

Automated identification of an aspirin-exacerbated respiratory disease cohort

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Background: Aspirin-exacerbated respiratory disease (AERD) is characterized by 3 clinical features: asthma, nasal polyposis, and respiratory reactions to cyclooxygenase-1 inhibitors (nonsteroidal anti-inflammatory drugs). Electronic health records (EHRs) contain information on each feature of this triad.

Objective: We sought to determine whether an informatics algorithm applied to the EHR could electronically identify patients with AERD.

Methods: We developed an informatics algorithm to search the EHRs of patients aged 18 years and older from the Partners Healthcare system over a 10-year period (2004-2014). Charts with search terms for asthma, nasal polyps, and record of respiratory (cohort A) or unspecified (cohort B) reactions to nonsteroidal anti-inflammatory drugs were identified as “possible AERD.” Two clinical experts reviewed all charts to confirm a diagnosis of “clinical AERD” and classify cases as “diagnosed AERD” or “undiagnosed AERD” on the basis of physician-documented AERD-specific terms in patient notes. **Results:** Our algorithm identified 731 “possible AERD” cases, of which 638 were not in our AERD patient registry. Chart review of cohorts A (n = 511) and B (n = 127) demonstrated a positive predictive value of 78.4% for “clinical AERD,” which rose to 88.7% when unspecified reactions were excluded. Of those with clinical AERD, 12.4% had no mention of AERD by any treating caregiver and were classified as “undiagnosed AERD.” “Undiagnosed AERD” cases were less likely than “diagnosed AERD” cases to have been seen by an allergist/immunologist (38.7% vs 93.2%; $P < .0001$).

Conclusions: An informatics algorithm can successfully identify both known and previously undiagnosed cases of AERD with a high positive predictive value. Involvement of an allergist/immunologist significantly increases the likelihood of an AERD diagnosis. (J Allergy Clin Immunol 2016;■■■:■■■-■■■.)

Key words: Aspirin-exacerbated respiratory disease, electronic health record, asthma, nasal polyps, nonsteroidal anti-inflammatory drugs, chronic rhinosinusitis, structured query language, clinical decision support

Electronic health records (EHRs) provide the advantage of an electronically searchable patient chart and are now being widely used in North America and Europe. One of the ways EHRs can be used to improve patient care is to develop informatics algorithms for disease diagnosis. Using this approach, cohorts of patients with disease-specific characteristics can be identified for diagnosis.¹ Identified patients may then benefit in various ways, such as from disease-targeted therapeutics and from participation in clinical trials and translational research investigations. This may be particularly important in the field of clinical allergy and immunology in which many of the common diseases encountered lack accurate disease-specific coding in our current systems.

In the classic triad form, aspirin-exacerbated respiratory disease (AERD), also referred to as Samter’s triad, is the unique clinical combination of chronic rhinosinusitis with nasal polyposis, asthma, and respiratory reactions to all inhibitors of cyclooxygenase-1 (COX-1). The syndrome affects 7.2% (95% CI, 5.26% to 9.03%) of adults with asthma and 14.9% (95% CI, 6.48% to 23.29%) of those with severe asthma, and therefore may affect up to 2 million US adults.² Ingestion of aspirin or any COX-1 inhibitor elicits hypersensitivity reactions within 30 minutes to 3 hours, which include worsening upper respiratory tract symptoms and acute bronchoconstriction, sometimes requiring emergency medical care. Although there are patients with respiratory reactions to COX-1 inhibitors who do not have all 3 components of this disease,³⁻⁵ we will consider the classic triad for the duration of this article. AERD is a chronic medical condition that dramatically impacts quality of life and medical resource utilization beyond that of most aspirin-tolerant patients with asthma or chronic rhinosinusitis with nasal polyposis.⁶ Despite the morbidity of the syndrome and its frequency in the adult population with asthma, our clinical experience is that there is a delay of many months to years between the onset of AERD symptoms and a formal diagnosis,⁴ and research efforts in AERD are hampered by modest sample sizes.

Unfortunately, AERD lacks a unifying International Classification of Diseases, Ninth Revision (ICD-9) or International Classification of Diseases, Tenth Revision (ICD-10) code. Because AERD is characterized by a unique triad, we hypothesized that the simultaneous use of ICD-9 codes

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Abbreviations used

AERD: Aspirin-exacerbated respiratory disease
 BWH: Brigham and Women's Hospital
 COX-1: Cyclooxygenase-1
 EHR: Electronic health record
 ICD-9: International Classification of Diseases, Ninth Revision
 ICD-10: International Classification of Diseases, Tenth Revision
 IQR: Interquartile range
 NSAID: Nonsteroidal anti-inflammatory drug
 PPV: Positive predictive value
 RPDR: Partners Research Patient Data Repository
 SQL: Structured query language

for asthma and nasal polyps, problem list entries, and medication allergy entries would automatically identify a cohort of possible AERD cases. Therefore, we developed and tested an EHR algorithm to identify subjects with AERD.

METHODS**Informatics algorithms**

Applying an informatics algorithm to the Partners Research Patient Data Repository (RPDR),^{1,7} the EHRs at 2 academic hospitals (Massachusetts General Hospital and Brigham and Women's Hospital [BWH]) and 1 community hospital (Faulkner Hospital) affiliated with the Partners Healthcare system were searched over a 10-year period (December 2004–November 2014). Institutional Review Board approval was obtained for this study. The EHR at the institutions searched is entirely electronic and included both inpatient and outpatient data from any affiliated hospital or clinic. All charts of patients aged 18 years or older who had 1 or more encounters during this time period were searched for AERD-relevant features. One RPDR query (see Table E1 in this article's Online Repository at www.jacionline.org) was designed to find patients with ICD-9 codes, problem list entries, laboratory values (eosinophils >500/ μ L) or medications associated with asthma and with ICD-9 codes, problem list entries, intranasal steroids, or surgical billing codes related to nasal polyposis. A second RPDR query was designed to find patients with nonsteroidal anti-inflammatory drug (NSAID) allergy. The union of the 2 RPDR queries resulted in data sets including 168,126 patients, which were further processed as described below.

The data sets obtained from RPDR were preprocessed, that is, decrypted and decompressed, and aggregation algorithms were used to summarize the resulting raw data tables, enabling first reviews of the data. Because the RPDR queries were designed to capture all patients of potential interest, structured query language (SQL) statements were used to filter and analyze patient data and allow for the identification of the most important structured terms used in the final algorithm.

Three preliminary SQL queries were developed for each characteristic of AERD, searching the data tables for specific terms, for example, "asthma," and misspellings such as "amaphylaxis," which were also considered. Each query returned 1 patient population with asthma (see Fig E1 in this article's Online Repository at www.jacionline.org), 1 population with nasal polyps (see Fig E2 in this article's Online Repository at www.jacionline.org), and 1 population with NSAID allergy (see Fig E3 in this article's Online Repository at www.jacionline.org). The NSAID allergy SQL was designed to identify charts that reported reactions typical of the respiratory symptoms triggered by NSAIDs in AERD or charts that reported unspecified ("unknown") reactions to NSAIDs. Reaction types not classically associated with AERD, for example, gastritis or urticaria, were excluded. The results (patient sets) of each query were used to further refine the SQL queries filtering more specific data about the identified populations. The BWH AERD patient registry ($n = 96$), a well-phenotyped database of patients with aspirin-challenge confirmed AERD, was also used to identify information of increased significance, and the SQL queries were iteratively revised several

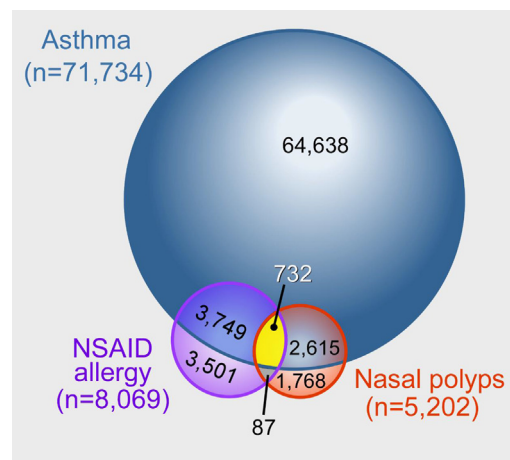


FIG 1. Venn diagram of the clinical characteristics of cases identified by an AERD bioinformatics algorithm. From 2,647,842 patients aged 18 years and older seen within the Partners Healthcare system between December 2004 and November 2014, we identified cases with a diagnosis of asthma, nasal polyps, and/or NSAID allergy. NSAID allergy was restricted to only those with a specified respiratory reaction to NSAIDs or an unspecified ("unknown") reaction. The cohort of "possible AERD" cases, in yellow, lies at the intersection of all 3 clinical characteristics. n represents sample size.

times. In the example of nasal polyps, if a problem was noted by a clinician that did not contain the necessary key words but one of the terms "sinus," "nasal," or "allergic rhinitis," then the problem-associated comment was searched for "polyp."

Over the course of these iterations, it became clear that *diagnoses* (ICD-9 codes), *problems* including associated *comments*, and *allergens*, focusing only on those with specified respiratory (eg, bronchospasm, wheeze, and nasal congestion) reactions, or unspecified reactions to any inhibitor of COX-1, were the most important components to identify potential patients with AERD. The intersection of the 3 populations identified "possible AERD" cases (Fig 1), which were further stratified by the type of reaction to an NSAID recorded in the EHR; cohort A included cases where specific respiratory symptoms were recorded, and cohort B included cases where the reaction symptoms were unspecified, that is, recorded as "unknown."

A number of cases identified as "possible AERD" were already recorded as having known AERD within structured information in the EHR, for example, problem lists and allergies and/or through involvement in the BWH AERD patient registry. Therefore, a fourth SQL query (see Fig E4 in this article's Online Repository at www.jacionline.org) was set up that searched only for AERD-specific terms within structured information in the EHR, to determine whether that more simplified approach would be sufficient to identify cases of AERD from the EHR.

Chart reviews

Two allergy/immunology experts with a clinical focus on AERD independently performed chart reviews. All charts from cohort A and cohort B were reviewed by at least 1 reviewer, with 20 charts from each cohort reviewed by both reviewers to assess the interrater agreement (kappa). Reviewers defined "clinical AERD" as the presence of an asthma diagnosis, nasal polyps, and a report of a classical respiratory reaction to 1 or more NSAIDs. The presence of nasal polyposis was confirmed during chart review if 1 of the following criteria was met: (1) documentation of rhinoscopic evidence of nasal polyposis, (2) surgical/pathologic report confirming nasal polyposis, or (3) radiologic evidence of nasal polyposis. Cases that carried a diagnosis of cystic fibrosis, sinus malignancy, or unilateral sinus disease or were determined by chart review to either not meet criteria for a diagnosis of AERD or not have sufficient information recorded within their chart to determine the diagnosis were labeled "Not AERD." During this review, unstructured EHR data,

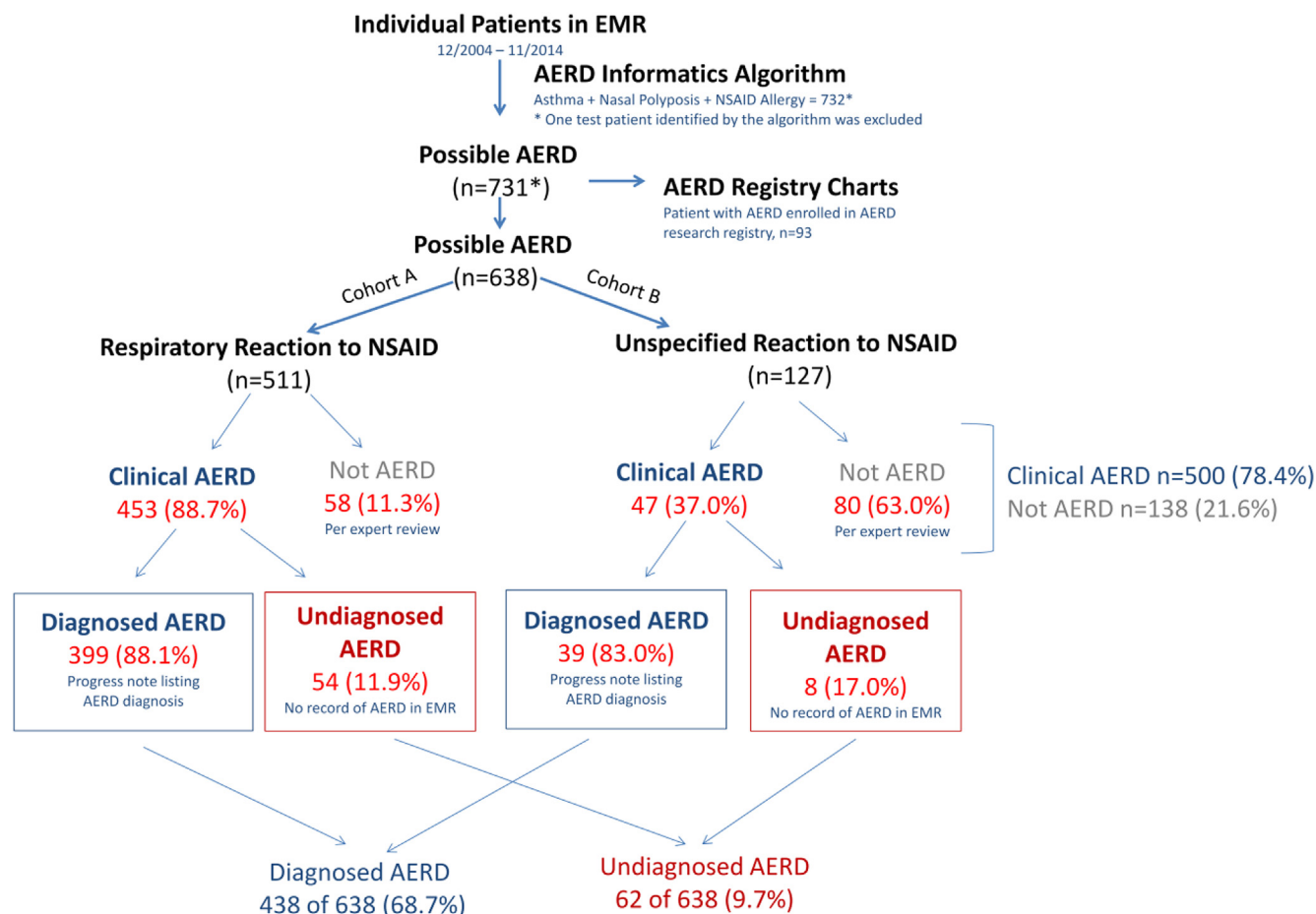


FIG 2. Flowchart for the assessment of the possible AERD cohort. The PPV for identifying AERD in subjects with asthma, nasal polyposis, and a recorded respiratory reaction to an NSAID (cohort A) was 88.7%. The PPV for identifying subjects with AERD having a recorded respiratory or unspecified reaction to an NSAID (cohorts A + B) not previously enrolled in the AERD registry was 78.4%. The PPV for algorithm identifying all patients with AERD (cohort A + cohort B + AERD registry) was 81.1%. *n* represents sample size. *A total of 732 charts were initially identified by the algorithm and 1 test chart was excluded.

including progress, hospital visit, and surgical procedure notes, were reviewed using a queriable patient inference dossier⁸ to identify whether a caregiver had made a prior diagnosis of AERD (or another term for the disease, including Samter's triad, aspirin-sensitive asthma, aspirin-intolerant asthma, or triad asthma) that was not recorded in the structured data. These cases were defined as "diagnosed AERD." Cases established by expert review as having "clinical AERD" but lacking any documentation of AERD in either the structured or unstructured data within the EHR were considered "undiagnosed AERD." Whether the patient had ever had clinical involvement of pulmonary, allergy/immunology, and otolaryngology specialists in each case was noted.

Statistical analyses

All data are represented as mean $\pm$ SD unless otherwise noted. Cohen's kappa coefficient was used to measure interrater agreement on the clinical diagnosis of AERD by our expert reviewers. Positive predictive values (PPVs) were calculated from chart reviews of cohort A, cohort B, and the BWH AERD registry. Fisher exact test was used to assess differences in sex and race between "diagnosed" and "undiagnosed" AERD; a Mann-Whitney *U* test was used to determine difference in age. Differences in rates of specialty physician evaluations were assessed using a contingency table and Fisher exact test. *T* tests were performed to determine differences in the number of encounters. GraphPad Prism version 6.07 for Windows (GraphPad Software, La Jolla, Calif, www.graphpad.com), SAS software, version 9.4 (Cary, NC), and/or R version 3.2.1 (R Foundation for Statistical Computing, Vienna, Austria) were used to complete these analyses.

RESULTS

A total of 2,647,842 charts were queried using RPDR between December 1, 2004, and November 30, 2014. The cohort defined by the intersection of the asthma (SQL #1), nasal polyp (SQL #2), and NSAID allergy (SQL #3) queries was considered to contain "possible AERD" cases (*n* = 732, Fig 1). One case was identified as a test patient, a virtual patient generated for training purposes, and excluded and 93 cases participated in the AERD registry and had known confirmed AERD. Of the remaining 638 cases, cohort A (*n* = 511) included cases with record of a respiratory reaction to NSAIDs and cohort B (*n* = 127) included cases with an unspecified reaction to an NSAID (Fig 2).

Cohorts A and B were independently reviewed by both reviewers. The interrater agreement value, kappa, for each cohort was 100%. The PPV for the identification of "clinical AERD" cases using this informatics algorithm is 81.1% (cohorts A, B, and the BWH AERD registry). The PPV excluding the AERD registry charts (cohorts A and B) is 78.4%, which rises to 88.7% if only cases with a specified respiratory reaction to an NSAID (cohort A) are considered. After expert review of progress notes, 12.4% of "clinical AERD" cases identified (11.9% in cohort A and 17.0% in cohort B) were labeled "undiagnosed AERD," indicating that the expert review agreed they had the triad of clinical symptoms

TABLE I. Allergist/immunologist involvement in undiagnosed and diagnosed clinical AERD

	AERD		Total
	Diagnosed	Undiagnosed	
Allergist/immunologist involvement	408	24	
No allergist/immunologist involvement	30	38	
Total, n	438	62	500
Allergy involvement (%)	93.2	38.7	

The charts of undiagnosed (n = 62) and diagnosed AERD (n = 438) cases were assessed for involvement by allergy/immunology specialists.

consistent with AERD but there was no mention of AERD or a similar term in the EHR (Fig 2). Significantly less involvement from allergy/immunology specialists was noted in the care of “undiagnosed AERD” cases as compared with “diagnosed AERD” cases (38.7% vs 93.2%; $P < .0001$; Table I). Among those “clinical AERD” patients who had been evaluated by only 1 type of specialty provider, 100% of the 6 cases seen by only allergy, 40.9% of the 44 cases seen by only otolaryngology, and 33.3% of the 3 cases seen by only pulmonary were recorded in the EHR as having been diagnosed with AERD ($P < .05$).

The patient demographics of “diagnosed” and “undiagnosed AERD” and the BWH AERD patient registry are reported in Table II. The diagnosed AERD cohort’s median age (interquartile range [IQR]) was slightly less than that of the undiagnosed cohort (54 [IQR, 45-65] vs 58 [IQR, 51-72]; $P < .01$). There was no significant difference in sex or race between cohorts. The median number of patient encounters with the Partners Healthcare system was not different between those with “diagnosed” and “undiagnosed” AERD (37.5 [IQR, 11-101] and 54.5 [IQR, 19-126], respectively; $P = .31$).

Application of SQL #4 (n = 255) identified only 28.9% (n = 211) of the “possible AERD” cases (Fig 3) and an additional 44 cases not identified by the EHR algorithm. Of the 42 charts in SQL #4 not identified by the EHR algorithm or included in the BWH AERD registry, 20 lacked 1 or more components of the triad and were considered “Not AERD” and 22 (52.4%) were labeled “clinical AERD” after expert chart review. Application of the primary EHR search algorithm to just the BWH AERD patient registry identified 93 of 96 patients (96.9%). Of the 3 cases from the BWH AERD patient registry that were not identified by the AERD algorithm, 2 had no NSAID allergy recorded, representing serious omissions that impact patient safety, and 1 lacked appropriate documentation of nasal polyps. Taken together, our primary algorithm failed to identify 3.7%—23 of 618 (Clinical AERD [n = 500] + BWH AERD registry [n = 96] + SQL #4 Clinical AERD [n = 22])—of the known patients with AERD in the EHR.

DISCUSSION

We demonstrate that an informatics algorithmic approach can be used to identify both diagnosed and previously undiagnosed cases of AERD. Our approach identified 593 known or expert-confirmed cases of AERD with a PPV of 81.1% while missing only 3.7% of the known patients with AERD in the EHR. Among those cases identified by our algorithm and confirmed by expert review as having “clinical AERD,” 12.4% (n = 62) carried no mention of AERD or an equivalent term in the medical chart. As far as could be determined from their medical chart, no caregiver

TABLE II. Demographic characteristics of diagnosed and undiagnosed AERD cases and the BWH AERD registry

Characteristic	Diagnosed AERD	Undiagnosed AERD	P value	AERD registry
Sample size, n	438	62		96
Sex: male, n (%) [*]	179 (40.9)	26 (41.9)	.9	42 (43.8)
Median age (y) (IQR) [†]	54 (45-65)	58 (51-72)	<.01	52 (42-60)
Race, n (%) [*]			.7	
White/Caucasian	356 (81.3)	53 (85.5)		87 (90.6)
Black/African American	27 (6.2)	2 (3.2)		3 (3.1)
Hispanic/Latino	16 (3.7)	3 (4.8)		2 (2.1)
Asian	5 (1.1)	1 (1.6)		3 (3.1)
Other/unknown	34 (7.8)	3 (4.8)		1 (1.0)
Encounters, total, median (IQR) [‡]	37.5 (11-101)	54.5 (19-126)	.3	

Statistical analyses run between diagnosed and undiagnosed AERD. The BWH AERD registry’s demographic characteristics have been included for reference. n represents sample size.

^{*}Fisher exact test.

[†]Mann-Whitney U test.

[‡]T test.

had ever realized the connection between their clinical triad of symptoms and therefore these cases had never been given the diagnosis of AERD (Fig 2). Patients in this “undiagnosed AERD” category were less likely to have been evaluated by an allergy/immunology specialist (Table I), highlighting the role of allergists/immunologists in correctly identifying this disease. Cases of “undiagnosed AERD” identified by the algorithm have not yet been exposed to the criterion standard for diagnosis of AERD, aspirin challenge, to confirm the assessment made by our expert clinicians. The current literature suggests that up to 15% of those cases meeting clinical criteria for AERD may have a negative aspirin challenge.^{9,10} However, the clinical experience from our institution involving more than 150 aspirin challenges is that less than 5% of patients with asthma, nasal polyposis, and a historical respiratory reaction to an NSAID go on to have a negative aspirin challenge.⁴ This suggests that our informatics algorithm can identify new diagnoses of AERD and could facilitate access to disease-specific treatments for these patients, which has been shown to improve their care.¹¹⁻¹³

Algorithm-identified cases of AERD, both “diagnosed” and “undiagnosed,” demonstrate the classical female predominance.^{9,10,14} The slightly younger age in the “diagnosed AERD” cases cannot easily be explained with the data generated in this study (Table II). One hypothesis drawn from our clinical experience is that younger patients with AERD are using electronic resources to connect their triad of symptoms and may present to their providers questioning a diagnosis of AERD, leading to greater consideration and confirmation of AERD. Previously there has been no racial predilection for the development of AERD reported and our racial demographics reflect the racial distribution of the Partners Healthcare patient population. Race does not predict whether a case is diagnosed or not. No data about asthma severity/control were collected/analyzed and no conclusions can be made about the nature of the upper or lower respiratory tract disease in the cohorts. The lack of a difference in the number of encounters between the groups suggests that both groups use the health care system at similar rates, had similar amounts of data available for chart review, and that the number of encounters with the health care

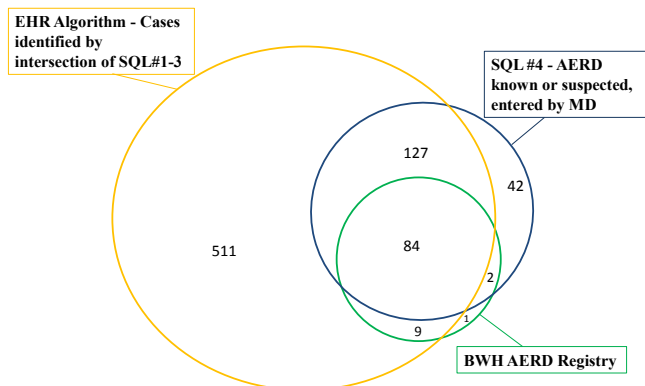


FIG 3. Venn diagram of the possible AERD cases identified by the AERD algorithm (SQL #1-3), AERD-specific search terms (SQL #4), and the BWH AERD registry.

system did not bias toward identifying an “undiagnosed” case of AERD.

The benefit of using such an algorithm to identify patients with AERD is multifactorial. In the short-term, patients with AERD would have better access to disease-specific therapy including zileuton, which improves nasal symptoms and FEV₁,¹⁵ and high-dose aspirin therapy, which improves sinus and asthma symptom scores and decreases nasal congestion, corticosteroid use (oral and inhaled), the number of sinus infections per year, and the need for repeat polypectomy.^{16,17} In addition, of the cases of AERD we identified, less than 20% are participating in the BWH AERD patient registry. Because patients who participate in the registry are provided with formal educational materials about their disease and are offered involvement in research opportunities, this highlights the potential to engage 500 new subjects in clinical or translational research focused on AERD at our or any other institution. Use of an informatics algorithm at any institution using an electronic medical record to identify patients with AERD, a disease lacking a unifying ICD-9 or ICD-10 code or diagnostic laboratory test, has the power to improve patient care immediately and to support the research endeavors that will yield future advances in patient care.

The algorithm we present used commonly coded information for diagnosis, billing, and allergy information that is captured in any electronic medical record. Our development of an EHR-based phenotyping algorithm for AERD can be deployed in other electronic medical record programs, both nationally and internationally, which are capturing data on the diagnosis of asthma, nasal polyps, and allergy to NSAIDs.¹⁸ Similar algorithms for rheumatoid arthritis, drug-induced liver injury, and genomic phenotyping have been successfully used across 2 to 13 different EHR platforms.¹⁹⁻²¹ The data model used by our EHR does not differ substantially from other EHRs both nationally and internationally. Minor adjustments for language and regional differences in terminology (eg, NERD, ie, NSAID-exacerbated respiratory disease, which is commonly used in Europe) would be required to maximize the success of adapting this algorithm. Although we have generated this algorithm and searched the patient charts from 2 large referral-based tertiary care centers with active research programs in asthma, nasal polyps, and AERD, the data used to identify potential cases of AERD are basic information that should be captured by primary care and specialist providers even if they have no knowledge of AERD.

As with all informatics algorithms, our algorithm is limited by the amount and the quality of the data contained within the EHR, specifically among the details of drug allergy recordings.²² The PPV of our algorithm drops from 88.7% (cohort A) to 78.4% (cohorts A and B) if we include cases in which the symptoms of reaction to NSAIDs are not specified. Of those cases in cohort A determined not to have AERD, 21 of 58 of them were classified as such because they lacked a sufficient NSAID allergy history in the chart to meet our prespecified criteria for characterization as AERD. The inclusion of SQL #4 confirms that the use of AERD-specific search terms alone vastly underestimates the potential cases of AERD in the EHR (Fig 3). A closer look at those 42 charts identified by SQL #4 that were not found by the primary EHR AERD algorithm or included in the BWH AERD registry highlights the danger of incomplete and inaccurate information contained within the EHR; 47.6% (n = 20) of these charts were eventually classified as “Not AERD” because of 1 of 2 reasons: (1) AERD had initially been considered and/or recorded by a provider but then ruled out by a negative aspirin challenge or (2) the EHR did not have enough information to confirm a diagnosis of AERD. Because of these data quality limitations, use of any algorithm is likely to underdetect possible cases of AERD and no conclusions about the prevalence of AERD can be drawn from this study. In primary care settings, relying on a single ICD-9 or ICD-10 code for the diagnosis of asthma lacks specificity.²³ The requirement for multiple ICD-9/ICD-10 codes and/or additional data, for example, concomitant prescriptions for disease-targeted therapy such as β -agonists, may be necessary to improve the specificity of this algorithm. However, no improvement in the algorithm methods can make up for the omission of information in the EHR. Our work underscores the need for complete and specific data entry in the EHR to maximize the patient safety and research potential.

In our health care system with more than 2,000,000 patient records between November 2004 and November 2014, given the known prevalence of asthma in US adults is 7%,²⁴ and the prevalence of AERD is estimated at 7% of adults with asthma,² we would have predicted to find more than 10,000 cases of AERD. In addition to the data quality issues our algorithm identified, patients referred from an outside provider to a tertiary care center for specialty care may lack complete EHR data, specifically ICD-9 coding or problem list entries for asthma or nasal polyps, if those problems are not being addressed by the specialty provider. We focused our efforts on the identification of the classic triad of AERD,²⁵ and did not focus on identifying those cases that lack either asthma or nasal polyposis but demonstrate the stereotypical respiratory reaction following the ingestion of a COX-1 inhibitor,³⁻⁵ likely missing these nonclassic presentations of AERD. In addition, our hospital system is known for oncology, rheumatology, and obstetric care and our starting population likely is overrepresented for these conditions that do not have any association with asthma.

The patient population searched presents 2 unique characteristics about the charts queried. First, the tertiary care setting may result in incomplete health records, as discussed above, and bias the algorithm and the chart review against assigning a diagnosis of AERD. Given the lack of disease-unique therapeutics or laboratory values in AERD, no other recorded data points can be depended upon to adequately replace missing diagnoses. Second, our cohort is likely to have more AERD-specific information available within the EHR, specifically in the problem

list in which an “aspirin-intolerant asthma with nasal polyposis” problem has been created at the request of BWH AERD center physicians. We anticipate that higher rates of “undiagnosed AERD” would be identified by the application of this algorithm to another setting that does not have an active AERD clinical and research program. The algorithm we present does not require an AERD-specific term, which SQL #4 demonstrated was neither sensitive nor specific for AERD, and the application of this algorithm approach to another EHR should have no impact on the clinically significant identification of cases that fall into cohorts A and B.

New strategies using the EHR to increase identification of patients with AERD and other allergic diseases hold great promise for improving clinical care and expanding access to specialists in the field. A recent survey of subjects with AERD highlighted the disconnect between beneficial therapies and their use in patients with AERD. A total of 91% of subjects with AERD reported that aspirin therapy was beneficial but less than 50% of the survey population had been offered aspirin therapy.⁶ The present algorithmic approach could be used to display automatic alert notifications to physicians to promote the consideration of AERD and improve documentation of AERD,²⁶ while offering evidence-based information and detailed advice including referral options.²⁷ Providing patients with an accurate diagnosis may empower them to seek out effective treatments for their disease and/or engage in clinical trials that have the potential to transform the future of AERD-specific care. The high PPV of our algorithm would likely generate notifications at low risk for inducing alert fatigue.²⁸ In addition, this algorithm could be used to prioritize the generation of medication alerts for NSAID prescriptions in those patients who have a record of NSAID allergy in conjunction with a history of asthma and/or nasal polyps.²⁹ Future work assessing the gains in patient care and safety from such an approach is needed.

AERD is an underrecognized but important disease in which current technology can be used to better serve the needs of our patients. Leveraging the power of the EHR to identify new diagnoses has the potential to shorten the length of time between symptom onset and diagnosis and to positively affect care for patients with AERD.

Key messages

- An informatics algorithm can be used to search EHRs to identify diagnosed and previously undiagnosed cases of clinical AERD.
- Incomplete recording of drug reaction data by caregivers limits the PPV of this algorithm.
- Involvement of allergy/immunology specialists in the care of subjects with asthma, nasal polyposis, and NSAID allergy increases the likelihood that a diagnosis of AERD will be made.

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```

-- ASTHMA
select distinct patient_id
from (
select patient_id
from diagnoses
where (
diagnosis like "*bronchitis and asthma age >17*" or
diagnosis like "*asthma, unspecified without mention of status asthmaticus*" or
diagnosis like "*extrinsic asthma without mention of status asthmaticus*" or
diagnosis like "*asthma, unspecified type, with acute exacerbation*" or
diagnosis like "*extrinsic asthma with acute exacerbation*" or
diagnosis like "*chronic obstructive asthma, without mention of status asthmaticus*"
or
diagnosis like "*intrinsic asthma without mention of status asthmaticus*" or
diagnosis like "*extrinsic asthma with status asthmaticus*" or
diagnosis like "*chronic obstructive asthma with acute exacerbation*" or
diagnosis like "*asthma, unspecified type, with status asthmaticus*" or
diagnosis like "*intrinsic asthma, with acute exacerbation*" or
diagnosis like "*cough variant asthma*" or
diagnosis like "*intrinsic asthma with status asthmaticus*" or
diagnosis like "*chronic obstructive asthma, with status asthmaticus*" or
diagnosis like "*asthma, unspecified*" or
diagnosis like "*asthma*" or
diagnosis like "*extrinsic asthma*" or
diagnosis like "*chronic obstructive asthma*" or
diagnosis like "*asthma-lmr 29*" or
diagnosis like "*asthmatic bronchitis-lmr 30*" or
diagnosis like "*exercise-induced asthma-lmr 1586*" or
diagnosis like "*asthma, acute exacerbation-lmr 1288*" or
diagnosis like "*asthma-oncall*" or
diagnosis like "*asthmatic bronchitis-oncall*" or
diagnosis like "*exercise induced asthma*" or
diagnosis like "*exercise induced bronchospasm*"
) and not (
diagnosis like "*bronchitis and asthma age 0-17*" or
diagnosis like "*family history of asthma*" or
diagnosis like "*antiasthmatics causing adverse effects in therapeutic use*" or
diagnosis like "*asthma care model patient-oncall*"
)
union
select patient_id
from problems
where (
problem = "asthma" or
problem = "h/o asthma" or
problem = "allergic asthma" or
problem = "cough variant asthma" or
problem = "asthma - resolved" or
problem = "asthma, acute exacerbation" or
problem = "asthma/allergic rhinitis" or
problem = "moderate persistent asthma" or
problem = "severe persistent asthma" or
problem = "asthmatic breathing" or
problem = "extrinsic asthma" or
problem = "asthma - or eosinophilic bronchitis" or
problem = "asthma,severe" or
problem = "chronic obstructive asthma" or
problem like "*asthma, aspirin sensitive*" or
problem like "*asthma, frequent steroids*" or
problem like "*asthma, intubated*"
))

```

FIG E1. SQL query #1 developed to identify a patient population with asthma.

```

-- NASAL POLYPS
select distinct patient_id
from (
select patient_id
from diagnoses
where (
diagnosis like "*polyp of nasal cavity*" or
diagnosis like "*nasal polyp*" or
diagnosis like "*other polyp of sinus*" or
diagnosis like "*polypoid sinus degeneration*" or
diagnosis like "*sinus surgery, polyp*" or
diagnosis like "*sinus polyp*"
)
union
select patient_id
from problems
where (
problem like "*polyp of nasal cavity*" or
problem like "*nasal polyp*" or
problem like "*other polyp of sinus*" or
problem like "*polypoid sinus degeneration*" or
problem like "*sinus surgery, polyp*" or
problem like "*sinus polyp*"
or (
problem like "*sinus*" or
problem like "*nasal*" or
problem like "*allergic rhinitis*"
) and (
comments like "*polyp*"
))
)
)

```

FIG E2. SQL query #2 developed to identify a patient population with nasal polyps.

```

-- NSAID HYPERSENSITIVITY
select distinct patient_id
from allergies
where (
allergen like "*aspirin*" or
allergen = "asa" or
allergen like "* asa *" or
allergen like "+asa *" or
allergen like "asa *" or
allergen like "+asa+" or
allergen like "asa-" or
allergen like "* asa, *" or
allergen like "* asa" or
allergen like "asa, *" or
allergen like "asa/*" or
allergen like "*/asa/*" or
allergen like "* asa, *" or
allergen like "*",asa, *" or
allergen like "*nsaid*" or
allergen like "*ibuprofen*" or
allergen like "*ibuprophen*" or
allergen like "*advil*" or
allergen like "*motrin*" or
allergen like "*naproxen*" or
allergen like "*naprosyn*" or
allergen like "*indomethacin*" or
allergen like "*ketorolac*" or
allergen like "*toradol*" or
allergen like "*salicylic acid*" or
allergen like "*sulfasalazin*" or
allergen like "*olsalazin*" or
allergen like "*sulindac*" or
allergen like "*etodolac*" or
allergen like "*flurbiprofen*" or
allergen like "*ketoprofen*" or
allergen like "*fenoprofen*" or
allergen like "*oxaprozin*" or
allergen like "*mefenamic acid*" or
allergen like "*meclofenamic acid*" or
allergen like "*piroxicam*" or
allergen like "*meloxicam*" or
allergen like "*diclofenac*"
) and (
reaction like "*bronchospasm*" or
reaction like "*brochospasm*" or
reaction like "*bronchoconstriction*" or
reaction like "*shortness of breath*" or
reaction like "*sob*" or
reaction like "*chest tightnes*" or
reaction like "*asthma*" or
reaction like "*ashtma*" or
reaction like "*anaphyla*" or
reaction like "*amaphyla*" or
reaction like "*anaphylla*" or

```

FIG E3. SQL query #3 developed to identify a patient population with NSAID hypersensitivity reactions typical of the respiratory symptoms triggered by NSAIDs in AERD or charts that reported unspecified ("unknown") reactions to NSAIDs. *Asa*, Aspirin; *Sob*, shortness of breath.

```

reaction like "*anaphlaxis*" or
reaction like "*cough*" or
reaction like "*wheez*" or
reaction like "*nasal polyp*" or
reaction like "*nasla polyp*" or
reaction like "*nasalpolyp*" or
reaction like "*asthma, polyp*" or
reaction like "*nasal stuffines*" or
reaction like "*nasal congestion*" or
reaction like "*congestion/nasal*" or
reaction like "*develops polyps*" or
reaction like "*rash*" or
reaction like "*flushing*" or
reaction like "*sneezing*" or
reaction like "*resp. react*" or
reaction like "*respiratory distres*" or
reaction like "*unable to breath*" or
reaction like "*difficulty breathing*" or
reaction like "*difficult to breath*" or
reaction like "*trouble breathing*" or
reaction like "*aerd*" or
reaction like "*sampter*" or
reaction like "*santer*" or
reaction like "*samter*" or
reaction like "*exacerbated respiratory disease*" or
reaction like "*unknown*"
)

```

FIG E3. (Continued).

```

-- KNOWN OR SUSPECTED AERD
select distinct patient_id
from (
select patient_id, problem as feature
from problems
union
select patient_id, comments as feature
from problems
union
select patient_id, problem_code_description as feature
from problems
union
select patient_id, allergen as feature
from allergies
union
select patient_id, reaction as feature
from allergies
)
where (
feature like "*aerd*" or
feature like "*aspirin-induced asthma*" or
feature like "*aspirin induced asthma*" or
feature like "*aspirin-induced respiratory*" or
feature like "*aspirin induced respiratory*" or
feature like "*aspirin exacerbated respiratory*" or
feature like "*aspirin-exacerbated respiratory*" or
feature like "*exacerbated respiratory disease*" or
feature like "*aspirin-sensitive asthma*" or
feature like "*aspirin sensitive asthma*" or
feature like "*aspirin causes shortness of breath*" or
feature like "*aspirin causes sob*" or
feature like "*nsaids, bronchospasm or wheezing*" or
feature like "*nsaid- breathing difficulty/bronchospasm*" or
feature like "*samter*" or
feature like "*sampter*" or
feature like "*santer*" or
feature like "*triad asthma*" or
feature like "*motrin, ibuprofen in high doses over a prolonged
periodbronchospasm, wheezing*" or
feature like "*tartrazine (yellow dye#5) - anaphylaxis, asa - asthma*" or
feature like "*intolerant to asa as it worsens her asthma symptoms*" or
feature like "*avoids nsaids because of effect on asthma*" or
feature like "*aspirin cuz asthma attack*" or
feature like "*asa and nsaids cause hives and sob*" or
feature like "*asthma*nasal polyp*intoleran*nsaid*" or
feature like "*asa sensitivity and nasal polyp*" or
feature like "*asa-sensitivity and nasal polyp*" or
feature like "*aspirin allergy*nasal*polyp*" or
feature like "*aspirin-allergy*nasal*polyp*" or
feature like "*aspirin sensitivity*nasal*polyp*" or
feature like "*aspirin-sensitivity*nasal*polyp*" or
feature like "*asa allergy*nasal*polyp*" or
feature like "*asa-allergy*nasal*polyp*" or
feature like "*motrine and tylenol gets sob*")

```

FIG E4. SQL query #4 developed to identify a patient population with known or suspected AERD. *Asa*, Aspirin; *Sob*, shortness of breath.

TABLE E1. Research patient data repository queries used to identify subjects from the electronic health record with possible asthma and nasal polyps and with possible aspirin/NSAID allergy

Asthma/nasal polyps RPDR query:	
Wheezing—786.07-.09	OR
Asthma, all types and exacerbation states—493.0-99	OR
Diagnosis related groups for bronchitis and asthma age >17	OR
Prescription, inpatient or outpatient, in all forms:	
Albuterol—inhaler and nebulizer	OR
Ipratropium plus albuterol	OR
Levalbuterol	OR
Zileuton	OR
Budesonide and all other inhaled corticosteroids (ICSs) in all formulation including ICS/long-acting beta-agonist combo	OR
Montelukast	OR
Zafirlukast	
AND	
Anosmia—781.1	OR
Chronic rhinitis—472.0	OR
Nasal polyp—471	OR
Prescriptions for any nasal steroid—generic and brand name	OR
Any procedure code for polypectomy—CPT 31288/30110, P2252/2264	OR
Any procedure code for nasal endoscopy—CPT 31231	
Aspirin/NSAID allergy RPDR query:	
Personal history of aspirin allergy—V14.6 code	OR
Desensitization—V071.XX code	OR
Drug allergy NOS—995.3	OR
Adverse effect of drug—995.27, 995.29	OR
Anaphylactic shock NOS—995.0	OR
Peripheral blood eosinophil count >500/ μ L	OR
Eosinophilia—288.3	

CPT, Current Procedural Terminology; NOS, not otherwise specified.