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Early View

Review

Identifying COPD in routinely collected electronic health records: a systematic scoping review

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Identifying COPD in routinely collected electronic health records: A systematic scoping review

256 character take-home message: Inconsistency in methods of identifying COPD in electronic health records and the lack of clinically important variables in healthcare databases widely used for research are persisting constraints in harnessing the potential of EHR worldwide.

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Abstract

Although routinely collected electronic health records (EHR) are widely used to examine outcomes related to chronic obstructive pulmonary disease (COPD), consensus regarding the identification of cases from electronic healthcare databases is lacking. We systematically examine and summarise approaches from the recent literature.

MEDLINE via EBSCOhost was searched for COPD-related studies using EHR published from 1 January 2018 to 30 November 2019. Data were extracted relating to the case definition of COPD and determination of COPD severity and phenotypes.

From 185 eligible studies, we found widespread variation in the definitions used to identify people with COPD in terms of code sets used (with 20 different code sets in use based on the ICD-10 classification alone) and requirement of additional criteria (relating to age (n=139), medication (n=31), multiplicity of events (n=21), spirometry (n=19) and smoking status (n=9)). Only 7 studies used a case definition which had been validated against a reference standard in the same dataset. Various proxies of disease severity were used since spirometry results and patient-reported outcomes were not often available.

To enable the research community to draw reliable insights from electronic health records and aid comparability between studies, clear reporting and greater consistency of the definitions used to identify COPD and related outcome measures is key.

Introduction

Chronic obstructive pulmonary disease (COPD) is a common, chronic condition characterised by persistent respiratory symptoms and irreversible expiratory airflow limitation, usually caused by chronic exposure to inhaled noxious substances. In clinical practice, COPD can be diagnosed in patients suspected to have the condition by use of spirometry, which also aids in the assessment of disease severity. Patients with COPD can also be grouped by their pattern of exacerbations and symptom burden, and this phenotyping guides treatment decisions [1]. Guidelines produced by the Global Initiative for Chronic Obstructive Lung Disease (GOLD) divide patients into 'GOLD groups' based on these characteristics when delineating treatment strategies.

Research using routinely collected data from electronic health records (EHR) and administrative databases to study COPD has seen an upsurge in recent years, as the wealth of data accumulated as a by-product of routine clinical care has made large, diverse populations accessible to researchers. However, this data has not been generated for the purpose of research, and important information such as spirometry results and patient-reported outcome measures are not often accessible in the data sources. Alternative measures are thus frequently used to identify individuals with COPD, as well as determine disease severity and phenotypes, though the extent to which the definitions used have been assessed for validity is unclear.

Although the need to focus on the accuracy of case definitions has been emphasised [2], there is still significant heterogeneity in the definitions used to identify common conditions in routinely collected data [3–5]. In this systematic scoping review, we sought to summarise the range of methods used to identify COPD, its severity and phenotypes in EHR, and determine what proportion of case definitions in use have been validated against reference standards.

Methods

We conducted a systematic scoping review [6] to answer our research questions: 1) how were individuals with COPD identified in EHR in the recent literature, 2) how many methods of case identification had been validated against reference standards, 3) how were COPD severity and phenotypes defined, and 4) what important data are missing from the data sources used in these studies?

Search strategy and eligibility criteria

A broad search strategy was developed to gather studies which used EHR to identify individuals with COPD (supplementary material S1). MEDLINE via EBSCOhost was searched 15th January 2020 for articles published between 1 January 2018 and 30 November 2019. Our search was limited to those written in the English language. There were no limitations as to study design.

EHR included routinely collected, individual level data from administrative databases, disease registries, electronic health records, and any other electronic databases that were generated as a by-product of routine healthcare. Studies using solely survey or trial data were excluded, along with studies not reporting original data. We included studies identifying a study population of individuals with COPD or using COPD as a primary outcome, but not those where COPD was just contained in a list of covariates.

Study selection and data extraction

Articles that did not fit the above eligibility criteria were excluded. Screening was initially conducted using titles and abstracts, and full-texts were accessed when necessary. Information extracted from articles deemed eligible for inclusion related to core study details, definitions of COPD diagnosis, severity and phenotypes, and quality appraisal (supplementary material S2).

Article screening and data extraction were performed independently by two authors (S.S. and M.A.A.) for 20% of studies. S.S. then completed screening and extraction, with discussion with the wider study group when necessary.

Results

Our search strategy identified 1226 articles for screening (supplementary material S1), of which 189 met our eligibility criteria. We were able to access the full text for 185 of these, which are included in our review. Most studies were conducted in North America, Taiwan, and the United Kingdom (UK) (supplementary material S3). We included studies with a range of designs, including retrospective cohort, self-controlled case series, quasi-experimental, nested case control, case crossover and descriptive/exploratory studies.

Identifying COPD

Studies often identified individuals with COPD using clinical codes. The most frequently used coding scheme was the International Statistical Classification of Diseases and Related Health Problems (ICD) [7], either alone or in conjunction with other coding schemes (supplementary material S4). However, studies using the same coding scheme did not always use the same list of codes ('code set') from within the scheme – 57 studies incorporating ICD-10 based code used 20 different code sets to detect COPD (supplementary material S5). Some studies did not report the specific code set used for case identification.

In order to achieve greater accuracy of case definitions, many studies used additional inclusion and exclusion criteria in their definition of COPD. 139 (75%) used age as a criterion, with the lower age limit varying from 18 to 66 (supplementary material S6). Some studies (21, (11%)) required multiple COPD-related event or claim codes. Some (25, (14%)) gave more weight to inpatient care codes, requiring multiple COPD-related codes if arising from primary care or outpatient care, but only one if arising from inpatient care. 19 (10%) mandated presence of a spirometry code, but results of spirometry were not always taken into account. 9 (5%) specified ever-smoking as a criterion (supplementary material S7). A COPD-related medication code was required by 31/171 (18%) studies (not including studies whose aim was to investigate COPD medications, since these would have automatically required presence of the medication). The specific medication requirements and reporting of this varied by study, from requiring 'the prescription of at least one bronchodilator'[8] to mandating a greater

frequency of medication use, with 'COPD medication use at least twice per year'[9] (where COPD medications were 'long-acting muscarinic antagonist, long-acting beta-2 agonist (LABA), inhaled corticosteroid (ICS), ICS plus LABA, short-active muscarinic antagonist (SAMA), short-acting beta-2 agonist (SABA), SAMA plus SABA, methylxanthines, systemic corticosteroids, and systemic beta agonists')[9]. One study stated only that patients were required to have been prescribed a 'respiratory medication' but did not elaborate further[10].

With regard to exclusion criteria, 25 (14%) studies excluded those with a previous asthma diagnosis, some excluded additional comorbid respiratory conditions, and a few excluded individuals using specific medications, such as leukotriene receptor antagonists which are mostly used in people with asthma.

COPD severity

Spirometry was utilised by 25 (14%) studies in their assessment of COPD severity, 8 (4%) as a binary measure, 17 (11%) as an ordinal measure. Most studies did not assess disease severity in any form, specifying that this was because they lacked the clinical data necessary. Proxies of severity were sometimes used, ranging from chronic medication use (n=16 (9%)) and measures relating to exacerbations (n=16 (9%)), to serum bicarbonate levels (n=1 (0.5%)) [11], to algorithms purporting to represent 'complexity' (n=1 (0.5%)) [12].

COPD phenotypes

Coexisting asthma was a phenotype examined by 15 (8%) studies and was generally identified by presence of a previous asthma diagnosis code, but the specific code sets or identification methods were not always reported. 12 (6%) studies compared those with high versus low blood eosinophil counts or concentrations, although the thresholds used to determine high and low differed by study (supplementary material S8) [13–15]. 3 studies performed sensitivity analyses to examine the effect of using differing thresholds [16–18]. 8 (4%) studies categorised individuals by their GOLD groups (i.e. taking into account both exacerbation history and symptom burden), and 18 (10%) examined individuals by exacerbation history. Again, there was variation in the code sets or

algorithms used to identify an exacerbation, and the thresholds for high versus low exacerbators.

Validation of case definitions

8 (4%) studies in our review compared their definition of COPD against a reference standard and provided sufficient information that a measure of validity could be calculated, although this may not have been their primary purpose. 2 of these studies identified themselves as 'validation studies' and went on to report measures of validity [19, 20].

Of the remaining 177 studies, a further 7 (4%) used a definition of COPD that had been previously validated against a reference standard in the same database used for their research. Additional studies referred to their case definition being 'based on' validated definitions, but used code sets different to those validated [21–23], or did not report the codes they used [18, 24, 25].

Some studies conducted analyses to justify the validity of their findings in different ways, such as performing sensitivity analyses using different definitions of COPD [26].

Reporting

Only one study referred to the REporting of studies Conducted using Observational Routinely collected Data (RECORD) guidance [27]. 15 (8%) studies stated that they used a particular coding scheme to identify people with COPD but did not report the code set used. 107 (58%) studies did not report whether they could access data related to (one of) smoking or spirometry. 44 (24%) reported that smoking information was not available within their data source (supplementary material S7), and 60 (32%) reported that spirometry events were unavailable.

Discussion

Principal findings

Electronic databases of routinely collected health data are used internationally to advance knowledge about 'real world' COPD by the research community. This systematic scoping

review has demonstrated significant variability in the methods used by researchers to identify individuals with COPD and describe disease severity and phenotypes using routine data.

Only a limited number of studies used definitions that had been validated against reference standards in the same database used for their study. Some studies referred to previous validation studies, but as they did not report the code list they had used, it was not clear whether they used the same validated case definition. The RECORD guidance [27] advocates for provision of a 'complete list of codes and algorithms used to classify exposures, outcomes, confounders, and effect modifiers' in order to enhance research transparency.

Interpretation and implications

Datasets generated as a by-product of routine clinical care are increasingly important and useful in research, given the size, heterogeneity, and unselected nature of the populations they provide access to. However, there are pitfalls to their use, and among them is the use of case definitions with unknown validity. Limitations in the reporting of code sets used by researchers further hinder comparability and reproducibility.

For EHR to provide meaningful insights, the case definitions used must be able to accurately detect individuals with the condition in question. One way of ensuring this is to use definitions validated against a reference standard. However, a definition validated in one database may not be transferable for use in others. One validated definition for COPD in the UK's Clinical Practice Research Datalink [28] specifies being a current or ex-smoker as an inclusion criterion, given that COPD is uncommon in never-smokers in the UK. However, in countries with a higher contribution of alternative risk factors to the development of COPD [29], necessitating being an ever-smoker would likely reduce the sensitivity of this definition, as will happen in all geographies where smoking prevalence is falling. Additionally, different research questions may necessitate different case definitions – if investigators wanted to prioritise specificity over sensitivity, a more

restrictive definition would be used, and vice versa – but clarity in the rationale would be useful to readers.

In addition to case definitions, the availability and accuracy of disease severity and phenotyping measures is imperative for studies to be able to adequately adjust for potential confounding. However, many administrative databases do not contain clinical detail at this level, so attempts at adjusting for severity in analyses often use proxy measures, the choice of which may be determined by data availability and not be validated against 'true' disease severity. More often, no attempt at adjusting for disease severity is made, leading to the potential of unmeasured confounding influencing results. Facilitating inclusion of clinically important variables (such as common investigation results and patient-reported outcome measures) into electronic health databases commonly used for research would be a useful and important intervention in improving research outputs. Through the lens of COPD, inclusion of spirometry results and UK Medical Research Council (MRC) dyspnoea scale scores would play a significant role in advancing research in the field. Similarly, inclusion of echocardiogram results and New York Heart Association (NYHA) class would likely be helpful for cardiovascular disease research. However, even when databases do hold such information, there may be a high rate of missing data (e.g., 65% of patients in one study had no spirometry recorded) [30]. This reflects real world patterns and levels of missingness are likely to vary geographically due to historic differences in clinical practice, or national incentive schemes.

Strengths and limitations

This is the first review, to our knowledge, to systematically examine methods of identifying individuals with COPD in routinely collected electronic health records. This approach has allowed us to objectively demonstrate the variability in research practice in the field. We applied broad inclusion criteria ensuring representation across the research field, but confined our review to recent literature in order to ensure relevancy. We did not include studies where COPD was only relevant due to being contained in a list of covariates (as is often done, for example as part of the Charlson Comorbidity Index) [31]

since an accurate case definition for this purpose holds less importance. However, this means that our review does not fully encompass the whole spectrum of the use of 'COPD' in electronic health data research.

Conclusions

Although the interrogation of routinely collected electronic health records is now commonplace in investigating important research questions related to COPD, and provides huge value when used carefully, persistent limitations constrain the quality of this research. The lack of clinically important variables in widely used databases limits researchers' ability to adjust for confounders such as disease severity. Variation in methods to identify COPD and define outcome measures restricts comparability between studies. With the contribution of EHR to COPD research continuing to increase internationally, ensuring greater consistency of case definitions and optimisation of reporting is key to enhancing the reliability of research outputs.

Footnotes

Ethics:

Ethical review was not required since this study was a review of previously published work.

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Supplementary material

Table S1: Search strategy

#	Query	Results
S1	(MH "Medical Records Systems, Computerized+") OR (MH "Medical Record Linkage") OR (MH "Electronic Health Records+") OR (MH "Clinical Coding") OR (MH "International Classification of Diseases")	50,268
S2	(MH "Databases as Topic+")	151,665
S3	medical record linkage or medical records linkage or clinical coding or code or codes or coding or codelist* or codeset* or algorithm* or International Classification of Disease* or ICD* or ICD-10 or ICD-9 or ICD-9-CM or ICD 9 or ICD 10	712,365
S4	emr or electronic medical record* or ehr or electronic health record*	44,324
S5	(data* or record*) and (insurance or claim* or administrative or routine* or electr* or digit* or computer* or linked)	1,667,252
S6	S1 OR S2 OR S3 OR S4 OR S5	2,297,452
S7	(MH "Pulmonary Disease, Chronic Obstructive+")	53,773
S8	copd or chronic obstructive pulmonary disease or coad or chronic obstructive airway disease or chronic obstructive lung disease or emphysema or chronic bronchitis or chronic airflow obstruction* or airflow obstruction, chronic or chronic airway obstruction* or airway obstruction, chronic	114,337
S9	S7 OR S8	114,337
S10	S6 AND S9 Limiters – Date of Publication: 20180101-20191130; English Language; Human	1,226

Table S2: Data extraction table

Variable	Variable value options
Core study details	
PubMed ID	Free text
Article title	Free text
Study location (country)	Free text
Study design	Free text
Data source	Free text
Study aim	Free text
Definition of COPD	
Inclusion criteria notes	Free text
Coding scheme used	ICD-9, ICD-9-CM, ICD-10, ICD-10-CM, ICD-10-CA, Read code, DRG, ATC, Other code, Mix of above codes, No codes reported
Code set used	Free text
Age as criterion?	Y/N
Age - lower limit	Free text
Requirement of multiple claims?	Y/N
More weight to inpatient claims?	Y/N
Requirement of specific treatment?	Y/N
Requirement of spirometry?	Yes spirometry required but results not specified, Yes spirometry required and results specified, No
Requirement of ever-smoker?	Y/N
Exclusion criteria notes	Free text
Exclusion criteria: are patients with asthma excluded?	Y/N
Definitions of COPD severity	

COPD severity notes	Free text
Spirometry- binary	Y/N
Spirometry- ordinal	Y/N
Related to chronic medication use?	Y/N
Related to exacerbations?	Y/N
Other proxies of severity	Free text
Definitions of COPD phenotype	
COPD phenotype notes	Free text
Co-existing asthma	Y/N
Blood eosinophil level	Y/N
Exacerbators	Y/N
GOLD groups	Y/N
Other	Free text
Quality appraisal	
Does the study validate definitions used?	Y/N
Have the definitions used been validated previously in the same dataset used for the study?	Y/N
Other justification of validity?	Free text
Missing data: smoking	Smoking data missing, smoking data not missing, not reported
Missing data: spirometry	Spirometry data missing, spirometry data not missing, not reported
Missing data: other	Free text
Other limitations and measure to minimise limitations	Free text
Reference to RECORD statement	Y/N

Table S3: Geographical distribution

Country	Number of studies
USA	52
Taiwan	29
United Kingdom	20
Canada	15
Spain	11
Korea	9
China	7
Italy	6
Sweden	5
Denmark	4
Netherlands	4
Hong Kong	3
Australia	3
Israel	3
Belgium	2
Poland	2
Austria	2
France	2
Scotland	1
Norway and Germany	1
Ireland	1
Singapore	1
Germany	1
Turkey	1

Table S4: Coding schemes used by studies

Coding scheme	Number of studies
ICD-9-CM	52
ICD-10	35
No codes reported	28
Mix of other named categories	25
ICD-9	23
Read code	15
Other codes*	4
ICD-10-CM	1
ICD-10-CA	1
N/A	1

ICD 10 = the International Statistical Classification of Diseases and Related Health Problems, 10th revision, the replacement of ICD-9. ICD-10-CM = clinical modification of the classification, replacing ICD-9-CM. ICD-10-CA is the Canadian modification.

*'Other codes' includes the Anatomical Therapeutic Chemical Classification System (ATC), Diagnosis-related Group codes (DRG), International Classification of Primary Care (ICPC)

Table S5: ICD-10 code sets used to identify COPD

ICD-10 code sets	Number of studies
J44	14
J41-44	10
J40-44	7
J41, J43-44	5
J43, J44	3
J42-44	2
J43-44, except J43.0	2
J44.1	2
J40, J41.0, J41.1, J41.8, J42, J43.0, J43.1, J43.2, J43.8, J43.9, J44.0, J44.1, J44.9	1
J40, J47	1
J40-42, J44	1
J40-44, J47	1
J41, J43	1
J41.0, J41.1, J41.8, J42, J43.9, J44.0, J44.1, J44.9	1
J41-43	1
J41-44, J47	1
J42, 44	1
J42-44, except J43.0	1
J44.0, J44.1, J44.9	1
J44.1, J44.8, J44.9	1

Includes studies which used ICD-10, ICD-10-CM or ICD-10-CA alone, or in combination with other coding schemes.

Table S6: Lower age limit used in definition of COPD

Lower age limit	Number of studies
40	76
35	13
18	12
20	8
45	6
65	6
66	5
55	5
50	4
30	2
25	1
60	1

Table S7: Smoking data

Is smoking data missing?*	Number of studies
Yes	44
No	66
Not reported	75
If study has access to smoking data, are never-smokers included in the analysis?	
Yes	33
No	9
Not reported	24

*Missing here means that information regarding smoking was not available in the database being interrogated

Table S8: Phenotyping by blood eosinophil level – thresholds used by studies

Blood eosinophil threshold	Number of studies
150 cells/μL	4
2% (of total white cell count)	3
300 cells/μL	2
200 cells/μL and/or 2%	1
'Always above', 'fluctuating above and below', and 'never above' cut off points of 100, 150, and 300 cells/μL	1
<2%, 2-4%, >4% and 150, 150–300, 300 cells per μL	1

% = blood eosinophil concentrations as percentage of total white blood cell count; cells/μL = absolute count of blood eosinophils

List of studies included in scoping review

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