Identification of Incident Atrial Fibrillation From Electronic Medical Records

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BACKGROUND: Electronic medical records are increasingly used to identify disease cohorts; however, computable phenotypes using electronic medical record data are often unable to distinguish between prevalent and incident cases.

METHODS AND RESULTS: We identified all Olmsted County, Minnesota residents aged ≥18 with a first-ever International Classification of Diseases, Ninth Revision (ICD-9) diagnostic code for atrial fibrillation or atrial flutter from 2000 to 2014 (N=6177), and a random sample with an International Classification of Diseases, Tenth Revision (ICD-10) code from 2016 to 2018 (N=200). Trained nurse abstractors reviewed all medical records to validate the events and ascertain the date of onset (incidence date). Various algorithms based on number and types of codes (inpatient/outpatient), medications, and procedures were evaluated. Positive predictive value (PPV) and sensitivity of the algorithms were calculated. The lowest PPV was observed for 1 code (64.4%), and the highest PPV was observed for 2 codes (any type) >7 days apart but within 1 year (71.6%). Requiring either 1 inpatient or 2 outpatient codes separated by >7 days but within 1 year had the best balance between PPV (69.9%) and sensitivity (95.5%). PPVs were slightly higher using ICD-10 codes. Requiring an anticoagulant or antiarrhythmic prescription or electrical cardioversion in addition to diagnostic code(s) modestly improved the PPVs at the expense of large reductions in sensitivity.

CONCLUSIONS: We developed simple, exportable, computable phenotypes for atrial fibrillation using structured electronic medical record data. However, use of diagnostic codes to identify incident atrial fibrillation is prone to some misclassification. Further study is warranted to determine whether more complex phenotypes, including unstructured data sources or using machine learning techniques, may improve the accuracy of identifying incident atrial fibrillation.

Key Words: atrial fibrillation ■ computable phenotype ■ electronic medical records

Atrial fibrillation (AF) is the most common cardiac arrhythmia affecting between 2.7 million and 6.1 million Americans, and with the aging population, the prevalence of AF is projected to increase to ~12 million by the year 2050. The outcomes of AF are of major clinical consequence as AF causes substantial morbidity, including a 5-fold increased risk of stroke, a tripling of risk for heart failure, and a doubling of the risk for dementia, and a nearly 2-fold increased risk of mortality.

Electronic medical records (EMR) are increasingly used to identify disease cohorts; study trends in incidence of a disease; characterize the demographics, clinical characteristics, and treatment strategies for a disease cohort; identify risk factors for and outcomes related to a disease; conduct comparative effectiveness research studies; and identify patients for enrollment in pragmatic clinical trials. However, accurate identification of a disease cohort is paramount to ensure valid study results. Several computable phenotypes for AF have been developed using EMR data. Some phenotypes for AF were created using cohorts of older populations, included only inpatient diagnoses, included only International Classification of Diseases, Ninth Revision (ICD-9) diagnostic codes, or were validated in a small number of cases, limiting the generalizability of previously
published computable phenotypes for AF. Furthermore, the majority of phenotypes were developed to identify AF cases and controls, and thus are unable to distinguish between prevalent and incident cases. Although identification of prevalent cases may be appropriate for genomic studies, accurate ascertainment of the onset of disease (incidence date) is necessary for many types of epidemiologic studies. Identification of incident AF is crucial for studies on temporal trends in incidence or outcomes of AF, case-control studies investigating risk factors for AF, or cohort studies developing a risk prediction tool for AF. Therefore, we sought to define and validate computable phenotypes for incident AF using structured EMR data from inpatient and outpatient visits over the past 2 decades in a well-characterized, geographically-defined community in Minnesota in which all diagnoses were confirmed by manual chart review.

METHODS

Study Population

Because of the sensitive nature of the data collected for this study, requests to access the data set from qualified researchers trained in human subject confidentiality protocols may be sent to the Rochester Epidemiology Project (REP) at Mayo Clinic at info@rochesterproject.org.

This study used the REP, a medical record-linkage system allowing virtually complete capture of health care provided to residents of Olmsted County, Minnesota.\textsuperscript{16-19} The retrieval of nearly all health care related events is possible through the linkage of information from the main health care providers in Olmsted County, which includes Mayo Clinic and its 2 affiliated hospitals and Olmsted Medical Center and its branch offices and affiliated hospital. Data captured include demographics, diagnostic codes, surgical procedure codes, outpatient drug prescriptions, and laboratory results from all participating institutions. In addition, the medical records from all providers in the REP are available to researchers for chart review to validate events, to identify the onset (incidence date) of events, and to abstract other relevant clinical information. Furthermore, demographic and ethnic characteristics of Olmsted County are representative of the state of Minnesota and the Midwest region of the United States, supporting the generalizability of REP data.\textsuperscript{17}

This study was approved by the Mayo Clinic and Olmsted Medical Center Institutional Review Boards. The study was considered minimal risk by both Institutional Review Boards; therefore, the requirement for informed consent was waived. However, records of any patient who had not provided authorization for their medical records to be used for research, as per Minnesota statute 144.335, were not reviewed.

Validation of Incident AF Diagnoses

An existing community cohort of people diagnosed with incident AF in Olmsted County, Minnesota has been established as part of ongoing surveillance.\textsuperscript{20} Briefly, incident AF or atrial flutter from 2000 to 2014 among adults (aged ≥18) was ascertained using ICD-9 codes 427.31 and 427.32 from all providers in the REP and electrocardiograms (ECGs) from Mayo Clinic. All medical records, including the clinical notes, tests, and procedures from inpatient and outpatient encounters, were reviewed in detail by trained nurse abstractors to validate the events. Evidence of AF or atrial flutter on 1 or more of the following was required to validate the diagnosis of AF: (1) on ECG or rhythm strip, (2) on Holter monitor, event monitor, or telemetry, (3) on monitor during an emergency department visit or hospitalization, (4) on the ECG during an echocardiogram, (5) on pacemaker interrogation, or (6) a physician diagnosis. The source(s) of documentation of AF were recorded and the date of onset (incidence date) was determined based on the documentation in the medical record(s). Consistent with other epidemiologic studies of AF, postoperative AF that occurred within 30 days of a
cardiac surgery (coronary artery bypass graft, surgery to repair or replace a heart valve, surgery to repair an atrial septal defect, or other open heart surgery) was excluded. However, if a postoperative patient with AF went on to experience a future episode of AF unrelated to a surgery (or occurring >30 days after a surgery), this episode of AF was considered incident AF. In addition to ascertainment of all incident AF occurring between 2000 and 2014, we also selected a random sample of 200 people with International Classification of Diseases, Tenth Revision (ICD-10) diagnostic code I48 between 2016 and 2018. The medical records of this random sample of 200 people were reviewed to validate the diagnosis as described previously.

AF Computable Phenotype Algorithm Development

Several computable phenotype algorithms were evaluated using combinations of the number (≥1, ≥2) and type (inpatient, outpatient) of diagnostic codes. The diagnostic codes used were ICD-9 codes 427.31 and 427.32 for the 2000 to 2014 time frame and ICD-10 code I48 for the 2016 to 2018 time frame. Codes that were preceded by cardiac surgery (such as coronary artery bypass graft, surgery to repair or replace a heart valve, surgery to repair an atrial septal defect, surgery on chordae tendineae, or other open heart surgery) within 30 days before the code were not used in the algorithms. When multiple diagnostic codes were required, different restrictions on timing between diagnostic codes was imposed. For example, some algorithms required ≥2 diagnostic codes that occurred at least 1 day apart whereas others required the ≥2 diagnostic codes to occur >30 days apart. In addition, we tested algorithms that required both diagnostic code(s) along with 1 of the following treatments: outpatient prescription for an anticoagulant drug, outpatient prescription for an antiarrhythmic drug, or electrical cardioversion. These algorithms were employed in a subset of patients starting in 2005 because of the availability of prescription data from the REP (prescription data are not routinely available before 2004). The anticoagulant drugs included warfarin, unfractionated heparin, low molecular weight heparin, and the nonvitamin K antagonist oral anticoagulants dabigatran, rivaroxaban, apixaban, and edoxaban. The antiarrhythmic drugs included amiodarone, disopyramide, dofetilide, dronedarone, flecainide, propafenone, and sotalol. Electrical cardioversions were identified using procedure codes (Current Procedural Terminology codes 92960 and 92961, ICD-9 procedure codes 99.61 and 99.62, and ICD-10 procedure code 5A2204Z).

Statistical Analysis

Analyses were performed using SAS, version 9.4 (SAS Institute Inc., Cary, NC). Patients with diagnostic code(s) before January 1, 2000 or who died within 30 days of their first diagnostic code were excluded. Between January 1, 2000 and December 31, 2014 there were a total of 6177 patients with at least 1 diagnostic code for AF, and an additional 70 patients with an ECG indicating AF (but without a diagnostic code). These 6247 patients were included in our analyses. For all analyses, we intended to replicate the development of our incident AF cohort where postoperative AF was ignored and a future episode of AF unrelated to a surgery was considered incident AF.

The index dates of the algorithms were defined differently for each type of algorithm. For the algorithms that did not specify the type of diagnostic code, the index date was the first AF code date. For the algorithms that specified either 1 inpatient or 2 outpatient codes, the date of the first outpatient AF code served as the index date if the criterion of 2 outpatient codes was met, the date of the inpatient code served as the index date if the criterion of 1 inpatient code was met, and the earlier of the 2 dates served as the index date if both criteria were met. As described, the records of all patients with a diagnosis code for AF were reviewed to validate the diagnosis, and the date of incident AF was recorded based on review of the medical records. Two approaches were used to analyze the data (Figure 1). In the first approach (prevalent approach), we included all patients who had a diagnostic code for AF from January 1, 2000 through December 31, 2014.
The positive predictive value (PPV, also referred to as precision) of each computable phenotype was calculated as the proportion of patients identified as having AF from the algorithm who have validated AF (true +/algorithm +). In addition, because electronic interpretations of ECGs were available in patients without a diagnostic code (N=70), we were able to estimate an upper limit of sensitivity (also referred to as recall) of the algorithms, defined as the proportion of validated AF that are identified as having AF from the algorithm (algorithm+/true +). Of note, we ignored any differences in dates between the algorithm date and the date of validated AF. Thus, any algorithm that was met between January 1, 2000 and December 31, 2013 was defined as algorithm +, and people who had validated incident AF during this same time frame were defined as true +.

In the second approach (incident approach), we aimed to determine whether the algorithms accurately identified the date of incident AF. For this analysis, we restricted to patients with a diagnostic code for AF, or an ECG indicating AF without any diagnostic codes, from February 1, 2000 through December 31, 2013 (n=5668). We imposed a window (−30 days to +1 year) around the index date of the algorithm to identify patients who had validated AF (gold standard). Specifically, patients with validated AF with an incidence date within 30 days before to 1 year after the index date determined by the algorithm were considered as true +, whereas those with validated AF that occurred outside this window were not included as true +. The PPV and upper limit of sensitivity were estimated using the formulas previously described. Analyses using the incident approach were repeated stratified by sex and age groups (<65, 65–74, 75–84, ≥85). Finally, analyses using the incident approach were completed for the random sample of 200 patients who had ICD-10 codes between February 1, 2016 and December 31, 2018. For this analysis, only the PPV was estimated because of the sampling of patients and the lack of information on patients who had AF but did not receive a diagnosis code in this time period.

RESULTS

Using EMR data from the providers captured in the REP, a total of 6177 patients had a diagnostic code for AF and an additional 70 people had an ECG indicating AF without any diagnostic codes between January 1, 2000 and December 31, 2014; thus 6247 people contributed to the analyses (Figure 1). Of the 6247 patients, the median (interquartile range) age was 73 (62–82) years, and 54% were male. Of the 6177 patients with a diagnostic code for AF between January 1, 2000 and December 31, 2014, 42 had a diagnostic code preceded by a cardiac surgery within 30 days before the code with no subsequent diagnostic codes for AF.

Therefore, all algorithms classified them as “no AF.” In addition to these 42, another 1759 patients (28%) did not have incident AF during the same time period (993 had no evidence of AF, 269 had isolated postoperative AF, and 497 had AF diagnosed before 2000, which was outside the time window of our study).

Using the prevalent approach, the PPVs ranged from 71.3% for the phenotype requiring 1 code of any type to 83.0% for the phenotype requiring 2 codes separated by more than 30 days but within 1 year (Figure 2; Table 1). However, the algorithm with the highest PPV (2 codes separated by >30 days but within 1 year) had the lowest sensitivity (78.7%). As expected, the sensitivity was highest for the model requiring a single code (98.4%). Requiring a medication or procedure in addition to diagnostic code(s) modestly improved the PPVs at the expense of large reductions in the sensitivity (Figure 2; Table 1).

In an attempt to distinguish between prevalent and incident cases and accurately identify not only the presence of AF but the diagnosis date of AF, we conducted analyses requiring the date of validated AF to occur within 30 days before to 1 year after the index date of the algorithm (incident approach). To allow for the time windows around the index date, the analysis was restricted to individuals with codes for AF (N=5602) or an ECG without any diagnostic codes (N=66) between February 1, 2000 and December 31, 2013 (Figure 1). Of the 5668 patients contributing to the incident analyses, 34 had a diagnostic code preceded by a cardiac surgery (within 30 days prior) with no subsequent codes for AF. Therefore, all algorithms classified these 34 as “no AF.” An additional 1982 (35%) patients did not have incident AF within the −30 days to +1 year time window. Records for 100 of these 1982 patients were reviewed. Nearly one-quarter had another type of cardiac dysrhythmia (n=23) and did not have AF despite receiving an AF diagnostic code. Other common reasons for incorrect AF diagnoses included prevalent AF (n=24) and failure to identify presence or date of incident AF after cardiac postoperative AF (n=21).

The PPVs were lower when attempting to more accurately ascertain the date of diagnosis of AF (incident approach; Figure 2; Table 2) compared with the prevalent approach. The lowest PPV was observed for the phenotype requiring 1 code (64.4%), and the highest PPV was observed for the phenotype requiring 2 codes (any type) >7 days apart but within 1 year (71.6%). The phenotype requiring either 1 inpatient code or 2 outpatient codes separated by >7 days but within 1 year appeared to have the best balance between PPV (69.9%) and sensitivity (95.5%). The sensitivities were quite similar between the incident and prevalent approaches. In addition, the PPVs and sensitivities were similar for men and women and across all age categories except for the phenotypes requiring a medication
or procedure in addition to the diagnostic code(s), for which the sensitivities were lower in women compared with men. Finally, the PPVs were slightly higher for the computable phenotypes using ICD-10 codes (Table 3). For example, the PPV for the phenotype requiring 1 code was 67.5% (compared with 64.4% using ICD-9 codes), and the PPV for the phenotype requiring 2 codes (any type) >7 days apart but within 1 year was 74.1% (compared with 71.6% using ICD-9 codes).

To better understand how well the algorithms identified the incidence date of AF, we compared the algorithm date and the validated incidence date of AF for the computable phenotype of 1 inpatient code or 2 outpatient codes separated by >7 days but within 1 year. Out of the 4936 patients meeting the algorithm definition, 3860 had validated incident AF. Of these 3860 with validated AF, 3451 (89%) occurred within our required time window (the date of validated AF had to occur within 30 days before to 1 year after the index date of the algorithm) with 1942 (50.3%) having the same date for the algorithm and the validated AF incidence date. The median (Q1, Q3) time between the algorithm date and validated date was 0 (−3, 0) days.

**DISCUSSION**

In this large study spanning decades, we observed that use of diagnostic codes from the EMR to identify AF is prone to some misclassification. We developed computable phenotypes with varying number and type of diagnoses as well as inclusion of AF treatment. The use of different time restrictions on the phenotypes requiring at least 2 diagnostic codes was employed to test varying degrees of certainty that the codes were assigned during separate encounters as an attempt to rule out false positive diagnoses. We observed that the best balance of PPV and sensitivity was achieved for the phenotype requiring 1 inpatient code or 2 outpatient codes separated by >7 days but within 1 year. Requiring a medication or procedure in addition to diagnostic code(s) modestly improved the PPVs at the expense of reductions in the sensitivity of the computable phenotypes, indicating that a large proportion of patients who have AF were missed when these additional data elements were required. As indicated by the low sensitivities, more than one-third of the patients with AF did not receive an anticoagulant or antiarrhythmic drug or an electrical cardioversion procedure within the year after their first diagnosis of AF. In addition, the sensitivities of the phenotypes incorporating AF treatment were lower in women compared with men, indicating that women were less likely to be treated with an anticoagulant drug, an antiarrhythmic drug, or an electrical cardioversion procedure. Nevertheless, the choice of the most appropriate computable phenotype may vary depending on the goal of...
Table 1. Positive Predictive Value and Upper Limit of Sensitivity* of Various Computable Phenotypes for Atrial Fibrillation Using the Prevalent Approach, January 1, 2000 to December 31, 2014

| Computable phenotype | Code only algorithms | Codes + medications/procedures† |
|----------------------|----------------------|----------------------------------|
|                      | PPV                  | Sensitivity                      | PPV                  | Sensitivity                      |
|                      | True+ / algorithm+  | Algorithm+ / true+               | True+ / algorithm+  | Algorithm+ / true+               |
|                      | %                   | %                                | %                   | %                                |
| 1 code (International Classification of Diseases, Ninth Revision 427.31 or 427.32; any type) | 4376/6135 | 71.3 | 4376/4446 | 98.4 | 1958/2645 | 74.0 | 1958/3143 | 62.3 |
| 2 codes (any type) ≥ 1 d apart and within 1 y | 4237/5419 | 78.2 | 4237/4446 | 95.3 | 1906/2422 | 79.9 | 1936/3143 | 61.6 |
| 2 codes (any type) > 7 d apart and within 1 y | 3933/4814 | 81.7 | 3933/4446 | 88.5 | 1862/2258 | 82.5 | 1862/3143 | 59.2 |
| 2 codes (any type) > 30 d apart and within 1 y | 3499/4216 | 83.0 | 3499/4446 | 78.7 | 1737/2074 | 83.8 | 1737/3143 | 55.3 |
| 1 inpatient code OR 2 outpatient codes ≥ 1 d apart and within 1 y | 4316/5638 | 76.6 | 4316/4446 | 97.1 | 1949/2484 | 78.5 | 1949/3143 | 62.0 |
| 1 inpatient code OR 2 outpatient codes > 7 d apart but within 1 y | 4223/5407 | 78.1 | 4223/4446 | 95.0 | 1920/2420 | 79.3 | 1920/3143 | 61.1 |
| 1 inpatient code OR 2 outpatient codes > 30 d apart but within 1 y | 4112/5226 | 78.7 | 4112/4446 | 92.5 | 1880/2356 | 79.8 | 1880/3143 | 59.8 |

PPV indicates positive predictive value.

*The sensitivity was estimated including patients with ECG evidence of atrial fibrillation without a diagnostic code. However, patients with true atrial fibrillation without an ECG or diagnostic code may have been missed, resulting in an overestimate of the sensitivity. Thus, our sensitivity estimates are an upper limit of the true sensitivity of the algorithms.

†The study period for this analysis was January 1, 2005 to December 31, 2014 (N=4459; 4430 with codes and 29 with ECG only). The algorithms incorporating both codes and medications/procedures require the patient to have the listed number and type of diagnostic codes plus a prescription for an anticoagulant drug or an antiarrhythmic drug or an electrical cardioversion procedure within 1 year of the first diagnostic code.
Table 2. Positive Predictive Value and Upper Limit of Sensitivity* of Various Computable Phenotypes for Atrial Fibrillation Using the Incident Approach, February 1, 2000 to December 31, 2013

| Computable phenotype | Code only algorithms | Codes + medications/procedures† |
|----------------------|----------------------|----------------------------------|
|                      | PPV                  | Sensitivity                      | PPV                  | Sensitivity                      |
|                      | True+ / algorithm+   | %                                | Algorithm+ / true+   | %                                | True+ / algorithm+   | %                                | Algorithm+ / true+   | %                                |
| 1 code (International Classification of Diseases, Ninth Revision 427.31 or 427.32; any type) | 3586/5568 64.4 | 3586/3652 98.2 | 1581/2288 69.1 | 1581/2572 61.5 |
| Sex                  |                      |                                  |                      |                                  |
| Male                 | 1919/2976 64.5       | 1919/1954 98.2                  | 890/1302 68.6        | 890/1398 63.9                    |
| Female               | 1667/2592 64.3       | 1667/1698 98.2                  | 688/986 69.8         | 688/1174 58.6                    |
| Age group, y         |                      |                                  |                      |                                  |
| Age <65              | 985/1626 60.6        | 985/1011 97.4                   | 431/661 65.2         | 431/728 59.2                     |
| Age 65–74            | 848/1314 64.5        | 848/861 98.5                    | 395/573 68.9         | 395/615 64.2                     |
| Age 75–84            | 1052/1608 65.4       | 1052/1064 98.9                  | 519/720 72.1         | 519/719 72.2                     |
| Age ≥85              | 701/1020 68.7        | 701/716 97.9                    | 236/334 70.7         | 236/510 46.3                     |
| 2 codes (any type) ≥1 d apart and within 1 y | 3480/4929 70.6 | 3480/3645 95.5 | 1515/2036 74.4 | 1515/2578 58.8 |
| Sex                  |                      |                                  |                      |                                  |
| Male                 | 1865/2627 71.0       | 1865/1956 95.3                  | 860/1157 74.3        | 860/1407 61.1                    |
| Female               | 1615/2302 70.2       | 1615/1689 95.6                  | 655/879 74.5         | 655/1171 55.9                    |
| Age group, y         |                      |                                  |                      |                                  |
| Age <65              | 937/1349 69.5        | 937/997 94.0                    | 421/575 73.2         | 421/718 58.6                     |
| Age 65–74            | 834/1160 71.9        | 834/886 96.3                    | 382/509 75.0         | 382/620 61.6                     |
| Age 75–84            | 1027/1470 69.9       | 1027/1062 96.7                  | 491/651 75.4         | 491/724 67.8                     |
| Age ≥85              | 682/950 71.8         | 682/720 94.7                    | 221/301 73.4         | 221/516 42.8                     |
| 2 codes (any type) >7 d apart and within 1 y | 3160/4411 71.6 | 3160/3554 88.9 | 1485/2004 74.1 | 1485/2536 58.6 |
| Sex                  |                      |                                  |                      |                                  |
| Male                 | 1681/2358 71.3       | 1681/1908 88.1                  | 837/1137 73.6        | 837/1285 60.4                    |
| Female               | 1479/2053 72.0       | 1479/1646 89.9                  | 648/867 74.7         | 648/1151 56.3                    |
| Age group, y         |                      |                                  |                      |                                  |
| Age <65              | 802/1131 70.9        | 802/964 83.2                    | 397/539 73.7         | 397/697 57.0                     |
| Age 65–74            | 784/1053 72.6        | 784/838 91.2                    | 373/503 74.2         | 373/608 61.3                     |
| Age 75–84            | 962/1346 71.5        | 962/1038 92.7                   | 491/659 74.5         | 491/715 68.7                     |
| Age ≥85              | 632/881 71.7         | 632/714 88.5                    | 224/303 73.9         | 224/516 43.4                     |
| 2 codes (any type) >30 d apart and within 1 y | 2732/3909 69.9 | 2732/3461 78.9 | 1411/1949 72.4 | 1411/2490 56.7 |

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| Computable phenotype | Code only algorithms | Codes + medications/procedures<sup>1</sup> |
|----------------------|----------------------|--------------------------------------------|
|                      | PPV                  | Sensitivity                                | PPV                  | Sensitivity                                |
|                      | True+ / algorithm+  | %                                            | Algorithm+ / true+  | %                                            |
|                      | 70%                  |                                              | 72%                  |                                              |
|                      | 80%                  |                                              | 82%                  |                                              |
|                      | 90%                  |                                              | 92%                  |                                              |
|                      | 95%                  |                                              | 97%                  |                                              |
|                      | 100%                 |                                              | 100%                 |                                              |
| Sex                  |                      |                                              |                      |                                              |
| Male                 | 1459/2100            | 69.5                                        | 1459/1858            | 78.5                                        |
| Female               | 1273/1809            | 70.4                                        | 1273/1603            | 79.4                                        |
|                      |                      |                                              |                      |                                              |
| Age group            |                      |                                              |                      |                                              |
| Age <65              | 665/965              | 68.9                                        | 665/313              | 71.4                                        |
|                      |                      |                                              |                      |                                              |
| Age 65–74            | 680/947              | 71.8                                        | 680/818              | 83.1                                        |
|                      |                      |                                              |                      |                                              |
| Age 75–84            | 860/1219             | 70.6                                        | 860/1012             | 85.0                                        |
|                      |                      |                                              |                      |                                              |
| Age ≥85              | 527/778              | 67.7                                        | 527/700              | 75.3                                        |
|                      |                      |                                              |                      |                                              |
| 1 inpatient code OR 2 outpatient codes ≥1 d apart and within 1 y | 3544/5125 | 69.2                                        | 3544/3645            | 97.2                                        |
|                      |                      |                                              |                      |                                              |
| Sex                  |                      |                                              |                      |                                              |
| Male                 | 1901/2735            | 69.5                                        | 1901/1955            | 72.7                                        |
| Female               | 1643/2390            | 68.7                                        | 1643/1690            | 72.7                                        |
|                      |                      |                                              |                      |                                              |
| Age group            |                      |                                              |                      |                                              |
| Age <65              | 960/1416             | 67.8                                        | 960/998              | 96.2                                        |
|                      |                      |                                              |                      |                                              |
| Age 65–74            | 845/1205             | 70.1                                        | 845/866              | 97.6                                        |
|                      |                      |                                              |                      |                                              |
| Age 75–84            | 1042/1518            | 66.6                                        | 1042/1062            | 98.1                                        |
|                      |                      |                                              |                      |                                              |
| Age ≥85              | 697/986              | 70.7                                        | 697/719              | 96.9                                        |
|                      |                      |                                              |                      |                                              |
| 1 inpatient code OR 2 outpatient codes >7 d apart but within 1 y | 3451/4936 | 69.9                                        | 3451/3614            | 95.5                                        |
|                      |                      |                                              |                      |                                              |
| Sex                  |                      |                                              |                      |                                              |
| Male                 | 1847/2636            | 70.1                                        | 1847/1943            | 95.1                                        |
| Female               | 1604/2300            | 69.7                                        | 1604/1671            | 96.0                                        |
|                      |                      |                                              |                      |                                              |
| Age group            |                      |                                              |                      |                                              |
| Age <65              | 901/1314             | 68.6                                        | 901/981              | 91.8                                        |
|                      |                      |                                              |                      |                                              |
| Age 65–74            | 829/1168             | 71.0                                        | 829/859              | 96.5                                        |
|                      |                      |                                              |                      |                                              |
| Age 75–84            | 1026/1478            | 69.4                                        | 1026/1055            | 97.3                                        |
|                      |                      |                                              |                      |                                              |
| Age ≥85              | 696/976              | 71.2                                        | 696/719              | 96.7                                        |
|                      |                      |                                              |                      |                                              |
| 1 inpatient code OR 2 outpatient codes >30 d apart but within 1 y | 3348/4801 | 69.7                                        | 3348/3578            | 93.6                                        |
|                      |                      |                                              |                      |                                              |
| Sex                  |                      |                                              |                      |                                              |
| Male                 | 1784/2569            | 69.4                                        | 1784/1917            | 93.1                                        |

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A research study. For example, surveillance studies or studies aiming to develop an early detection system may opt for a computable phenotype with the highest sensitivity, whereas a computable phenotype with higher PPV may be more appropriate for identification of patients for a survey study or a clinical trial.

A distinct advantage of our study was the medical record review to confirm diagnosis of AF as well as to identify the date of onset (incidence date). We observed that the computable phenotypes had lower PPVs when attempting to more accurately ascertain the date of diagnosis of AF (incident approach) compared with the prevalent approach. These findings have important implications when interpreting the performance of published computable phenotypes, which are often developed to identify prevalent cases. For example, the Electronic MEdical Records and Gnomics Network has developed more than 50 computable phenotypes to identify cases and controls for genome-wide association studies, and these computable phenotypes have been published on the Phenotype Knowledgebase allowing other investigators to reuse the published algorithms.13,21 Accurate identification of cases and controls is appropriate for genomic studies. However, the ability to distinguish between prevalent and incident cases and to accurately identify the diagnosis date of a disease is often essential for epidemiologic studies. For example, identification of incident AF is needed to study temporal trends in incidence or outcomes of AF, for case-control studies investigating risk factors for AF, and for cohort studies developing a risk prediction tool for AF. Nevertheless, the majority of published computable phenotypes for AF have been developed to identify prevalent AF11–13,15 or were developed to identify incident AF but lacked record review to validate the diagnoses and assess algorithm performance.14

The simplicity of our computable phenotypes for AF, which include only number and type of diagnosis code, is another advantage of our study. Our AF phenotypes are easily exportable and can be implemented using electronic health records, claims data, and large research networks such as the National Patient-Centered Clinical Research Network, allowing large-scale national surveillance.22–24 Although inclusion of more than 1 type of structured data element may generally increase the ability to correctly identify a disease of interest,14,25,26 we found that for AF, inclusion of prescriptions for anticoagulant or antiarrhythmic drugs or procedure codes for electrical cardioversion procedures did not improve the performance of our computable phenotypes. Nevertheless, more complex phenotypes that include natural language processing of the unstructured text of the medical record, or machine learning approaches applied to the EMR, could be developed to improve the accuracy of identifying
incident AF.\textsuperscript{26–28} However, these complex phenotypes may be more difficult to implement across large data networks or in nonacademic settings, or may not improve the ability to identify incident AF over simpler approaches.\textsuperscript{29}

**Limitations and Strengths**

We acknowledge the following limitations. AF is often asymptomatic and may go undiagnosed for some time before coming to clinical attention. Our algorithms were developed to identify the date of diagnosis of AF but may not accurately identify the true onset of disease. The performance of the algorithms may differ across medical systems due to differences in coding practices, patient populations, or completeness of data capture. We used a medical records-linkage system (the REP) that captures the majority of medical care delivered to local residents. Thus, when the computable phenotypes are implemented in other medical systems or data sources such as claims, the PPVs and sensitivities may be lower than reported herein. We did not have an external data set with validated AF events to estimate how the performance of the algorithms may differ across data sources. Finally, due to the limited geographic and racial diversity of our local population, our results may not be generalizable to all patient populations.

Our study also has a number of strengths, including the large sample size and inclusion of all people with a diagnosis code for AF over a 15-year period. In addition, we included a random sample of patients with ICD-10 diagnosis codes to allow for comparison of the PPVs over time. The records of all patients were reviewed to manually validate all AF events and to ascertain the date of first diagnosis of AF (incidence date). As a result, we created computable phenotypes not only to identify prevalent AF but also to identify incident AF. We also had the ability to identify patients with ECG evidence of AF without a diagnosis code in order to estimate an upper limit of sensitivity of the computable phenotypes. Finally, all computable phenotypes included structured data and are easy to implement in other research settings.

**CONCLUSIONS**

We developed simple, exportable, computable phenotypes to identify incident AF using structured data from the EMR. However, use of diagnostic codes to identify incident diagnoses of AF remains prone to some misclassification. Creation and validation of more complex algorithms including unstructured data sources, such as natural language processing of the medical record notes, or machine learning approaches applied to the EMR, may improve the accuracy of identifying AF and warrant further study.

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