Defining asthma and assessing asthma outcomes using electronic health record data: a systematic scoping review

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Short Title

Defining and assessing asthma using EHR data

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Abstract

There is currently no consensus on approaches to defining asthma or assessing asthma outcomes using electronic health record (EHR)-derived data. We explored these approaches in the recent literature, and examined the clarity of reporting.

We systematically searched for asthma-related articles published between 1-1-2014 and 31-12-2015, extracted the algorithms used to identify asthma patients and assess severity, control and exacerbations, and examined how the validity of these outcomes was justified.

From 113 eligible articles, we found significant heterogeneity in the algorithms used to define asthma (n=66 different algorithms), severity (n=18), control (n=9), and exacerbations (n=24). For the majority of algorithms (n=106), validity was not justified. In the remaining cases, approaches ranged from using algorithms validated in the same databases, to using non-validated algorithms that were based on clinical judgement or clinical guidelines. The implementation of these algorithms was sub-optimally described overall.

Although EHR-derived data are now widely used to study asthma, the approaches being used are significantly varied and are often underdescribed, rendering it difficult to assess the validity of studies and compare their findings. Given the substantial growth in this body of literature, it is crucial that scientific consensus is reached on the underlying definitions and algorithms.

Keywords: Algorithms; asthma; electronic health records; quality of reporting; reproducibility.

Take home message (117 characters for social media)

Inconsistent/underdescribed #asthma case definitions are common in research, limiting #reproducibility/#comparability

Introduction

Asthma is in clinical practice a diagnosis based on the patient history, examination and objective tests [1]. It is however increasingly considered to represent a heterogeneous group of disorders with different phenotypes and endotypes [2]. The clinical definitions of asthma and its key outcomes, including disease severity, control, and attacks/exacerbations have been the subject of vigorous debate [3–8].

Particular challenges arise in the context of epidemiologic studies where validated operational definitions are needed [9, 10]. These studies are, increasingly, being undertaken using electronic health record (EHR)-derived data, which adds a further layer of complexity as the use of valid and reliable approaches is essential in order to ensure the reproducibility of research findings [11].

In order to assess current approaches, we systematically interrogated the recent EHR-based asthma literature. Our specific objectives were to: i) describe the different methods of defining asthma and assessing disease severity, control and exacerbations in EHR-based studies; ii) investigate whether authors reported on the validity of those methods; and iii) assess their reporting practices.

Methods

We conducted a systematic scoping review based on Arksey and O'Malley's five-stage framework, including identifying the research question, identifying relevant studies, study selection, data charting and collating, summarising and reporting the results [12]. The research questions were: (1) How were asthma and its key outcomes defined using EHR data in the recent literature? (2) How did authors report on the validity of their EHR-based algorithms? (3) How clearly were the EHR-related methods reported?

Eligibility criteria and search strategy

We searched PubMed using a broad query (Table E1) to retrieve asthma studies that used EHR-derived data and were published between January 1, 2014 and December 31, 2015. The search query was iteratively improved by adding many variations and equivalents of the keywords "EHR" and "routinely collected data" as well as named data sources found in the literature. Only articles written in English were included.

Study selection

We excluded non-relevant articles by reviewing titles and abstracts, referring to the full-text when needed. We included only articles where asthma was a main finding. For the purpose of this review, we limited the concept of EHR-derived data to coded, objective, individual-level data that were generated as a by-product of routine health care.

Data extraction and synthesis

From each of the eligible articles, we extracted and summarised information from the full text and online supplements, including basic bibliography, setting (country) and design; names and types of EHR-derived data sources used; algorithms to identify asthma patients, assess disease severity, control, exacerbation; and how authors reported on algorithm validity. In this context, we referred to 'validation' as any attempt to assess the algorithm's concurrent or construct validity. We used the RECORD Statement's 13-items checklist to assess the clarity of reporting of other EHR-related aspects such as clinical code lists used in the algorithms, and the implications of using EHR data in asthma research. The RECORD Statement is a recently introduced extension to the STROBE Statement which helps improve the reporting of observational studies conducted using routinely collected data [13]. Table E2 describes the data extraction and charting tool. Article screening and data extraction were performed independently by two authors (MAS and EV) with a third author arbitrating (GAD).

Role of the funding sources

The funding sources had no role in study design; in the collection, analysis, and interpretation of data; in the writing of the report; or in the decision to submit the paper for publication.

Results

We included 113 articles in the review. Figure 1 shows the study selection process. Most studies were conducted in the United States (US), Taiwan, and Canada (Table E3), and employed longitudinal designs (Table E4). The most commonly used data types were health insurance claims followed by medical record repositories and dispensing databases (Table E5).

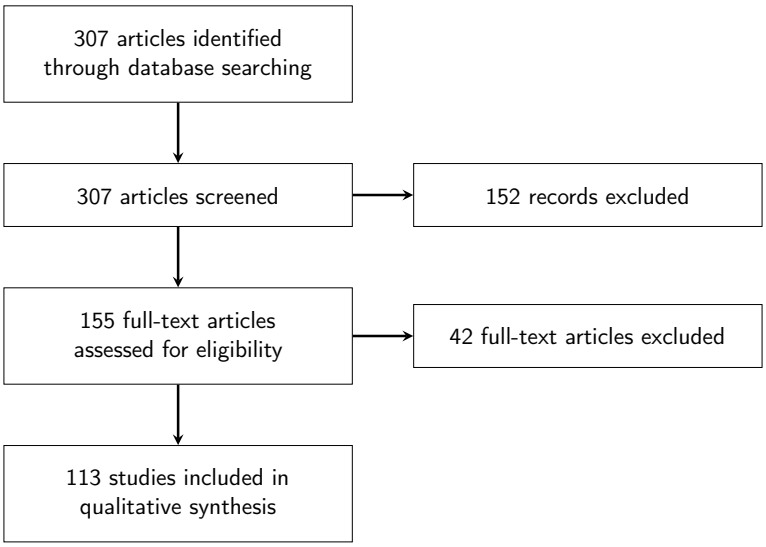

Figure 1: Flowchart for study selection in this scoping review.

Defining asthma

We identified 66 different algorithms to define asthma under seven diagnostic labels (Table E6).

'Persistent asthma' was defined over 12 and 24 months using the US Healthcare Effectiveness Data and Information Set (HEDIS) criteria [14], which involved assessing for any of the following asthma-related events: (1) emergency department (ED) visit, (2) hospitalisation, (3) outpatient visit and two asthma prescriptions, or (4) four asthma prescriptions [15–18]; by HEDIS criteria except "four asthma prescriptions" [19]; and by any asthma encounter (hospitalisation or ED visit) or using oral corticosteroids (OCS) for three or more days [20].

'Current asthma' was defined by any asthma encounter in the last three years [21].

'Current general practitioner (GP)-reported and diagnosed asthma' was defined as any asthma encounter in the last 12 months, and *'current GP-reported, diagnosed and treated asthma'* as the same plus any asthma prescription in the same period [22].

Patients with treated asthma were otherwise required to have at least three dispensing events of asthma treatments in three different quarters of the year [23].

'Acute asthma' was defined using any asthma diagnosis codes in ED or inpatient data [24].

In the remaining studies, the label *'asthma'* was defined using various algorithms, some of which were similar to those of the aforementioned more specific labels.

The intervals over which asthma diagnostic/management and prescription codes where queried were specified in 31 and 8 studies, respectively. The positions of diagnostic codes in the encounter (i.e. primary or secondary) were specified in 37 studies.

We identified five approaches in these algorithms: requiring diagnostic/management events, prescription events, or both (Table E7). In addition, to exclude likely non-asthma patients, some studies applied additional non-asthma criteria to restrict the study population based on age (Table E8) and/or comorbidities (Table E9).

Assessing asthma severity

Eighteen studies used 20 different algorithms to assess asthma severity (Table E10), as binary (i.e. severe vs. non-severe asthma) [15, 23, 25–38] or ordinal variables (mild, moderate, and severe asthma [39]; or low, moderate, and high-risk asthma [40]). The algorithms were based on one or more of the following asthma-related variables: number and/or dosage of prescriptions—namely SABA, inhaled corticosteroids (ICS), OCS, and leukotriene receptor antagonist (LTRA)—and number of hospitalisations, ED and outpatient visits. Almost all algorithms (17) used prescriptions (either alone or with other variables), while one algorithm was based only on hospitalisations and ED visits [36]. The intervals over which asthma severity was assessed were three [29], six [38], 12 [15, 23, 28, 30–32, 34, 36, 37, 39, 40], 24 months [33, 35], or unclear [26, 27].

Assessing asthma control

Nine studies assessed asthma control using 11 algorithms, in 9 of which the interval was 12 months, in one 1-3 months, and in the remaining study this was unclear (Table E12). Uncontrolled asthma was defined by a minimum number/dose of SABA prescriptions [30, 31, 39, 41, 42]; any or short-course OCS prescriptions [30, 31, 41–44]; any hospitalisation or ED visit with either diagnosis of asthma [27, 30, 31, 41–43, 45] or — in already diagnosed asthma patients — diagnosis of status asthmaticus, pneumonia, dyspnoea, or respiratory insufficiency [30]; unscheduled outpatient visits for asthma or lower respiratory tract infections (LRTI) [31]; and GP consultations for LRTI requiring antibiotics in asthma patients [31]. Asthma impairment was defined based on the required SABA use, namely an average of more than two salbutamol puffs per day [31]. One study assessed asthma control based on number of OCS and SABA prescriptions per year (without giving any further details about the actual algorithm) [41].

Defining exacerbations

Twenty-four studies defined exacerbations using EHR-derived data (Table E11), as a dichotomous variable (absent vs. present) [16, 17, 23, 27, 30–32, 35, 37–39, 42–44, 46–54], or stratified into absent, moderate and severe [55]. Oral corticosteroid prescriptions were used as a marker for exacerbations in 17 studies, either alone [23, 30, 31, 35, 39, 42, 47, 48, 53] or with a concurrent asthma encounter (e.g., a GP, outpatient, or ED visit, or hospitalisation within five or seven days) [16, 17, 32, 37, 38, 46, 52, 54]. In one study, exacerbations were defined by a minimum of six short-acting beta-2 agonist (SABA) prescriptions per year [47]. Other definitions included an outpatient code of ‘asthma exacerbation’ [52], asthma hospitalisation [23, 30, 32, 35, 37, 39, 43,

Table 1: Practices of reporting or justifying the validity of algorithms to define and assess asthma using EHR-derived data.

Algorithm validity was justified by	Number of algorithms				
	Identifying asthma patients	Assessing severity	Assessing control	Defining exacerbation	Total per category
Validation of the same algorithm in the same database	14	1	1	1	17
Validation of the same algorithm in different database(s)	2	6	3	2	13
Validation of other diseases' algorithms in the same database	2	0	0	0	2
Validation of other diseases' algorithms in different database(s)	1	0	0	0	1
Being consistent with similar studies in the same database	1	0	1	0	2
Being consistent with similar studies in different database(s)	1	0	0	1	2
Validation or concordance analysis in the same study	4	0	0	0	4
Being based on nationally developed algorithms	3	0	0	2	5
Relying on the validity of database coding	5	0	0	0	5
Being based on clinical guidelines	0	3	0	0	3
Not justified	76	8	4	18	106

44, 46, 48, 50, 51, 53–55], asthma ED visit [16, 30–32, 35, 37, 38, 43, 44, 46, 48, 51–54], or hospitalisation with diagnosis of status asthmaticus, or — in already diagnosed asthma patients — diagnosis of pneumonia, dyspnoea, or respiratory insufficiency [30].

Clarity of reporting

Overall, the reporting of methodological aspects of using EHR-derived data was suboptimal. The majority of studies presented no information on the algorithms' validity. Among studies that reported on the validity, we identified 10 practices of reporting or justifying on the validity of algorithms (Table 1): (1) performing validation or concordance analysis in the same study against other measures based on different data sources (e.g., medical record review or patient-reported measures); (2) referring to previous validation of similar algorithms in the same or (3) different databases; (4) referring to previous validation of similar algorithms for different diseases in the same or (5) different database (6); using algorithms 'consistent' with previous studies in the same or (7) different databases; (8) using nationally developed algorithms; (9) using algorithms based on clinical guidelines; (10) and relying on previous validation of the database content. Some studies did not provide clear algorithms for asthma severity or control, but only referred to their components [23, 35, 37, 38, 41].

Of the 113 reviewed studies, 40 studies used record-linkage, of which 17 mentioned it in the abstract, and 28 provided at least some explanation in the full text. The geographical region, time frame of data, and types or names of the data sources were mentioned in 83, 91, and 104 abstracts, respectively. Eighty-three studies reported their extent of access to the data sources. The intervals over which the algorithms were applied were often not reported. One hundred and eleven studies touched on the implications of using EHR data to study asthma. Of these, 64 and 63 studies discussed the risk of misclassification bias and unmeasured confounding, respectively. Six studies acknowledged the possible changes over time in data quality and coding practices and the entailing changes in case definition eligibility and accuracy. Five studies explained their data cleansing procedures. Finally, no study shared the programming codes of data preparation and analysis.

Discussion

Statement of principal findings

This systematic analysis of the contemporaneous asthma literature has found evidence of considerable international activity in using EHR-derived data to study a variety of asthma populations and outcomes. Importantly, we also found wide variations in the approaches used with limited attention being paid to the validity of the underlying algorithms used and suboptimal reporting of studies. This poses a major challenge to the interpretation and reproducibility of this important, emerging body of research inquiry.

Strengths and limitations

To our knowledge, this is the first systematic exercise to investigate the quality of reporting on EHR-based studies, especially the validity of measures, in the context of asthma. In undertaking this work, we used robust approaches which involved two people independently selecting studies and undertaking data extraction. The findings may also apply to other chronic diseases. This review had no geographic limits, but it was confined to assessing the recent literature. Examining the most recent asthma literature is most likely to provide meaningful insights on current practices. A limitation is that we did not systematically check whether the references provided to support the claimed validity of algorithms in question actually provided sufficient evidence of validity. For example, differences might exist between the algorithms used in a given study and those previously validated.

Interpretation in the light of previous studies

Although EHR-derived data are convenient resources for research, they are originally collected for other purposes, and usually suffer from missing or incorrect data and potential biases [56–58]. In addition, EHR systems usually fail to capture complete and accurate clinical information at the point of care due to design limitations and inefficient use of these systems by clinicians to document clinical data [59, 60].

These issues impose challenges on their use to assess a complex and heterogeneous condition such as asthma. For example, asthma diagnosis codes, which are commonly used solely for patient identification, may be recorded after a trial or wrong diagnosis, and do not capture undiagnosed patients [61]. In addition, many EHR-derived databases often lack important variables, such as lung function, indication of dispensed medications, adherence to treatment, and lifestyle, which are vital for identifying and assessing asthma patients. These challenges are however not insurmountable. In this review, we found several techniques intended to improve algorithm accuracy such as age limitation, comorbidity exclusion, and diagnosis position restriction.

Ideally, algorithms should be validated in the databases in which they are used. However, this was often not the case. Instead, using algorithms with only reasonable face validity based on clinical guidelines or clinical judgement is a very common practice in EHR-based studies

[62, 63]. These approaches assume that clinical codes in the database accurately represent the patient's actual health care events [62].

Under-reporting on implementation details and methods' validity compromises transparency and reproducibility, a crucial issue in medical research. It has been previously found that in EHR-based studies, full lists of clinical codes were often not reported [64]. A recent, large-scale reproducibility exercise identified similar challenges due to suboptimal reporting of EHR-based studies, particularly sharing code lists and algorithms [65].

The significant methodological heterogeneity we found in EHR-based asthma assessment algorithms reflects, in addition to the content differences between the databases used, the lack of consensus on the clinical definitions in the first place despite continuous standardisation efforts [5, 6, 66, 67]. The focus of our work was to examine asthma definitions and their validity specifically in the context of EHR, but this highlights the fundamental need to reach consensus on clinical asthma definitions and the appropriate validation of asthma diagnosis. For example, there is still an active debate on whether lung function is essential to establish asthma diagnosis [7, 8]. A recent study also found significant variation in algorithms to assess asthma severity from health insurance data [68]. Unjustified inter-study variation in the operational definitions of the same clinical concepts creates challenges for comparability, meta-analysis and evidence synthesis. These issues have been raised for asthma [69] and other allergic conditions such as peanut allergy [70, 71] and anaphylaxis [72], where wide variations in findings were potentially attributed to inconsistent case definitions.

Implications for policy, practice and research

This review sheds light on the opportunities offered by the increasingly ubiquitous EHRs, but also highlights considerable heterogeneity and suboptimal reporting of EHR-based asthma assessment algorithms and the implications of these practices on comparability and reproducibility of studies.

Developing reliable algorithms to assess asthma outcomes using EHR data is a non-trivial challenge. In addition, standardising such algorithms across different populations may be impractical since databases differ in content, validity may not hold across different populations, and no best practice currently exists [68]. Similar challenges arise when comparing asthma epidemiology between multiple populations [73]. These methodologic issues, in addition to suboptimal reporting, should be considered when interpreting and synthesising evidence from geographically dispersed studies.

With the accelerating availability of EHR-derived data and their use to study asthma, we believe that consideration needs to be given to convening an international task force to work on the harmonisation of those algorithms under uniform and consistent clinical labels, while considering the differences between populations and databases. In addition, validation of these algorithms in the respective populations should be given a high priority. Furthermore, to allow more accurate assessment of asthma from EHR data, efforts are needed to improve the capture and coding of asthma-related data at the point of care [74] which requires more efficient EHR systems [59, 60]. In addition, emerging data sources such as patient-generated data and wearables need to be harnessed [75]. Finally, to improve the clarity of reporting on EHR-related methodological aspects, we strongly advocate the adoption of the RECORD Statement as an extension of the STROBE Statement by both authors and journal editors [13]. Optimal reporting should include complete code lists, detailed algorithms and validity assessment. Implications of using EHR-

derived data to study a complex condition such as asthma should be clearly communicated to enable judgement of internal and external validity.

In summary, we have found that there is considerable international interest in exploiting EHR-derived data to study asthma, but that there are considerable variations in the approaches used. These variations are compounded by sub-optimal reporting of methods, which makes it difficult to assess the reproducibility of research. Given the substantial investments taking place in EHRs globally, this body of work is likely to grow significantly in the coming years. It is therefore important that the asthma-interested research community works to place it on a solid footing in order to ensure the quality and reproducibility of this work.

Authors' contributions

MAS, SER and GAD, AS, and RAL developed the concept and methods. MAS conducted the literature search. MAS and EV independently reviewed the studies with GAD arbitrating. All authors contributed to the development of methods, interpretation of findings, and manuscript writing, and critically reviewed and approved the final manuscript.

Conflict of Interest Statement

Aziz Sheikh reports grants from Asthma UK during the conduct of the study.

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Supplementary Materials

Table E1: Search query (adapted from [E1])

Search ID	Query
#1	Search ("humans"[mh] AND English[lang] AND ("2014/01/01"[PDat] : "2015/12/31"[PDat]) AND "loattrfull text"[sb] AND (Asthma[m "Anti-Asthmatic Agents"[mh]) AND (Asthma[tiab] OR Asthmatic[tiab] OR Asthmatics[tiab]) NOT "Comment" [pt] NOT "Editorial"["Letter" [pt] NOT "review"[pt] NOT "Meta-Analysis" [pt] NOT "clinical trial"[pt] NOT "Randomized Controlled Trial" [pt] NOT "Clini Phase I" [pt] NOT "Clinical Trial, Phase II" [pt] NOT "Clinical Trial, Phase III" [pt] NOT "Clinical Trial, Phase IV" [pt] NOT "Controll Trial" [pt] NOT "Clinical Trials as Topic" [Mesh] NOT "double-blind" [All] NOT "placebo-controlled" [All] NOT "case reports" [pt] NOT [All] NOT "pilot projects" [Mesh] NOT "Prospective Studies" [Mesh])
#2	"GPRD" OR "CPRD" OR "Clinical Practice Research Datalink" OR "General Practice Research Database" OR "SAIL databank" OR "Se Anonymised Information Linkage Databank" OR "Hospital Episode Statistics" OR ("HES" AND "England") OR "Mediplus" OR "DIN-L "QResearch" OR "RiRL" OR "Research in Real Life" OR "Paediatric Intensive Care Audit Network" OR "PICANet" OR "Scottish Drug Database" OR "Prescribing Information System" OR "Maternity and Neonatal Linked Database" OR "Office for National Statistics" OR ("UK" OR "United Kingdom")) OR "Primary Care Mortality Database" OR "PCMD" OR "Emergency department Data Set" OR "Nati Community Child Health Database" OR "Outpatient Dataset" OR "Patient Episode Database for Wales" OR "PEDW" OR "Primary Car OR "Primary Care GP dataset" OR "Maternity and Neonatal Linked Database" OR "Prescribing Information System" OR "Scottish Birt "Scottish Drug Misuse Database" OR "Scottish Morbidity Records" OR "Scottish morbidity" OR "SMR01" OR "SMR00" OR "Outpatie dataset" OR "SMR01" OR "General / Acute Inpatient and Day Case dataset" OR "Department of Health Victoria Australia" OR "Clalit computerized databases" OR "National Health Insurance Research Database" OR "NHIRD" OR "Portuguese Anti-Doping authority data "Children's Hospital Srebrnjak Database" OR "CHSD" OR "Practice Team Information" OR "Norwegian Prescription Database" OR "N "National Health Insurance Claims Database" OR "Longitudinal Health Insurance Database" OR "LHID" OR "Medical Birth Registry" O Birth Register" OR "Statistics Norway" OR "National Insurance Scheme" OR "Medco Health Solutions administrative database" OR "D Abstract Database") OR "Ontario Asthma Database" OR "Ontario COPD Database" OR "Ontario Hypertension Database" OR "Ontari Database" OR "Surveillance, Epidemiology and End Results" OR "SEER" OR "National Board of Health and Welfare and Statistics" OR Drug Register" OR "National Patient Registry" OR "Optimum Patient Care Research Database" OR "OPCRD" OR "Hospital Discharge "Cause of Death Register" OR "Register of Population and Population Changes" OR "British Thoracic Society Difficult Asthma Registry "InterAction Database" OR "IADB" OR "Total Population Register" OR "Multi-Generation Register" OR "Prescribed Drug Register" O "National Patient Register" OR "NPR" OR "Statistics Denmark" OR "Odense Pharmaco-Epidemiological Database" OR "Register of M Product Statistics" OR "RMPS" OR "Register of Medical Product Statistics" OR "RMPS" OR "National Hospital Register" OR "Hospi Enquiry" OR "HIPE" OR "Utrecht General Practitioner Research Network" OR "Christelijke Mutualiteiten health insurance" OR "MigM "Hospital Discharge Registers" OR "Ambulatory Care Classification System" OR "ACCS" OR "Physician Claims Database" OR "Medica Plan" OR "Discharge Abstracts Database" OR "Régie de l'Assurance Maladie du Quebec" OR "RAMQ" OR "MED-ECHO" OR "Fichie événements démographiques" OR "The Health Improvement Network" OR "Oxford Record Linkage" OR "PharMetrics" OR "National In Sample" OR "Mutuelle Générale de l'Education Nationale" OR "INSS Unified Benefit System"

Search ID	Query
#3	("Premier" [All] OR "Solucient" [All] OR "Cerner" [All] OR "Ingenix" [All] OR "LabRx" [All] OR "IHCIS" [All] OR "marketscan" [All] OR scan" [All] OR "Medstat" [All] OR "Thomson" [All] OR "pharmetrics" [All] OR "healthcore" [All] OR "united healthcare" [All] OR "Uni [All] OR "UHC" [All] OR "Research Database" [All] OR "Group Health" [All] OR "HCUP" [All] OR ("Healthcare Cost" [All] AND "Utiliz [All]) OR ("Health Care Cost" [All] AND "Utilization Project" [All]) OR "MEPS" [All] OR "Medical Expenditure Panel Survey" [All] OR [All] OR "National Hospital Ambulatory Medical Care Survey" [All] OR "National Ambulatory Medical Care Survey" [All] OR "NHIS" [A "National Health Interview Survey" [All] OR "Kaiser" [All] OR "Kaiser-Permanente" [All] OR "Kaiser Permanente" [All] OR "HMO Rese "Health Maintenance Organization" [All] OR "HMO" [All] OR "Cleveland Clinic" [All] OR "Lovelace" [All] OR "Department of Defense "Henry Ford" [All] OR "i3 Drug Safety" [All] OR "i3" [All] OR "Aetna" [All] OR "Humana" [All] OR "Wellpoint" [All] OR "IMS" [All] "Intercontinental Marketing Services" [All] OR "IMS Health" [All] OR "Geisinger" [All] OR "GE Healthcare" [All] OR "MQIC" [All] OR [All] OR "Institute for Drug Outcome Research" [All] OR "Pilgrim" [All] OR "Puget Sound" [All] OR "Regenstrief" [All] OR "Saskatche "Tayside" [All] OR "MEMO" [All] OR "Veterans Affairs" [All] OR "Partners Healthcare" [All] OR "Mayo Clinic" [All] OR "Rochester Ep [All] OR "Indiana Health Information Exchange" [All] OR "Indiana Health" [All] OR "Intermountain" [All] OR "blue cross" [All] OR "he [All] OR "health plan" [All] OR "health services" [All] OR "Nationwide Inpatient Sample" [All] OR "National Inpatient Sample" [All] OR [All] OR "medicare" [All] OR "MediPlus" [All] OR "Outcome Assessment" [All] OR (TennCare [tiab]) OR (RAMQ [tiab]) OR (Cigna [tia ((british columbia [tiab]) AND ((health [tiab]) OR (data [tiab]) OR (database [tiab]) OR (population [tiab]))) OR (CIHI [All Fields]) OR [tiab]) AND ((center for health policy [all fields]) OR (population [tiab]) OR (health insurance [tiab]))) OR ((ontario [tiab]) AND ((popu OR (OHIP [tiab]) OR (registered persons database [tiab]) OR (health insurance [tiab]) OR (ICES [All Fields]) OR (Institute for Clinical E Sciences [All Fields]))) OR ((Alberta [tiab]) AND ((health [tiab]) OR (data [tiab]) OR (database [tiab]) OR (population [tiab]) OR (Albe Wellness [All Fields]))) OR "ICD-9-CM" [All Fields] OR "ICD-10-CM" [All Fields] OR "ICD-9" [All] OR "ICD-10" [All] OR "internationa classification" [All] OR "international classification of diseases" [All] OR "Database Management Systems" [Mesh] OR "Medical Records Computerized" [Mesh] OR "CPT" [All] OR "Current procedural terminology" [All] OR "OPCS4" OR "OPCS-4" OR "Read code*" OR " OR "J45*" OR "H33*" OR "insurance database" [All] OR "insurance databases" [All] OR "health insurance claim*" OR "health insuran "claim data" OR "claims data" OR ("claims" [tw] AND "administrative" [tw]) OR "Insurance Claim Review"[mh] OR ((medical OR pha claim) OR ((medical OR pharmacy) AND claims) OR "Insurance Claim Reporting"[mh] OR "routine data" OR "routine health data" OR clinical data" OR "routine electronic data" OR "routinely collected data" OR "routinely-collected data" OR "routinely-collected health d surveillance" [All] OR "pharmacy data" OR "dispensing data" OR "administrative data" OR "administrative health data" OR "health ad data" OR ("data" [tw] AND "administrative" [tw]) OR "database analysis" OR "register" OR "registry" OR "Databases, Factual" [Mes "Databases as topic" [Mesh] OR "Data Warehouse" [All] OR "Medical Record Linkage" [Mesh] OR "record-linkage" OR "record linkage
#4	#1 AND (#2 OR #3)

Table E2: Charting table including data extracted from the reviewed articles.

Variable	Notes
General	
Title/Year	
Country	
Study design	
Routine data sources used	We extracted the routine datasets fro measured or derive
Algorithms and case definitions	
Asthma	Includes asthma comorbidity and validity reporting. study between the and the study-sp selection which can
Asthma severity	Also includes validit
Asthma control	Also includes validit
Asthma exacerbation	Also includes validit
Clarity of reporting routine data-related methods	
Title and abstract	
RECORD 1.1: Types or names of routine data sources used are mentioned	
RECORD 1.2: Geographical regions covered by the routine data sources used are mentioned	
RECORD 1.2: Study-time frame is mentioned	
RECORD 1.3: Record linkage is mentioned (if used)	
Methods	
RECORD 6.1: Selection process of study population is mentioned in detail; clinical codes for asthma case definitions are reported	Clinical codes coul section or in supple
RECORD 6.2: Validation for case definitions	
RECORD 6.3 and 12.3: Record-linkage, if used, is sufficiently explained	
RECORD 7.1: List of codes used in study variables	
RECORD 12.1: Authors explained their level of access to database population	
RECORD 12.2: Data cleaning is explained	
Results	
RECORD 13.1: Details of study population selection	
Discussion	

Variable	Notes
RECORD 19.1: Implications of using routine data for asthma research (e.g. misclassification bias, unmeasured confounding, missing data, and changing eligibility over time)	
RECORD 22.1: Information on how to access study protocol, raw data, and programming code is mentioned	

Table E3: Geographical distribution of the reviewed studies.

Country	Number of studies
USA	52
Taiwan	20
Canada	12
Sweden	4
Denmark	4
UK	3
Republic of Korea	2
Israel	2
France	2
Finland	2
Europe	2
USA, UK	1
Spain	1
Singapore	1
Portugal	1
Netherlands	1
Korea	1
Italy	1
Iran	1
Australia	1

Table E4: Study designs of the reviewed studies.

Study design	Number of studies
cohort study, retrospective, using routine database(s)	62
cross-sectional / prevalence study	27
nested case-control	5
cohort study, prospective, using routine database(s)	5
validation study	3
time series analysis	3
population based cross-sectional ecological study	2
cohort study, retrospective, linked to self-reported data	1
cohort study, retrospective, linked to medical charts	1
cohort study, retrospective, linked to death registry	1
case-crossover study	1
case-control study	1
case-control	1

Table E5: Types of EHR-derived data sources used in the reviewed articles.

Type	Number of studies
health insurance claim	72
medical records or medical administrative data	39
dispensing	13
mortality with causes of death	2
public health surveillance database	1
medical birth register	1
health insurance claim + medical records	1
drug adverse effect surveillance	1
disease register	1

Table E6: Algorithms used to identify asthma patients.

Label	Algorithm
asthma	asthma encounter (position = unspecified) ≥ 1
	IP (position = unspecified) ≥ 1
	Rx ≥ 1
	IP (position = unspecified) ≥ 1 OR OP (position = unspecified) ≥ 1 OR ED (position = unspecified) ≥ 1
	asthma encounter (position = 1) ≥ 1
	IP (position = unspecified) ≥ 1 OR OP (position = unspecified) ≥ 2
	IP (position = unspecified) ≥ 1 OR OP (position = unspecified) ≥ 2
	IP (position = unspecified) ≥ 1 OR OP (position = unspecified) ≥ 1
	IP (position = 1) ≥ 1
	ED (position ≤ 3) ≥ 1
	asthma encounter (position = unspecified) ≥ 1 OR Rx ≥ 1
	asthma encounter (position = unspecified) ≥ 1 AND Rx ≥ 2 within 12 months
	SABA ≥ 1 AND (ICS, inhaled anticholinergics, Theo, LTRA, OCS, Combo) ≥ 2 OR LABA-ICS ≥ 1
	Rx ≥ 1 within 12 months
	Rx > 1 OR omalizumab ≥ 1 within 12 months
	OP (position = unspecified) ≥ 3 OR IP (position = unspecified) ≥ 1
	OP (position = unspecified) ≥ 2 OR IP (position = unspecified) ≥ 2
	OP (position = unspecified) ≥ 2 OR IP (position = 1) ≥ 1 within 12 months
	OP (position ≤ 2) ≥ 2 OR IP (position = unspecified) ≥ 1 OR ED (position = unspecified) ≥ 1
	OP (position ≤ 2) ≥ 2 OR ED (position = 1) ≥ 1 OR IP (position = 1) ≥ 1
	IP OR ED (position = 1 or second to a repiratory diagnosis) ≥ 1
	IP (position ≥ 1) ≥ 1 OR OP (position ≥ 1) ≥ 2 within 2 years
	IP (position ≥ 1) ≥ 1 OR OP (position ≥ 1) ≥ 2
	IP (position ≥ 1) ≥ 1 OR OP (position ≥ 1) ≥ 1
	IP (position = unspecified) ≥ 1 OR OP (position = unspecified) ≥ 3 within 36 months
	IP (position = unspecified) ≥ 1 OR OP (position = unspecified) ≥ 2 within 12 months
	IP (position = unspecified) ≥ 1 OR OP (position = unspecified) ≥ 2 OR ED (position = unspecified) ≥ 2 O
	IP (position = unspecified) ≥ 1 OR OP (position = unspecified) ≥ 1 OR ED (position = unspecified) ≥ 1
	IP (position = unspecified) ≥ 1 OR OP (position = unspecified) ≥ 1 within 1 year
	IP (position = unspecified) ≥ 1 OR OP (position = unspecified) ≥ 1 OR Rx ≥ 4 within 12 months
	IP (position = unspecified) ≥ 1 OR (OP (position = unspecified) + ED (position = unspecified)) ≥ 2

ED = emergency department visit ; GP = general practitioner visit ; ICS = inhaled corticosteriod ; IP = inpatient hospitalisation ; LABA
leukotriene receptor antagonist ; OCS = oral corticosteroids ; OP = outpatient visit ; RSV = respiratory syncytial virus ; SABA = short-a

Table E6: Algorithms used to identify asthma patients.(cont'd)

Label	Algorithm
	IP (position = unspecified) $\geq$ 1 AND Rx $\geq$ 1
	IP (position = 1) OR OP (position = 1) ever
	IP (position = 1) $\geq$ 1 OR IP (position = 2 or 3, following pneumonia/influenza, respiratory failure, RSV/bro
	IP (position $\leq$ 2) $\geq$ 1
	GP (position $\leq$ 2) $\geq$ 1 OR IP (position $\leq$ 2) $\geq$ 1 OR ED (position $\leq$ 2) $\geq$ 1 OR asthma urgent care visit (po $\geq$ 1
	ED (position = any) $\geq$ 1 OR wheeze $\geq$ 1
	ED (position = 1) $\geq$ 1
	ED (position = 1 to 11) $\geq$ 1
	based on ICS
	based on asthma medications
	asthma encounter (position = unspecified) $\geq$ 2 within 12 months
	asthma encounter (position = unspecified) $\geq$ 2 ever
	asthma encounter (position = unspecified) $\geq$ 2
	asthma encounter (position = unspecified) $\geq$ 1 within 12 months
	asthma encounter (position = unspecified) $\geq$ 1 OR Rx within 6 months
	asthma encounter (position = unspecified) $\geq$ 1 OR Rx $\geq$ 2 ever
	asthma encounter (position = unspecified) $\geq$ 1 OR Rx $\geq$ 1 ever
	asthma encounter (position = unspecified) $\geq$ 1 OR ICS $\geq$ 1 within 12 months
	asthma encounter (position = unspecified) $\geq$ 1 OR asthma medications $\geq$2
	asthma encounter (position = unspecified) $\geq$ 1 ever
	asthma encounter (position = unspecified) $\geq$ 1 AND Rx $\geq$ 2 within 24 months
	asthma encounter (position = unspecified) $\geq$ 1 AND Rx $\geq$ 2
	asthma encounter (position = unspecified) $\geq$ 1 AND Rx $\geq$ 1 within 12 months
	asthma encounter (position = unspecified) $\geq$ 1 AND Rx $\geq$ 1
	asthma encounter (position = unspecified) $\geq$ 1 AND current Rx $\geq$ 2
	asthma encounter (position = unspecified) $\geq$ 1 AND current Rx $\geq$ 1
	asthma encounter (position = unspecified) $\geq$ 1 AND Rx $\geq$ 2
	asthma encounter (position = unspecified) $\geq$ 1 AND Rx $\geq$ 1
	(asthma encounter (position = 1) $\geq$ 1 OR asthma encounter (position $\geq$ 1) $\geq$ 4) AND (asthma prescriptions $\geq$ 1) within 5 years
current asthma	asthma encounter (position = unspecified) $\geq$ 1

ED = emergency department visit ; GP = general practitioner visit ; ICS = inhaled corticosteriod ; IP = inpatient hospitalisation ; LABA leukotriene receptor antagonist ; OCS = oral corticosteroids ; OP = outpatient visit ; RSV = respiratory syncytial virus ; SABA = short-a

Table E6: Algorithms used to identify asthma patients.(cont'd)

Label	Algorithm
current GP-reported asthma	asthma encounter (position = unspecified) $\geq$ 1 within 12 months
current treated asthma	asthma encounter (position = unspecified) $\geq$ 1 AND Rx $\geq$ 1 within 12 months
treated asthma	Rx > = 3 within 12 months
persistent asthma	Rx $\geq$ 4 OR IP $\geq$ 1 OR ED (position = 1) $\geq$ 1 OR (OP (position = any) $\geq$ 1 AND Rx $\geq$ 2) within 12 month
	Rx $\geq$ 4 OR IP $\geq$ 1 OR ED (position = 1) $\geq$ 1 OR (OP (position = any) $\geq$ 1 AND Rx $\geq$ 2) within 24 month
	Rx $\geq$ 4 OR IP $\geq$ 1 OR ED (position = 1) $\geq$ 1 OR (OP (position = any) $\geq$ 1 AND Rx $\geq$ 2) within 12 month
	Rx $\geq$ 4 OR IP $\geq$ 1 OR ED (position = 1) $\geq$ 1 OR (OP (position = any) $\geq$ 1 AND Rx $\geq$ 2)
	IP (position = unspecified) $\geq$ 1 OR ED (position = unspecified) $\geq$ 1 OR OCS $\geq$ 3) within 12 months

ED = emergency department visit ; GP = general practitioner visit ; ICS = inhaled corticosteriod ; IP = inpatient hospitalisation ; LABA
leukotriene receptor antagonist ; OCS = oral corticosteroids ; OP = outpatient visit ; RSV = respiratory syncytial virus ; SABA = short-a

Table E7: Approaches used in identifying asthma patients.

Criteria base on	Diagnostic label used	Number of studies
Asthma diagnostic/management codes	'asthma'	68
	persistent asthma	1
	acute asthma	1
	current asthma	1
	current GP-reported and diagnosed asthma	1
Asthma diagnostic/management codes AND asthma prescription codes	'asthma'	11
	current treated asthma	1
	persistent asthma	2
Asthma prescription codes	asthma	22
	treated asthma	1
	persistent asthma	4

Table E8: Approaches used in identifying asthma patients.

Age limits	Studies	Number of studies
Minimum age limits		
6 months	E2	1
2 years	E3–E8	6
3 years	E9–E11	3
5 years	E12–E14	3
Maximum age limits		
44 years	E15	1
55 years	E16	1
60 years	E17	1
64 years	E18	1

Table E9: Co-morbidities and conditions based on which asthma patients were excluded.

Condition	Number of studies
COPD	11
Cystic fibrosis	13
Pulmonary embolism	3
Bronchiectasis	4
Pulmonary hypertension	4
Congestive heart failure	3
Emphysema	3
Chronic bronchitis	2
Immunodeficiency	2
Churg Strauss syndrome	1
Wegener syndrome	1
Sarcoidosis	1
Smoker over age of 60	1
Pneumonia	1
Anti-cholinergic prescription as a proxy of COPD	1
Chronic respiratory failure	1
Achondroplasia	1
Bronchopulmonary dysplasia	1
Respiratory cancer	1
Active or past tobacco use	1
Primary ciliary dyskinesia	1
Tracheomalacia	1
Bronchiolitis/RSV infection	2
Pneumoconiosis	1
Other lung diseases due to external agents	1
Psychosis	1
"Perinatal respiratory condition"	1
Tracheostomy	1
Gastrostomy	1

Table E10: Algorithms used to ascertain asthma severity using EHR data.

Variable	Algorithm	Interval (months)	Appears in
Mild asthma	either 500 mg/day of ICS monotherapy (in beclomethasone chlorofluorocarbon equivalents) **OR** 250 mg/day of ICS + additional controller **AND** either $\leq$ 3 SABA doses per week on average (each = 2 salbutamol 100mg puffs) **OR** both 4−10 doses of SABA per week on average **AND** no moderate to severe asthma exacerbation (defined as asthma ED visit **OR** asthma hospitalization **OR** short−course OCS)	12	[E19]
Moderate asthma	**NOT** mild asthma **NOR** severe asthma as defined in the same study	12	[E19]
Severe asthma	$>$ 1000 mg/day of ICS **AND** one of $>$ 3 SABA per week on average **OR** $\geq$ 1 moderate to severe asthma exacerbation **OR** both lower doses of ICS with >10 SABA doses per week on average **AND** 1 moderate to severe asthma exacerbation	12	[E19]
	$>$ 6 albuterol refills per year	12	[E3]
	GINA step 4 or higher	unclear	[E20]
	continuous treatment with ICS (at least 800 mg budesonide daily or equivalent [500 mg fluticasone]) and (LABA)	12	[E21]
	presence of persistent asthma according to the HEDIS criteria associated with readmission **OR** presence of complex chronic condition within the prior year associated with readmission	12	[E5]
	based on number of ICS, LABA, and OCS prescriptions	24	[E22]
	based on number of asthma prescriptions (including OCS)	12	[E23]

ED = emergency department; GINA = Global Initiative for Asthma; HEDIS = Healthcare Effectiveness Data and Information Set; IC
long-acting β2 agonists; OCS = oral corticosteroids; OP = outpatient; SABA = short-acting β2 agonists
.

Table E10: Algorithms used to ascertain asthma severity using EHR data.(cont'

Variable	Algorithm	Interval (months)	Appears in
	based on asthma hospitalisation, asthma Ed visits, outpatient visits for asthma exacerbation, number of SABA dispensings, number of OCS dispensings	12	[E24]
	based on number of of asthma hospitalisations, asthma ED visits, SABA prescriptions, OCS prescriptions, and asthma exacerbations over 6 months	6	[E14]
	based on acute OCS course, mean daily SABA dose, number of asthma consultations with no acute OCS	12	[E17]
	ICS (>800 mg budesonide daily) **AND** second controller **OR** ICS−LABA **OR** omalizumab	12	[E15]
	According to GINA 2006 classification of severity	unclear	[E25]
	Based on OCS prescriptions	unclear	[E26]
	Number of OP over variable follow−up periods	variable	[E27]
'More severe asthma'	$\geq$ 2 SABA prescriptions within 90 days of ICS prescriptions	3	[E28]
	HEDIS criteria for persistent asthma: $\geq$ 1 asthma hospitalisation **OR** $\geq$ 1 asthma ED visit **OR** $\geq$ 4 asthma prescriptions **OR** both $\geq$ 4 asthma outpatient visits **AND** $\geq$ 2 asthma prescriptions	24	[E7]
	$\geq$ 1 asthma hospitalisations or ED visits	12	[E29]
Low-risk asthma	no asthma ED visits **AND** no asthma hospitalisations **AND** $<$ 15 β−agonist canisters dispensed **AND** no OCS dispensed	12	[E10]

ED = emergency department; GINA = Global Initiative for Asthma; HEDIS = Healthcare Effectiveness Data and Information Set; IC
long-acting β2 agonists; OCS = oral corticosteroids; OP = outpatient; SABA = short-acting β2 agonists
.

Table E10: Algorithms used to ascertain asthma severity using EHR data.(cont'

Variable	Algorithm	Interval (months)	Appears in
Moderate-risk asthma	no asthma ED visits **AND** no asthma hospitalisations **AND** only one of: $\geq$ 15 $\beta-$agonist canisters dispensed **OR** $\geq$ 1 OCS dispensings	12	[E10]
High-risk asthma	$\geq$ 1 asthma ED visits **OR** $\geq$ 1 asthma hospitalisations **OR** both: $\geq$ 15 $\beta-$agonist canisters dispensed **AND** $\geq$ 1 OCS dispensings	12	[E10]

ED = emergency department; GINA = Global Initiative for Asthma; HEDIS = Healthcare Effectiveness Data and Information Set; IC
long-acting β2 agonists; OCS = oral corticosteroids; OP = outpatient; SABA = short-acting β2 agonists
.

Table E11: Algorithms used to ascertain asthma exacerbation using EHR data

Variable	Study	Algorithm	OCS				IP	ED
			alone	+ OP	+ IP, ED, OP or GP	+ IP or ED		
Exacerbation	[E30]	$\geq$ 1 OCS prescription for $<$ 21 days **OR** $\geq$ 4 asthma GP visits per year **OR** $\geq$ 5 SABA prescriptions per year	$<$ 21 days					
	[E15]	$\geq$ 1 OCS prescription **OR** Hospitalisation or ED visit for asthma, status asthmaticus, pneumonia, dyspnoea, or respiratory insufficiency	$\geq$ 1				p	p
	[E32]	asthma hospitalisation **OR** asthma ED visit **OR** OCS pharmacy claim	p				p	p
	[E20]	OCS prescription within 7 days of any asthma encounter (which may include hospitalisation, ED, outpatient, or GP visit, ascertained with the ICD−9 code 493 as a primary diagnosis or as a secondary diagnosis provided the primary diagnosis is another respiratory condition) Variation: asthma encounter = asthma hospitalisation or ED visit only			within 7 days	within 7 days		
	[E22]	OCS with asthma as indication **OR** asthma ED visit **OR** asthma hospitalisation	indication is asthma				p	p

p = present; a = absent; OCS = oral corticosteroids; AE = asthma exacerbation; SABA = short-acting $\beta 2$ agonists; ED = emergency depa
of Diseases; IP = inpatient hospitalisation; OP = outpatient; GP = general practitioner.

Table E11: Algorithms used to ascertain asthma exacerbation using EHR data. (co

Variable	Study	Algorithm	OCS				IP	ED
			alone	+ OP	+ IP, ED, OP or GP	+ IP or ED		
	[E23]	OCS prescription **OR** number of asthma GP visits **OR** hospitalisation for asthma (as a primary diagnosis; variation: as a priamry or secondary diagnosis)	p				p	
	[E33]	Occurrence, after 3 months from previous asthma hospitalisation, if any, of: OCS short−course **OR** asthma ED visit (ICD−9−CM = 493) **OR** asthma hospitalisation (ICD−9−CM = 493)	p				p	p
	[E34]	Primary hospital discharge diagnosis of asthma exacerbation					p	
	[E35]	ED visit with primary diagnosis of asthma **OR** outpatient visit with diagnosis of asthma exacerbation **OR** diagnosis of asthma with OCS prescription (< 14−day supply) within 5 days **OR** hospitalization with diagnosis of asthma (primary) or asthma exacerbation (any position)		< 14-day supply; within 5 days			p	p
	[E36]	OCS use **OR** asthma ED visit **OR** asthma hospitalisation	p				p	p

p = present; a = absent; OCS = oral corticosteroids; AE = asthma exacerbation; SABA = short-acting β2 agonists; ED = emergency depa
of Diseases; IP = inpatient hospitalisation; OP = outpatient; GP = general practitioner.

Table E11: Algorithms used to ascertain asthma exacerbation using EHR data. (co

Variable	Study	Algorithm	OCS				IP	ED
			alone	+ OP	+ IP, ED, OP or GP	+ IP or ED		
	[E24]	outpatient visit with primary diagnosis of asthma (ICD−9−CM = 493) and OCS dispensing within 5 days **OR** asthma ED visit (ICD−9−CM = 493.xx) **OR** asthma hospitalization (ICD−9−CM = 493.xx)		within 5 days			p	p
	[E37]	ED visit with any asthma diagnosis **OR** hospitalization with primary diagnosis asthma **OR** OCS with asthma claim within 7 days			within 7 days		p	p
	[E38]	one−off OCS prescription (short−course)	p					
	[E39]	OCS within 7 days of an encounter with diagnosis of exacerbation or uncontrolled asthma			P			
	[E40]	$\geq$ 1 asthma ED visits **OR** $\geq$ 1 asthma hospitalizations **OR** OCS prescriptions	p				p	p
	[E41]	asthma ED visit (ICD−9−CM = 493) **AND/OR** asthma hospitalisation (ICD−9−CM = 493)					p	p
	[E9]	Encounter with asthma exacerbation code						

p = present; a = absent; OCS = oral corticosteroids; AE = asthma exacerbation; SABA = short-acting β2 agonists; ED = emergency depa
of Diseases; IP = inpatient hospitalisation; OP = outpatient; GP = general practitioner.

Table E11: Algorithms used to ascertain asthma exacerbation using EHR data. (co

Variable	Study	Algorithm	OCS				IP	ED
			alone	+ OP	+ IP, ED, OP or GP	+ IP or ED		
	[E17]	acute OCS **OR** unscheduled asthma hospitalisation **OR** ED visit	p				p	p
	[E18]	new occurrence (after >= 8−day wash−up period) of: Both Asthma outpatient visit (with a code for acute exacerbation, status asthmaticus, acute asthma attack, uncontrolled asthma, asthmatic bronchitis) **AND** OCS dispensing within 7 days **OR** Asthma ED visit or hospitalization (asthma diagnosis position = 1 **OR** position = 2 following a primary respiratory diagnosis)		p			p	p
	[E42]	Asthma hospitalization **OR** Asthma ED visit **OR** Asthma OP visit with OCS prescription		p			p	p
	[E25]	Based on rescue medications						
Moderate-to-severe exacerbation	[E19]	OCS short−course **OR** asthma ED visit **OR** asthma hospitalisation	p				p	p
	[E14]	OCS within 7 days of asthma outpatient visit **OR** Asthma ED visit		within 7 days				p

p = present; a = absent; OCS = oral corticosteroids; AE = asthma exacerbation; SABA = short-acting β2 agonists; ED = emergency depa
of Diseases; IP = inpatient hospitalisation; OP = outpatient; GP = general practitioner.

Table E11: Algorithms used to ascertain asthma exacerbation using EHR data. (co

Variable	Study	Algorithm	OCS				IP	ED
			alone	+ OP	+ IP, ED, OP or GP	+ IP or ED		
Moderate exacerbation	[E43]	$\geq$ 1 ED visits for asthma **AND** no hospitalisation for asthma					a	p
Severe exacerbation	[E43]	$\geq$ 1 hospitalisation for asthma as a primary or admission diagnosis					p	

p = present; a = absent; OCS = oral corticosteroids; AE = asthma exacerbation; SABA = short-acting β2 agonists; ED = emergency depa
of Diseases; IP = inpatient hospitalisation; OP = outpatient; GP = general practitioner.

Table E12: Algorithms used to assess asthma control using EHR data

Variable	Algorithm	Interval	Appe
Low control/ uncontrolled asthma	$\geq$ 600 doses (1 dose = 1 puff) of SABA in the recent year **OR** $\geq$ 1 exacerbation in the recent year, defined as: $\geq$ 1 hospitalisation or ED visit associated with ICD−10 code for asthma, status asthmaticus, pneumonia, dyspnoea, or respiratory insufficiency **OR** $\geq$ 1 OCS prescription	12 months	[E15
	$\geq$ 1 hospitalisation or ED visit **OR** dispensing of OCS for $\geq$ 3 days	12 months	[E40
	$\geq$ 1 ED or OP visit for asthma **OR** $\geq$ 1 antibiotic prescriptions	unclear	[E44
	$\geq$ 1 moderate to severe asthma exacerbation **AND** $>$ 3 and 10 SABA doses per week on average for mild and moderate/severe asthma, respectively	12 months	[E19
	$\geq$ 2 acute care contact within 1 month **OR** $\geq$ 3 reliever inhaler uses per week **OR** severe exacerbation requiring ICU/intubation in the last 3 months **OR** asthma hospitalisation in the last 3 months	1-3 months	[E25
	at the assessment date $>$ 2 asthma drug classes **OR** $\geq$ 1 SABA **OR** in 12 months $\geq$ 1 OCS **OR** $\geq$ 6 SABA **OR** $\geq$ 1 asthma ED visits **OR** $\geq$ 1 asthma hospitalisations	12 months	[E38

LRTI = lower respiratory tract infection; SABA = short-acting β agonists; OCS = oral corticosteroids; GP = general practitioner; E
International Classification of Diseases

Table E12: Algorithms used to assess asthma control using EHR data (cont'd

Variable	Algorithm	Interval	Appe
Low-risk asthma control	Absence of all the following: hospitalisation, ED, and unscheduled outpatient visits for asthma (ascertained by any asthma or LRTI codes) GP consultation for LRTI requiring antibiotics acute course of OCS	12 months	[E17
	based on number of OCS prescriptions per year	12 months	[E45
Impairment-domain asthma control	based on number of $\beta-$agonists prescriptions per year	12 months	[E45
	$>$ 2 salbutamol puffs per day ($> 200\mu$g in the UK and $> 180\mu$g in the US)	12 months	[E17
Overall asthma control	based on impairment−domain and risk−domain asthma control algorithms used by the same study	12 months	[E17

LRTI = lower respiratory tract infection; SABA = short-acting β agonists; OCS = oral corticosteroids; GP = general practitioner; E
International Classification of Diseases

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