Web Material

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Web Table 2. Description of ICD codes used to define comorbidities in both ARIC heart failure

National Inpatient Sample. The codes are similar to those suggested by National Inpatient Sample clinical classification software.

WEB APPENDIX

1. Derivation of model to predict ADHF probability from the ARIC HF surveillance

Additional details regarding derivation of the validation models as well as additional results from model-building are provided here.

Models were developed separately for the three ICD code 428 code groups: 428 primary, nonprimary, and absent (non428 eligible ICD codes). We used a structured approach to build multivariate logistic regression models to predict the probability of ADHF. All models included age, race, sex, and teaching hospital status. We collapsed certain groups of HF codes defining conceptually similar and low prevalent conditions such as hypertensive heart failure, hypertensive-renal heart failure, rheumatic heart failure, pulmonary heart failure etc. into an 'other heart failure group'. We then identified comorbidities that are common in patients with heart failure (coronary atherosclerosis, chronic kidney disease, electrolyte imbalancehyponatremia), those that may precipitate ADHF (atrial fibrillation, acute myocardial infarction), or may represent a treatment complication (acute kidney injury) and considered those with > 5% prevalence in at least one of the three ICD code 428 groups.

Model selection was conducted to achieve adequate model fit, discrimination and calibration while minimizing model complexity to avoid over-fitting. Variables defining presence of HF codes, position of the 428 code (second position vs. 3-26 included in the ICD code 428 nonprimary group only) and comorbidity codes were selected using a forward stepwise procedure (Wald test *P* value < 0.20) and then eliminated in a stepwise fashion until measures of model fit, discrimination and calibration (Hosmer-Lemeshow, AUC and Integrated discrimination improvement [IDI], respectively) were impacted. See Supplementary Tables 5a-c for a summary of the results. In these reduced models, we replaced comorbidity in any position variables with two code position variables (primary vs. nonprimary) to test the significance of code position. Position variables were kept only if both were significant (Wald *P* value < 0.20); otherwise the presence variable was maintained in the model. We also examined Arjas plots to assess final model fit (Supplementary Figure 2).

To assess internal validity of the final models, we examined AUC and calibration slope corrected for optimism (1000 bootstrap samples).^{12,13}. We fitted models with interaction terms and examined Arjas plots in subgroups to assess consistency of model fit across ARIC community and study year.

Final models with optimism-corrected statistics are presented in Supplementary Tables 6a-c, ROC curves are presented in Supplementary Figure 1 and Arjas plots are presented in Supplementary Figures 2-4.

2. Variance of the Estimator of ADHF Hospitalizations Count and Rate

We applied the ADHF validation models derived in ARIC to NIS data to estimate the total number of ADHF hospitalizations. Population estimates were then used to calculate rates. The count estimator and derivation of the variance of the count estimator are presented here as well as the variance of the rate estimator.

The count estimator is composed of the sum of validation model-based predicted probabilities restricted to the domain defined by inclusion criteria described in Figure 1, summed over NIS strata, sampled hospitals within strata and hospitalizations within sampled hospitals. The validation model applied differs by ICD code 428 code group (primary, nonprimary, absent).

The set of NIS strata is $A = \{1, \ldots, a, \ldots, N_A\}$, the set of hospitals in stratum *a* is U_{al} = $\{1,\ldots,i,\ldots,N_{al}\}\$ and the set of hospitalizations in stratum a, hospital *i* is $H_{ai} = \{1,\ldots,k,\ldots,N_{ail}\}\$. The inclusion probability for hospital *i* from stratum *a* is π_{ai} and the set of sampled hospitals is *Sa*.

The estimator of the number of ADHF hospitalizations for domain *D* is therefore given in Equation (1).

$$
\hat{T}_D = \sum_{a=1}^{N_A} \sum_{i=1}^{N_{ai}} \sum_{k=1}^{N_{aiH}} \pi_{ai}^{-1} I(i \in S_a) I(k \in D) \logit^{-1}(x_{aik}\hat{\beta}_c | c, x_{aik}) \tag{1}
$$

where *D* is the domain satisfying inclusion criteria described in Figure 1. NIS data and logistic regression coefficient estimates from the ARIC validation model used to calculate predicted probabilities are represented by the vectors x_{aik} and $\hat{\beta}_c$, respectively. ICD code 428 code group is represented by c . $I(z)$ is an indicator variable taking on the value 1 when *z* is true, 0 otherwise.

The variance of the estimate in (1) is therefore given by (2):

$$
Var(\widehat{T}_D) = E\{Var(\widehat{T}_D \mid \widehat{\beta}) + Var\{E(\widehat{T}_D \mid \widehat{\beta})\}\
$$
 (2)

Since $\hat{\beta}$ is an unbiased estimate, $\mathrm{E}\{\mathrm{Var}\big(\widehat{T}_{D} \bigm| \hat{\beta}\big)\} \ = \ \mathrm{Var}\big(\widehat{T}_{D} \bigm| \beta\big).$

To calculate Var $\left(\widehat{T}_{D}\left\vert \beta\right. \right)$, let the number of estimated ADHF hospitalizations for domain *D* in hospital *I* and stratum *a*, be represented by t_{aip} defined in (3).

$$
t_{aiD} = \sum_{k=1}^{N_{aiH}} I(k \in D) \logit^{-1}(x_{aik}\beta_c \mid c, x_{aik})
$$
 (3)

Then the variance of \hat{T}_D given β is defined in (4).

$$
Var(\hat{T}_D | \beta) = \sum_{a=1}^{A} \sum_{i=1}^{N_{al}} \sum_{j=1}^{N_{al}} \frac{\pi_{aij} - \pi_{ai} \pi_{ai}}{\pi_{aij}} \frac{t_{aiD}}{\pi_{ai}} \frac{t_{ajD}}{\pi_{aj}}
$$
(4)

where π_{aij} = Pr(hospital *i* and hospital *j* in stratum *a* are both selected).

Denote \tilde{t}_{aib} as $\sum_{k=1}^{N_{aiH}} I(k \in D)$ $\text{logit}^{-1}(x_{aik}\hat{\beta}_{y_k}|y_k,x_{aik})$ $\lim_{k=1}^{N_{ail}} I(k \in D)$ logit⁻¹ $(x_{aik}\hat{\beta}_{y_k} | y_k, x_{aik})$, and

$$
\widehat{\text{Var}}(\widehat{T}_D \mid \beta) = \sum_{a=1}^A \sum_{i=1}^{N_{al}} \sum_{j=1}^{N_{al}} \frac{\pi_{aij} - \pi_{ai}\pi_{ai}}{\pi_{aij}} \frac{\tilde{t}_{aiD}}{\pi_{ai}} \frac{\tilde{t}_{ajD}}{\pi_{aj}} \ . \tag{5}
$$

Note: in the case of simple random cluster sampling (as in NIS),

$$
\pi_{ai} = \frac{n_{as}}{N_{al}}
$$

$$
\pi_{aij} = \pi_{ai}, \text{if } i = j
$$

$$
\pi_{aij} = \frac{n_{as} (n_{as} - 1)}{N_{al} (N_{al} - 1)}, \text{if } i \neq j
$$

Where n_{as} is the number of selected hospitals in stratum *a* and N_{al} is the number of all hospitals in stratum *a*.

For the second term in (2),

$$
E(\hat{T}_D | \hat{\beta}) = \sum_{a=1}^{N_A} \sum_{i=1}^{N_{ai}} \sum_{k=1}^{N_{aiH}} I(k \in D) \logit^{-1}(x_{aik}\hat{\beta}_c | c, x_{aik}). \quad (6)
$$

To estimate the variance of (6) we apply the delta method to the asymptotic distribution of $\hat{\beta}$:

$$
\widehat{\text{Var}}\{\mathbf{E}(\hat{T}_D \mid \hat{\beta})\} = \sum_{c=1}^3 f(\hat{\beta}_c) \mathbf{A} \mathbf{V}(\hat{\beta}_c) f(\hat{\beta}_c)^T \tag{7}
$$

Where the vector function of $\hat{\beta}_c$, $f(\hat{\beta}) = \sum_{a=1}^{N_A} \sum_{i=1}^{N_{al}} \sum_{k=1}^{N_{ail}} I(k \in D \text{ and } k \in c) x_k$ $k=1$ $\exp(x_{aik}\hat{\beta}_c)$ $_{i=1}^{N_{al}}$ $\sum_{k=1}^{N_{ail}} I(k \in D \text{ and } k \in c)$ $x_k \frac{\exp(x_{aik}\beta_c)}{\left\{1+\exp(x_{aik}\widehat{\beta}_c)\right\}^2}$, $i=1$ N_A $a=1$

and $\operatorname{AV}(\hat{\beta}_c)$ is the asymptotic covariance matrix of $\hat{\beta}_c.$

Thus, by combining the variance estimates in (5) and (7), we obtain the variance estimate of \hat{T}_D :

$$
\widehat{\text{Var}}(\widehat{r}_D) = \sum_{a=1}^A \sum_{i=1}^{N_{al}} \sum_{j=1}^{N_{al}} \frac{\pi_{aij} - \pi_{ai}\pi_{ai}}{\pi_{aij}} \frac{\tilde{t}_{aiD}}{\pi_{ai}} \frac{\tilde{t}_{ajD}}{\pi_{aj}} + \sum_{c=1}^3 f(\widehat{\beta}_c) \text{AV}(\widehat{\beta}_c) f(\widehat{\beta}_c)^T
$$

The rate estimator is simply the count estimator divided by the corresponding inter-censal population estimate. For the variance calculation, the population estimate is treated as fixed.

Web Table 4. Results of model selection to predict ADHF among those hospitalizations with ICD code

The basic model includes variables forced into all models.

The reduced model includes variables selected through forward stepwise procedure (Wald *P* value < 0.20) and excludes those eliminated through consideration of model fit, discrimination and calibration. The reduced model forms the basis for final validation models (after consideration of position of HF codes).

The extended model Includes all variables selected through forward stepwise procedure (Wald *P* value < 0.20).

* Compared to basic model.

† Compared to optimal model.

Web Table 5. Results of model selection to predict ADHF among those hospitalizations with ICD code

The reduced model includes variables selected through forward stepwise procedure (Wald *P* value < 0.20) and excludes those eliminated through consideration of model fit, discrimination and calibration. The reduced model forms the basis for final validation models (after consideration of position of HF codes).

The extended model Includes all variables selected through forward stepwise procedure (Wald *P* value < 0.20).

* Compared to basic model.

† Compared to optimal model.

Web Table 6. Results of model selection to predict ADHF among those hospitalizations with ICD code 428 absent with other eligible codes

The reduced model includes variables selected through forward stepwise procedure (Wald *P* < 0.20) and excludes those eliminated through consideration of model fit, discrimination and calibration. The reduced model forms the basis for final validation models (after consideration of position of HF codes).

The extended model Includes all variables selected through forward stepwise procedure (Wald *P* < 0.20). * Compared to basic model.

† Compared to reduced model.

Web Table 8. Characteristics of heart failure eligible* hospitalizations in ARIC ADHF surveillance and

Abbreviations: ADHF, acute decompensated heart failure; AF, atrial fibrillation; ARIC, Atherosclerosis Risk in Communities; COPD, chronic obstructive pulmonary disease; HF, heart failure.

* Eligible sample of hospitalizations among age ≥55 years are defined by hospital ICD codes as detailed in methods and Web Table 1.

† Estimated among those with nonmissing values as race is missing for 23% hospitalizations in the NIS.

Web Table 11. Multivariable model to predict ADHF among those hospitalizations with ICD code 428

Web Figure 1. Area under the receiver operating characteristic (ROC) curve (AUC) for risk score to predict hospitalized ADHF with predictors that include age, sex, teaching hospital status, and comorbidity defined with discharge codes for 428 primary (A), nonprimary (B), and absent (C).

Web Table 13. Annual percentage change in the estimates for hospitalizations, hospitalization

Estimates were based on National Inpatient Sample of hospitalizations with ICD code 428.xx in the primary position, vs. nonprimary position, vs. other absent with other eligible ICD code. ADHF frequency and rates are based on estimations using validated models in the ARIC study. US Census data were used for estimation of rates. Figure 3 shows the trends. CI, confidence interval.

Inpatient Sample.

WEB FIGURES 2 AND 3

Web Figure 2. Predicted versus observed probability of acute decompensated heart failure (ADHF) hospitalization by decile of risk scores derived for 428 primary (A), nonprimary (B), and absent (C), separately.

Web Figure 3. Comparison of hospitalizations with ICD-9-CM code 428 primary with acute decompensated heart failure (ADHF) in the United States during 1998–2011, by age group. Panels show discharge code 428 in primary position (A), estimated ADHF hospitalizations (B), and corresponding rates per 1000 persons for 428 primary (C), and estimated ADHF (D). Trends for 1998–2004 and 2005–2011 are shown as annual percent change.