Mortality Among Patients Hospitalized With Heart Failure and Diabetes Mellitus

Results From the National Inpatient Sample 2000 to 2010

Theingi Tiffany Win, MD; Herbert T. Davis, PhD; Warren K. Laskey, MD, MPH

Background—Case fatality and hospitalization rates for US patients with heart failure (HF) have steadily decreased during the past several decades. Diabetes mellitus (DM), a risk factor for, and frequent coexisting condition with, HF continues to increase in the general population.

Methods and Results—We used the National Inpatient Sample to estimate overall as well as age-, sex-, and race/ethnicity-specific trends in HF hospitalizations, DM prevalence, and in-hospital mortality among 2.5 million discharge records from 2000 to 2010 with HF as primary discharge diagnosis. Multivariable logistic and Poisson regression were used to assess the impact of the above demographic characteristics on in-hospital mortality. Age-standardized hospitalizations decreased significantly in HF overall and in HF with DM. Age-standardized in-hospital mortality with HF declined from 2000 to 2010 (4.57% to 3.09%, \( P_{\text{trend}<0.0001} \)), whereas DM prevalence in HF increased (38.9% to 41.9%, \( P_{\text{trend}<0.0001} \)) as did comorbidity burden. Age-standardized in-hospital mortality in HF with DM also decreased significantly (3.53% to 2.27%, \( P_{\text{trend}<0.0001} \)). After adjusting for year, age, and comorbid burden, males remained at 17% increased risk versus females, non-Hispanics remained at 12% increased risk versus Hispanics, and whites had a 30% higher mortality versus non-white minorities. Absolute mortality rates were lower in younger versus older patients, although the rate of decline was attenuated in younger patients.

Conclusions—In-hospital mortality in HF patients with DM significantly decreased during the past decade, despite increases in DM prevalence and comorbid conditions. Mortality rate decreases among younger patients were significantly attenuated, and mortality disparities remain among important demographic subgroups. (Circ Heart Fail. 2016;9:e003023.)

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Key Words: diabetes mellitus ■ heart failure ■ hospitalization ■ mortality ■ risk factor

There are nearly 5 million individuals in the United States with a diagnosis of heart failure (HF), and HF is the principal diagnosis in >1 million hospitalizations annually. During the past decade, overall HF hospitalization and in-hospital mortality rates have declined. Diabetes mellitus (DM), a disease that is increasing in prevalence, is a significant risk factor for the development of cardiovascular disease and amplifies the risk for the development of HF. In addition, HF itself is considered an insulin-resistant state and is associated with significant risk for the future development of DM. Given these relationships, it is not surprising that DM and HF may commonly coexist.

See Clinical Perspective

Although the true population-based prevalence of DM in patients with HF (ambulatory or hospitalized) is unknown, prevalences range from 20% to 30% in clinical trial populations to >40% in recent registries of hospitalized patients. What is clear is that the absolute number of individuals with HF will continue to increase world-wide as well as in the United States over the next decade, whereas the number of individuals with DM will also continue to increase world-wide and in the United States. Given the increasing prevalence of DM and HF and comparatively worse clinical outcomes of concomitant HF and DM in the general population, we examined trends in hospitalizations and in-hospital mortality in patients with HF and DM from 2000 to 2010. We also describe the factors associated with in-hospital mortality with a focus on the impact of time, age, sex, race, and ethnicity for this interval.

Methods

Data Source

The National Inpatient Sample (NIS), sponsored by the Agency for Healthcare Research and Quality Healthcare Cost and Utilization Project, is the largest all-payer in-patient database publicly available in the United States consisting of discharge data from >1000 hospitals across a majority of states and is designed to =20% stratified sample of US community hospitals.

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The NIS provides discharge-level demographic and clinical characteristics that are searchable using *International Classification of Diseases, Ninth revision*, codes. Each annual release of the NIS includes patient-level hospital discharge abstracted data for 100% of discharges from the sample of hospitals in participating states. We used NIS security files to extract administratively coded comorbid conditions of patients as established by Agency for Healthcare Research and Quality. The study was considered exempt from formal review by the University of New Mexico institutional review board because the NIS is a public database without personal identifiers.

**Data Quality**

A summary data quality report is available for review for each year of the NIS. Individual reports for the years 2000 to 2010 were reviewed by one of the authors (W.K.L.). With the exception of data for race and ethnicity (see below), edit check failure rates were consistently <0.5% for other key data elements.

**Study Population**

A total of 71 million hospital discharges were reported to the NIS from 2000 to 2010. We analyzed data for patients ≥18 years of age. HF hospital stays were defined as those with a primary discharge diagnosis of HF on the basis of the following *ICD-9-CM* codes: 402.01, 402.11, 402.91, 404.01, 404.03, 404.11, 404.13, 404.91, 404.93, and 428. We excluded any record containing an *ICD-9-CM* code for acute coronary syndrome or acute myocardial infarction to obviate the confounding issue of acute ischemia on in-hospital outcome. The total number of HF hospitalizations was calculated as the sum over all HF *ICD-9-CM* codes. We then obtained the proportion of HF discharges that occurred during the same time interval with a diagnosis of type 2 DM, identified by *ICD-9-CM* code 250.0 to 250.9 with a fifth digit of 0 or 2 because the majority of diagnosed cases of DM in adults are of type 2.

**Data Analysis**

Figure 1 shows the sequence of data analysis. We recorded the number of records for each year and stratified these records by age group (<60, 60–69, 70–79, and ≥80 years) sex, race, and ethnicity. We also computed a measure of medical comorbidities used by Healthcare Cost and Utilization Project in NIS data sets—the Elixhauser comorbidity index.28,29

Statistical weights provided by the NIS allow extrapolation to estimate discharge rates for the nation. After weighting, this reflects >95% of hospital discharges within the United States.

**Statistical Analysis**

Hospitalizations are summarized as raw counts as well as counts per 100000 adults (>18 years of age) for that year obtained using the US Census Bureau intercensal estimates for 2000 to 2010.31 Categorical data are summarized as percents. The outcome of interest in our analysis was in-hospital mortality. In keeping with our stated objectives, exposure variables were year, age on admission, sex, the discharge record specified race, and ethnicity and the Elixhauser comorbidity index. Survey analysis methods were used that used hospital-level discharge weights provided by the NIS to estimate the number of HF hospitalizations and in-hospital mortality on a national level.32 Direct standardization of age was performed using the average of the 2000 and 2010 NIS data sets as the standard population. Age-standardized in-hospital mortality rates for HF with DM were calculated and reported (in percent) for the overall sample and stratified by sex. All other sub–group-specific mortality rates are reported as crude mortality rates (CMR). Rates were plotted and smoothed for display using a Hamming window filter.

To distinguish changes in population age or sex composition versus age/sex-independent factors driving the observed decrease in CMR over time, the method of rate decomposition was used.33 Briefly, the difference in CMR from 2000 to 2010 can be viewed as the sum of a composition effect (reflecting the difference in the age or sex composition of the sample from 2000 to 2010) and a rate effect (reflecting differences in the distribution of stratum-specific mortality rates from 2000 to 2010; Δ CMR2000–2010=composition effect+rate effect). Calculations were performed for age and sex, separately and combined.

*P* values are based on χ² tests for all categorical row variables or χ² rank–based group means score statistics for continuous/ordinal row variables (equivalent to Wilcoxon tests). All such tests treat the column variable as nominal. Trends in categorical variables were tested using χ² statistics. Multivariable logistic regression that accounted for survey methodology and hospital clustering was used to estimate the magnitude of association between clinical, temporal, and demographic covariates and in-hospital mortality. Year was modeled as a continuous linear variable. An interaction term, age (group)xsex, was added to the model to test for the influence of sex on the association between age and mortality. Estimated measures of association are expressed as odds ratios (ORs) and 95% confidence intervals (CIs). Adjusted annual rates of change in mortality were estimated from a Poisson regression model, which estimated linear time trends in in-hospital mortality and included all variables used in the logistic regression model. Hospital length of stay (days) was used as the offset (exposure) variable in the Poisson model.

A sensitivity analysis was performed in the subgroup of hospitals with >90% completion of race/ethnicity data because missing rates of the latter frequently exceeded 10% in the overall sample. Additional sensitivity analyses examining the impact of the inclusion of *ICD-9-CM* codes for nonacute ischemic heart disease (*ICD-9-CM* 412.X, 413.X, and 414.X) on the associations between age, sex, race/ethnicity, time and comorbid burden, and in-hospital mortality was performed. We assessed the frequency of any acute manifestation of ischemic heart disease (*ICD-9-CM* codes 410.0–410.8) using the clinical classifications software provided by Healthcare Cost and Utilization Project.

The study was considered exempt from formal review by the University of New Mexico institutional review board because the NIS is a public database without personal identifiers.

A *P* value of < 0.05 was considered statistically significant. All analyses were performed using SAS (version 9.1 or higher) or STATA (version 14).

**Results**

**Characteristics of HF Hospitalizations From 2000 to 2010**

Hospitalization with a primary diagnosis of HF steadily decreased from 227595 in 2000 to 207593 in 2010 and translates to a decrease from 555/100 000 US adults to 460/100 000 US adults (*P* value < 0.0001; Table I in the Data Supplement). The overall prevalence of women was 52.5% and decreased from...
55.4% in 2000 to 49.9% in 2010 ($P_{\text{trend}}<0.0001$). The mean (±SD) age of the sample was 72.6±14.4 years and approximately two thirds (65.4% in 2000 and 62.4% in 2010) were ≥70 years of age. The majority were of white race (representing about 73% in 2000 and 66% in 2010), although non-white minority prevalence increased significantly from 27% to 34%. The prevalence of Hispanic ethnicity increased significantly from 5.3% in 2000 to 6.9% in 2010 ($P_{\text{trend}}<0.0001$). The mean (±SE) Elixhauser comorbidity index increased from 3.32±0.04 in 2000 to 5.67±0.07 in 2010 ($P_{\text{trend}}<0.0001$). The prevalence of DM increased from 38.9% to 41.9% ($P_{\text{trend}}<0.0001$) whereas the cumulative prevalence of nonwhite minorities increased from 32% to 39% ($P_{\text{trend}}<0.0001$). Minorities were noted with, however, persistent absolute differences between whites and non-white minorities.

The overall decrease in in-hospital mortality was not shared equally among the selected subgroups. As seen in Figures 3 and 4, larger decreases in case fatality rates were noted in the oldest groups when compared with their younger counterparts. Women exhibited smaller decreases in mortality over time with the largest decreases noted in the oldest group. Poisson regression analysis indicated a lower overall mortality rate and rate of decline in younger age groups (Table 2). As seen in Figures 5 and 6, declines in case fatality rates in Hispanics and non-Hispanics and whites versus non-white minorities were noted with, however, persistent absolute differences between whites and non-white minorities.

Demographic, temporal and clinical factors associated with in-hospital death were assessed using multivariable regression (Table 3) with the results supporting significant disparities within and among our selected subgroups. Males remained at 17% increased risk compared with females (OR, 1.17; 95% CI, 1.14–1.20); white populations remained at 30% higher risk compared with non-white minorities (OR, 1.30; 95% CI, 1.26–1.34); non-Hispanics remained at 12% increased risk compared with Hispanics (OR, 1.12; 95% CI, 1.06–1.19); and older patients (280 years) remained at 4× higher risk compared with their younger counterparts <60 years (OR, 4.08; 95% CI, 3.87–4.29). There was no significant interaction between age and sex on the association of either with in-hospital mortality ($P_{\text{interaction}}=0.19$).

Analysis of the above associations for only those records containing ICD-9-CM codes specific to ischemic heart disease yielded no meaningful differences in effect size (difference in magnitude of β-coefficients <2%) between models. In addition, there was minimal variation in the frequency of acute coronary syndromes coded in a secondary position with an average rate for the interval of 3.1%.

Sensitivity analysis confined to those hospitals with >90% data completion for race/ethnicity confirmed the above-mentioned significant trends in prevalences over time. As well, Poisson regression utilizing data from hospitals with >90% complete records yielded similar results to those in Table 3.

### Discussion

Using a nationally representative all-payer in-patient sample of US hospital admissions from 2000 to 2010, our observations support the following conclusions. First, the total number of hospitalizations with a primary diagnosis of HF decreased during this interval. Second, the prevalence of DM as well as a measure of the burden of comorbidities among hospitalized HF patients increased. Third, despite the increased prevalence of DM and comorbidity burden there was a 36% decrease in age-standardized in-hospital mortality among HF with DM. Fourth, in-hospital mortality rates varied by age, sex, race, and ethnicity. Fifth, the decrease in in-hospital mortality rate is the...
Reduction in In-Hospital Mortality in HF Patients With Coexisting DM

Several studies have now documented a decrease in hospitalization rates in the United States for patients with HF during a time interval similar to this study. The inclusion of hospitalizations in all adults, that is, >18 years of age, distinguishes this study from previous Medicare-derived data and the focus on the DM subgroup distinguishes this study from previous NIS studies. The inclusion of patient hospitalizations with age <65 years allows for analysis of an important group of relatively younger patients who comprised one fifth of all HF hospitalizations in the NIS database.

Our study was limited to hospitalized patients. Nevertheless, secular changes in the management and characteristics of patients with HF from 2000 to 2010 are relevant to these data. A decrease in HF-related hospitalization rates and in-hospital mortality was first reported from the Medicare and Medicaid population beginning in 1998 but reflects changes beginning before that date. The period from 2000 to 2010 was a period of increasing attention to improved management strategies for all patients with HF, which would likely affect hospitalization and in-hospitality mortality rates. The observed trend in this study is consistent with the time frame for the diffusion of evidence-based and clinical trial data into mainstream practice, and reflects many changes in the timing and extent of pharmacotherapy for HF. Improved adherence to contemporary guideline-based therapies for HF and DM in conformance with national guidelines during this time interval may also have contributed to improved in-hospital outcomes in HF and DM patients. Changes in the underlying cardiovascular risk profile of patients presenting with HF and DM, whether a cohort effect or a true indicator of intensified risk factor recognition and treatment, is another possible explanation for the reduction in in-patient mortality—a finding supported by our rate decomposition analysis.

Similar or lower in-hospital CMRs in patients with HF and DM compared with those with HF without DM have been previously observed. Of note is the similarity of our current observations in hospitalized patients to trends in the US population from 2005 to 2011. In this latter study, although...
hospitalizations and mortality rates declined in patients with DM, including those with HF, decreases in event rates, and mortality were lower or absent in those without DM. Thus, although hospitalized patients are a highly selected group from the general population, the above-noted secular trends may be powerful enough to beneficially affect this selected group of patients.

### In-Hospital Mortality Trends in HF With DM by Age, Sex, Race, and Ethnicity

Our study also indicated that the reduction in in-hospitality mortality over time varied by age, sex, race, and ethnicity. The current national focus on disparities in health care and health outcomes was the main driver for these additional analyses. Of particular concern is the lack of concordance in trends in-hospital mortality rates between younger and older age groups, notwithstanding higher event rates in the latter.

### Results

Continuing increases in the incidence of obesity and DM, both contributors to the development of HF, in the young will likely further adversely affect these trajectories and could reverse much of the gain in survival noted to date. At the beginning of this study, females had higher rates of HF as well as HF with DM hospitalizations than males. However, the reverse trend was found by the end of the study period. These results are consistent with previous studies that suggested that the prevalence of HF in males is increasing in comparison with females.3 Age-standardized in-patient HF with DM mortality rates in both sexes decreased from 2000 to 2010. However, the age-standardized mortality in males remained higher than females throughout the study period until around 2006 and then became more comparable with females by the end of the study period.

Concordance in trends for in-hospital mortality between Hispanic and non-Hispanics was observed—findings similar to previous reports from a national HF registry.4 In the adjusted logistic regression model, Hispanics were at

### Table 2. In-Hospital Mortality in Patients With Heart Failure and Coexisting Diabetes Mellitus

<table>
<thead>
<tr>
<th>Variable</th>
<th>IRR</th>
<th>SE</th>
<th>P Value</th>
<th>95% Confidence Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age ≥80 y</td>
<td>1.00</td>
<td>…</td>
<td>…</td>
<td>…</td>
</tr>
<tr>
<td>Age 70–79 y</td>
<td>0.58</td>
<td>0.01</td>
<td>&lt;0.0001</td>
<td>0.56–0.59</td>
</tr>
<tr>
<td>Age 60–69 y</td>
<td>0.39</td>
<td>0.01</td>
<td>&lt;0.0001</td>
<td>0.38–0.40</td>
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<tr>
<td>Age &lt;60 y</td>
<td>0.27</td>
<td>0.01</td>
<td>&lt;0.0001</td>
<td>0.25–0.27</td>
</tr>
<tr>
<td>Female (vs male)</td>
<td>0.81</td>
<td>0.01</td>
<td>&lt;0.0001</td>
<td>0.79–0.83</td>
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<tr>
<td>Hispanic (vs non-Hispanic)</td>
<td>0.86</td>
<td>0.02</td>
<td>&lt;0.0001</td>
<td>0.82–0.89</td>
</tr>
<tr>
<td>Year (per year from 2000)</td>
<td>0.95</td>
<td>0.01</td>
<td>&lt;0.0001</td>
<td>0.94–0.94</td>
</tr>
<tr>
<td>Elixhauser comorbidity index (per 1 U increase)</td>
<td>1.03</td>
<td>0.01</td>
<td>&lt;0.0001</td>
<td>1.03–1.04</td>
</tr>
</tbody>
</table>

Results from Poisson regression model. IRR indicates incidence rate ratio.
Win et al In-Patient Mortality in Heart Failure and Diabetes Mellitus

...diminished risk for in-patient mortality compared with non-Hispanics. Racial differences in in-hospital mortality persist notwithstanding overall similar declines in both white and non-white groups. Lower mortality rates in the composite nonwhite minority group have been observed previously and remain unexplained but may be of relevance as the relative proportions of whites and non-whites in the United States changes during the next several decades.

Limitations

The NIS remains the largest publicly available database with a statistically sound sampling design allowing for accurate identification of trends in specific diseases. However, analyses and conclusions from this large administrative database have many caveats. Observations reflect admissions and not unique patients. Thus, the current unit of analysis is the admission. Given the inability to account for multiple admissions for a given patient in the NIS, our observations and conclusions may be confounded by the nontrivial risk for repeat hospitalization. Thus, our reported rates may be viewed as overestimates of a per patient admission rate. Mortality rates, however, are unlikely to be affected (a patient can only die once). Misclassification (under- or overcoding) cannot be completely ruled out without more extensive and rigorous data verification, although the large number of patients in the database strongly mitigates against substantial misclassification bias. Previous studies have shown excellent positive and negative predictive capability for ICD-9-CM codes for HF. Our analysis could be biased by upcoding or diagnosis-related group creep, which may have resulted in over-reporting of comorbidities. However, the impact of such would likely have been uniform across the groups, would be unlikely to bias CMRs, and would bias the results of comparisons toward the null if applied nondifferentially. It is even more unlikely that the highly statistically significant trend in hospitalizations, and mortality from 2000 to 2010 is attributable to downward coding bias given the consistent trends across all subgroups, the concordance with other published studies and the fact that there was no meaningful modification or revision of ICD-9-CM codes for HF or DM during the study interval. However, the possibility of bias against coding of comorbid or chronic conditions on discharge abstracts of patients who die is acknowledged. Given the statistically significant and uniform increases in the prevalence of DM and the Elixhauser index over time, the extent of systematic undercoding is admittedly unquantifiable but likely small.

Data quality assessment of the NIS is performed annually and ensures the internal validity of the data. Our data are also in agreement with a report from the National Hospital Discharge Survey, a separate and independent (from NIS) analysis of hospitalization for HF in the United States during the same time interval from the Centers for Disease Control and Prevention.

We were only able to assess in-hospital mortality and do not have data on longer-term outcomes that may be more

<p>| Table 3. Factors Associated With In-Hospital Mortality in Patients With Heart Failure and Coexisting Diabetes Mellitus |
|---------------------------------------------------------------|----------------|----------------|</p>
<table>
<thead>
<tr>
<th>Factor</th>
<th>Odds Ratio</th>
<th>95% Confidence Interval</th>
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</thead>
<tbody>
<tr>
<td>Sex</td>
<td>Male (vs female)</td>
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</tr>
<tr>
<td>Age, y</td>
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<td></td>
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<tr>
<td></td>
<td>&lt;60</td>
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<td></td>
<td>60–69</td>
<td>1.51</td>
</tr>
<tr>
<td></td>
<td>70–79</td>
<td>2.29</td>
</tr>
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<td></td>
<td>≥80</td>
<td>4.08</td>
</tr>
<tr>
<td>Race</td>
<td>White (vs Non-White Minority)</td>
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<tr>
<td>Ethnicity</td>
<td>Non-Hispanic (vs Hispanic)</td>
<td>1.12</td>
</tr>
<tr>
<td>Year</td>
<td></td>
<td>0.92</td>
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<tr>
<td>Elixhauser comorbidity index</td>
<td>1.06</td>
<td>1.06–1.07</td>
</tr>
</tbody>
</table>

Results from a logistic regression model.
relevant, particularly for younger patients. Observational studies may not be able to fully adjust for residual or unmeasured confounding that might affect our estimates for the reported associations between in-hospital mortality and included covariates. Therefore, inferences based on these observational data can only be viewed as associational and hypothesis generating and not causal in nature. Selection (survival) bias must be considered operational in all cross-sectional studies. In the absence of a prospective cohort design, it is certain that hospitalized patients represent just the fraction of all HF patients, with and without DM, who survived to hospitalization. We indeed observed such a potential source of bias in our data noting that the risk ratio for mortality in HF with DM (data not shown) declined over the age spectrum (higher ratio in the younger age groups which decreases with age), consistent with a (non-testable) hypothesis in this data set that it is the older subjects with HF and DM who survive to hospitalization.46 The absence of specific data on pre- or in-hospital medical therapy for HF and DM in the NIS database precludes further analysis about the impact of prevalent treatment on outcomes. The absence of information on pre-hospitalization functional classification, for example, New York Heart Association class and left ventricular function, precludes stratification on these important measures. However, modest differences in hospital mortality between patients with preserved and depressed left ventricular function would not likely affect the observed trends or rates in the absence of large changes in the proportion of these entities over time.57

Finally, these observations pertain to the population with HF in the United States and may not be generalizable to other populations with HF in other countries. In a recent overview of HF hospitalization on a global scale,48 it was pointed out that, at least within randomized clinical trials, there is much variability in HF hospitalization rates and that outside of the clinical trial universe, the lack of standardized, nonadministrative HF-specific registries represent a major limitation to assessing and comparing HF hospitalization rates within and between countries. Population-based and registry data from several European countries with integrated health information systems indicate a decrease in HF hospitalization rates49 consistent with the data herein, but such trends have not been seen in other European countries.

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Disclosures

None.

References


In-Patient Mortality in Heart Failure and Diabetes Mellitus


**CLINICAL PERSPECTIVE**

Given the increased incidence and prevalence of obesity and diabetes mellitus (DM), both risk factors for heart failure, the impact of DM on heart failure outcomes warrants close study. Using a nationally representative all-payer in-patient sample of US hospital admissions from 2000 to 2010, our observations indicate that the total number of hospitalizations with a primary diagnosis of heart failure decreased, whereas the prevalence of DM as well as a measure of comorbidity burden increased. Despite the increased prevalence of DM and comorbid burden, there was a 36% decrease in age-standardized in-hospital mortality among heart failure with DM. The decrease in in-hospital mortality was the result of a change in the stratum-specific risk for mortality, rather than a change in age or sex structure of the 2000 and 2010 samples. However, in-hospital mortality rates varied by age, sex, race, and ethnicity, and emphasize the need to survey relevant strata within an overall population as well.
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Data Supplement (unedited) at:
http://circheartfailure.ahajournals.org/content/suppl/2016/05/04/CIRCHEARTFAILURE.115.003023.DC1

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Supplemental Table 1. Characteristics among Patients with Heart Failure from 2000 to 2010 (N = 2,492,425)

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<td>N (Weighted)</td>
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Sex (%)

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<tr>
<td>CHF/100,000 US Census</td>
<td>46.1</td>
<td>54.5</td>
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Age (%)

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<th>Age</th>
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Race (%)

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N = numbers, CHF = Congestive Heart Failure, AI/NA = American Indian/Native Alaskan, T2DM = Type 2 Diabetes mellitus, SE = Standard error
Supplemental Figure Legend

**Supplemental Figure 1.** Decrease in age-standardized in-hospital mortality rate among men and women with heart failure, 2000-2010. $P_{\text{linear trend}} < 0.0001$