UCLA
UCLA Previously Published Works

Title

Temporal trends in risk profiles among patients hospitalized for heart failure

Permalink

https://escholarship.org/uc/item/7v24z2g2

Authors

Hamo, Carine E
Fonarow, Gregg C
Greene, Stephen J
et al.

Publication Date

2021-02-01

DOI

10.1016/j.ahj.2020.11.015

Peer reviewed

eScholarship.org Powered by the California Digital Library
University of California

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

HHS Public Access

Author manuscript

Am Heart J. Author manuscript; available in PMC 2022 February 01.

Published in final edited form as:

Am Heart J. 2021 February ; 232: 154–163. doi:10.1016/j.ahj.2020.11.015.

Temporal trends in risk profiles among patients hospitalized for heart failure

Carine E. Hamo, MD[a], **Gregg C. Fonarow, MD**[b], **Stephen J. Greene, MD**[c,d], **Muthiah Vaduganathan, MD,MPH**[e], **Clyde W. Yancy, MD**[f], **Paul Heidenreich, MD**[g], **Di Lu, MS**[c], **Roland A. Matsouaka, PhD**[c,h], **Adam D. DeVore, MD,MHS**[c,d], **Javed Butler, MD,MPH,MBA**[i]

[a]Division of Cardiology, Johns Hopkins University, Baltimore, MD

[b]Ahmanson-UCLA Cardiomyopathy Center, Ronald Reagan UCLA Medical Center, Los Angeles, CA

[c]Duke Clinical Research Institute, Durham, NC

[d]Division of Cardiology, Duke University School of Medicine, Durham, NC

[e]Brigham and Women's Hospital Heart & Vascular Center, Boston, MA

[f]Division of Cardiology, Northwestern University Feinberg School of Medicine, Chicago, IL

[g]Division of Cardiology, Veterans Affairs Palo Alto Healthcare System, Palo Alto, CA

[h]Department of Biostatistics and Bioinformatics, Duke University, Durham, NC

[i]University of Mississippi Medical Center, Jackson, MS

Abstract

Background—Postdischarge mortality following hospitalization for heart failure with reduced ejection fraction (HFrEF) has remained high and unchanged over the past 2 decades, despite effective therapies for HFrEF. We aimed to explore whether these patterns could in part be explained by changes in longitudinal risk profile and HF severity over time.

Methods—Among patients hospitalized for HF in the GWTG-HF registry from January 2005 to December 2018 with available data, we evaluated GWTG-HF and ADHERE risk scores, observing in-hospital mortality per-year. The risk profiles and outcomes were described overall and by subgroups based on ejection fraction (EF), diabetes mellitus (DM), sex, and age.

Results—Overall, 335,735 patients were included (50% HFrEF, 46% DM, 48% female, mean age 74 years). In-hospital mortality increased by 2.0% per year from 2005 to 2018. There was no significant change in mean GWTG-HF risk score overall or when stratified by EF groups ($P = 0.46$ HFrEF, $p = 0.26$ HF mid-range EF [HFmrEF], and $P = 0.72$ HF preserved EF [HFpEF]), age, sex, or presence of DM. The observed/expected ratio based on the GWTG-HF risk score was 0.93

Reprint requests: Javed Butler, MD, MPH, MBA, Department of Medicine, University of Mississippi, 2500 North State Street, Jackson, MS 39216. Jbutler4@umc.edu.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.ahj.2020.11.015.

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

(0.91-0.96), 0.83 (0.77-0.90), 0.92 (0.89-95) for HFrEF, HFmrEF, and HFpEF, respectively. Similar findings were seen when risk was assessed using ADHERE risk score.

Conclusions—There were no significant changes in average risk profiles among hospitalized HF patients over the study duration. These data do not support the notion that worsening risk profile explains the lack of improved outcomes despite therapeutic advances, underscoring the importance of aggressive implementation of guideline-recommended therapies and investigation of novel treatments.

Patients hospitalized with heart failure (HF) continue to experience high rates of postdischarge mortality and readmission,[1,2] and account for a large proportion of overall HF-related cost.[3,4] These patients also carry a high comorbidity burden. In a study of Medicare beneficiaries with HF, ~40% of patients had 5 or more noncardiac comorbidities.[5] Approximately 40% of patients hospitalized with HF have concomitant diabetes mellitus (DM), and this portends a worse prognosis with higher mortality and rehospitalization.[6] HF outcomes postdischarge have remained largely unchanged with some data suggesting a trend toward increased mortality.[7-9] It may be hypothesized that this could be related to an increase in HF severity and comorbidity burden over time, and as such stability in event rates may represent improved outcomes compared with expected. However, no comprehensive longitudinal data evaluating the evolution of risk profiles of patients hospitalized for HF exist. In this study, we assessed the temporal trends in estimated risk profile and observed in-hospital mortality among patients hospitalized with HF participating in the Get With The Guidelines- Heart Failure (GWTG-HF) centers to better elucidate whether the risk profile for these patients has increased, remained unchanged, or decreased over time.

Methods

Data source

GWTG-HF is a national quality improvement program by the American Heart Association that began in 2005 and includes patients admitted for worsening HF, de novo HF, and those who develop symptoms attributable to HF during hospitalization (all with a primary discharge diagnosis of HF). The program design and objectives have been published previously.[10] Consecutive patients or a random sample at each enrolling site are identified using methods similar to those employed by the Joint Commission. Baseline characteristics, patient disposition, and in-hospital outcomes are collected via a point-of-service web-based tool managed by (IQVIA, Parsippany, NJ) and stored and analyzed at the Duke Clinical Research Institute. Participating centers are required to obtain institutional review board approval for the GWTG-HF protocol. A waiver of informed consent is granted under the Common Rule given that the data collection is primarily for the purpose of quality improvement.

Study population and design

The initial study population for this analysis consisted of 810,689 GWTG-HF patients. The study period was from January 2005 through December 2018. We sequentially excluded patients with a completely missing medical history panel (n = 32,636), with missing or not documented discharge disposition (n = 3,615), with missing ejection fraction (EF) (n =

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

20,527), and with missing GWTG-HF risk or Acute Decompensated Heart Failure National Registry (ADHERE) risk score (n = 418,176). This yielded 335,735 patients from 508 hospitals. Additional exclusions were then applied to evaluate the trend of in-hospital mortality, discharge home, and length of stay. From 335,735 participants, we excluded patients who left the hospital against medical advice (n = 3,355), who were transferred to an acute care facility (ie, short-term hospitals) (n = 5,358), and those who were discharged to hospice care (n = 11,232). This resulted in 315,790 patients from 505 hospitals serving as Cohort A. We then excluded patients who died in the hospital (n = 8601) yielding 307,189 patients from 503 hospitals serving as Cohort B. An additional 20,060 patients who were transferred to the hospital were excluded resulting in 287, 129 patients from 503 hospitals as Cohort C. To investigate hospital variation in clinical risk profiles we excluded from the initial 335,735 the participants the patients from hospitals with less than ten eligible hospitalizations during the study period (n = 281). (Figure 1)

HF was defined by EF measurements with HF with preserved EF (HFpEF) defined as EF ≥50%, HF with mid-range EF (HFmrEF) defined as EF 41%-49%, and HF with reduced EF (HFrEF) defined as EF ≤40%. DM was defined as a medical history of insulin or noninsulin treated DM or a new diagnosis of DM during the index hospitalization. The primary outcome was time trend of in-hospital mortality from 2005 to 2018. The secondary outcomes were time trend in discharge home and hospital length of stay from 2005 to 2018.

The GWTG-HF and ADHERE risk scores

The GWTG-HF risk score is a validated score using readily available clinical variables including systolic blood pressure (SBP), blood urea nitrogen (BUN), sodium, age, heart rate, black race, and history of chronic obstructive pulmonary disease (COPD)/asthma to predict in-hospital mortality among patients admitted with HF. The score ranges from 0 to 101, with scores ≤33 indicating a <1% probability of death and scores ≥79 indicating a >50% probability of death.[11] GWTG-HF risk scores were computed in the present analysis for patients with nonmissing SBP, BUN, sodium, age, heart rate, black race, or COPD/asthma history (n = 337,245).

The ADHERE score, developed prior to the GWTG-HF score, uses BUN, SBP, and creatinine obtained on hospital admission for HF to predict in-hospital mortality. Scores are categorized into low (BUN level <43 mg/dL and SBP ≥115 mm Hg), intermediate (intermediate risk 1: BUN level ≥43 mg/dL, SBP <115 mmHg, and creatinine level <2.75 mg/dL, intermediate risk 2: BUN level ≥43 mg/dL, and SBP ≥115 mm Hg, intermediate risk 3: BUN level <43 mg/dL and SBP <115 mm Hg), and high (BUN level ≥43 mg/dL, SBP <115 mmhg, and creatinine level ≥2.75 mg/dL) with mortality ranging from 2.1% to 21.9%.[12] In the present analysis, ADHERE risk scores for in-hospital mortality were computed among patients with nonmissing BUN, SBP, or creatinine (n = 338,617).

Statistical analysis

Patient demographics, medical history, laboratory values, and HF medications were studied and compared stratified by incremental time periods (20052009, 2010-2014, and 2015-2018). Continuous variables were reported as medians with 25th and 75th percentiles

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

and categorical variables as counts and percentages. The overall risk profiles and outcomes were described by different subgroups, including EF groups (HFpEF, HFmrEF, HFrEF as defined above), DM (presence or absence), sex (male, female), and age (<65 or ≥65 years). Observed to expected (O/E) ratios with 95% confidence intervals (CI) based on a binomial distribution were calculated among patients with nonmissing expected mortality and nonmissing observed in-hospital mortality.

The time trends of risk profiles from 2005 to 2018 were analyzed, including stratified analyses by the key, prespecified subgroups mentioned above. For continuous GWTG-HF risk score, linear regression models were used to assess the temporal trend. For high ADHERE risk as defined above, logistic regression models were used to assess the temporal trend. For all the regression models, the generalized estimating equation (GEE) method with exchangeable working correlation structure were used to account for within-hospital clustering of patients and to determine robust variance estimates.

The time trend of in-hospital mortality was assessed from 2005 to 2018 among Cohort A, using a logistic regression model. The results for in-hospital morality are presented as odds ratio (OR) with 95% CI. For discharge disposition comparison from 2005 to 2018, we performed the analysis among Cohort B (excluding in-hospital deaths from Cohort A) using also a logistic regression model. For length of stay assessment, we analyzed Cohort C (excluding transfer-ins from Cohort B). Poisson regression model with log link was used to assess the association between temporal trend and the length of stay; the results are presented as risk ratio with the corresponding 95% CI. Similarly, the GEE method with exchangeable working correlation structure was used to account for within-hospital clustering of patients and to determine robust variance estimates. Both unadjusted and adjusted (for risk factors) analyses were performed and reported. Standard GWTG-HF adjustment variables were included in the adjusted analysis, that is, age, sex, white race, anemia, ischemic history, cerebrovascular accident/transient ischemic attack (CVA/TIA), DM, hyperlipidemia, hypertension, COPD or asthma, peripheral vascular disease (PVD), renal insufficiency, smoking, EF groups, SBP at admission, heart rate, sodium, BUN) and hospital-level factors (hospital region, hospital type, number of beds, and rural location).

For hospital-level variation in clinical risk profiles, we created histograms of mean GWTG-HF risk score for each hospital and the proportions of high risk ADHERE score for each hospital. To determine hospital-level variation in risk-standardized mortality rates (RSMR), we used a hierarchical multivariable logistic regression model with a random intercept for hospital to derive hospital-specific in-hospital RSMR. In-hospital RSMR was calculated for each hospital for the study period by multiplying the ratio of predicted/expected in-hospital mortality by the observed overall in-hospital mortality rate. For the ratio of predicted/expected in-hospital mortality, the predicted number of deaths for each hospital was calculated by the hierarchical model given the patients' risk factors and the hospital-specific effect, and the expected number of deaths for each hospital given the patients' risk factors and the average of all hospital-specific effects overall. The clinical factors of the GWTG HF Risk Score prediction model were included in the model. Another similar hierarchical multivariable logistic regression model using the factors from the ADHERE Risk Score prediction model was also fitted.

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

Missing history of smoking was imputed as “no”. Missing hospital characteristics were not imputed. For sodium values at admission, values <90 mEq/L were truncated at 90 mEq/L, and the values >190 mEq/L were truncated at 190 mEq/L. For BUN at admission, the values <4 mg/dL were truncated at 4 mg/dL, up to maximum values of 150 mg/dL. Linearity of continuous variables was checked before fitting the model. If found nonlinear, flexible spline transformations of adjustment continuous variables were used, and linear splines of temporal trend were fitted when appropriate. For discharge home, the linear spline knot for time trend was chosen at year 2014 that balanced model fit by maximizing model likelihood and interpretation of results. Collinearity was checked for these models as well. A 2-sided $P < 0.05$ was considered statistically significant for all tests. All statistical analyses were performed at the Duke Clinical Research Institute using SAS (version 9.3; SAS; Cary, NC).

Results

Baseline characteristics

Of the 335,735 patients analyzed, the mean age was 74 years (Table 1). Across three time periods (2005-2009, 2010-2014, and 2015-2018), 49.3%, 48.5%, and 46.6% of patients were female with approximately 68% white and 19% black. Comorbidity burden was similar across the three time periods with exception of a notable increase in hypertension from 76.4% in 2005-2009 to 85.4% in 2015-2018, and an increase in chronic or recurrent atrial fibrillation from 30.6% in 2005-2009 to 39.8%. in 2015—2018. In 2005-2009, 38.2% of patients had HFpEF and 54.2% had HFrEF, while in 2015-2018 45.0% of patients had HFpEF and 45.3% of patient had HFrEF.

Risk profiles

Overall—Mean GWTG-HF risk score in the overall cohort was 39.9. Of 338,617 individuals in whom ADHERE risk data was available, 5,598 (1.7%) had high risk, 110,114 (32.5%) had intermediate risk, and 222,905 (65.8%) had low risk. The overall O/E ratios for all subgroups were <1.0.

Subgroups—Risk profiles and outcomes of in-hospital mortality among patients by subgroup are presented in Table 2. GWTG-HF risk scores ranged from 34.4 among individuals < 65 years to 42.3 among individuals ≥65 years. Expected mortality ranged from 1.57% among those aged <65 years to 3.10% among those ≥65 years. GWTG-HF risk score was 39.4 among HFpEF patients and 40.5 among HFrEF patients. The percentage of individuals with high ADHERE risk ranged from 1.1% among HFpEF patients to 2.2% among those with HFrEF. Expected mortality was 2.69% in HFpEF patients compared to 3.04% in HFrEF patients. The O/E ratio was 0.88 (95% CI 0.86-0.91) among individuals with DM, 0.94 (95% CI 0.92-0.97) among individuals without DM, 0.91 (95% CI 0.89-0.93) among those aged ≥65 years, and 0.95 (95% CI 0.90-1.00) among those < 65 years.

Change over time—GWTG-HF and ADHERE risk profiles remained stable when stratified by admission year (Online Table 1). From 2005 to 2018, there was no significant change in mean GWTG-HF score when stratified by EF groups ($P = 0.46$ HFrEF, $P = 0.26$ HFmrEF, and $P = 0.72$ HFpEF), DM ($P = 0.42$ DM, $P = 0.86$ without DM), sex ($P = 0.99$ for

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

female, and $P = 0.93$ for male), or age ($P = 0.054$ for age< 65 years, and $P = 0.56$ for age ≥65 years) (Figure 2). There was no significant change in the distribution of ADHERE risk groups. Among patients with high ADHERE risk, there was no significant change in the distribution of patients by EF, sex, or age (Figure 3).

Outcomes—In an unadjusted model, there was a nonstatistically significant trend in the change in-hospital mortality per year from 2005 to 2018 (OR 1.01, 95% CI 1.00-1.02; $P = 0.052$). When adjusted for all covariates, there was a relative increase in-hospital mortality of 2% per year from 2005 to 2018 (OR 1.02, 95% CI 1.01-1.04; $P = 0.001$) (Table 3). The estimated odds of being discharged home from 2005 to 2014 was 2% less with each calendar year (OR 0.98, 95% CI 0.96-0.99; $P = 0.003$). From 2015 to 2018, the estimated odds of being discharged home was 3% greater with each calendar year (OR 1.03, 95% CI 1.01-1.04; $P = 0.004$). For every calendar year (from 2005 to 2018), there was a 1% reduction in the length of stay in both unadjusted and adjusted models (risk ratio 0.99, 95% CI 0.98-0.99; $P <0.001$)

Hospital variation—Mean GWTG-HF risk score was relatively similar across hospitals with a median of 40.5 and a range from 30.5 to 49.3 (Figure 4A). Median proportion of patients with a high ADHERE risk score was 1.4%, with the proportion ranging from 0% to 16.7% across hospitals. (Figure 4B). Intermediate ADHERE risk was observed in a median of 31.1% of hospitals with a range from 0% to 58.8%. Low ADHERE risk was observed in a median of 68.9% of hospitals with a range from 41.2% to 100%. Using covariates from the GWTG-HF risk score prediction model, median in-hospital RSMR was 2.6% with a range from 1% to 7.1% (Figure 5A). Using covariates from the ADHERE risk score prediction model, median in-hospital RSMR was 2.5% with a range from 1% to 6.8% (Figure 5B).

Discussion

In this large registry-based cohort of U.S. patients hospitalized for HF, the level of intrinsic patient risk as defined by the GWTG-HF and ADHERE risk scores has remained unchanged over time. These findings were consistent across all prespecified subgroups, showing temporally stable levels of risk irrespective of EF, DM status, sex, or age. Unadjusted in hospital-mortality did not change significantly between 2005 and 2018; however, the adjusted odds of in-hospital mortality was 2% greater with each calendar year. The odds of being discharged home was 2% lower with each calendar year between 2005 and 2014 and 3% greater with each year from 2015 to 2018. Length of stay decreased by 1% annually from 2005 to 2018. The GWTG-HF risk score distribution was similar across hospitals while the distribution of ADHERE risk appeared more variable. In-hospital RSMR were relatively similar using either the covariates from the GWTG-HF or ADHERE risk score prediction models.

To our knowledge, we present the first longitudinal analysis of temporal trends in the risk profile of patients hospitalized with HF utilizing clinical variables. We have shown, similar to previous studies, that overall the comorbidity burden, particularly noncardiac comorbidities, of HF patients has increased over time.[13] However, this may be driven in whole or in part by electronic health record adoption along with public reporting and

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

Hospital Readmissions Reduction Program incentivized increases in severity coding also at times referred to as “upcoding”. The use of validated risk models such as the GWTG-HF and ADHERE scores are based largely on clinical variables (eg, vital signs and laboratory values) and provide an alternative to claims-based risk adjustment which may be subject to financially incentivized increases in severity coding. Therefore, they may represent a more objective means to evaluate temporal trends in risk profiles than those based on administratively coded data alone. The current study found that from 2005 to 2018, there was no observed change in GWTG-HF or ADHERE risk overall or among subgroups.

In the evaluation of temporal trends in-hospital mortality we found that unadjusted mortality rates were unchanged over 2005-2018. When adjusted for GWTG-HF and ADHERE risk, there was a very slight but statistically significant increase in-hospital mortality of 1% relative odds per calendar year and a 2% relative odds increase when adjusted for all covariates. These findings are consistent with those of another analysis of the GWTG-HF cohort and support the potential differing effect of adjustment for clinical variables versus billing and diagnostic codes. For example, using claims-based adjustment, data from the National Inpatient Sample from 2000 to 2010 found age-standardized in-hospital mortality among patients hospitalized with HF to decline from 4.57% to 3.09% (P-trend <0.0001) with a concomitant increase in DM prevalence and comorbidity burden.[14] Likewise, in an analysis of Medicare patients hospitalized for HF between 2006 and 2014 to determine trends following the Hospital Readmissions Reduction Program, investigators reported a substantial increase in the severity/risk score among hospitalized HF patients. This was accompanied by a decrease in-hospital mortality by 0.014% per month.[7] A recent study of Veterans hospitalized with HF from 2009 to 2015 compared 30-day mortality trends using claims-based versus clinical risk-adjustment models, finding that use of clinical variables attenuated or eliminated the observed decline in mortality using claims-based risk adjustment. While predicted mortality risk using claims-based data increased, the predicted risk of mortality declined, or remained constant with clinical variable-based models.[15]

While patient risk profiles as determined by GWTG-HF and ADHERE risk scores remained relatively stable and observed unadjusted in-hospital mortality remained unchanged over time, we found that adjusted in-hospital mortality after accounting for risk scores increased very slightly. The GWTG-HF and ADHERE risk scores were primarily developed to address the risk of in-hospital mortality that could be expected based on admission characteristics, albeit they have also been shown to predict early postdischarge mortality.[16] Over time, the observed in-hospital mortality may be influenced by a variety of factors including treatment rendered, transfers out of the hospital, or changes in length of stay regardless of the risk expected based on admission characteristics. It is also important to note that the observed mortality is for the entire cohort of patients in each study period whereas the unadjusted and risk adjusted odds of mortality reported utilized GEEs which account for the clustering of data within hospitals. The observed mortality, both unadjusted and risk adjusted, is also not a measure of the intrinsic risk unless there is no impact of management or these other factors. The slight increase in risk adjusted mortality observed in the present study may suggest worse or incomplete treatment, less transfers out before death, or an increase in intrinsic risk that was not fully captured in the risk models.

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

Study limitations

Due to the observational nature of this study, there is the potential for residual confounding. There are additional clinical and biomarker data that were not available that may have identified differences in risk over time that were not captured in the risk scores utilized. Data was obtained from among the hospitals who voluntarily participated in the GWTG program and therefore findings may not be generalizable to hospitals with different practices or resources. A large proportion (48%) of patients were excluded due to missing GWTG-HF or ADHERE risk scores which may have resulted in an under-representation of illness severity. Finally, data on cause-specific mortality were unavailable.

Conclusions

Among patients hospitalized with HF between 2005 and 2018, we assessed patient characteristics and previously derived and validated GWTG-HF and ADHERE risk scores to evaluate temporal trends in estimated mortality. While comorbidity burden increased over time, risk profile on admission measured by GWTG-HF and ADHERE risk scores remained unchanged. This was accompanied by no increase in unadjusted but a slight and statistically significant increase in risk-adjusted in-hospital mortality.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

Disclosures

CEH: Reports support from the National Heart, Lung, and Blood Institute, National Institutes of Health (Grant Number T32 HL007024). GCF: Reports grant support from NIH, consulting for Abbott, Amgen, AstraZeneca, Bayer, CHF Solutions, Janssen, Medtronic, Merck, and Novartis. SJG: Reports support by a Heart Failure Society of America/ Emergency Medicine Foundation Acute Heart Failure Young Investigator Award funded by Novartis; has received research support from Amgen, Bristol-Myers Squibb, and Novartis; has served on advisory boards for Amgen and Cytokinetics; and has served as a consultant for Amgen and Merck. MV: Reports grant funding from the KL2/Catalyst Medical Research Investigator Training award from Harvard Catalyst (NIH/NCATS Award UL 1TR002541) and serves on advisory boards for Amgen, AstraZeneca, Baxter Healthcare, Bayer AG, Boehringer Ingelheim, Cytokinetics, and Relypsa. ADD: Reports grant support from the AHA, Amgen, AstraZeneca, Bayer, Intra-Cellular Therapies, Luitpold Pharmaceuticals, Merck, the NHLBI, Novartis and PCORI; consulting for Amgen, AstraZeneca, Bayer, InnaMed, LivaNova, Mardil Medical, Novartis, Procyrion, scPharmaceuticals, and Zoll. JB: Served as a consultant for Abbott, Amgen, Array, AstraZeneca, Bayer, Boehringer Ingelheim, CVRx, Eli Lilly, G3 Pharmaceutical, Impulse Dynamics, Innolife, Janssen, Luitpold, Medtronic, Merck, Novartis, Novo Nordisk, Relypsa, Sequana, StealthPeptide, and ViforXXX. All other authors have reported that they have no relationships to disclose.

Sources of Funding: This work was supported in part by an American Heart Association grant award #16SFRN30180010. The Get With The Guidelines-Heart Failure (GWTG-HF) program is provided by the American Heart Association. GWTG-HF is sponsored, in part, by Amgen Cardiovascular and has been funded in the past through support from Medtronic, GlaxoSmithKline, Ortho-McNeil, and the American Heart Association Pharmaceutical Roundtable.

References

1. Ross JS, Chen J, Lin Z, et al. Recent national trends in readmission rates after heart failure hospitalization. Circ Heart Fail 2010; 3:97–103. [PubMed: 19903931]

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

2. Lee DS, Austin PC, Rouleau JL, Liu PP, Naimark D, Tu JV. Predicting mortality among patients hospitalized for heart failure: derivation and validation of a clinical model. JAMA 2003;290:2581–7. [PubMed: 14625335]

3. Benjamin EJ, Virani SS, Callaway CW, et al. Heart Disease and Stroke Statistics-2018 Update: a Report From the American Heart Association. Circulation 2018;137:e67–e492. [PubMed: 29386200]

4. Ambrosy AP, Pang PS, Khan S, et al. Clinical course and predictive value of congestion during hospitalization in patients admitted for worsening signs and symptoms of heart failure with reduced ejection fraction: findings from the EVEREST trial. Eur Heart J 2013;34:835–43. [PubMed: 23293303]

5. Braunstein JB, Anderson GF, Gerstenblith G, et al. Noncardiac comorbidity increases preventable hospitalizations and mortality among Medicare beneficiaries with chronic heart failure. J Am Coll Cardiol 2003;42:1226–33. [PubMed: 14522486]

6. Mentz RJ, Felker GM. Noncardiac comorbidities and acute heart failure patients. Heart Fail Clin 2013;9:359–67 vii. [PubMed: 23809421]

7. Khera R, Dharmarajan K, Wang Y, et al. Association of the hospital readmissions reduction program with mortality during and after hospitalization for acute myocardial infarction, heart failure, and pneumonia. JAMA Network Open 2018;1.

8. Gupta A, Allen LA, Bhatt DL, et al. Association of the Hospital Readmissions Reduction Program Implementation With Readmission and Mortality Outcomes in Heart Failure. JAMA Cardiol 2018;3:44–53. [PubMed: 29128869]

9. Gupta A, Fonarow GC. The Hospital Readmissions Reduction Program-learning from failure of a healthcare policy. Eur J Heart Fail 2018;20:1169–74. [PubMed: 29791084]

10. Smaha LA. The American Heart Association Get With The Guidelines program. Am Heart J 2004;148(5 Suppl):S46–8. [PubMed: 15514634]

11. Peterson PN, Rumsfeld JS, Liang L, et al. A validated risk score for in-hospital mortality in patients with heart failure from the American Heart Association get with the guidelines program. Circ Cardiovasc Qual Outcomes 2010;3:25–32. [PubMed: 20123668]

12. Fonarow GC, Adams KF, Abraham WT. et al. Risk stratification for in-hospital mortality in acutely decompensated heart failure: classification and regression tree analysis. JAMA 2005;293:572–80. [PubMed: 15687312]

13. Sharma A, Zhao X, Hammill BG, et al. Trends in noncardiovascular comorbidities among patients hospitalized for heart failure: insights from the Get With The Guidelines-Heart Failure Registry. Circ Heart Fail 2018;11.

14. Win TT, Davis HT, Laskey WK. Mortality among patients hospitalized with heart failure and diabetes mellitus: results from the National Inpatient Sample 2000 to 2010. Circ Heart Fail 2016;9.

15. Silva GC, Jiang L, Gutman R, et al. Mortality trends for veterans hospitalized with heart failure and pneumonia using claims-based vs clinical risk-adjustment variables. JAMA Intern Med 2020;180(3):347–55. [PubMed: 31860015]

16. Win S, Hussain I, Hebl VB, Dunlay SM, Redfield MM. Inpatient mortality risk scores and postdischarge events in hospitalized heart failure patients: A community-based study. Circ Heart Fail 2017;10(7):e003926 [PubMed: 28701328]

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

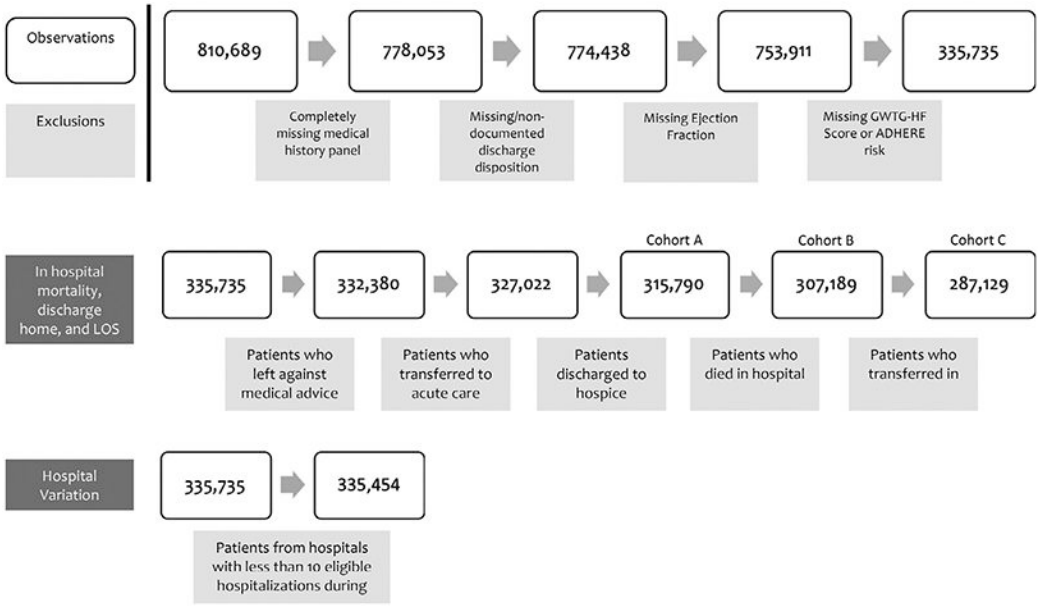

Figure 1.
Study population selection. LOS, length of stay.

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

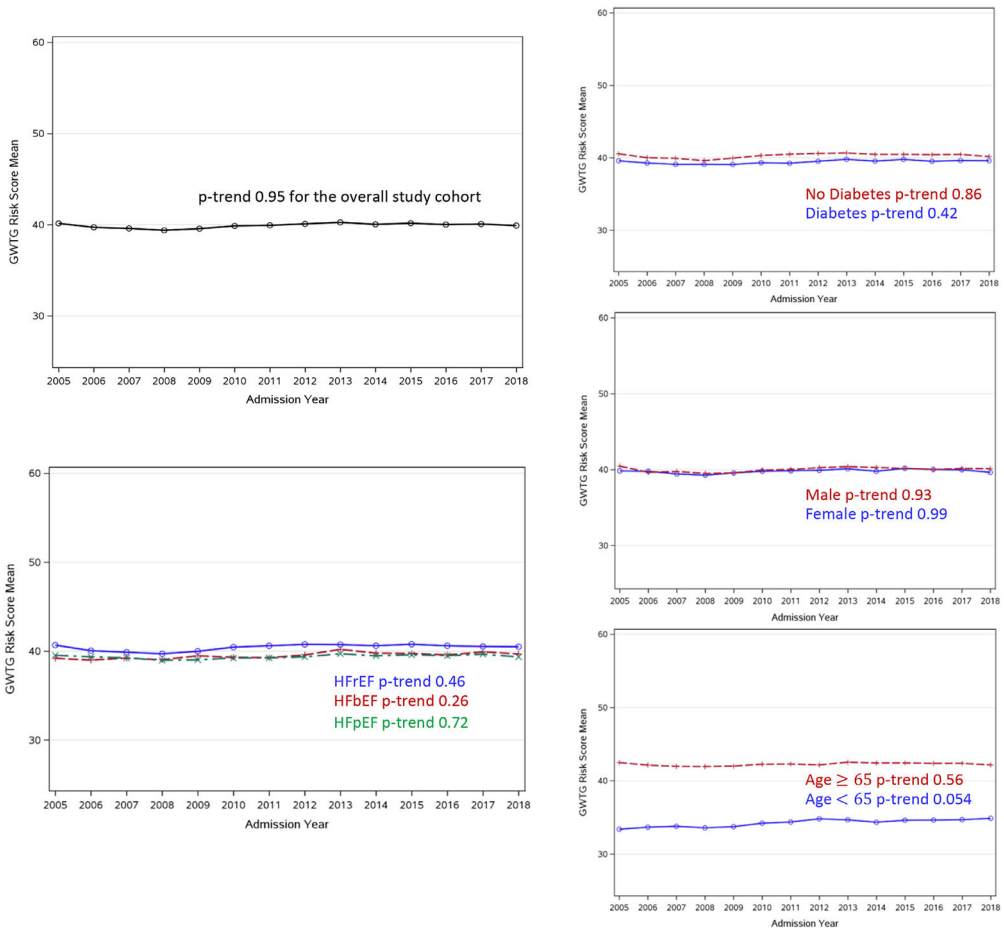

Figure 2.

Temporal Trends in GWTG-HF Risk Scores Stratified by Subgroups. Mean GWTG-HF risk score from 2005 through 2018 in (a) overall cohort and stratified by (b) HF subgroup (HFrEF, HFmrEF, and HFpEF), (c) diabetes mellitus status (present or absent), (d) sex (male, female), and (e) age (≥65 years, < 65 years). GWTG-HF, Get With The Guidelines-Heart Failure Registry; HFrEF, heart failure with reduced ejection fraction; HFmrEF, heart failure with mid-range ejection fraction; HFpEF, heart failure with preserved ejection fraction.

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

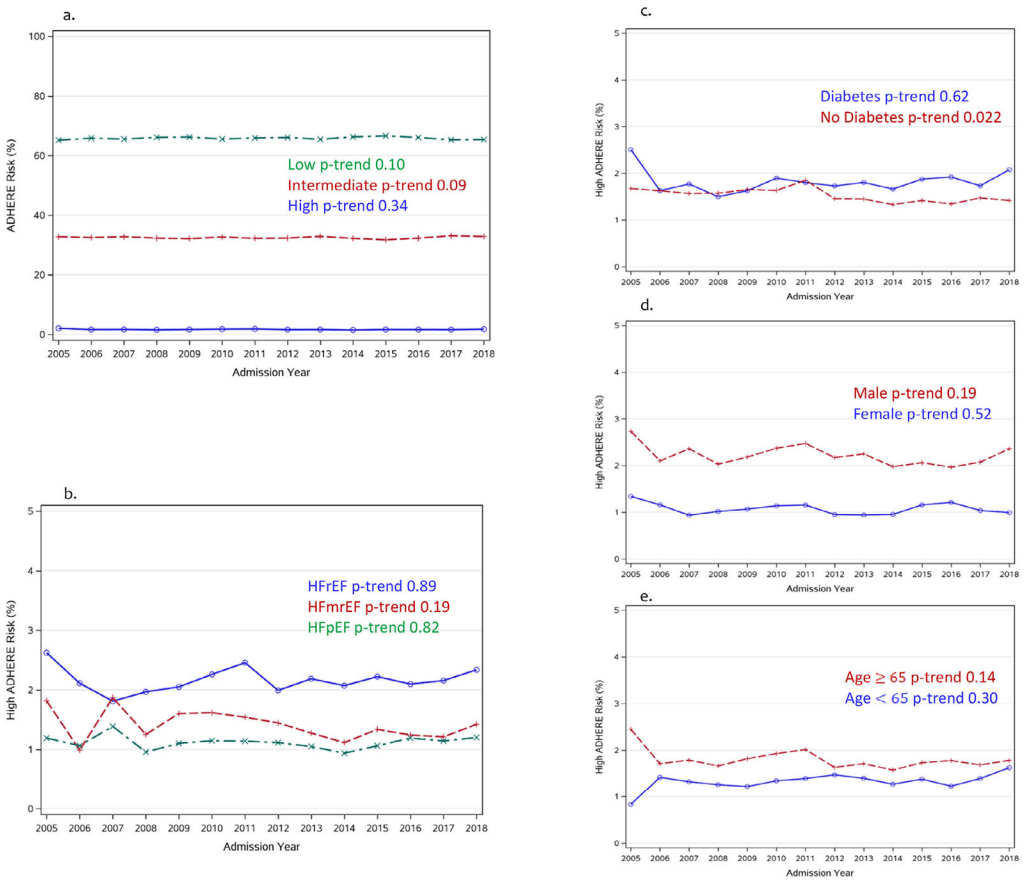

Figure 3.

Temporal Trends in ADHERE Risk Stratified by Subgroups. (a) Percent distribution of Low, Intermediate, and High ADHERE risk from 2005 through 2018 in overall cohort. Percent distribution of High ADHERE risk from 2005 through 2018 stratified by (b) HF subgroup (HFrEF, HFmrEF, and HFpEF), (c) diabetes mellitus status (present or absent), (d) sex (male, female), and (e) age (≥65 years, < 65 years). ADHERE, Acute Decompensated Heart Failure National Registry; HFrEF, heart failure with reduced ejection fraction; HFmrEF, heart failure with mid-range fraction; HFpEF, heart failure with preserved ejection fraction.

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

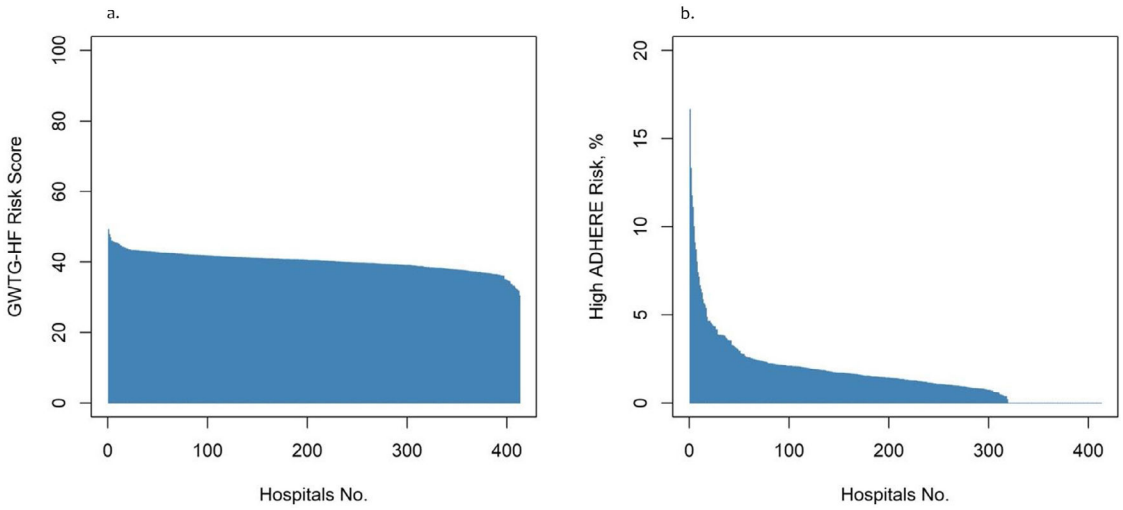

Figure 4.

Histograms of hospital-level (a) GWTG-HF risk score and (b) High ADHERE risk. ADHERE, Acute Decompensated Heart Failure National Registry; GWTG-HF, Get With The Guidelines-Heart Failure Registry.

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

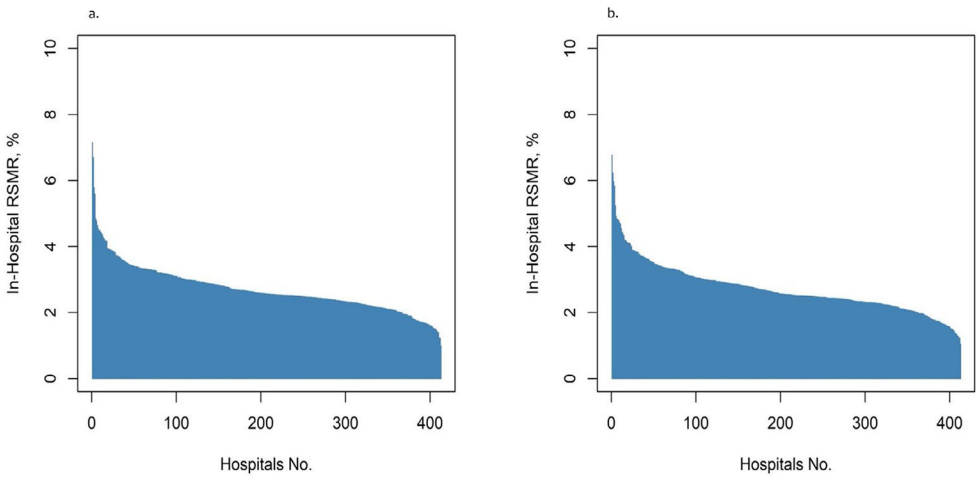

Figure 5.

In-hospital Risk-Standardized Mortality Rates (RSMR) using covariates from the (a) GWTG-HF Risk Score prediction model and the (b) ADHERE Risk Score prediction model. ADHERE, Acute Decompensated Heart Failure National Registry; GWTG-HF, Get With The Guidelines-Heart Failure Registry.

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

Am Heart J. Author manuscript; available in PMC 2022 February 01.

Table 1.

Baseline patient characteristics stratified by time periods.

	2005-2009 ***N*** **= 75,430**	**2010-2014** ***N*** **= 118,495**	**2015-2018** ***N*** **= 141,810**
Age	74.0 (62.0-83.0)	74.0 (62.0-84.0)	73.0 (62.0-83.0)
Sex			
Female	37,195 (49.3%)	57,485 (48.5%)	66,026 (46.6%)
Male	38,235 (50.7%)	61,010 (51.5%)	75,784 (53.4%)
Race			
UTD	1,632 (2.2%)	2,352 (2.0%)	2,229 (1.6%)
Native Hawaiian or Pacific Islander	126 (0.2%)	272 (0.2%)	504 (0.4%)
White	51,874 (68.8%)	80,679 (68.1%)	95,537 (67.4%)
Asian	695 (0.9%)	1,636 (1.4%)	2,285 (1.6%)
American Indian or Alaska Native	304 (0.4%)	644 (0.5%)	641 (0.5%)
Black or African American	15,719 (20.8%)	21,221 (17.9%)	27,547 (19.4%)
Hispanic	5,080 (6.7%)	11,691 (9.9%)	13,067 (9.2%)
Coronary Artery Disease	37,128 (49.2%)	59,591 (50.3%)	68,927 (48.6%)
Chronic or Recurrent Atrial Fibrillation	23,072 (30.6%)	43,651 (36.8%)	56,487 (39.8%)
Diabetes Mellitus	32,684 (43.3%)	55,667 (47.0%)	66,780 (47.1%)
Hypertension	57,653 (76.4%)	97,713 (82.5%)	121,149 (85.4%)
Hyperlipidemia	32,371 (42.9%)	63,588 (53.7%)	80,779 (57.0%)
Dialysis (Chronic)	3,104 (4.1%)	4,859 (4.1%)	5,589 (3.9%)
Renal Insufficiency (Chronic)	15,162 (20.1%)	27,163 (22.9%)	33,683 (23.8%)
COPD or Asthma	22,451 (29.8%)	41,224 (34.8%)	52,783 (37.2%)
Anemia	13,571 (18.0%)	27,644 (23.3%)	33,839 (23.9%)
Ischemic history	42,188 (55.9%)	66,301 (56.0%)	74,996 (52.9%)
CVA/TIA	11,170 (14.8%)	19,162 (16.2%)	24,264 (17.1%)
Peripheral Vascular Disease	9,292 (12.3%)	15,933 (13.4%)	17,651 (12.4%)
Smoking	12,978 (17.4%)	20,372 (17.2%)	25,044 (17.7%)
Serum Creatinine, mg/dL	1.3 (1.0-1.9)	1.3 (1.0-1.8)	1.3 (1.0-1.9)
BUN, mg/dL	25.0 (17.0-38.0)	25.0 (17.0-38.0)	25.0 (17.0-38.0)
eGFR (mL/min/1.73m^2)	51.0 (34.5-70.5)	53.7 (36.6-73.7)	54.4 (36.2-74.3)

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

Am Heart J. Author manuscript; available in PMC 2022 February 01.

	2005-2009 ***N*** **= 75,430**	**2010-2014** ***N*** **= 118,495**	**2015-2018** ***N*** **= 141,810**
Sodium, mEq/L	138.0 (135.0-141.0)	138.0 (135.0-140.0)	139.0 (136.0-141.0)
HbA1C,%	7.0 (6.1-8.0)	6.6 (5.9-7.8)	6.5 (5.8-7.7)
Ejection Fraction,%	38.0 (25.0-55.0)	40.0 (25.0-55.0)	45.0 (27.0-58.0)
HFpEF	28,791 (38.2%)	49,934 (42.1%)	63,870 (45.0%)
HFmrEF	5,740 (7.6%)	10,145 (8.6%)	13,741 (9.7%)
HFrEF	40,899 (54.2%)	58,416 (49.3%)	64,199 (45.3%)
Systolic Blood Pressure, mmHg	138.0 (119.0-159.0)	139.0 (119.0-160.0)	138.0 (119.0-159.0)
Diastolic Blood Pressure, mmHg	75.0 (64.0-88.0)	76.0 (64.0-89.0)	77.0 (66.0-90.0)
Heart Rate, bpm	82.0 (70.0-97.0)	83.0 (71.0-98.0)	84.0 (72.0-98.0)
Region			
West	8,729 (11.6%)	16,046 (13.5%)	28,914 (20.4%)
South	28,502 (37.8%)	36,829 (31.1%)	43,437 (30.6%)
Midwest	18,188 (24.1%)	25,048 (21.1%)	24,038 (17.0%)
Northeast	20,011 (26.5%)	40,572 (34.2%)	45,421 (32.0%)
Hospital Type - Academic	55,291 (73.8%)	87,990 (77.5%)	117,202 (85.0%)
Number of Beds	400.0 (297.0-585.0)	400.0 (294.0-581.0)	400.0 (276.0-608.0)
Rural Location	3,441 (5.0%)	4,849 (4.3%)	2,070 (1.5%)
Beta Blocker prior to admission	28,803 (41.1%)	74,445 (69.2%)	86,192 (68.8%)
ACE inhibitor prior to admission	28,093 (40.1%)	38,677 (35.9%)	36,141 (28.8%)
Angiotensin receptor blocker prior to admission	10,720 (15.3%)	15,688 (14.6%)	19,128 (15.3%)
Aldosterone antagonist prior to admission	7,517 (10.7%)	13,901 (12.9%)	16,700 (13.3%)
Hydralazine prior to admission	5,163 (7.4%)	10,805 (10.0%)	14,696 (11.7%)
Nitrate prior to admission	13,295 (19.0%)	19,686 (18.3%)	19,817 (15.8%)
Diuretic prior to admission	47,106 (67.3%)	70,612 (65.6%)	81,994 (65.4%)

ACE, angiotensin converting enzyme; BUN, blood urea nitrogen; COPD, chronic obstructive pulmonary disease; CVA, cerebrovascular event; EF; ejection fraction; eGFR, estimated glomerular filtration rate; HbA1C, hemoglobin A1C; HFmrEF, Heart failure mid-range ejection fraction; HFpEF, Heart failure preserved ejection fraction; HFrEF, heart failure reduced ejection fraction; UTD, unable to determine.

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

Table 2.

Risk profiles and in-hospital mortality among patients stratified by subgroup.

Subgroups	GWTG-HF Risk Score Mean(SD)	ADHERE High Risk N (%)	Expected In-Hospital Mortality (%)	Observed Unadjusted Hospital Mortality (%)	O/E ratio (95% CI)
HFrEF (EF ≤40%)	40.5(9.1)	3,540 (2.2%)	3.04	2.84	0.93 (0.91-0.96)
HFmrEF (EF 41-49%)	39.6(9.0)	404 (1.4%)	2.78	2.31	0.83 (0.77-0.90)
HFpEF (EF≥50%)	39.4(8.8)	1,600 (1.1%)	2.69	2.46	0.92 (0.89-0.95)
DM Absent	40.3(9.0)	2,719 (1.5%)	2.98	2.81	0.94 (0.92-0.97)
DM Present	39.5(8.9)	2,825 (1.8%)	2.74	2.42	0.88 (0.86-0.91)
Male	40.0(9.2)	3,827 (2.2%)	2.94	2.67	0.91 (0.88-0.93)
Female	39.8(8.7)	1,717 (1.1%)	2.79	2.59	0.93 (0.90-0.96)
Age ≥65 years	42.3(8.1)	4,190 (1.8%)	3.40	3.10	0.91 (0.89-0.93)
Age < 65 years	34.4(8.3)	1,354 (1.4%)	1.57	1.48	0.95 (0.90-1.00)

DM, diabetes mellitus; HFmrEF, Heart failure mid-range ejection fraction; HFpEF, Heart failure preserved ejection fraction; HFrEF, heart failure reduced ejection fraction, O/E, observed/expected.

Am Heart J. Author manuscript; available in PMC 2022 February 01.

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

Table 3.

Time trend in in-hospital mortality, discharge home, and length of stay.

Cohort	Outcome	Variable	Unadjusted		Adjusted for GWTG-HF risk score		Adjusted for ADHERE risk		Adjusted for all covariates	
			OR (95% CI)	*P*-value	OR (95% CI)	*P*-value	OR (95% CI)	*P*-value	OR (95% CI)	*P*-value
A	In-hospital mortality	Per year (2005-18)	1.01 (1.00, 1.02)	0.052	1.01 (1.00, 1.03)	0.021	1.01 (1.00-1.03)	0.023	1.02 (1.01, 1.04)	0.001
B	Discharge home	Per year (2005-14)	0.98 (0.96, 1.00)	0.011	0.98 (0.96, 0.99)	<0.001	0.98 (0.96-0.99)	0.003	0.98 (0.96, 0.99)	0.003
		Per year (2015-18)	1.02 (1.00, 1.04)	0.037	1.02 (1.00, 1.04)	0.013	1.02 (1.00-1.04)	0.030	1.03 (1.01, 1.04)	0.004
C	Length of stay	Per year (2005-18)	0.99 (0.98, 0.99)	<0.001	0.99 (0.98, 0.99)	<0.001	0.99 (0.98-0.99)	<0.001	0.99 (0.98, 0.99)	<0.001

Am Heart J. Author manuscript; available in PMC 2022 February 01.