 Tetanus	072 Mumps	
	045 Acute poliomyelitis		
	320.0 Hemophilus meningitis		
Grand mal status/epileptic convulsions	345 Epilepsy and recurrent seizures		
Convulsion	780.3 Convulsions		
Severe ENT infections	382 Suppurative and unspecified otitis media	381 Nonsuppurative otitis media and Eustachian tube disorders	ENT19 (Pharyngitis: Non-Streptococcal)*
	462 Acute pharyngitis		ENT21 (Sinusitis 2/3)**
	463 Acute tonsillitis		
	465 Acute upper respiratory infections of multiple or unspecified sites		
	472.1 Chronic pharyngitis		
Tuberculosis	011 Pulmonary tuberculosis	010 Primary tuberculous infection	
	012 Other respiratory tuberculosis	137 Late effects of tuberculosis	
	013 Tuberculosis of meninges and central nervous system		
	014 Tuberculosis of intestines, peritoneum, and mesenteric glands		
	015 Tuberculosis of bones and joints		
	016 Tuberculosis of genitourinary system		
	017 Tuberculosis of other organs		
	018 Miliary tuberculosis		
Bacterial pneumonia	481 Pneumococcal pneumonia [Streptococcus pneumoniae pneumonia]	482.0 Pneumonia due to Klebsiella pneumoniae	
	482.2 Pneumonia due to Hemophilus influenzae [H. influenzae]	482.1 Pneumonia due to Pseudomonas	
	482.3 Pneumonia due to Streptococcus	482.4 Pneumonia due to Staphylococcus	
	482.9 Bacterial pneumonia	482.8 Pneumonia due to	

+ From Shi, L. & Lu, N. Individual Sociodemographic Characteristics Associated with Hospitalization for Pediatric Ambulatory Care Sensitive Conditions. *Journal of Health Care for the Poor and Underserved*. 2000; 11(4): 373-384.

* Expansion of condition included in Shi and Lu

** Addition to conditions in Shi and Lu

	unspecified	other specified bacteria	
	483 Pneumonia due to other specified organism		
	485 Bronchopneumonia, organism unspecified		
	486 Pneumonia, organism unspecified		
Asthma	493 Asthma		
Cellulitis	681 Cellulitis and abscess of finger and toe		
	682 Other cellulitis and abscess		
	683 Acute lymphadenitis		
	686 Other local infections of skin and subcutaneous tissue		
	707 Chronic ulcer of skin		
Diabetes	250.1 Diabetes with ketoacidosis		
	250.2 Diabetes with hyperosmolarity		
	250.3 Diabetes with other coma		
	250.8 Diabetes with other specified manifestations		
	250.9 Diabetes with unspecified complication		
	250.0 Diabetes mellitus without mention of complication		
Gastroenteritis	558.9 Other and unspecified noninfectious gastroenteritis and colitis	008.6 Enteritis due to specified virus	GIS32 (Salmonellosis)**
		008.8 Other organism, not elsewhere classified	GIS37 (Ulcerative Colitis 2/3)**
		009 Ill-defined intestinal infections	
		007 Other protozoal intestinal diseases	
		558.2 Toxic gastroenteritis and colitis	
		558.4 Eosinophilic gastroenteritis and colitis	
Kidney and urinary infection	590 Infections of kidney	595.0 Acute cystitis	GUS10(Urinary Tract Infections 2/3)*
	~~599.0 Urinary tract infection, site not specified~~	595.9 Cystitis, unspecified	GUS83(Other Disorders of Kidney or Ureter 2/3)*
	599.9 Unspecified disorder of urethra and urinary tract		
Dehydration-volume depletion	276.5 Volume depletion		
Iron deficiency anemia	280.1 Secondary to inadequate dietary iron intake		
	280.8 Other specified iron deficiency anemias		
	280.9 Iron deficiency anemia, unspecified		
Nutritional deficiencies	260 Kwashiorkor		
	261 Nutritional marasmus		
	262 Other severe protein-calorie malnutrition		
	268.0 Rickets, active		
	268.1 Rickets, late effect		

Failure to thrive	783.4 Lack of expected normal physiological development in childhood		
Dental conditions	521 Diseases of hard tissues of teeth		
	522 Diseases of pulp and periapical tissues		
	523 Gingival and periodontal diseases		
	525 Other diseases and conditions of the teeth and supporting structures		
	528 Diseases of the oral soft tissues, excluding lesions specific for gingiva and tongue		
Pelvic inflammatory disease	614 Inflammatory disease of ovary, fallopian tube, pelvic cellular tissue, and peritoneum		
Hypoglycemia	251.2 Hypoglycemia, unspecified	251.0 Hypoglycemic coma	
		251.1 Other specified hypoglycemia	
		775.0 Syndrome of "infant of a diabetic mother"	
Appendicitis (stage 2 or 3)			GIS05(Appendicitis 2/3)*
Congenital Syphilis		090.9 Congenital syphilis, unspecified	
Cardiovascular disease (including CHF)		428 Heart failure	
Trauma (including Head Injury)			TRA01(Acetaminophen Toxicity)*
			TRA02(Adverse Drug Reactions)*
			TRA04(Burns)*
			TRA05(Burns, Chemical: Esophagus, Stomach, or Small Intestine)*
			TRA09(Toxic Effects of Nonmedicinal Agents)*
			NEU11(Injury: Craniocerebral)*
			TRA80(Effects of Environment and Other External Causes 3)*
Rheumatic fever	390 Rheumatic fever without mention of heart involvement		
	391 Rheumatic fever with heart involvement		
Monotropic hormone deficiency			END10 (Monotropic hormone deficiency 2/3)*
Foreign Body: Nasopharynx, Throat or Bronchus			ENT04 (Foreign Body: Nasopharynx, Throat or Bronchus)*
Gastritis			GIS17 (Gastritis 2/3)*

Appendix 2: Admissions for a complication of selected conditions

Condition Category	ICD-9-CM Code	Disease Staging Category includes Admissions for a Complication of Selected Conditions*
Immunization preventable conditions	033 Whooping cough	RES28(Pertussis)
	037 Tetanus	INF28 (Tetanus)
	045 Acute poliomyelitis	INF20 (Poliomyelitis)
	320.0 Hemophilus meningitis	NEU14(Meningitis: Bacterial)
	052 Chickenpox	INF30 (Varicella (Chickenpox))
	055 Measles	INF18 (Measles or Rubeola)
	056 Rubella	INF25 (Rubella: Acquired)
	072 Mumps	INF32 (Mumps)
Grand mal status/epileptic convulsions	345 Epilepsy and recurrent seizures	NEU07(Epilepsy)
Convulsion	780.3 Convulsions	
Severe ENT infections	381 Nonsuppurative otitis media and Eustachian tube disorders	ENT18 (Otitis Media),ENT19 (Pharyngitis: Non-Streptococcal),ENT81 (Other Ear, Nose and Throat Disorders), ENT82(Other Ear, Nose, and Throat Infections)
	382 Suppurative and unspecified otitis media	
	462 Acute pharyngitis	
	463 Acute tonsillitis	
	465 Acute upper respiratory infections of multiple or unspecified sites	
	472.1 Chronic pharyngitis	
Tuberculosis	010 Primary tuberculous infection	RES27 (Tuberculosis)
	011 Pulmonary tuberculosis	
	012 Other respiratory tuberculosis	
	013 Tuberculosis of meninges and central nervous system	
	014 Tuberculosis of intestines, peritoneum, and mesenteric glands	
	015 Tuberculosis of bones and joints	
	016 Tuberculosis of genitourinary system	
	017 Tuberculosis of other organs	
	018 Miliary tuberculosis	
	137 Late effects of tuberculosis	
Bacterial pneumonia	481 Pneumococcal pneumonia [Streptococcus pneumoniae pneumonia]	RES12(Mycoplasma pneumoniae Infection), RES15(Pneumonia: Bacterial), RES16(Pneumonia: Chlamydial), RES17(Pneumonia: Legionella), RES24 (Rhino, Adeno, and Corona Virus Infections)
	482.0 Pneumonia due to Klebsiella pneumoniae	
	482.1 Pneumonia due to Pseudomonas	
	482.2 Pneumonia due to Hemophilus influenzae [H. influenzae]	
	482.3 Pneumonia due to Streptococcus	
	482.4 Pneumonia due to Staphylococcus	
	482.8 Pneumonia due to other specified bacteria	
	482.9 Bacterial pneumonia unspecified	
	483 Pneumonia due to other specified organism	
	485 Bronchopneumonia, organism unspecified	
	486 Pneumonia, organism unspecified	
Asthma	493 Asthma	RES02 (Asthma)
Cellulitis	681 Cellulitis and abscess of finger and toe	

	682 Other cellulitis and abscess	
	683 Acute lymphadenitis	
	686 Other local infections of skin and subcutaneous tissue	
	707 Chronic ulcer of skin	
Diabetes	250.1 Diabetes with ketoacidosis	END04(Diabetes Mellitus Type 1), END05(Diabetes Mellitus Type 2, Unspecified Types of Diabetes, and Hyperglycemic States)
	250.2 Diabetes with hyperosmolarity	
	250.3 Diabetes with other coma	
	250.8 Diabetes with other specified manifestations	
	250.9 Diabetes with unspecified complication	
	250.0 Diabetes mellitus without mention of complication	
Gastroenteritis	008.6 Enteritis due to specified virus	GIS81(Gastroenteritis)
	008.8 Other organism, not elsewhere classified	
	009 Ill-defined intestinal infections	
	007 Other protozoal intestinal diseases	
	558.2 Toxic gastroenteritis and colitis	
	558.4 Eosinophilic gastroenteritis and colitis	
	558.9 Other and unspecified noninfectious gastroenteritis and colitis	
	599.9 Unspecified disorder of urethra and urinary tract	
	595.0 Acute cystitis	
	595.9 Cystitis, unspecified	
Kidney and urinary infection	590 Infections of kidney	GUS10(Urinary Tract Infections, 1.02 above), GUS83(Other Disorders of Kidney or Ureter), GUS01(Bladder Disorders), END04(Diabetes Mellitus Type 1), END05(Diabetes Mellitus Type 2),HEM06(Anemia: Sickle Cell), INF03(Candida (Monilial) Infections), MGS08(Prostatitis), PED06(Anomaly: Defects of Kidney), GUS02(Calculus of the Urinary Tract), GYN34(Vulvovaginitis), HEM19(Neoplasm, Malignant: Leukemia, Acute Nonlymphocytic), MGS01(Benign Prostatic Hypertrophy), NEU23(Injury: Spine and Spinal Cord: Low Back), PED09(Anomaly: Neural Tube Defects)
Dehydration-volume depletion	276.5 Volume depletion	GIS12 (Food Poisoning: Other Organisms, 1.02 above), GIS13(Food Poisoning: S. aureus), PED05(Anomaly: Congenital Megacolon), NUT80(Other Electrolyte Disorders), CVS12(Digoxin Toxicity), PSY05(Drug Abuse, Dependence, Intoxication: Alcohol)
Iron deficiency anemia	280.1 Secondary to inadequate dietary iron intake	HEM05(Anemia: Iron Deficiency)
	280.8 Other specified iron deficiency anemias	
	280.9 Iron deficiency anemia, unspecified	
Nutritional deficiencies	260 Kwashiorkor	NUT81 (Other Nutritional and Metabolic Disorders),END18 (Vitamin D Deficiency), PSY13(Eating disorders: Anorexia Nervosa), GIS06(Celiac Disease)
	261 Nutritional marasmus	
	262 Other severe protein-calorie malnutrition	
	268.0 Rickets, active	
	268.1 Rickets, late effect	
Failure to thrive	783.4 Lack of expected normal physiological development in childhood	

Dental conditions	521 Diseases of hard tissues of teeth	DEN02(Dental Disease), DEN04 (Gingival and Periodontal Disease), DEN81(Other Disorders of Oral Cavity)
	522 Diseases of pulp and periapical tissues	
	523 Gingival and periodontal diseases	
	525 Other diseases and conditions of the teeth and supporting structures	
	528 Diseases of the oral soft tissues, excluding lesions specific for gingiva and tongue	
Pelvic inflammatory disease	614 Inflammatory disease of ovary, fallopian tube, pelvic cellular tissue, and peritoneum	GYN28 (Pelvic Inflammatory Disease), INF04(Chlamydial Infection Except Trachoma or Pneumonia)
Hypoglycemia	251.2 Hypoglycemia, unspecified	END08(Hypoglycemia)
	251.0 Hypoglycemic coma	
	251.1 Other specified hypoglycemia	
	775.0 Syndrome of "infant of a diabetic mother"	
Appendicitis (stage 2 or 3)		NA
Congenital Syphilis	090.9 Congenital syphilis, unspecified	PED30 (Syphilis: Congenital)
Cardiovascular disease	428 Heart failure	CVS05(Aortic Stenosis), CVS07(Cardiomyopathies), CVS09(Congestive Heart Failure), CVS10(Coronary Artery Disease Prior Coronary Revascularization), CVS11(Coronary Artery Disease w/o Prior Coronary Revascularization), CVS13(Essential Hypertension,CVS16 Mitral Stenosis), CVS14(Infective Endocarditis), CVS15(Mitral Regurgitation), CVS16(Mitral Stenosis), CVS18(Pericarditis: Chronic), CVS19(Pericarditis: Viral or Traumatic) , CVS83(Other Cardiac Conditions), END07(Hyperthyroidism), END09(Hypothyroidism), END15(Neoplasm: Pheochromocytoma), END16(Primary Amyloidosis), GEN01(Down's Syndrome), HEM03(Anemia: Folic Acid Deficiency), HEM04(Anemia: Hemolytic, HEM05 Anemia: Iron Deficiency), HEM06(Anemia: Sickle Cell, HEM07(Anemia: Thalassemia), HEM08(Anemia: Vitamin B-12 Deficiency), HEM34(Neoplasm, Malignant: Multiple Myeloma), HEM35(Neoplasm, Malignant: Waldenstrom's Macroglobulinemia), HEM36(Polycythemia Vera), HEP12(Pancreatitis, INF23 Rheumatic Fever), INF27(Syphilis: Acquired), MUS32(Muscular Dystrophy), MUS39(Progressive Systemic Sclerosis), MUS40(Rheumatoid Arthritis), PED02(Anomaly: Atrial Septal Defect), PED10(Anomaly: Other Congenital Heart Disease), PED11(Anomaly: Pulmonary Valve Stenosis), PED12(Anomaly: Tetralogy of Fallot), PED14(Anomaly: Transposition of the Great Arteries), PED15(Anomaly: Ventricular Septal Defects), PSY05(Drug Abuse, Dependence, Intoxication: Alcohol), RES15(Pneumonia: Bacterial)
Trauma (Head Injury)		NA

Rheumatic fever	390 Rheumatic fever without mention of heart involvement	INF23 (Rheumatic fever)
	391 Rheumatic fever with heart involvement	
Monotropic hormone deficiency		NA
Foreign Body: Nasopharynx, Throat or Bronchus		NA
Gastritis		NA

Appendix 3. Regression coefficients and significance levels

Male 1-2 years old

Variable	Coefficient	P-value
Intercept	-4.4619	<.0001
Age at end of 2012	-0.1783	0.013
Number of ER visits labeled as 'C: Critical': 1+	0.6582	0.3476
Number of ER visits labeled as 'A: Acute': 1	0.4812	0.0001
Number of ER visits labeled as 'A: Acute': 2+	0.6205	0.0099
Number of ER visits labeled as 'U: Urgent but could be deferred': 1	0.2002	0.02
Number of ER visits labeled as 'U: Urgent but could be deferred': 2+	0.4258	<.0001
Number of ER visits labeled as 'N: Not Urgent': 1+	0.255	0.003
Cancer (specialty visit)	0.5055	0.2369
Cancer (hospital admission)	1.3543	0.013
Cardiovascular (drug use)	1.5456	0.008
Cardiovascular (hospital admission)	0.3149	0.3629
Skin (specialty visit)	-0.0047	0.9725
Dental Conditions (hospital admission)	-0.7102	0.3781
Endocrine (specialty visit)	1.3936	<.0001
Endocrine (hospital admission or drug use)	0.8038	0.0182
Ear, Nose, Throat (specialty visit)	0.5473	<.0001
Ear, Nose, Throat (hospital admission)	0.0494	0.839
Eye (hospital admission)	-0.2042	0.728
Genetic Conditions (hospital admission)	-0.285	0.6631
Gastrointestinal (specialty visit)	0.3153	0.2036
Gastrointestinal (hospital admission with primary diagnosis)	0.3776	0.086
Gastrointestinal (hospital admission with secondary diagnosis)	0.0525	0.8635
Genitourinary (specialty visit)	-0.2778	0.3841
Genitourinary (hospital admission)	0.5299	0.0697
Hematological (hospital admission)	0.7983	0.0046
Hepatobiliary (hospital admission)	0.4004	0.5696
Immunologic Disease (hospital admission)	1.0591	0.1003
Infectious Disease (hospital admission)	0.6027	0.0406
Male Genital (hospital admission)	-0.1114	0.8129
Musculoskeletal (hospital admission)	0.3921	0.2235
Neurologic Diseases (drug use)	0.3671	0.4453
Neurologic Diseases (hospital admission)	0.7566	0.0106
Nutrition (hospital admission)	-0.0472	0.9119
Other Conditions (hospital admission)	0.8184	0.0002
Pediatric medical specialty visit	0.4803	0.0005
Neonatal Conditions (hospital admission)	-0.0838	0.8757
Inappropriate Rx	-0.0338	0.8686
Psychological (hospital admission)	0.2778	0.5749

Respiratory (specialty visit)	0.2825	0.4175
Respiratory (drug use)	-0.095	0.4871
Respiratory (hospital admission)	0.3919	0.0211
Antibiotics Usage (number of Rx): 1	0.0662	0.5353
Antibiotics Usage (number of Rx): 2	0.2095	0.068
Antibiotics Usage (number of Rx): 3+	0.447	<.0001
Skin (hospital admission)	0.4547	0.2407
Pediatric surgical specialty visit	0.1926	0.187
Trauma (hospital admission)	0.0413	0.9339
Other conditions vs healthy newborns	0.0793	0.5959
Abnormal birth weight vs healthy newborns	0.1125	0.2604
Low income (exemption variables from AFT/FED and ASA)	0.2345	0.0045
Disabled (exemption variables from AFT/FED and ASA)	0.1821	0.5097
Immigrants	-0.0417	0.6379
Mom: Age at delivery 24 and less	-0.0979	0.5097
Mom: Age at delivery 35-39	0.0212	0.8208
Mom: Age at delivery 40 and over	0.0234	0.8733
Mom: Age at delivery NA	0.1158	0.3462
Mom: First delivery	0.1875	0.0263
Mom: C-section	-0.05	0.5649
Mom: Number of hospitalizations 1 year prior to delivery 1	0.078	0.5319
Mom: Number of hospitalizations 1 year prior to delivery 2+	0.264	0.2263
Mom: Inappropriate prescription during pregnancy (class D)	0.2514	0.1184
Mom: Inappropriate prescription during pregnancy (class X)	-0.3009	0.193
Mom: >=1 Rx for antibiotic during pregnancy	0.0123	0.8801
Mom: Abortion	0.115	0.3047
Mom: Asthma	0.1245	0.1754
Mom: Cardiovascular disease	0.263	0.0161
Mom: Diabetes	0.0993	0.6942
Mom: Infection	-0.3891	0.3948
Mom: Psychological condition	0.00668	0.9664
Mom: Bacterial pneumonia	-11.361	0.9739
Mom: Hypertension	-11.339	0.9689

Male 3-5 years old

Variable	Coefficient	P-value
Intercept	-4.3908	<.0001
Age at end of 2012	-0.1851	<.0001
Number of ER visits labeled as 'C: Critical': 1+	-0.0642	0.9443
Number of ER visits labeled as 'A: Acute': 1	0.1502	0.2516
Number of ER visits labeled as 'A: Acute': 2+	0.2391	0.4166
Number of ER visits labeled as 'U: Urgent but could be deferred': 1	0.1307	0.0589
Number of ER visits labeled as 'U: Urgent but could be deferred': 2+	0.2037	0.0201
Number of ER visits labeled as 'N: Not Urgent': 1+	0.0885	0.272
Cancer (specialty visit)	-0.8693	0.1277
Cancer (hospital admission)	2.2189	0.0003
Cardiovascular (drug use)	0.453	0.4879
Cardiovascular (hospital admission)	-0.2452	0.6019
Skin (specialty visit)	0.0923	0.3485
Dental Conditions (hospital admission)	-0.0628	0.9371
Endocrine (specialty visit)	-0.6416	0.1776
Endocrine (drug use)	-1.1204	0.1659
Endocrine (hospital admission)	0.6101	0.2156
Ear, Nose, Throat (specialty visit)	1.524	<.0001
Ear, Nose, Throat (hospital admission)	-0.7479	<.0001
Eye (hospital admission)	-0.7131	0.3525
Genetic Conditions (hospital admission)	0.4159	0.5152
Gastrointestinal (specialty visit)	-0.157	0.5272
Gastrointestinal (hospital admission with primary diagnosis)	0.933	<.0001
Gastrointestinal (hospital admission with secondary diagnosis)	0.00379	0.9928
Genitourinary (specialty visit)	0.1998	0.5642
Genitourinary (hospital admission)	0.2243	0.623
Hematological (hospital admission)	0.2777	0.4688
Hepatobiliary (hospital admission)	0.015	0.9882
Immunologic Disease (hospital admission)	-0.5462	0.6782
Infectious Disease (hospital admission)	0.9351	0.0112
Male Genital (hospital admission)	-1.1519	0.0347
Musculoskeletal (hospital admission)	-1.1269	0.0187
Neurologic Diseases (drug use)	0.3605	0.3631
Neurologic Diseases (hospital admission)	0.803	0.0021
Nutrition (hospital admission)	-0.3288	0.4881
Neonatal/other condition (hospital admission)	0.9366	<.0001
Pediatric medical specialty visit	0.1763	0.2109
Inappropriate Rx	-0.1163	0.3507
Psychological (hospital admission)	-0.1213	0.7529

Respiratory (specialty visit)	0.6986	0.0002
Respiratory (drug use)	-0.0033	0.9767
Respiratory (hospital admission)	0.6469	0.001
Antibiotics Usage (number of Rx): 1	0.3154	0.0009
Antibiotics Usage (number of Rx): 2	0.4605	<.0001
Antibiotics Usage (number of Rx): 3+	0.8373	<.0001
Skin (hospital admission)	-0.8752	0.2465
Pediatric surgical specialty visit	0.1381	0.3299
Trauma (hospital admission)	-12.786	0.9467
Other conditions vs healthy newborns	0.0693	0.692
Abnormal birth weight vs healthy newborns	-0.1385	0.1889
Low income (exemption variables from AFT/FED and ASA)	0.1382	0.0352
Disabled (exemption variables from AFT/FED and ASA)	-0.0398	0.8437
Immigrant	-0.1255	0.1239
Mom: Age at delivery 24 and less	0.092	0.4172
Mom: Age at delivery 35-39	-0.0953	0.1981
Mom: Age at delivery 40 and over	-0.1726	0.1823
Mom: Age at delivery NA	0.00579	0.9547
Mom: First delivery	0.0862	0.2102
Mom: C-section	0.064	0.3488
Mom: Number of hospitalizations 1 year prior to delivery 1	0.1719	0.0713
Mom: Number of hospitalizations 1 year prior to delivery 2+	0.4186	0.0092
Mom: Inappropriate prescription during pregnancy (class D)	0.345	0.0015
Mom: Inappropriate prescription during pregnancy (class X)	-0.1565	0.4248
Mom: >=1 Rx for antibiotic during pregnancy	0.0643	0.3298
Mom: Abortion	0.0611	0.5114
Mom: Asthma	-0.067	0.4507
Mom: Cardiovascular disease	0.0794	0.4534
Mom: Diabetes	0.2278	0.3482
Mom: Infection	-0.3829	0.5266
Mom: Psychological condition	0.0282	0.8502
Mom: Hypertension	-12.352	0.9701
History: Cancer (hospital admission)	-0.0872	0.9335
History: Cardiovascular (hospital admission)	-1.7855	0.0597
History: Dental Conditions (hospital admission)	0.1191	0.4171
History: Endocrine (hospital admission)	0.2455	0.4269
History: Ear, Nose, Throat (hospital admission)	0.2496	0.2975
History: Eye (hospital admission)	-0.088	0.4598
History: Genetic Conditions (hospital admission)	-0.1924	0.5286
History: Gastrointestinal (hospital admission with primary diagnosis)	-0.1531	0.6886
History: Gastrointestinal (hospital admission with secondary diagnosis)	0.2482	0.0296

History: Genitourinary (hospital admission)	-0.0753	0.6449
History: Hematological (hospital admission)	-0.2199	0.3188
History: Hepatobiliary (hospital admission)	0.4456	0.1529
History: Immunologic Disease (hospital admission)	0.4059	0.3341
History: Infectious Disease (hospital admission)	0.0303	0.8035
History: Male Genital (hospital admission)	-0.263	0.2335
History: Musculoskeletal (hospital admission)	-0.4993	0.0254
History: Neurologic Diseases (hospital admission)	0.2836	0.1162
History: Nutrition (hospital admission)	0.4121	0.0231
History: Other Conditions (hospital admission)	0.4624	0.0793
History: Neonatal Conditions (hospital admission)	-0.0783	0.5494
History: Psychological (hospital admission)	0.0445	0.8625
History: Respiratory (hospital admission)	0.0854	0.3347
History: Skin (hospital admission)	0.0851	0.7052
History: Trauma (hospital admission)	-0.0237	0.9288
History: Skin (specialty visit)	0.1423	0.0518
History: Pediatric surgical specialty visit	0.00376	0.9665
History: Gastrointestinal (specialty visit)	0.2392	0.1128
History: Endocrine (specialty visit)	0.0858	0.7584
History: Genitourinary (specialty visit)	0.1166	0.671
History: Cancer (specialty visit)	0.1478	0.6408
History: Ear, Nose, Throat (specialty visit)	0.5316	<.0001
History: Pediatric medical specialty visit	0.0864	0.1887
History: Respiratory (specialty visit)	0.5207	0.0064
History: Cardiovascular (drug use)	0.0362	0.9379
History: Respiratory (drug use)	-0.3478	<.0001
History: Endocrine (drug use)	0.6752	0.3485
History: Neurologic Diseases (drug use)	0.4141	0.334
History: Inappropriate Rx	0.00895	0.9274
History: Antibiotics Usage (number of years history)	0.0111	0.705
History: Number of ER visits labeled as 'C: Critical': 1+	0.6068	0.0612
History: Number of ER visits labeled as 'A: Acute': 1	0.0277	0.7708
History: Number of ER visits labeled as 'A: Acute': 2+	0.0285	0.8146
History: Number of ER visits labeled as 'U: Urgent but could be deferred': 1	0.1429	0.0952
History: Number of ER visits labeled as 'U: Urgent but could be deferred': 2+	0.0699	0.337
History: Number of ER visits labeled as 'N: Not Urgent': 1+	-0.0249	0.6872

Male 6-13 years old

Variable	Coefficient	P-value
Intercept	-5.0608	<.0001
Age at end of 2012	-0.0988	<.0001
Number of ER visits labeled as 'C: Critical': 1+	0.5905	0.397
Number of ER visits labeled as 'A: Acute': 1	0.254	0.09
Number of ER visits labeled as 'A: Acute': 2+	-0.4226	0.3826
Number of ER visits labeled as 'U: Urgent but could be deferred': 1	0.1963	0.0093
Number of ER visits labeled as 'U: Urgent but could be deferred': 2+	0.3353	0.002
Number of ER visits labeled as 'N: Not Urgent': 1+	0.0694	0.4921
Cancer (specialty visit)	0.0895	0.8435
Cancer (hospital admission)	1.0735	0.0669
Cardiovascular (drug use)	-0.0648	0.8959
Cardiovascular (hospital admission)	0.251	0.5673
Skin (specialty visit)	-0.1038	0.3095
Dental Conditions (hospital admission)	0.6784	0.1429
Endocrine (specialty visit)	0.5	0.0384
Endocrine (drug use)	-0.5023	0.4691
Endocrine (hospital admission)	0.2352	0.6721
Ear, Nose, Throat (specialty visit)	1.3841	<.0001
Ear, Nose, Throat (hospital admission)	-1.0555	0.0003
Eye (hospital admission)	-0.7516	0.343
Genetic Conditions (hospital admission)	-0.2224	0.7612
Gastrointestinal (specialty visit)	-0.0155	0.9528
Gastrointestinal (hospital admission with primary diagnosis)	1.0092	0.0004
Gastrointestinal (hospital admission with secondary diagnosis)	0.2371	0.5723
Genitourinary (specialty visit)	-0.199	0.5697
Genitourinary (hospital admission)	0.9503	0.0159
Hematological (hospital admission)	0.4117	0.2535
Hepatobiliary (hospital admission)	-1.0456	0.4125
Immunologic Disease (hospital admission)	0.5324	0.6289
Infectious Disease (hospital admission)	0.7537	0.0819
Male Genital (hospital admission)	-0.0609	0.8806
Musculoskeletal (hospital admission)	-0.497	0.1098
Neurologic Diseases (drug use)	0.7414	0.0279
Neurologic Diseases (hospital admission)	0.9324	<.0001
Nutrition (hospital admission)	0.1509	0.7591
Neonatal/other condition (hospital admission)	0.4672	0.1678
Pediatric medical specialty visit	0.0984	0.5306
Inappropriate Rx	0.3362	0.1756
Psychological (hospital admission)	0.0188	0.9642

Respiratory (specialty visit)	0.4092	0.0829
Respiratory (drug use)	-0.0899	0.5566
Respiratory (hospital admission)	0.6178	0.0156
Antibiotics Usage (number of Rx): 1	0.1123	0.1765
Antibiotics Usage (number of Rx): 2	0.2957	0.0022
Antibiotics Usage (number of Rx): 3+	0.6045	<.0001
Skin (hospital admission)	0.3592	0.4646
Pediatric surgical specialty visit	-0.2561	0.1962
Trauma (hospital admission)	0.2288	0.6719
Low income (exemption variables from AFT/FED and ASA)	0.1108	0.0876
Disabled (exemption variables from AFT/FED and ASA)	0.0562	0.7407
Immigrant	0.1941	0.0171
History: Cancer (hospital admission)	-0.1893	0.7004
History: Cardiovascular (hospital admission)	-0.331	0.2351
History: Dental Conditions (hospital admission)	0.0863	0.7781
History: Endocrine (hospital admission)	0.1744	0.549
History: Ear, Nose, Throat (hospital admission)	-0.0818	0.4303
History: Eye (hospital admission)	-0.0877	0.7598
History: Genetic Conditions (hospital admission)	0.2786	0.3979
History: Gastrointestinal (hospital admission with primary diagnosis)	0.0912	0.5373
History: Gastrointestinal (hospital admission with secondary diagnosis)	-0.2858	0.2282
History: Genitourinary (hospital admission)	0.1141	0.6252
History: Hematological (hospital admission)	0.2059	0.3073
History: Hepatobiliary (hospital admission)	0.7768	0.0281
History: Immunologic Disease (hospital admission)	-0.7195	0.3302
History: Infectious Disease (hospital admission)	0.1183	0.6089
History: Male Genital (hospital admission)	-0.192	0.287
History: Musculoskeletal (hospital admission)	0.1894	0.1981
History: Neurologic Diseases (hospital admission)	0.5886	0.0002
History: Nutrition (hospital admission)	0.2161	0.3529
History: Other Conditions (hospital admission)	0.3105	0.2424
History: Neonatal Conditions (hospital admission)	-0.3908	0.6064
History: Psychological (hospital admission)	0.0745	0.7265
History: Respiratory (hospital admission)	0.3742	0.0029
History: Skin (hospital admission)	0.1594	0.5364
History: Trauma (hospital admission)	-0.2875	0.3379
History: Skin (specialty visit)	0.00041	0.9953
History: Pediatric surgical specialty visit	0.0781	0.3987
History: Gastrointestinal (specialty visit)	-0.1624	0.4098
History: Endocrine (specialty visit)	-0.1416	0.5324
History: Genitourinary (specialty visit)	0.1667	0.5171

History: Cancer (specialty visit)	0.5712	0.0242
History: Ear, Nose, Throat (specialty visit)	0.3662	<.0001
History: Pediatric medical specialty visit	0.1406	0.0412
History: Respiratory (specialty visit)	0.2227	0.2056
History: Cardiovascular (drug use)	0.4739	0.2013
History: Respiratory (drug use)	-0.1722	0.0587
History: Endocrine (drug use)	0.1974	0.7629
History: Neurologic Diseases (drug use)	0.0465	0.8891
History: Inappropriate Rx	-0.0067	0.9478
History: Antibiotics Usage (number of years history)	0.0642	0.0063
History: Number of ER visits labeled as 'C: Critical': 1+	-0.113	0.8007
History: Number of ER visits labeled as 'A: Acute': 1	-0.1029	0.3904
History: Number of ER visits labeled as 'A: Acute': 2+	0.0835	0.5636
History: Number of ER visits labeled as 'U: Urgent but could be deferred': 1	0.1123	0.1878
History: Number of ER visits labeled as 'U: Urgent but could be deferred': 2+	0.1706	0.019
History: Number of ER visits labeled as 'N: Not Urgent': 1+	0.0356	0.6004

Female 1-2 years old

Variable	Coefficient	P-value
Intercept	-4.5571	<.0001
Age at end of 2012	-0.2066	0.0083
Number of ER visits labeled as 'C: Critical': 1+	0.9244	0.1671
Number of ER visits labeled as 'A: Acute': 1	0.1969	0.2132
Number of ER visits labeled as 'A: Acute': 2+	0.7359	0.0083
Number of ER visits labeled as 'U: Urgent but could be deferred': 1	0.4261	<.0001
Number of ER visits labeled as 'U: Urgent but could be deferred': 2+	0.4671	<.0001
Number of ER visits labeled as 'N: Not Urgent': 1+	0.0731	0.4675
Cancer (specialty visit)	-0.1589	0.8328
Cancer (hospital admission)	2.161	0.0004
Cardiovascular (drug use)	0.5362	0.4646
Cardiovascular (hospital admission)	0.8576	0.0182
Skin (specialty visit)	0.184	0.1983
Dental Conditions (hospital admission)	-0.9622	0.3726
Endocrine (specialty visit)	-0.3798	0.5293
Endocrine (hospital admission or drug use)	0.3949	0.3608
Ear, Nose, Throat (specialty visit)	0.6081	0.0002
Ear, Nose, Throat (hospital admission)	0.4674	0.08
Eye (hospital admission)	0.431	0.4151
Genetic Conditions (hospital admission)	1.0638	0.074
Gastrointestinal (specialty visit)	-0.1407	0.6559
Gastrointestinal (hospital admission with primary diagnosis)	0.3972	0.1327
Gastrointestinal (hospital admission with secondary diagnosis)	0.2011	0.5735
Genitourinary (specialty visit)	0.0847	0.8286
Genitourinary (hospital admission)	0.0645	0.891
OB/GYN (hospital admission)	-11.007	0.9775
Hematological (hospital admission)	-0.1244	0.7917
Hepatobiliary (hospital admission)	-11.698	0.9635
Infectious Disease (hospital admission)	0.5415	0.1206
Musculoskeletal (hospital admission)	0.3153	0.3954
Neurologic Diseases (drug use)	1.9836	<.0001
Neurologic Diseases (hospital admission)	-0.0008	0.9983
Nutrition (hospital admission)	0.4527	0.2304
Other Conditions (hospital admission)	0.694	0.0125
Pediatric medical specialty visit	0.4988	0.0017
Neonatal Conditions (hospital admission)	-0.1669	0.7809
Inappropriate Rx	0.2409	0.2714
Psychological (hospital admission)	0.7913	0.1063
Respiratory (specialty visit)	0.0595	0.9006

Respiratory (drug use)	0.1825	0.2547
Respiratory (hospital admission)	0.5431	0.0032
Antibiotics Usage (number of Rx): 1	0.1048	0.3403
Antibiotics Usage (number of Rx): 2	0.3254	0.0059
Antibiotics Usage (number of Rx): 3+	0.2723	0.0176
Skin (hospital admission)	0.5242	0.2614
Pediatric surgical specialty visit	0.0184	0.9507
Trauma (hospital admission)	-1.3538	0.2004
Other conditions vs healthy newborns	0.3338	0.0187
Abnormal birth weight vs healthy newborns	-0.1441	0.2722
Low income (exemption variables from AFT/FED and ASA)	0.1929	0.0307
Disabled (exemption variables from AFT/FED and ASA)	0.2458	0.3869
Immigrant	0.1709	0.068
Mom: Age at delivery 24 and less	-0.0148	0.9227
Mom: Age at delivery 35-39	-0.0742	0.4664
Mom: Age at delivery 40 and over	-0.1103	0.502
Mom: Age at delivery NA	0.091	0.503
Mom: First delivery	0.2184	0.0176
Mom: C-section	0.1219	0.1914
Mom: Number of hospitalizations 1 year prior to delivery 1	0.0709	0.6003
Mom: Number of hospitalizations 1 year prior to delivery 2+	0.2905	0.1941
Mom: Inappropriate prescription during pregnancy (class D)	-0.1674	0.4037
Mom: Inappropriate prescription during pregnancy (class X)	0.086	0.6881
Mom: >=1 Rx for antibiotic during pregnancy	0.0725	0.4081
Mom: Abortion	0.1205	0.3247
Mom: Asthma	0.2316	0.0176
Mom: Cardiovascular disease	-0.1599	0.2254
Mom: Diabetes	0.4683	0.0481
Mom: Infection	0.4508	0.1694
Mom: Psychological condition	0.3314	0.0323
Mom: Bacterial pneumonia	0.5788	0.4408
Mom: Hypertension	0.6761	0.5213

Female 3-5 years old

Variable	Coefficient	P-value
Intercept	-4.6056	<.0001
Age at end of 2012	-0.2234	<.0001
Number of ER visits labeled as 'C: Critical': 1+	1.5291	0.0242
Number of ER visits labeled as 'A: Acute': 1	0.2541	0.1171
Number of ER visits labeled as 'A: Acute': 2+	0.5921	0.0611
Number of ER visits labeled as 'U: Urgent but could be deferred': 1	0.1159	0.1775
Number of ER visits labeled as 'U: Urgent but could be deferred': 2+	0.3232	0.0037
Number of ER visits labeled as 'N: Not Urgent': 1+	0.0931	0.3538
Cancer (specialty visit)	-0.7706	0.35
Cancer (hospital admission)	-0.1399	0.9057
Cardiovascular (drug use)	-0.3416	0.7265
Cardiovascular (hospital admission)	0.4549	0.3553
Skin (specialty visit)	-0.1928	0.144
Dental Conditions (hospital admission)	0.3988	0.579
Endocrine (specialty visit)	0.481	0.2104
Endocrine (drug use)	0.1423	0.8601
Endocrine (hospital admission)	0.6761	0.1341
Ear, Nose, Throat (specialty visit)	1.5774	<.0001
Ear, Nose, Throat (hospital admission)	-0.3541	0.1076
Eye (hospital admission)	-0.5433	0.5958
Genetic Conditions (hospital admission)	-0.7183	0.3049
Gastrointestinal (specialty visit)	-0.1286	0.6569
Gastrointestinal (hospital admission with primary diagnosis)	0.4361	0.1608
Gastrointestinal (hospital admission with secondary diagnosis)	-0.1194	0.7893
Genitourinary (specialty visit)	-0.5411	0.3296
Genitourinary (hospital admission)	2.1019	<.0001
OB/GYN (hospital admission)	-12.569	0.9572
Hematological (hospital admission)	0.0931	0.8231
Hepatobiliary (hospital admission)	-0.7794	0.5574
Immunologic Disease (hospital admission)	-0.6438	0.5935
Infectious Disease (hospital admission)	0.8241	0.0627
Musculoskeletal (hospital admission)	0.1936	0.6165
Neurologic Diseases (drug use)	0.1575	0.7742
Neurologic Diseases (hospital admission)	0.5916	0.0909
Nutrition (hospital admission)	0.7261	0.092
Neonatal/other condition (hospital admission)	0.7359	0.024
Pediatric medical specialty visit	0.1741	0.3278
Inappropriate Rx	0.1276	0.415
Psychological (hospital admission)	-0.911	0.2026

Respiratory (specialty visit)	0.7151	0.0078
Respiratory (drug use)	-0.2092	0.1685
Respiratory (hospital admission)	0.9109	<.0001
Antibiotics Usage (number of Rx): 1	0.00781	0.9441
Antibiotics Usage (number of Rx): 2	0.2729	0.0175
Antibiotics Usage (number of Rx): 3+	0.5587	<.0001
Skin (hospital admission)	0.4143	0.5171
Pediatric surgical specialty visit	-0.3071	0.417
Trauma (hospital admission)	0.6426	0.2586
Other conditions vs healthy newborns	-0.0286	0.8313
Abnormal birth weight vs healthy newborns	0.0403	0.8428
Low income (exemption variables from AFT/FED and ASA)	0.1281	0.1019
Disabled (exemption variables from AFT/FED and ASA)	-0.2122	0.4469
Immigrant	-0.1857	0.058
Mom: Age at delivery 24 and less	0.4048	0.0012
Mom: Age at delivery 35-39	0.0281	0.7534
Mom: Age at delivery 40 and over	-0.1245	0.4175
Mom: Age at delivery NA	0.3277	0.0081
Mom: First delivery	0.2424	0.0043
Mom: C-section	0.0588	0.4802
Mom: Number of hospitalizations 1 year prior to delivery 1	0.1992	0.0751
Mom: Number of hospitalizations 1 year prior to delivery 2+	0.1744	0.3781
Mom: Inappropriate prescription during pregnancy (class D)	0.00365	0.9796
Mom: Inappropriate prescription during pregnancy (class X)	-0.18	0.4421
Mom: >=1 Rx for antibiotic during pregnancy	0.1996	0.0109
Mom: Abortion	0.0806	0.4681
Mom: Asthma	0.03	0.7731
Mom: Cardiovascular disease	0.0892	0.4937
Mom: Diabetes	0.3871	0.1656
Mom: Infection	0.0938	0.8747
Mom: Psychological condition	0.1887	0.2588
Mom: Bacterial Pneumonia	-1.0059	0.468
Mom: Hypertension	0.9258	0.2283
History: Cancer (hospital admission)	-0.7613	0.4968
History: Cardiovascular (hospital admission)	-0.1357	0.4844
History: Dental Conditions (hospital admission)	-0.0641	0.8721
History: Endocrine (hospital admission)	-0.321	0.3353
History: Ear, Nose, Throat (hospital admission)	0.1229	0.4029
History: Eye (hospital admission)	-0.0508	0.8818
History: Genetic Conditions (hospital admission)	0.799	0.0191
History: Gastrointestinal (hospital admission with primary diagnosis)	0.1729	0.2373

History: Gastrointestinal (hospital admission with secondary diagnosis)	-0.1618	0.4496
History: Genitourinary (hospital admission)	0.1015	0.677
History: OB/GYN (hospital admission)	-0.0352	0.9506
History: Hematological (hospital admission)	0.3412	0.1549
History: Hepatobiliary (hospital admission)	0.5836	0.1771
History: Immunologic Disease (hospital admission)	0.1294	0.815
History: Infectious Disease (hospital admission)	-0.3508	0.0383
History: Musculoskeletal (hospital admission)	0.1377	0.5135
History: Neurologic Diseases (hospital admission)	0.1388	0.5723
History: Nutrition (hospital admission)	0.1641	0.4831
History: Other Conditions (hospital admission)	0.6846	0.0305
History: Neonatal Conditions (hospital admission)	0.1031	0.5163
History: Psychological (hospital admission)	-0.3948	0.2789
History: Respiratory (hospital admission)	0.2487	0.0197
History: Skin (hospital admission)	0.1305	0.5923
History: Trauma (hospital admission)	0.6773	0.0161
History: Skin (specialty visit)	0.1008	0.2576
History: Pediatric surgical specialty visit	-0.1367	0.4052
History: Gastrointestinal (specialty visit)	-0.0783	0.7024
History: Endocrine (specialty visit)	-0.501	0.1488
History: Genitourinary (specialty visit)	-0.4215	0.3296
History: Cancer (specialty visit)	0.1303	0.736
History: Ear, Nose, Throat (specialty visit)	0.5018	<.0001
History: Pediatric medical specialty visit	0.0626	0.4364
History: Respiratory (specialty visit)	-0.6453	0.0757
History: Cardiovascular (drug use)	0.3177	0.5455
History: Respiratory (drug use)	0.1378	0.1819
History: Endocrine (drug use)	0.1246	0.8816
History: Neurologic Diseases (drug use)	1.0076	0.0729
History: Inappropriate Rx	0.0338	0.7872
History: Antibiotics Usage (number of years history)	0.0117	0.7383
History: Number of ER visits labeled as 'C: Critical': 1+	-0.183	0.752
History: Number of ER visits labeled as 'A: Acute': 1	0.0778	0.5103
History: Number of ER visits labeled as 'A: Acute': 2+	-0.1193	0.4529
History: Number of ER visits labeled as 'U: Urgent but could be deferred': 1	0.0555	0.5856
History: Number of ER visits labeled as 'U: Urgent but could be deferred': 2+	0.1819	0.031
History: Number of ER visits labeled as 'N: Not Urgent': 1+	-0.0098	0.8966

Female 6-13 years old

Variable	Coefficient	P-value
Intercept	-5.8784	<.0001
Age at end of 2012	-0.0548	0.0008
Number of ER visits labeled as 'C: Critical': 1+	0.5528	0.4286
Number of ER visits labeled as 'A: Acute': 1	0.5618	0.0007
Number of ER visits labeled as 'A: Acute': 2+	0.8879	0.0091
Number of ER visits labeled as 'U: Urgent but could be deferred': 1	0.2361	0.0074
Number of ER visits labeled as 'U: Urgent but could be deferred': 2+	0.5049	<.0001
Number of ER visits labeled as 'N: Not Urgent': 1+	0.0593	0.6033
Cancer (specialty visit)	0.8804	0.0421
Cancer (hospital admission)	1.9472	0.0019
Cardiovascular (drug use)	0.0531	0.9215
Cardiovascular (hospital admission)	-0.1109	0.8265
Skin (specialty visit)	-0.0202	0.8567
Dental Conditions (hospital admission)	-0.789	0.2343
Endocrine (specialty visit)	-0.4513	0.0949
Endocrine (drug use)	0.1639	0.7554
Endocrine (hospital admission)	0.1729	0.6192
Ear, Nose, Throat (specialty visit)	1.5421	<.0001
Ear, Nose, Throat (hospital admission)	-0.467	0.0722
Eye (hospital admission)	-0.3721	0.604
Genetic Conditions (hospital admission)	1.3712	0.0286
Gastrointestinal (specialty visit)	-0.4065	0.1273
Gastrointestinal (hospital admission with primary diagnosis)	0.5999	0.045
Gastrointestinal (hospital admission with secondary diagnosis)	0.8453	0.0224
Genitourinary (specialty visit)	0.0925	0.8232
Genitourinary (hospital admission)	-0.0319	0.9572
OB/GYN (hospital admission)	-10.576	0.9463
Hematological (hospital admission)	-0.0211	0.9641
Hepatobiliary (hospital admission)	0.3693	0.6164
Immunologic Disease (hospital admission)	0.5725	0.4888
Infectious Disease (hospital admission)	0.1486	0.7992
Musculoskeletal (hospital admission)	-0.6102	0.0649
Neurologic Diseases (drug use)	0.6316	0.1157
Neurologic Diseases (hospital admission)	1.327	<.0001
Nutrition (hospital admission)	0.3239	0.5243
Neonatal/other condition (hospital admission)	0.2169	0.614
Pediatric medical specialty visit	0.3156	0.0413
Inappropriate Rx	-0.1339	0.7061
Psychological (hospital admission)	-0.4714	0.344

Respiratory (specialty visit)	0.0964	0.7649
Respiratory (drug use)	-0.0021	0.9908
Respiratory (hospital admission)	0.3228	0.2791
Antibiotics Usage (number of Rx): 1	0.2231	0.0191
Antibiotics Usage (number of Rx): 2	0.5496	<.0001
Antibiotics Usage (number of Rx): 3+	0.7316	<.0001
Skin (hospital admission)	-0.4769	0.5205
Pediatric surgical specialty visit	0.163	0.6316
Trauma (hospital admission)	0.6965	0.2614
Low income (exemption variables from AFT/FED and ASA)	0.2506	0.0006
Disabled (exemption variables from AFT/FED and ASA)	0.3811	0.0453
Immigrant	0.0669	0.4837
History: Cancer (hospital admission)	-1.2579	0.0794
History: Cardiovascular (hospital admission)	-0.5369	0.0971
History: Dental Conditions (hospital admission)	0.6569	0.0201
History: Endocrine (hospital admission)	-0.0114	0.9665
History: Ear, Nose, Throat (hospital admission)	0.1263	0.2948
History: Eye (hospital admission)	0.1505	0.5917
History: Genetic Conditions (hospital admission)	-0.2005	0.6414
History: Gastrointestinal (hospital admission with primary diagnosis)	0.32	0.0332
History: Gastrointestinal (hospital admission with secondary diagnosis)	0.0424	0.8574
History: Genitourinary (hospital admission)	-0.0075	0.9806
History: OB/GYN (hospital admission)	0.9705	0.0427
History: Hematological (hospital admission)	0.3297	0.1683
History: Hepatobiliary (hospital admission)	0.1931	0.7029
History: Immunologic Disease (hospital admission)	0.469	0.2754
History: Infectious Disease (hospital admission)	0.0864	0.7466
History: Musculoskeletal (hospital admission)	0.3058	0.0805
History: Neurologic Diseases (hospital admission)	0.2079	0.3002
History: Nutrition (hospital admission)	-0.1424	0.6003
History: Other Conditions (hospital admission)	-1.1015	0.0258
History: Neonatal Conditions (hospital admission)	-0.054	0.9358
History: Psychological (hospital admission)	0.2273	0.3797
History: Respiratory (hospital admission)	0.0871	0.5762
History: Skin (hospital admission)	0.0572	0.8443
History: Trauma (hospital admission)	0.4149	0.1635
History: Skin (specialty visit)	-0.135	0.0878
History: Pediatric surgical specialty visit	0.011	0.9465
History: Gastrointestinal (specialty visit)	0.4319	0.0093
History: Endocrine (specialty visit)	0.4559	0.0118
History: Genitourinary (specialty visit)	-0.1484	0.6694

History: Cancer (specialty visit)	-0.2097	0.604
History: Ear, Nose, Throat (specialty visit)	0.3035	<.0001
History: Pediatric medical specialty visit	0.00862	0.9143
History: Respiratory (specialty visit)	-0.0033	0.9886
History: Cardiovascular (drug use)	0.7729	0.0742
History: Respiratory (drug use)	0.1033	0.3109
History: Endocrine (drug use)	0.3977	0.453
History: Neurologic Diseases (drug use)	0.1549	0.7028
History: Inappropriate Rx	0.1035	0.3876
History: Antibiotics Usage (number of years history)	0.0952	0.0004
History: Number of ER visits labeled as 'C: Critical': 1+	0.7989	0.0396
History: Number of ER visits labeled as 'A: Acute': 1	-0.1075	0.451
History: Number of ER visits labeled as 'A: Acute': 2+	0.3286	0.043
History: Number of ER visits labeled as 'U: Urgent but could be deferred': 1	0.2086	0.0248
History: Number of ER visits labeled as 'U: Urgent but could be deferred': 2+	0.1974	0.0158
History: Number of ER visits labeled as 'N: Not Urgent': 1+	-0.0564	0.4744

STROBE 2007 (v4) checklist of items to be included in reports of observational studies in epidemiology*

Checklist for cohort, case-control, and cross-sectional studies (combined)

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2-3
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4-5
Objectives	3	State specific objectives, including any pre-specified hypotheses	5
Methods			
Study design	4	Present key elements of study design early in the paper	6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	6
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	7
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	7-11
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	*7-11*
Bias	9	Describe any efforts to address potential sources of bias	7-11
Study size	10	Explain how the study size was arrived at	7
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	7-11
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	11-12
		(*b*) Describe any methods used to examine subgroups and interactions	
		(*c*) Explain how missing data were addressed	
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed	

		Cross-sectional study—If applicable, describe analytical methods taking account of sampling strategy	
		(*e*) Describe any sensitivity analyses	
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	12
		(b) Give reasons for non-participation at each stage	
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	12-14, Table 1 and 2
		(b) Indicate number of participants with missing data for each variable of interest	
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	12-14, Table 3
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	
		Cross-sectional study—Report numbers of outcome events or summary measures	
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	14-15, Table 4, Fig. 1
		(*b*) Report category boundaries when continuous variables were categorized	
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	
Discussion			
Key results	18	Summarise key results with reference to study objectives	15
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	16
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	17
Generalisability	21	Discuss the generalisability (external validity) of the study results	17
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	18

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.
Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.