External validation of a claims-based model to predict left ventricular ejection fraction class in patients with heart failure

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NOTE: This preprint reports new research that has not been certified by peer review and should not be used to guide clinical practice.
ABSTRACT

BACKGROUND:

Ejection fraction (EF) is an important prognostic factor in heart failure (HF), but administrative claims databases lack information on EF. We previously developed a model to predict EF class from Medicare claims. Here, we evaluated the performance of this model in an external validation sample of commercial insurance enrollees.

METHODS:

Truven MarketScan claims linked to electronic medical records (EMR) data (IBM Explorys) containing EF measurements were used to identify a cohort of US patients with HF between 01-01-2012 and 10-31-2019. By applying the previously developed model, patients were classified into HF with reduced EF (HFrEF) or preserved EF (HFpEF). EF values recorded in EMR data were used to define gold-standard HFpEF (LVEF ≥45%) and HFrEF (LVEF<45%). Model performance was reported in terms of overall accuracy, positive predicted values (PPV), and sensitivity for HFrEF and HFpEF.

RESULTS:

A total of 7,001 HF patients with an average age of 71 years were identified, 1,700 (24.3%) of whom had HFrEF. An overall accuracy of 0.81 (95% CI: 0.80-0.82) was seen in this external validation sample. For HFpEF, the model had sensitivity of 0.96 (95%CI, 0.95-0.97) and PPV of 0.81 (95% CI, 0.81-0.82); while for HFrEF, the sensitivity was 0.32 (95%CI, 0.30-0.34) and PPV was 0.73 (95%CI, 0.69-0.76). These results were consistent with what was previously published in US Medicare claims data.

CONCLUSIONS:

The successful validation of the Medicare claims-based model provides evidence that this model may be used to identify patient subgroups with specific EF class in commercial claims databases as well.
INTRODUCTION

Ejection fraction (EF) is an important prognostic factor in heart failure (HF). HF with reduced ejection fraction (HFrEF) is well characterized and there are a number of evidence-based therapies available.\(^1\) In contrast, HF with preserved EF (HFpEF) is more heterogeneous, poorly characterized and there are no approved therapies that improve outcomes.\(^1\)

Insurance claims databases allow for longitudinal follow-up at the patient level and are very useful in evaluation of disease epidemiology and treatment outcomes in routine care.\(^2\) However, a major limitation with claims databases in studying HF is the lack of available results from procedures such as echocardiograms or cardiac catheterization, which are used to measure EF. Consequently, one cannot directly distinguish between HFrEF and HFpEF based on administrative claims. To address this limitation, we previously developed a model to predict EF class using Medicare claims and validated using electronic medical record (EMR) data from two large healthcare provider networks from the Boston metropolitan area.\(^3\) The primary objective of the current study was to evaluate the performance of this prediction model in an external validation cohort.

METHODS

Data Source

Claims data derived from the Truven MarketScan database linked to EMRs from the IBM Explorys database were used. Truven MarketScan covers 235 million lives of US citizens consisting of two core claims databases; 1) MarketScan Commercial Claims and Encounters - which contains healthcare data commercially insured individuals, encompassing employees, their spouses, and their dependents from the United States, 2) Medicare Supplemental and Coordination of Benefits - which contains the healthcare experiences of Medicare-eligible retirees with employer-sponsored Medicare Supplemental plans. Both these data sources contain longitudinally traceable information for their enrollees' medical
diagnoses recorded with International Classification of Disease, 9th and 10th Clinical Modification (ICD-9/ICD-10 CM) codes, medical procedures recorded as Current Procedure Terminology (CPT) or ICD-9 procedure codes, and medication dispensing recorded using National Drug Codes (NDC). The IBM Explorys data platform is a data network that comprises integrated information from 360 hospitals and approximately 31,700 providers, covering approximately 50 million patient lives. The Explorys data has been used for multiple prior observational studies and contain data derived from ambulatory electronic medical records (EMRs), inpatient EMRs, laboratory, pharmacy, health plans, billing and accounting, data warehouses, patient portals, satisfaction surveys, and care management systems. The Marketscan and Explorys linked population represent approximately 10% of the total MarketScan population.

**Study Design**

Adult patients were included in the study if they had ≥1 diagnosis code for HF (ICD-9 or ICD-10) from the Truven MarketScan claims database after 6 months of continuous enrollment in their health plans and ≥1 recorded EF result, within 6 months prior or 1 month after the HF diagnosis date, from the IBM Explorys EMR database. The study period was between January 1st of 2012 and October 31 of 2019 and the HF diagnosis date successfully paired with a qualifying EF measurement was defined as the cohort entry date.

The study protocol was approved by the Brigham and Women’s Hospital Institutional Review Board.

**Model Validation:**

A patient level analytic data file with information on the predictor variables ([Appendix Table 1](#)) was created for the whole cohort of eligible HF patients from the Marketscan-Explorys linked dataset. All predictors were measured in the 6 months prior to and 1-month post cohort entry. Using the regression coefficients for each individual predictor variables reported in Desai et al., we estimated the probabilities of patient belonging to HFrEF or HFpEF and classified patients into one of these two classes using the recommended
We used EF data from IBM Explorys to define gold standard classification into HFP EF (LVEF ≥45%) and HFrEF (LVEF<45%). In case of ≥1 EF results, values recorded on days closest to the cohort entry dates were used to define the gold standard. The predicted classification was compared against the gold standard to complete this validation exercise.

**Statistical analysis**

Patient characteristics including demographics, HF-related variables (e.g. diagnosis code recorded for HF, HF-related hospitalizations), HF-related medications and various co-morbid conditions (e.g. hyperlipidemia, hypertension, cardiomyopathy) were described stratified by HFrEF or HFP EF for this validation cohort. We calculated overall accuracy (correct classification rate = number of accurate predictions/number of total predictions), positive predictive value (probability of being a true case, given algorithm prediction) and sensitivity (the probability of being identified as a case of specific HF class by the algorithm for a true case out of the overall population) along with 95% confidence intervals. Further, the performance of this model was also tested in the following pre-specified subgroups: males and females, age <65 and >=65 years, index date prior to October 2015 (ICD9 period) and after October 2015 (ICD10 period). It should be noted that we allowed multiple entries in the cohort, therefore some patients may contribute to both the ICD9 and ICD10 period subgroups. We also described patient characteristics in categories of patients accurately and inaccurately classified by our model to characterize misclassified populations.

**RESULTS**

**Study Cohort**

We identified 157,203 patients with at least 1 HF diagnosis following 6 months eligibility of continuous medical and pharmacy benefits. Of these patients, we included 7,001 who were at least 18 years old at
cohort entry date and who had at least one EF result available between 180 days before and 30 days after index date. Details of the cohort construction are provided in Figure 1.

**Figure 1: Cohort consort diagram**

![Cohort consort Diagram](image)

Table 1 contains data on baseline characteristics by EF class identified via the gold standard criteria using EMR-recorded EF values. We identified 5,301 patients as HFrEF and 1,700 patients as HFrEF. The average age was similar across both the groups (HFrEF = 71 years vs HFrEF = 69 years) while males comprised 68% of HFrEF compared to 51% of HFrEF. The mean (SD) EF was 59% (7) in the HFrEF group while it was 32% (9) in the HFrEF group.
Table 1: Baseline Characteristics of HF Patients Stratified by Ejection Fraction Class (HFrEF, < 0.45; or HFpEF, ≥ 0.45)

| Variable                                      | Gold standard HFrEF (N=1,700) | Gold standard HFpEF (N=5,301) |
|-----------------------------------------------|--------------------------------|--------------------------------|
|                                               | N (%)                          | N (%)                          |
| Mean LVEF (in %), (SD)                        | 32 (9)                         | 59 (7)                         |
| **Demographics**                              |                                |                                |
| Male                                          | 1152 (67.76)                   | 2687 (50.69)                   |
| Age in years, mean (SD)                       | 69.2 (14.0)                    | 70.6 (13.7)                    |
| **HF-related variables**                      |                                |                                |
| HF-specific ICD-9 and ICD-10 codes             |                                |                                |
| Systolic HF                                   | 657 (38.65)                    | 476 (8.98)                     |
| Diastolic HF                                  | 83 (4.88)                      | 1360 (25.66)                   |
| Left HF                                       | 94 (5.53)                      | 239 (4.51)                     |
| Unspecified HF                                | 790 (46.47)                    | 2930 (55.27)                   |
| HF Hospitalizations, mean (SD)                | 0.16 (0.37)                    | 0.08 (0.27)                    |
| Implantable cardioverter-defibrillator        | 245 (14.41)                    | 111 (2.09)                     |
| HF diagnosis identified in outpatient claims  | 886 (52.12)                    | 3146 (59.35)                   |
| **HF-related medication use**                 |                                |                                |
| ACE inhibitors                                | 968 (56.94)                    | 2108 (39.77)                   |
| Mineralocorticoid receptor antagonists        | 389 (22.88)                    | 467 (8.81)                     |
| Beta blockers                                 | 998 (58.71)                    | 2587 (48.80)                   |
| Digoxin                                       | 101 (5.94)                     | 118 (2.23)                     |
| Loop diuretics                                | 952 (56.00)                    | 2489 (46.95)                   |
| Nitrates                                      | 285 (16.76)                    | 519 (9.79)                     |
| Thiazide diuretics                            | 629 (37.00)                    | 1581 (29.82)                   |
| **Comorbidities**                             |                                |                                |
| Atrial fibrillation or flutter                | 723 (42.53)                    | 1956 (36.90)                   |
| Anemia                                        | 583 (34.29)                    | 2121 (40.01)                   |
| Coronary artery bypass graft                  | 132 (7.76)                     | 292 (5.51)                     |
| Cardiomyopathy                                | 789 (46.41)                    | 572 (10.79)                    |
| Chronic obstructive pulmonary disease         | 422 (24.82)                    | 1539 (29.03)                   |
| Depression                                    | 209 (12.29)                    | 941 (17.75)                    |
| Hypertensive nephropathy                      | 241 (14.18)                    | 772 (14.56)                    |
| Hyperlipidemia                                | 1063 (62.53)                   | 3356 (63.31)                   |
| Hypertension                                  | 1365 (80.29)                   | 4375 (82.53)                   |
| Hypotension                                   | 293 (17.24)                    | 811 (15.30)                    |
| Myocardial infarction                         | 436 (25.65)                    | 608 (11.47)                    |
Performance of the HF model

The model showed an overall accuracy of 0.81 (95% CI: 0.80-0.82). For HFrEF, the model had sensitivity of 0.96 (95% CI, 0.95-0.97) and PPV of 0.81 (95% CI, 0.81-0.82); while for HFrEF, the sensitivity was 0.32 (95% CI, 0.30-0.34) and PPV was 0.72 (95% CI, 0.69-0.76).

The overall accuracy was similar across the different subgroups; however, some variation was observed in sex subgroups. The overall accuracy was higher among female patients compared to male patients, due to a higher sensitivity and PPV in HFrEF. While, the male subgroup performed better for HFrEF. The model demonstrated very similar performance when using ICD-9 HF diagnoses compared to ICD-10 coded HF diagnoses. This was an important finding as the original model was developed using ICD-9 codes only and these finding support its use for data currently using both ICD-9 and ICD-10 diagnoses codes. Details of the performances of the primary model as well as the subgroup analyses are presented in Table 2.

Patient characteristics in categories of patients accurately and inaccurately classified by our model are summarized for both HFrEF and HFrEF, in Appendix Table 2.
Table 2. Primary Analysis and Subgroup-Specific Performance

| Analysis                          | Overall Accuracy With 95% CIs | Reduced Ejection Fraction | Preserved Ejection Fraction |
|----------------------------------|------------------------------|---------------------------|-----------------------------|
|                                  |                              | Positive Predicted Value With 95% CIs | Sensitivity With 95% CIs | Positive Predicted Value With 95% CIs | Sensitivity With 95% CIs |
| Primary analysis                 | 0.81 (0.80 - 0.82)           | 0.72 (0.69 - 0.76)        | 0.32 (0.30 - 0.34)          | 0.81 (0.81 - 0.82) | 0.96 (0.95 - 0.97) |
| Subgroup 1: Age 65–75 y          | 0.80 (0.78 - 0.82)           | 0.73 (0.66 - 0.80)        | 0.32 (0.28 - 0.37)          | 0.81 (0.79 - 0.83) | 0.96 (0.95 - 0.97) |
| Subgroup 2: Age 75 y and older   | 0.80 (0.79 - 0.82)           | 0.73 (0.66 - 0.79)        | 0.20 (0.17 - 0.23)          | 0.81 (0.79 - 0.82) | 0.98 (0.97 - 0.98) |
| Subgroup 3: Males                | 0.77 (0.75 - 0.78)           | 0.73 (0.69 - 0.77)        | 0.35 (0.32 - 0.38)          | 0.77 (0.76 - 0.79) | 0.95 (0.94 - 0.95) |
| Subgroup 4: Females              | 0.85 (0.84 - 0.86)           | 0.70 (0.63 - 0.76)        | 0.27 (0.23 - 0.30)          | 0.86 (0.85 - 0.88) | 0.98 (0.97 - 0.98) |
| Subgroup 5: Entry HF diagnosis in inpatient claims | 0.80 (0.78 - 0.81)           | 0.76 (0.72 - 0.80)        | 0.37 (0.34 - 0.40)          | 0.80 (0.78 - 0.82) | 0.96 (0.95 - 0.96) |
| Subgroup 6: Entry HF diagnosis in outpatient claims | 0.81 (0.80 - 0.82)           | 0.68 (0.63 - 0.73)        | 0.28 (0.25 - 0.31)          | 0.83 (0.81 - 0.84) | 0.96 (0.96 - 0.97) |
| Subgroup 7: ICD-9 coded HF       | 0.80 (0.78 - 0.81)           | 0.72 (0.66 - 0.77)        | 0.28 (0.25 - 0.32)          | 0.80 (0.79 - 0.82) | 0.96 (0.96 - 0.97) |
| Subgroup 8: ICD-10 coded HF      | 0.79 (0.78 – 0.80)           | 0.72 (0.68 – 0.75)        | 0.34 (0.31 – 0.36)          | 0.80 (0.79 – 0.81) | 0.95 (0.95 – 0.96) |

DISCUSSION

As EF information is unavailable in administrative claims databases, it is important to develop claims-based models that can be used as a proxy to identify EF classes in patients with HF. In this external validation study, we assessed the accuracy of a claims-based model to predict EF class developed in Medicare data, by applying it to commercial claims data to establish generalizability of this model outside of Medicare claims.

The performance with commercial claims was noted to be equivalent to the performance previously reported for the internal validation sample using Medicare claims. In this study, we observed sensitivity of 0.96 and PPV of 0.81 in identifying HFrEF patients. This is very similar to what was reported by Desai et al. in Medicare claims data (sensitivity of 0.97, PPV of 0.84). For HFrEF patients a substantially lower sensitivity (0.32) and a relatively lower PPV (0.72) was seen, which is also consistent with what was previously published (sensitivity of 0.29, PPV of 0.73).

We want to emphasize certain cautions that must be weighed carefully when using this model to identify EF classes in HF. First, the low sensitivity in identifying HFrEF would result in a considerable amount of sample being lost. Further, the group that is identified as HFrEF may systematically differ than the group...
that is misclassified by the model. On comparing the accurately classified HFrEF patients (547) with the misclassified HFrEF patients (1,153), we observed that EF was lower in accurately classified patients (average of 29% versus 33%, Appendix Table II). Compared to the misclassified HFrEF patients, the accurately classified HFrEF patients showed a higher prevalence of HF-related comorbidities, such as cardiomyopathy (85% versus 28%), myocardial infarction (34% versus 21%) and other dysrhythmias (67% versus 55%). Thus, patients identified as HFrEF by this model represents a sicker group.

Some limitations deserve mention. Although EMR data includes rich clinical information, high amount of missing data is to be expected. Consequently, generalizability may be limited if the patients with recorded EF values are not representative of the full HF population. Further, in the clinical setting, the diagnosis of HFpEF is typically a diagnosis of exclusion and may require confirmatory information about structural changes of the heart, beyond EF alone. Consequently, even though EF improves the accuracy of the diagnosis, there might be false positive HFpEF patients.

In conclusion, results from this study provide evidence regarding the generalizability of an approach using claims data to identify EF classes in HF patients outside of Medicare claims. This will aid future studies evaluating health outcomes, healthcare utilization as well as cost of care among HF patients in routine care when EF measurements are not available.
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Disclosures

Dr. Desai has received unrestricted research grants from Merck and Bayer for unrelated projects. Dr. Studer and Ms. Lahoz are employees of Novartis Pharma AG. Mr. Kumar is an employee of Novartis Healthcare Pvt. Ltd., India and Dr. Barve is an employee of Novartis Ireland Pvt. Ltd., Ireland. There are no conflicts of interest to disclose for the other co-authors.
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Appendices
| Variable | Variable name in SAS algorithm | ICD-9 codes Definition (Codes are ICD-9 diagnosis unless otherwise specified, all medical claims, inpatient and outpatient, should be used to define the conditions unless otherwise specified) | Corresponding ICD-10 Diagnosis / Procedure codes, or prescription codes | When measured |
|----------|--------------------------------|-------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------|---------------|
| Gender   | Male                           | N/A                                                                                              | N/A                                                                                              | On index date |
| Age      | Age                            | N/A                                                                                              | N/A                                                                                              | On index date |
| Systolic heart failure | hf_systolic | ICD-9 code of 428.2x (not co-occurring with 428.3x) 428.2x or 428.3x | ICD-9 code of 428.2x (not co-occurring with 428.3x) 428.2x or 428.3x | On index date |
| Diastolic heart failure | hf_diastolic | a code of 428.1x (not co-occurring with more specific systolic or diastolic HF codes of 428.3x) 428.1x or 428.3x | a code of 428.1x (not co-occurring with more specific systolic or diastolic HF codes of 428.3x) 428.1x or 428.3x | On index date |
| Left heart failure | hf_left | N/A                                                                                              | I50.1 (not co-occurring with more specific systolic or diastolic HF codes of I50.2x or I50.3x) | On index date |
| Unspecified heart failure | hf_unspecified | codes of 428.0x, 428.4x, 428.9x as well as instances of recording of both 428.2x and 428.3x | codes of 428.0x, 428.4x, 428.9x as well as instances of recording of both 428.2x and 428.3x | On index date |
| Index diagnosis recorded during an outpatient visit | index_dx_out | If index diagnosis occurs in an outpatient claim | N/A                                                                                              | On index date |
| Number of hospitalizations for CHF | hosp_chf | Count variable where CHF is the primary diagnosis in an inpatient stay | N/A                                                                                              | 6 month prior to the index date (including index date) |
| Implantable cardioverter defibrillator | dx_defibrillator | V45.02 (ICD-9 diagnosis code) 295.810. | 295.810, | On index date |
| Ace inhibitor | rx_ace | Benazepril, captopril, enalapril, fosinopril, lisinopril, moexipril, perindopril, quinapril, ramipril, trandolapril from prescription claims | Benazepril, captopril, enalapril, fosinopril, lisinopril, moexipril, perindopril, quinapril, ramipril, trandolapril from prescription claims | 6 month prior to the index date to (index date+30 days) |
| Mineralocorticoid receptor antagonist | rx_antagonist | Eplerenone, spironolactone from prescription claims | Eplerenone, spironolactone from prescription claims | 6 month prior to the index date to (index date+30 days) |
| Beta blocker | rx_bblocker | Acebutolol, atenolol, betaxolol, bisoprolol, carvedilol, esmolol, labetalol, metoprolol, nadolol, nebivolol, pindolol, propranolol, timolol from prescription claims | Acebutolol, atenolol, betaxolol, bisoprolol, carvedilol, esmolol, labetalol, metoprolol, nadolol, nebivolol, pindolol, propranolol, timolol from prescription claims | 6 month prior to the index date to (index date+30 days) |
| Digoxin | rx_digoxin | Digoxin from prescription claims | Digoxin from prescription claims | 6 month prior to the index date to (index date+30 days) |
| Loop diuretic | rx_loop_diuretic | Bumetanide, furosemide, torsemide, ethacrynic acid from prescription claims | Bumetanide, furosemide, torsemide, ethacrynic acid from prescription claims | 6 month prior to the index date to (index date+30 days) |
| Nitrate | rx_nitrates | Nitroglycerin, isosorbide dinitrate, isosorbide mononitrate, ranolamine from prescription claims | Nitroglycerin, isosorbide dinitrate, isosorbide mononitrate, ranolamine from prescription claims | 6 month prior to the index date to (index date+30 days) |
| Thiazide diuretic | rx_thiazide | Bendroflumethiazide, Benztiazide, Chlorothiazide, Chlorothalidone, Hydrochlorothiazide, Indapamide, Methylthiazide, Metolazone, Polychloroethane, Trichlormethiazide from prescription claims | Bendroflumethiazide, Benztiazide, Chlorothiazide, Chlorothalidone, Hydrochlorothiazide, Indapamide, Methylthiazide, Metolazone, Polychloroethane, Trichlormethiazide from prescription claims | 6 month prior to the index date to (index date+30 days) |
| Atrial fibrillation | dx_afib | 427.3x 414.x | 427.3x 414.x | 6 month prior to the index date to (index date+30 days) |
| Anemia | dx_anemia | 280.xx 281.xx 282.xx 283.xx 285.xx | 280.xx 281.xx 282.xx 283.xx 285.xx | 6 month prior to the index date to (index date+30 days) |
| Description                              | ICD-10 Codes                      | CPT Codes                      | Start Date | End Date |
|------------------------------------------|-----------------------------------|--------------------------------|------------|----------|
| Cardiomyopathy                           | dx_cardiomyopathy                 |                               | 6 month     | prior to  |
|                                          |                                   |                               | index date  | the index |
|                                          |                                   |                               | date to     | date +30  |
|                                          |                                   |                               | days        | days      |
| COPD                                     | dx_copd                           |                               | 6 month     | prior to  |
|                                          |                                   |                               | index date  | the index |
|                                          |                                   |                               | date to     | date +30  |
|                                          |                                   |                               | days        | days      |
| Depression                               | dx_depression                     |                               | 6 month     | prior to  |
|                                          |                                   |                               | index date  | the index |
|                                          |                                   |                               | date to     | date +30  |
|                                          |                                   |                               | days        | days      |
| Hypertensive nephropathy                 | dx_hyp_nephropathy                |                               | 6 month     | prior to  |
|                                          |                                   |                               | index date  | the index |
|                                          |                                   |                               | date to     | date +30  |
|                                          |                                   |                               | days        | days      |
| Hypertension                             | dx_hyperension                    |                               | 6 month     | prior to  |
|                                          |                                   |                               | index date  | the index |
|                                          |                                   |                               | date to     | date +30  |
|                                          |                                   |                               | days        | days      |
| Hypotension                              | dx_hypotension                    |                               | 6 month     | prior to  |
|                                          |                                   |                               | index date  | the index |
|                                          |                                   |                               | date to     | date +30  |
|                                          |                                   |                               | days        | days      |
| Myocardial infarction                    | dx_mi                             |                               | 6 month     | prior to  |
|                                          |                                   |                               | index date  | the index |
|                                          |                                   |                               | date to     | date +30  |
|                                          |                                   |                               | days        | days      |
| Obesity                                  | dx_obesity                        |                               | 6 month     | prior to  |
|                                          |                                   |                               | index date  | the index |
|                                          |                                   |                               | date to     | date +30  |
|                                          |                                   |                               | days        | days      |

**Notes:**
- The CPT codes listed are for reference purposes and may not be exhaustive.
- The ICD-10 codes are specific to medical conditions and diagnoses.
- CPT codes are for procedural services and may vary.
- The time frames refer to the period before the index date and are inclusive of the index date itself.
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| Condition | ICD-9/CPT Code(s) | 6 month prior to the index date to (index date+30 days) |
|-----------|-----------------|--------------------------------------------------|
| Psychosis | dx_psychosis    | 290.8x, 290.9x, 295.xx, 297.xx, 299.xx, 780.1x |
|           |                 | I47.9, I49.01, I49.02, I49.0, I49.03, I49.49 |
|           |                 | I49.40, I49.1, I49.2, I49.3, I49.49            |
|           |                 | I49.5, R00.1, I49.8                             |
|           |                 | I49.9                                             |
| Rheumatic heart disease | dx_rheumatic_heart | 393-398.x |
| Sleep apnea | dx_sleep_apnea | 327.2x, 780.51, 780.53, 780.57 |
| Stable angina | dx_stable_angina | 413.xx |
| Valve disorder | dx_valve_disorder | 35.1x, 35.2x |
| Other dysrythmias | dx_oth_dysrhythmia | 427.2x, 427.4x, 427.6x, 427.8x, 427.9x |
| Sleep apnea | dx_sleep_apnea | 785.0x |
| OR | ICD-9 procedure code |
| Valve disorder | dx_valve_disorder | 35.2x |
| OR | one of the following CPT codes: |
| Other dysrythmias | dx_oth_dysrhythmia | 785.0x |
| Rheumatic heart disease | dx_rheumatic_heart | 6 month prior to the index date to (index date+30 days) |
| Sleep apnea | dx_sleep_apnea | 327.2x, 780.51, 780.53, 780.57 |
| Stable angina | dx_stable_angina | 413.xx |
| Valve disorder | dx_valve_disorder | 35.1x, 35.2x |
| OR | ICD-9 procedure code |
| Valve disorder | dx_valve_disorder | 6 month prior to the index date to (index date+30 days) |
| Other dysrythmias | dx_oth_dysrhythmia | 427.2x, 427.4x, 427.6x, 427.8x, 427.9x |
| Sleep apnea | dx_sleep_apnea | 785.0x |
| Rheumatic heart disease | dx_rheumatic_heart | 6 month prior to the index date to (index date+30 days) |
| Sleep apnea | dx_sleep_apnea | 327.2x, 780.51, 780.53, 780.57 |
| Stable angina | dx_stable_angina | 413.xx |
| Valve disorder | dx_valve_disorder | 35.1x, 35.2x |
| OR | ICD-9 procedure code |
| Valve disorder | dx_valve_disorder | 6 month prior to the index date to (index date+30 days) |
## Appendix Table 2. Baseline Characteristics of HF Patients correctly and incorrectly classified by algorithm compared to Gold standard classification.

| Variable | Correctly classified rEF cases \(N=547\) | rEF cases incorrectly classified as pEF \(N=1,153\) | Gold standard HFrEF \(N=1,700\) | Correctly classified pEF cases \(N=5,094\) | pEF cases incorrectly classified as rEF \(N=207\) | Gold standard HFpEF \(N=5,301\) |
|----------|----------------------------------------|----------------------------------------|----------------------------------------|----------------------------------------|----------------------------------------|----------------------------------------|
| N (%)    | 64 (11.7)                              | 71 (6.15)                              | 69.2 (54.0)                            | 70.9 (13.3)                            | 72.4 (15.8)                            | 70.7 (13.7)                            |
| Mean LVEF, (SD) | 0.29 (0.09)                              | 0.33 (0.08)                              | 0.32 (0.09)                            | 0.59 (0.07)                            | 0.53 (0.07)                            | 0.59 (0.07)                            |
| Demographics |                                         |                                         |                                         |                                         |                                         |                                         |
| Male     | 401 (73.31)                             | 751 (65.13)                             | 1152 (67.76)                           | 2542 (49.90)                           | 145 (70.05)                            | 2687 (50.69)                           |
| Age, mean (SD) | 64.3 (13.7)                             | 71.6 (13.5)                             | 69.2 (54.0)                            | 70.9 (13.3)                            | 72.4 (15.8)                            | 70.7 (13.7)                            |
| HF-related variables |                                         |                                         |                                         |                                         |                                         |                                         |
| HF-specific ICD-9 and ICD-10 codes |                                         |                                         |                                         |                                         |                                         |                                         |
| Systolic HF |                                         |                                         |                                         |                                         |                                         |                                         |
| Diastolic HF |                                         |                                         |                                         |                                         |                                         |                                         |
| Left HF |                                         |                                         |                                         |                                         |                                         |                                         |
| Unspecified HF |                                         |                                         |                                         |                                         |                                         |                                         |
| HF Hospitalizations, mean (SD) |                                         |                                         |                                         |                                         |                                         |                                         |
| HF-related medication use |                                         |                                         |                                         |                                         |                                         |                                         |
| ACE inhibitors |                                         |                                         |                                         |                                         |                                         |                                         |
| Aldosterone receptor antagonists |                                         |                                         |                                         |                                         |                                         |                                         |
| Beta-blockers |                                         |                                         |                                         |                                         |                                         |                                         |
| Digoxin |                                         |                                         |                                         |                                         |                                         |                                         |
| Diuretics |                                         |                                         |                                         |                                         |                                         |                                         |
| Comorbidities |                                         |                                         |                                         |                                         |                                         |                                         |
| Atrial fibrillation or flutter |                                         |                                         |                                         |                                         |                                         |                                         |
| Anemia |                                         |                                         |                                         |                                         |                                         |                                         |
| Coronary artery bypass graft |                                         |                                         |                                         |                                         |                                         |                                         |
| Cardiomyopathy |                                         |                                         |                                         |                                         |                                         |                                         |
| Chronic obstructive pulmonary disease |                                         |                                         |                                         |                                         |                                         |                                         |
| Depression |                                         |                                         |                                         |                                         |                                         |                                         |
| Hypertensive nephropathy |                                         |                                         |                                         |                                         |                                         |                                         |
| Hypertension |                                         |                                         |                                         |                                         |                                         |                                         |
| Hypothyroidism |                                         |                                         |                                         |                                         |                                         |                                         |
| Rheumatic fever |                                         |                                         |                                         |                                         |                                         |                                         |
| Rheumatoid arthritis |                                         |                                         |                                         |                                         |                                         |                                         |
| Sleeping apnea |                                         |                                         |                                         |                                         |                                         |                                         |
| Sleep disorders |                                         |                                         |                                         |                                         |                                         |                                         |
| Stable angina |                                         |                                         |                                         |                                         |                                         |                                         |
| Valve disorders |                                         |                                         |                                         |                                         |                                         |                                         |

### Notes

- Variable abbreviations: rEF: reduced ejection fraction, pEF: preserved ejection fraction, HFrEF: heart failure with reduced ejection fraction, HFpEF: heart failure with preserved ejection fraction.
- All data are presented as N (%) unless otherwise specified (mean (SD)).
- The table compares baseline characteristics of HF patients correctly classified by the algorithm to those classified incorrectly and compared to the Gold standard classification for both HFrEF and HFpEF.
- The data includes demographics, HF-related variables, HF-related medication use, and comorbidities.

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