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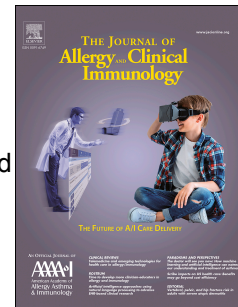
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Developing and evaluating a pediatric asthma severity computable phenotype derived from electronic health records

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Abstract

Background: Extensive data available in electronic health records (EHR) have the potential to improve asthma care and understanding of factors influencing asthma outcomes. However, this work can only be accomplished when the EHR data allow for accurate measures of severity, which at present are complex and inconsistent.

Objective: To create and evaluate a standardized pediatric asthma severity phenotype based in clinical asthma guidelines for use in EHR-based health initiatives and studies; and to examine the presence and absence of these data in relation to patient characteristics.

Methods: We developed an asthma severity computable phenotype and compared the concordance of different severity components contributing to the phenotype to trends in the literature. We used multivariable logistic regression to assess the presence of EHR data relevant to asthma severity.

Results: The asthma severity computable phenotype performs as expected in comparison to national statistics and the literature. Severity classification for a child is maximized when based on the long-term medication regimen component and minimized when based only on the symptom data component. Use of the severity phenotype results in better, clinically-grounded classification. Children for whom severity could be ascertained from these EHR data were more likely to be seen for asthma in the outpatient setting, and less likely to be older or Hispanic. Black children were less likely to have lung function testing data present.

Conclusion: We developed a pragmatic computable phenotype for pediatric asthma severity that is transportable to other EHRs.

Clinical Implication: Ascertainment of asthma severity from the EHR is viable but depends on intensity of patient engagement in healthcare and demographic characteristics.

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47 **Capsule Summary**

48 We present a pragmatic approach to use electronic health record (EHR) data to classify pediatric
49 asthma severity.

50

51 **Key Words**

52 Asthma

53 Electronic health records

54 Big data

55 Respiratory function tests

56 Selection bias

57 Healthcare disparities

58 Delivery of Health Care

59 Observer Variation

60 National Heart, Lung, and Blood Institute (U.S.)

61 Pediatrics

Abbreviations

Electronic health records (EHRs)

Machine learning (ML)

Artificial intelligence (AI)

National Institutes of Health (NIH)

National Heart, Lung, and Blood Institute (NHLBI)

2007 National Asthma Education and Prevention Program Expert Panel Report 3 (NAEPP
EPR3)

Global Initiative for Asthma (GINA)

Healthcare Effectiveness Data and Information Set (HEDIS)

International Classification of Diseases codes (ICD)

Percent predicted forced expiratory volume in one second (FEV1%)

Boston Medical Center (BMC)

Concept Unique Identifier (RxCUI)

Inhaled corticosteroid (ICS)

Informatics for Integrating Biology with the Bedside Platform at Boston University (BU-i2b2)

Asthma Control Test (ACT)

Patient Health Questionnaire (PHQ)

Natural Language Processing (NLP)

82 Introduction

83 Electronic health records (EHRs) are potentially rich “big data” sources of detailed
84 longitudinal health information. EHRs are increasingly used for research to advance therapeutics,
85 improve patient care, and epidemiology^{1–3}. Despite the potential opportunities EHR data present
86 to conduct large-scale studies in a timely fashion and at a lower cost than traditional studies,
87 there are significant challenges in their application in research, such as data quality (incomplete,
88 incorrect, and discordant)⁴, standardization⁵, and interoperability⁶.

89 The data in the EHR may not reflect the underlying disease that researchers are interested in
90 studying, but rather the totality of complex patient, clinician, and health system interactions and
91 documentation (or lack thereof.)⁷. Data in EHRs represent complex visit and documentation
92 processes—a concept that has been termed *informed presence*⁸. Thus to study a disease of
93 interest, researchers must understand the idiosyncrasies of the healthcare process that give rise to
94 the data documented in the EHR⁹. Idiosyncrasies such as the effect of the weekend on hospital
95 admissions¹⁰ or treatment options sought by patients varying by distance from healthcare
96 facilities¹¹ may or may not be relevant to the disease and the EHR data a researcher is analyzing.
97 A researcher must first understand the potential biases that result from informed presence, and
98 only then can such biases be addressed¹² or creatively exploited^{13,14} using approaches only
99 recently described in the epidemiological and informatics literature.

100 Characterizing and defining asthma severity and its components has varied in the clinical
101 literature, claims-based guidelines, and clinical practice guidelines^{15–21}. Idiosyncrasies of asthma
102 EHR data relevant to severity include: lung function testing is often performed on severe
103 patients; the frequency of interactions with the health care system varies by severity; and
104 assessment may be clinically subjective given the diffuse clinical definition of severity. In spite

of these complexities of standardized ascertainment of asthma severity status from EHR data, it is important to tackle because asthma severity is: 1) integral to an asthma diagnosis and treatment plan in the clinical setting; 2) a key element of valid and interpretable research; 3) highly associated with significant economic burden nationally and internationally²²⁻²⁴; 4) relevant to advancing risk prediction of asthma morbidity and mortality²⁵⁻²⁸.

To date, relatively few research studies using sophisticated methodologies²⁹⁻³¹ applied to “big data” have been translated into clinical practice with documented improvement in asthma care^{32,33}. Limitations of EHR data^{4,34,35} can be mitigated through interdisciplinary collaboration³². Thus, an aim of our research was to integrate the knowledge and skill base of a team of clinicians, informaticians, and health scientists to advance pediatric asthma research using EHR data, with the goal of developing a computable phenotype. A computable phenotype is “a clinical condition or characteristic that can be ascertained via a computerized query to an EHR system or clinical data repository using a defined set of data elements and logical expressions so as to be able to identify patients from clinical data for research purposes”^{36,37}. Computable phenotyping is therefore the process used to identify and understand the actual patient population in the EHR sample under study^{9,38}. A goal of phenotyping is to leverage clinical and informatics knowledge in such a way that phenotypes are transportable across health systems, thus supporting the scale-up of “big data” health research³⁹.

The objectives of this study are to create a standardized pediatric asthma severity phenotype that is based in clinical asthma guidelines and to evaluate documentation of visit processes and patient characteristics that give rise to the presence of these data in the EHR. The following two research questions were posed for our second objective: what data are observed for those patients for whom we can ascertain an asthma severity classification compared to those patients for

whom we cannot? And among those with severity data, why do some patients have different data elements related to asthma severity components while others do not (e.g. lung function test, recorded asthma symptoms)?⁴⁰ This study extends the current science of mainly binary phenotypes (e.g. asthmatic versus non-asthmatic)⁴¹ by creating a multi-class computable phenotype for asthma severity. While an asthma computable phenotype exists in the literature^{42,43}, to our knowledge, no validated and standardized computable phenotype that is based on clinical asthma guidelines exists for asthma severity^{20,21}.

Methods

The Boston University Medical Campus Institutional Review Board approved The Asthma Simulation Tool for Housing, Medication, and Social Adversity (ASTHMA) Study in May 2018. Figure 1 provides a high-level summary of our study design and analyses.

Severity phenotype development

Interdisciplinary team: The asthma severity phenotype presented in Table 1 was iteratively developed between July 2018 and January 2020 by a team of clinicians, informaticians, and health scientists using best practices for phenotype development from the National Institutes of Health (NIH)³⁶.

Basis of asthma severity phenotype definition: Our phenotype is based on clinical guidelines established in the National Heart, Lung, and Blood Institute (NHLBI) 2007 National Asthma Education and Prevention Program Expert Panel Report 3 (NAEPP EPR3)⁴⁴ and supplemented with the 2019 Global Initiative for Asthma (GINA) Report⁴⁵. The Classifying Asthma Severity Table⁴⁶ outlined in the NAEPP EPR3 reflects the culmination of significant clinical iteration and expertise and is ideally summarized for translation into an informatics approach (Table 1). Thus, the NAEPP EPR3 was considered preferential to other approaches (Healthcare Effectiveness Data and Information Set (HEDIS) or the Leidy method)^{20,21}.

Pragmatic approach for replication: We applied a set of principles when building the severity phenotype: to build upon existing phenotypes, ground the phenotype in clinical guidelines, and develop a transportable phenotype³⁶. The phenotype was built on ontologies based on standard national reference codes⁴⁷. The timescale of the phenotype is one calendar year and the phenotype indicates the worst severity observed based on any of the EHR data elements in the given year. This logic was based on the NAEPP EPR3 severity guidelines, the clinical expertise

of the team and literature, and for comparability to the time-scale of claims-based asthma severity algorithms^{19–21}.

EHR database & asthma phenotype: We constructed a database of children (ages 0 to 18) seen at Boston Medical Center (BMC) from 2003 onward (CHILD-DB) as an aim of the ASTHMA Study. BMC, located in Boston, Massachusetts, USA, is the largest urban safety net hospital in New England and primarily serves a low-income and minority population. CHILD-DB is a limited dataset that includes individual child attributes from the EHR as well as geospatial data (e.g. air pollution, census data.) Children in CHILD-DB were first classified as having asthma by applying criteria from a published asthma computable phenotype⁴³ that was iteratively developed and validated in adults, children (ages 5 and older), and across health institutions^{42,43}. Because the asthma phenotype was created with ICD-9 codes, we updated it to include corresponding exclusionary ICD-10 codes (Table S1.)

Asthma severity phenotype: We defined severity (detailed in Table 1) on an annual basis (calendar year) according to the NAEPP EPR3, specifically the “Classifying Asthma Severity Table”⁴⁶. The phenotype is a deterministic rule-based algorithm for children ages 5 to 18 and based on the following EHR data elements that align with the NAEPP EPR3 components of impairment for asthma severity: 1) prescribed asthma medications (Rx), 2) International Classification of Diseases codes (ICD-10), 3) percent predicted forced expiratory volume in one second (FEV1%) as a measure of lung function, and 4) asthma symptoms. Since the range of FEV1% values for intermittent and mild persistent are the same (>80%) according to NHLBI guidelines, the risk component of severity was integrated into the phenotype for these categories: annual corticosteroids were used to distinguish intermittent (0-1/year) from mild persistent ($\geq$

2/year). Asthma severity was assigned to asthmatic children in CHILD-DB based on the following EHR data elements and the logic outlined in Table 1:

Rx: Medications prescribed to children with an asthma ICD-9 or ICD-10 code recorded in their chart were extracted from CHILD-DB. Medications were matched to generic or tradename for asthma medications obtained from the 2017 NAEPP EPR3 and 2019 GINA Report (Table S2), flagged, and the associated medication Concept Unique Identifiers (RxCUIs) from the RxNorm⁴⁸ ontology were identified. For all asthma medications except inhaled corticosteroids (ICSs), the RxCUI codes were categorized according to the medication class listed in Table S2. For ICSs, the medication instruction data field was also extracted to determine whether a patient was on a low, medium or high daily dose. Using the dosage indicated by the RxCUI code, the administrations per day that were mined from instructions, and the patient's age, we determined the associated severity classification (Table S3).

ICD-10: ICD-10 diagnosis codes conveying asthma severity (listed in Table 1) were identified (primary, secondary, admitting, or problem list.)

FEV1%: The lowest FEV1% lab value in a given year was identified in accordance with the NAEPP ERP3 guidelines. The number of RxCUI codes for a systemic corticosteroid in a year was used to differentiate intermittent and mild persistent asthma since both are defined as <80% in the NAEPP ERP3.

Symptoms: Asthma symptom data were available until 2015 when BMC transitioned from GE Centricity to Epic EHR software. Symptom data were collected in HDID fields (GE Centricity EHR software specific codes) as structured data or free-text, which were coded to correspond to a severity (e.g. "every day not all the time" in the structured HDID field is coded as severe.)

Informatics work was conducted in Microsoft SQL Server 2008 as part of the Informatics for Integrating Biology with the Bedside Platform at Boston University (BU-i2b2)⁴⁹.

In summary, severity was defined, per NAEPP EPR3 as the worst severity observed based on any of the four EHR data elements in the given year. For subjects who did not have severity ascertained, there was no EHR data element available in any of the four data elements (Rx, ICD-10, FEV1% and symptom severity).

Data analyses

Sample for analysis: A sample of the most recent five years of data (2013-2017) was created. There were 5,047 asthmatic children (contributing 14,054 patient-years) seen at BMC classified according to the Afshar et al (2018)⁴³ asthma phenotype during this time. A random, independent sample consisting of one year of data per patient was compiled for analysis (5,047 patients contributing 5,047 patient-years). The Mantel-Haenszel chi-square test was used to assess the relationship between increasing severity and patient, visit, and documentation characteristics.

Phenotype evaluation: The distribution of asthma severity among children at BMC produced by the asthma severity phenotype was qualitatively compared to what has been documented in the literature. Concordance assessments appropriate for paired, ordinal data were conducted (Weight Kappa & McNemar Test of Direction of Change) to determine agreement and direction of change between pair-wise comparisons of the different EHR data elements (Rx, ICD-10, FEV1%, symptoms.)

Influence of informed presence: To answer our questions about what data are observed and why⁴⁰, we applied multivariable logistic regression models associating dependent variables (severity ascertainment, the presence of long term Rx regimen, the presence of ICD-10 severity,

the presence of a lung function test, the presence of symptom data) with independent variables (sex, age, race/ethnicity, language spoken at home, number of years active, number of visits per year, asthma care during the year.) For the four models where EHR data elements were the outcome, data were restricted to patients for whom NHLBI severity was ascertained, ascertained severity was included as an independent variable, and if needed, data were restricted to the timeframe in which that element was available. Bivariate associations between dependent and independent variables that were statistically significant at $p < 0.05$ (chi-square test results) were entered into the multivariable logistic regression models. Candidate model variables were removed from the multivariable models using backward selection ($p < 0.05$). Analyses were conducted in SAS 9.4 and using the Marginal Homogeneity Program v.1.2⁵⁰.

Results

Severity phenotype

Table 1 details the computable phenotype algorithm and Tables S1-S3 provide standardized guidance and codes to implement the phenotype on EHR data. When the severity phenotype was applied to our random sample of independent severity-years, severity was ascertainable for about half our random sample (n=2,461) (Table 2). For those patients for whom severity could be ascertained in our random sample, 80% of patients had Rx data, 50% had ICD-10 data, 26% had FEV1% data, and 17% had symptom data relevant to severity in a given year. The three most common combinations of EHR data elements relevant to asthma severity accounted for two-thirds of the patients with severity data: 28% had Rx and ICD-10 data, 26% had Rx data only, and 12% had Rx, ICD-10, and FEV1% data. The more “complete” a patient’s severity data, the more years a patient was active during the study period, and the more visits a patient had in the year, the more severe their asthma was documented to be (Table 2). While differences in race/ethnicity and age existed across levels of severity, there were no significant differences in sex and language spoken at home (Table 2).

Phenotype evaluation

Overall distribution: The asthma severity computable phenotype produces a similar distribution in comparison to nationally representative and inner-city pediatric populations. Our study estimated 45% intermittent and 55% persistent asthmatics, as compared with 40% and 60% respectively in a national study⁵¹. A sample of children from the National Cooperative Inner-City Asthma Study (of which BMC is a member) were found to be approximately 40% intermittent, 15% mild persistent, and 45% moderate or severe persistent¹⁷. Our study had a similar distribution (45% intermittent, 17% mild persistent, and 37% moderate or severe persistent).

Concordance and direction of change analyses: Table 3 summarizes the results of assessments of pairwise comparisons between the four different EHR data elements that correspond to components of asthma severity, which can be compared with similar assessments from the clinical and claims literature¹⁵⁻¹⁹. While categorization based on Rx and ICD-10 show moderate agreement, there is minimal agreement for all other pairwise comparisons (Table 3, weighted kappa). In regards to direction of change, severity based on Rx is generally more severe than when based on ICD-10, which is generally more severe than when based on FEV1%, which is generally more severe than when based on symptom data (Table 3, McNemar Test). These findings agree with the clinical literature on asthmatic children that asthma severity classified by symptoms does not correlate well with FEV1% categorization^{18,19,52} and that classification is more severe when based on lung function and symptoms compared to symptoms only¹⁷. Our results also agree with the claims-based literature, which finds that claims-based approaches categorize asthmatic patients as more severe compared to lung function measures¹⁶ or symptom-based approaches¹⁵. Claims-based approaches can be considered loosely comparable to Rx and ICD-10 severity.

Influence of informed presence

Children for whom severity could be ascertained compared to children for whom severity could not were more likely to be: seen for asthma in the outpatient setting in a calendar year, younger (ages 5-11), White (compared to Hispanic), seen for any reason two or more times in a calendar year, and continually active patients for the five year period (Table 4). Among patients for whom severity could be ascertained, the presence of lung function test data, ICD-10 data, Rx data, and symptom data varied most by disease severity and asthma care pattern during the year. Asthma care pattern during the year was positively correlated with lung function data and ICD-

10 data, whereas Rx data and symptom data were negatively correlated with asthma care pattern during the year. Severity was also positively correlated with lung function, ICD-10 and Rx data presence, but was negatively correlated with symptom data (Table 4). Symptom data and Rx data were positively correlated with healthcare frequency or duration, whereas ICD-10 data and lung function test data were not. Symptom data were positively correlated with all racial/ethnic groups relative to White children with Black and Other races attaining statistical significance; except for Hispanic children, lung function data were negatively correlated with all racial/ethnic groups relative to White, with Black race attaining statistical significance (Table 4).

Discussion

We created a clinically based and transportable⁴¹ computable phenotype for pediatric asthma severity based on EHR data because documentation of asthma severity in a standardized manner in the EHR is not common practice nor are clinical guidelines consistently implemented. Knowledge and selection of asthma clinical guidelines⁵³, implementation^{53–55}, and adherence to use of such guidelines^{54,55} by clinicians as well as a clear referral pathways from primary care to asthma specialists⁵⁵ remain current challenges. We have documented an approach through which “big data” from the EHR can contribute to pediatric asthma research that is low-cost, standardized, leverages existing data, and does not add to clinician or clinical staff burden.

Overall, the computable phenotype produces a distribution and behaves as expected in comparison to the literature and national statistics. As anticipated, children for whom severity could be ascertained were characteristically different in terms of their healthcare use and data documented, and ascertainment was also less likely among older and Hispanic children. Lastly, asthma severity based on different severity components (i.e. ICD-10 versus FEV1%) leads to different severity classifications for the same patient when using EHR data. This lack of concordance has been shown to be the case for clinical research and claims data as well^{16,19}.

Disparities: Black children are four times more likely to suffer from severe persistent asthma compared to White children⁵⁶; moreover, in our analysis they were less likely to have documentation of severity based on lung function testing in their EHR. Racial/ethnic differences in clinical documentation of asthma severity classification is a recognized barrier to eliminating racial disparities⁵³ and may be an indicator of structural racism in health care. Our analyses of a largely urban, Black, pediatric population also highlight challenges outlined in the growing “big data” health disparities literature⁵⁷. Fitzpatrick et al (2019) found Blacks were less likely to

receive outpatient care for asthma⁵⁸. Our study corroborates their findings: 1) we found Black children were more likely to have symptom data and less likely to have lung function testing; 2) lung function testing, but not symptom data, was positively and significantly associated with being seen for asthma in the outpatient setting. Uncovering such trends can inform clinical care management plans, interventions, and policies to reduce disparities.

Clinical practice: The strength of the asthma severity computable phenotype is that it circumvents issues related to inconsistent documentation of asthma severity components and the use of varying asthma severity definitions by clinicians. The computable phenotype for asthma severity could be implemented as a clinically relevant and impactful population management tool, much like the patient-administered Asthma Control Test (ACT) score or the clinically-administered Patient Health Questionnaire (PHQ -2 or PHQ-9) for depression screening. The value of the ACT and PHQ are that they are standardized tools; the computable severity phenotype can identify the most severe asthmatics to target for intervention, with the added advantage that it can be automatically generated from existing EHR data. This application of the phenotype is valuable for EHR-based decision support and population health.

Research: The influence of informed presence on data in the EHR relevant to asthma severity varies largely by disease severity, being seen for asthma, and being seen in the outpatient setting. This has significant implications in terms of what research questions are appropriate or not appropriate within EHR-based data analyses for pediatric asthma. For example, a traditional study may be better suited to conclude the true association between changes in FEV1% and ER visits for asthmatics since FEV1% is documented mainly for moderate and severe persistent asthmatics in the EHR. On the other hand, a longitudinal analysis of EHR data may be well-

suited to advance our understanding of asthma remission and the evolution of illness trajectories (e.g. can patients “outgrow” asthma?)

Clinical research: A clinical research area of particular importance that EHR data may be ideally suited for is risk prediction of adverse events (exacerbations, death.) In regards to designing novel studies for risk prediction, the presence and absence of data in the EHR due to the healthcare process itself can be predictive of health status or adverse events^{13,14}. Asthma exacerbations are a significant contributor to morbidity and mortality across all levels of severity⁵⁹, and the variation in the presence and absence of EHR asthma severity components could be exploited for risk prediction. The computable phenotype could contribute to differentiating risk factors for exacerbations across severity levels²⁶ or be linked to omics data to further elucidate clinically-relevant asthma phenotypes⁶⁰.

Epidemiological research: While statistical methods are well established to conduct valid and unbiased studies (i.e. methods for the common missingness patterns such as missing completely at random (MCAR) and missing at random (MAR)), the concept of informed presence when it comes to EHR data automatically disqualifies most traditional statistical methodologies since EHR data are not missing at random (NMAR). Our study showed increasing asthma severity and the number of EHR data elements with severity data (i.e. completeness of severity data) were associated, and there were racial/ethnic and healthcare utilization pattern disparities in the EHR data elements recorded relevant to severity. This is consistent with the broader literature, which shows that more complete records in EHRs are biased toward sicker patients^{61,62} or certain populations (older, female)⁶³.

Studies like ours are important to discover which missingness mechanisms exist as a result of informed presence NMAR patterns so researchers can address these patterns in traditional

analyses^{8,12,64} and develop novel studies that creatively exploit the nature of EHR data. The epidemiological and informatics literatures are beginning to coalesce to create interdisciplinary solutions for “big data” health research^{8,13,40}. Both literatures have demonstrated approaches through which bias can be mitigated in EHR studies, ranging from the simple (adjusting for the number of health encounters⁶⁴ or accounting for the context in which laboratory results are collected⁶⁵) to utilizing a general framework to guide the research⁴⁰.

Limitations. There are a number of limitations to our work. This was an evaluation of a computable phenotype and not a validation study. While validation by clinically assessed (“gold standard”) chart review is a component of building a valid computable phenotype, our study emphasized the impact of unstandardized and inconsistent EHR data. The ICD-10 code indicating severity was assigned by the clinician seeing the patient and can therefore be considered a reflection of clinically assessed severity, lending confidence to our findings, but future work should incorporate chart review as a key element prior to widespread utilization.

In developing the severity phenotype, the time-scale of the phenotype (one calendar year) was a pragmatic choice and aligns with other population level, administrative timescales (i.e. HEDIS); however, other time-scales may be more clinically appropriate. The team was also guided by the NAEPP EPR3’s definition for asthma severity that is relevant to research: “For population-based evaluations, clinical research, or subsequent characterization of the patient’s overall severity, asthma severity can be inferred after optimal therapy is established by correlating levels of severity with the lowest level of treatment required to maintain control.” Thus, our study assumed the documented long-term asthma medication regimen was the treatment required to maintain control. Additionally, this study was conducted at a single institution and not across multiple institutions/EHRs. While the phenotype was constructed

largely from structured EHR data (versus unstructured EHR data), this limitation may not exist at other institutions to which this phenotype can be transported (i.e. those institutions may have the infrastructure and resources to leverage unstructured data through Natural Language Processing (NLP).) Lastly, while the proportion of asthmatics for whom we could classify severity may seem low, it is important to note that in the sample assessed, 40% of asthmatic patients did not receive care for asthma in the year their severity was assessed.

Our study demonstrates the impact of visit and documentation processes on pediatric asthma severity at New England's largest safety net hospital. Our pragmatic approach to classifying asthma severity can advance clinical practice and future research using EHR data.

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636 **Figure 1.** Flowchart of study design and analyses

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Table 1. Asthma severity phenotype algorithm for pediatric patients ages 5-18

Category basis	Intermittent	Persistent			Component annual severity select most severe from row(s)	Final annual severity select most severe from previous column
		Mild	Moderate	Severe		
Presence of Annual Long-term Rx's ⁴⁶	Step 1 medication regimen: SABA only	Step 2 medication regimen: low dose ICS OR cromolyn, LTRA, or theophylline	Step 3 medication regimen: low dose ICS AND LABA, LTRA, theophylline, or (age 12 and up only: zileuton) OR medium dose ICS	Step 4 or more medication regimen: medium dose ICS AND LABA, LTRA, theophylline, or (age 12 and up only: zileuton) OR high dose ICS OR age 12 and up only: omalizumab	Rx severity	PHENOTYPE: National Heart, Lung, and Blood Institute (NHLBI) criteria severity
Presence of Annual ICD-10	J45.2x Mild intermittent asthma...	J45.3x Mild persistent asthma...	J45.4x Moderate persistent asthma...	J45.5x Severe persistent asthma...	ICD-10 severity	
Minimum Annual FEV1% & # Annual Corticosteroids ⁴⁶	>80 FEV1% & 1 or less steroid	>80 FEV1% & 2+ steroid	60-80	<60	FEV1% severity	
SABA use for symptom control ⁴⁶	≤ 2 days/week	> 2 days/ week but not daily and not more than once on any day	Daily	throughout the day	Symptom severity	
Symptoms ⁴⁶	≤ 2 days/week	> 2 days/ week but not daily	Daily	throughout the day		
Nighttime awakening due to symptoms ⁴⁶	≤ 2x/month	3-4x/month	> 1x/week but not nightly	often 7x/week		

Abbreviations:

Medication prescription (Rx)
Short-acting beta₂-agonists (SABA)
Inhaled Corticosteroid (ICS)

Leukotriene receptor antagonists (LTRA)
Long-acting beta₂-agonists (LABA)
Percent predicted forced expiratory volume in 1 second (FEV1%)

Table 2. Sample characteristics by asthma severity ascertainment from EHR over 5-year period (n=5,047 patients)

	No severity ascertained	Severity ascertained (n=2,461)				MH chi- square p- value***
		Intermittent	Mild persistent	Moderate persistent	Severe persistent	
n	2,586	1,115	423	447	476	
Male (vs female)	1,490 (58%)	608 (55%)	236 (56%)	230 (52%)	274 (58%)	0.19
Age: 5 to 11 (vs 12 to 18)	1,205 (47%)	594 (53%)	288 (68%)	235 (53%)	352 (74%)	<0.0001
Race/ethnicity						0.009
Asian	70 (3%)	25 (2%)	15 (4%)	6 (1%)	6 (1%)	
Black	1,479 (57%)	637 (57%)	219 (52%)	260 (58%)	257 (54%)	
Hispanic	134 (5%)	22 (2%)	7 (2%)	11 (2%)	13 (3%)	
Not Recorded	634 (25%)	329 (30%)	135 (32%)	121 (27%)	148 (31%)	
Other	43 (2%)	15 (1%)	5 (1%)	3 (1%)	3 (1%)	
White	226 (9%)	87 (8%)	42 (10%)	46 (10%)	49 (10%)	
English spoken at home (vs not English)	1,975 (76%)	849 (76%)	318 (75%)	315 (70%)	375 (79%)	0.58
Duration of HCU (# years active)						0.0007
1	685 (26%)	246 (22%)	111 (26%)	121 (27%)	121 (25%)	
2	640 (25%)	263 (24%)	99 (23%)	109 (24%)	94 (20%)	
3	472 (18%)	177 (16%)	72 (17%)	68 (15%)	70 (15%)	
4	372 (14%)	169 (15%)	53 (13%)	47 (11%)	71 (15%)	
5	417 (16%)	260 (23%)	88 (21%)	102 (23%)	120 (25%)	
Total HCU (approx. quartiles: # visits/year)						<0.0001
Q1 (30%): 1 visit	1,106 (43%)	242 (22%)	84 (20%)	63 (14%)	48 (10%)	
Q2 (20%): 2 visits	517 (20%)	231 (21%)	82 (19%)	79 (18%)	80 (17%)	
Q3 (30%): 3-5 visits	655 (25%)	381 (34%)	153 (36%)	164 (37%)	165 (35%)	
Q4 (20%): 6-45 visits	308 (12%)	261 (23%)	104 (25%)	141 (32%)	183 (38%)	
Type of asthma specific HCU						<0.0001
Seen in OP for asthma*	325 (13%)	773 (69%)	325 (77%)	390 (87%)	434 (91%)	
Seen in ER and/or IP only for asthma*	470 (18%)	170 (15%)	66 (16%)	43 (10%)	30 (6%)	
No visit for asthma in the year	1,791 (69%)	172 (15%)	32 (8%)	14 (3%)	12 (3%)	
# EHR elements with data (i.e. completeness of severity data)						<0.0001
1	0 (0%)	722 (65%)	158 (37%)	98 (22%)	75 (16%)	
2	0 (0%)	368 (33%)	225 (53%)	235 (53%)	191 (40%)	
3	0 (0%)	25 (2%)	38 (9%)	109 (24%)	205 (43%)	
4	0 (0%)	0 (0%)	2 (<1%)	5 (1%)	5 (1%)	
Severity data present in specific EHR element						
Rx – long term regimen present (vs not)	0 (0%)	735 (66%)	377 (89%)	391 (87%)	471 (99%)	<0.0001
ICD-10 severity** present (vs not)	0 (0%)	414 (37%)	243 (57%)	283 (63%)	302 (63%)	<0.0001
FEV1% present (vs not)	0 (0%)	133 (12%)	70 (17%)	182 (41%)	253 (53%)	<0.0001
Symptoms present** (vs not)	0 (0%)	251 (23%)	40 (9%)	59 (13%)	66 (14%)	<0.0001

Notes: *Seen in the outpatient setting for asthma = OP, IP & ER; OP & ER; OP & IP; OP only. Seen in ER and/or IP only for asthma = ER & IP; ER only; IP only

**ICD-10 asthma codes with severity indication were implemented in 2015 and the EHR form used to record asthma symptom data was discontinued in 2015

***MH test is inclusive of no severity ascertained category

Abbreviations:

MH: Mantel-Haenszel

HCU: healthcare use

OP: outpatient visit

IP: inpatient visit

ER: emergency room visit

Table 3. Concordance and direction of change of pair-wise comparisons of EHR data elements representing asthma severity

	# patients with data in both EHR elements	Weighted Kappa	McNemar Test of Direction of Change Interpretation*
Rx & ICD-10**	1,002	0.46 (0.42,0.50)	Rx severity > ICD-10 severity
Rx & FEV1%	502	0.05 (0.01,0.09)	Rx severity > FEV1% severity
Rx & symptoms**	227	0.07 (0.02,0.12)	Rx severity > symptom severity
ICD-10** & FEV1%	343	0.02 (-0.04,0.07)	ICD-10 severity > FEV1% severity
ICD-10** & symptoms**	34	0.09 (-0.07,0.25)	ICD-10 severity > symptom severity
FEV1% & symptoms**	114	-0.11 (-0.18,-0.04)	FEV1% severity > symptom severity

Notes: * The McNemar Test of Direction of Change is a non-parametric test used to evaluate changes in directionality of paired data. In this case, it indicates whether the proportion of patients in the four severity levels differed when based on a different EHR data element. ">" is interpreted as "generally higher than" (e.g. for the first result, severity based on Rx is generally higher than when severity is based on ICD-10.) All McNemar results were significant at $p < 0.05$

**ICD-10 asthma codes with severity indication were implemented in 2015 (backdating of ICD-10 codes is possible in the system) and the EHR form used to record asthma symptom data was discontinued in 2015

Table 4. The influence of informed presence on severity ascertainment and data elements relevant to asthma severity

	Multivariable Models				
	Odds Ratio (95% confidence interval)				
	Severity ascertained versus not	Long term Rx regimen present versus not	ICD-10 severity present versus not*	Lung function test present versus not**	Symptom data present versus not***
Total n	5,047	2,461	1,625	2,461	836
Data Present	2,461	1,974	1,179	638	378
Not Present	2,586	478	446	1,823	458
Age: 5 to 11 (vs 12 to 18)	1.66 (1.42,1.94)				
Race/ethnicity					
Asian	0.76 (0.43,1.34)			0.53 (0.22,1.30)	1.65 (0.43,6.27)
Black	0.97 (0.73,1.28)			0.47 (0.32,0.69)	2.37 (1.26,4.48)
Hispanic	0.47 (0.29,0.77)			1.40 (0.62, 3.20)	2.08 (0.84, 5.11)
Not Recorded	1.08 (0.80,1.46)			0.69 (0.47,1.03)	1.62 (0.83,3.18)
Other	0.61 (0.29,1.27)			0.66 (0.21,2.05)	5.91 (1.90,18.41)
White	Reference			Reference	Reference
# years active					
1	Reference				Reference
2	1.02 (0.82, 1.27)				0.94 (0.59,1.49)
3	0.81 (0.64,1.04)				0.92 (0.54, 1.58)
4	0.95 (0.73,1.24)				1.91 (1.18,3.10)
5	1.30 (1.01,1.66)				2.41 (1.54,3.79)
# visits/year					
1 visit	Reference	Reference			
2 visits	1.40 (1.12,1.75)	1.20 (0.86,1.68)			
3-5 visits	1.60 (1.30,1.97)	1.52 (1.13,2.06)			
6-45 visits	1.62 (1.27,2.07)	1.85 (1.33,2.58)			
Asthma care during year^^					
Seen in OP for asthma		0.40 (0.27,0.58)	253 (97,663)	12 (5,29)	1.34 (0.83,2.15)
OP, IP & ER	102 (31,334)				
OP & ER	46 (32,68)				
OP & IP	49 (27,89)				
OP only	39 (32,47)				
Not seen in OP for asthma		1.64 (0.98,2.75)	26 (10,67)	0.27 (0.06, 1.27)	0.13 (0.05,0.35)
ER & IP	13 (7,24)				
ER only	4 (3,5)				
IP only	11 (8,15)				
No visit for asthma	Reference	Reference	Reference	Reference	Reference
Severity	N/A				
Intermittent		Reference	Reference	Reference	Reference
Mild		4.63 (3.31,6.48)	2.53 (1.50,4.26)	1.31 (0.92,1.86)	0.29 (0.18,0.46)
Moderate		4.18 (3.05,5.71)	4.08 (2.26,7.36)	4.27 (3.17,5.76)	0.48 (0.31,0.73)
Severe		57 (23,139)	8.65 (3.60,20.81)	6.76 (5.05,9.05)	0.41 (0.28,0.62)

Notes: **Bold:** p<0.05

*ICD-10 asthma codes with severity indication were implemented in late 2015 so data reflected is for 2016-2017

** Lung function test present means that there was a lung function test done and there is a recorded FEV1% in the patient's record

***the EHR form used to record asthma symptom data was discontinued in 2015 so data reflected is for 2013-2014

^^In the first column (severity ascertained versus not logistic model), the variable "Asthma care during year" is made up of 8 categories: from the reference category of "No visit for asthma" up to "OP, IP & ER"; however, for the remaining models, the variable is collapsed into 3 categories: No visit for asthma, Not seen in OP for asthma, and Seen in OP for asthma

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Figure 1. Flow chart of study design and analyses