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National rate of tobacco and substance use disorders among hospitalized heart failure patients

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Abstract

Background: Several cardiotoxic substances impact heart failure incidence. The burden of comorbid tobacco or substance use disorders among heart failure patients is under-characterized. We describe the burden of tobacco and substance use disorders among hospitalized heart failure patients in the U.S.

Methods: We calculated the proportion of primary heart failure hospitalizations in the 2014 National Inpatient Sample with tobacco or substance use disorders accounting for demographic factors.

Results: Of 989,080 heart failure hospitalizations, 15.5% (n=152,965) had documented tobacco (n= 119,285, 12.1%) or substance (n=61,510, 6.2%) use disorder. Female sex was associated with lower rates of tobacco (OR 0.72; 95% CI, 0.70 to 0.74) and substance (OR 0.37; 95% CI, 0.36 to 0.39) use disorder. Tobacco and substance use disorder rates were highest for hospitalizations <55 years of age. Native American race was associated with increased risk of alcohol use disorder (OR 1.67; 95% CI, 1.27 to 2.20) and Black race with alcohol (OR 1.09; 95% CI, 1.02 to 1.16) or drug (OR 1.63; 95% CI, 1.53 to 1.74) use disorder. Medicaid insurance or income in the lowest quartile were associated with increased risk of tobacco and substance use disorders.

Conclusions: Tobacco and substance use disorders affect vulnerable heart failure populations, including those of male sex, younger age, lower socioeconomic status, and racial/ethnic minorities. Enhanced screening for tobacco and substance use disorders in hospitalized heart failure patients may reveal opportunities for treatment and secondary prevention.

Introduction

Heart failure is the fourth overall principal diagnosis and first among cardiovascular conditions as the reason for hospitalization in the U.S.[1] Heart failure is a prevalent condition with several preventable etiologies including uncontrolled hypertension or ischemic heart disease.[2] Behavioral risk factors such as tobacco, alcohol, and drug use are known to contribute to heart failure incidence.[3–5] Alcohol,[6,7] cocaine,[8,9] and amphetamines[10–12] have cardiotoxic effects. Drug overdose death rates in the U.S. are rising, especially in younger persons.[15] The burden of active tobacco and substance use disorders among hospitalized heart failure patients in the U.S. has not been well described.

Nationally representative administrative data facilitates understanding the burden of tobacco and substance use disorders among heart failure patients and its potential influence on health outcomes. Vulnerable populations, including patients from racial/ethnic minorities or lower socioeconomic status, may be at increased risk of developing tobacco or substance use disorders for multiple reasons including social stressors, lack of economic opportunity, and community factors.[16–18] Identifying heart failure patients with tobacco or substance use disorders is critical to developing treatment strategies to address observed cardiovascular health disparities.

We describe the national burden of heart failure and comorbid tobacco or substance use disorder among hospitalized patients in the U.S. We used data from the 2014 National Inpatient Sample (NIS) to describe diagnosis rates of tobacco and substance use disorders among hospitalized heart failure patients and examined demographic groups that may be at higher risk for these disorders.

Methods

Data Source

The NIS dataset provides hospital administrative data through the Agency for Healthcare Research and Quality's Healthcare Cost and Utilization Project. It contains approximately 7 million weighted hospital discharges representing 35 million inpatient hospitalizations.[19] The NIS unit of analysis is a discharge; therefore, readmissions are not identified. The sample is drawn from forty-four states and the District of Columbia, covering more than 96% of the U.S. population. A 20% stratified sample is obtained from 4,411 U.S. community hospitals. All insurance payer sources are included. Survey weights are provided to obtain national estimates for relevant statistics.

Study Cohort

Heart failure was defined by any International Classification of Diseases, Ninth Revision-Clinical Modification (ICD-9-CM) code that mentioned a heart failure syndrome (eTable 1). A primary heart failure hospitalization was defined as any heart failure ICD-9-CM code used as the first listed discharge code, consistent with prior publications.[20,21] Patients less than 18 years were excluded. Race/ethnicity was classified as white, black, Hispanic, Asian/Pacific Islander (PI), or Native American as captured by administrative hospital data. Additional demographic factors included age, sex, payer source, geographic Census division, and median household income based on zip code.

Substance use disorder was defined as any alcohol or drug use disorder, excluding tobacco, which was a separate outcome. Tobacco, alcohol, and drug use disorders were defined using Clinical Classifications Software (CCS) and ICD-9-CM codes (eTable 2).[22] Drug use disorder was sub-divided into cocaine, cannabis, opioid, amphetamine, psychotherapeutic (pain

relievers, tranquilizers, stimulants, and sedatives), hallucinogen, and other use disorder categories (eTable 3).[23]

Statistical Analysis

Overall and for each tobacco and substance use disorder category, we estimated the national proportion of hospitalized heart failure patients and provided descriptive statistics for patient characteristics, select comorbidities, hospital length of stay, and inpatient mortality. We next stratified heart failure hospitalizations by sex and other demographic factors (age, race/ethnicity, geographic Census division, payer source, and median household income of patient's zip code). For each stratum, we reported the percent of patients in each tobacco or substance use disorder category.

Tobacco and substance use disorder rates were age-standardized (by single year of life for ages between 18 and 90 or greater) using the 2000 US Standard Population, per Center for Disease Control and Prevention recommendations.[24] To evaluate demographic factors (sex, race/ethnicity, region, health insurance, and median household income) associated with each co-morbid tobacco or substance use disorder category, we used logistic regression models accounting for clustering (region and hospital level) and non-linear age-adjustment using multivariable fractional polynomials.[25] Selection of best-fit multivariable fractional polynomial models used a closed-test algorithm.[26] This curvilinear adjustment was used to reduce residual confounding that may arise secondary to model misspecification using age as a single linear term.[27]

All estimation procedures were performed with appropriate NIS survey weights to account for sampling design, and all results are presented as the weighted national 2014

hospitalized population. Analyses were performed in STATA 15.1 (StataCorp, College Station, TX). Institutional IRB provided an exemption for this research.

Results

There were 989,080 heart failure hospitalizations in the U.S. in 2014 (Table 1) of which 15.5% (n=152,965) had documented tobacco or substance use disorder. Tobacco use disorder was found in 12.1% (n=119,285), substance use disorder in 6.2% (n=61,510), alcohol use disorder in 3.5 % (n=34,285) and drug use disorder in 3.5% (n=34,600). Both tobacco and substance use disorder were documented on 2.8% (n=27,830) of heart failure hospitalizations, while both alcohol and drug use disorder were found in 0.7% (n=7,375).

In the overall heart failure cohort, mean patient age was 72.0 (SD 14.2), and females comprised almost half (48.5%) of the hospitalizations. The majority of heart failure hospitalizations were for patients age 65 or older (71.2%), of white race/ethnicity (64.3%), and with payer source of Medicare (74.2%). The most common comorbidities were hypertension (81.8%) and coronary artery disease (55.3%). Demographic patterns of the cohort with no tobacco or substance use disorder mirrored that of the overall heart failure cohort.

Tobacco use disorder and heart failure hospitalizations

Tobacco use disorder patients were younger (mean age 61.2, SD 12.7) than the overall heart failure cohort and 36.0% female (Table 1). Tobacco use disorder was more common among males than females across demographic subcategories (Table 2). Rates were highest for both sexes between ages 45 and 55 (30.8% males, 26.6% females). Native American males had highest age-adjusted rates (31.4%), while white and Native American females had highest age-adjusted rates (21.8% and 21.1% respectively). Tobacco use disorder rates were highest in the

East South Central region (17.5% males, 11.3% females) and for payer status of no charge (34.8% males, 19.5% females), self-pay (33.5% males, 24.5% females), or Medicaid (32.8% males, 23.1% females). Rates of tobacco use disorder increased as median household income decreased.

Substance use disorder and heart failure hospitalizations

Heart failure hospitalizations with documented substance use disorder represented younger patients (mean age 57.6, SD 13.0) than the overall or tobacco use disorder cohorts and were 22.9% female (Table 1). Substance use disorder diagnosis rates were highest for males 45 to 55 years of age (25.1%) and females <45 years of age (13.9%) (Table 2). Native Americans had highest rates of substance use disorder when age-adjusted (31.2% males, 13.1% females). Substance use disorder was highest for heart failure hospitalizations in the Pacific region, payer status of Medicaid, self-pay or no-charge, and for lower income quartiles.

Alcohol use disorder and heart failure hospitalizations

Alcohol use disorder was less common among female heart failure hospitalizations relative to tobacco and drug use disorder (Table 1). Heart failure hospitalizations for those age 45 to 55 years had highest rates of alcohol use disorder (13.2% males, 3.7% females) (Table 2). Alcohol use disorder rates were highest among Native Americans (23.8% males, 8.3% females, age-adjusted), the Pacific region (8.1% males, 1.6% females), payer status of no charge (16.6% males, 4.1% females), Medicaid (14.0% males, 3.4% females) or self-pay (13.6% males, 3.1% females), and the lowest income quartile.

Drug use disorder and heart failure hospitalizations

Heart failure hospitalizations with drug use disorder were the youngest cohort (mean age 53.9, SD 12.3) and 29.1% female (Table 1). Racial/ethnic minorities had higher representation among drug use disorder hospitalizations, as 44.9% of drug use disorder hospitalizations were for black race/ethnicity. Medicaid insurance (43.3%) and lowest quartile income (47.3%) was more prevalent among heart failure hospitalizations with drug use disorder compared to no use, tobacco, or alcohol use disorder (Table 1).

Cocaine was the most frequent substance-specific drug use (11,700 hospitalizations), followed by other unspecified drugs (n=8,855), cannabis (n=8,060), opioids (n=5,840) and amphetamines (n=5,280) (Table 4). Drug use disorder was generally most common for both sexes age <45 years. For males, highest rates of drug use disorder were for Asian/PI hospitalizations (age-adjusted 26.5%), while for females, highest rates were for black hospitalizations (age-adjusted 9.4%) (Table 2). Asian/PI males and females had highest rates of amphetamine use (age-adjusted 12.8% and 4.0% respectively) (Table 4). Black males and females had highest rates of cannabis (age-adjusted 5.8% and 3.8% respectively) and cocaine use (age-adjusted 5.8% and 4.5% respectively) (Table 4).

The Pacific region had highest rates of drug use disorder (11.9% males, 4.7% females) (Table 2). Medicaid hospitalizations had highest rates of drug use disorder overall and for cocaine, opioid, and amphetamine use disorders for both sexes. Those in the lowest income quartile had highest rates of drug use disorder overall and for most subcategories.

Associated Demographic Factors

Black race ethnicity was associated with substance (OR 1.30; 95% CI, 1.24 to 1.36), alcohol (OR 1.09; 95% CI, 1.02 to 1.16), and drug (OR 1.63; 95% CI, 1.53 to 1.74) use disorder.

Native American race/ethnicity was associated with alcohol use disorder (OR 1.67; 95% CI, 1.27 to 2.20). All census divisions when compared to New England were associated with tobacco use disorder. The Pacific region was associated with substance (OR 1.81; 95% CI, 1.63 to 2.02), alcohol (OR 1.15; 95% CI, 1.01 to 1.32), and drug (OR 2.85; 95% CI, 2.43 to 3.33) use disorder, while the Mountain region was associated with drug use disorder (OR 1.44; 95% CI, 1.20 to 1.73). Payer status of Medicaid was associated with tobacco (OR 1.50; 95% CI, 1.44 to 1.57), substance (OR 1.98; 95% CI, 1.88 to 2.09), alcohol (OR 1.75; 95% CI, 1.63 to 1.88), and drug (OR 2.15; 95% CI, 2.01 to 2.30) use disorder. Payer status of self-pay, no charge, or other was also associated with each use disorder. The lowest income quartile was associated with substance use disorder (OR 1.25; 95% CI, 1.17 to 1.33), while all income quartiles were associated with tobacco or drug use disorder when compared to the highest income quartile. Curvilinear relationships are noted between age and risk of tobacco, alcohol, and drug use disorder (eFigure 1-3).

Female sex was associated with lower odds of tobacco (OR 0.72; 95% CI, 0.70 to 0.74), substance (OR 0.37; 95% CI, 0.36 to 0.39), alcohol (OR 0.23; 95% CI, 0.22 to 0.25), and drug (OR 0.58; 95% CI, 0.55 to 0.62) use disorder. All racial/ethnic groups had decreased risk of tobacco use disorder when compared to whites except for Native Americans. Hispanic race/ethnicity was associated with less substance (OR 0.80; 95% CI 0.74 to 0.86) or drug (OR 0.76; 95% CI, 0.69 to 0.83) use disorder, and Asian/PI race/ethnicity was associated with less substance (OR 0.65; 95% CI, 0.57 to 0.75), alcohol (OR 0.53; 95% CI, 0.43 to 0.65), and drug (OR 0.83; 95% CI, 0.70 to 0.97) use disorder. Private insurance was associated with less tobacco (OR 0.80; 95% CI, 0.76 to 0.83), substance (OR 0.81; 95% CI, 0.76 to 0.86), and drug (OR 0.59; 95% CI, 0.54 to 0.65) use disorder.

Discussion

Among national heart failure hospitalizations, 15.5% had comorbid tobacco or substance use disorders. Tobacco use disorder was most common at 12.1% overall, a rate similar to prior studies (15.9% of heart failure patients in OPTIMIZE-HF[40] smoked cigarettes in the past year, while 17% of males and 10% of females in ADHERE[41] were current smokers). For certain male heart failure subgroups, including those age 45 to 55 years, Native American race/ethnicity, and payer status of Medicaid, self pay, or no charge, our results show that approximately one-third of hospitalizations had tobacco use disorder. Tobacco use in OPTIMIZE-HF patients contributed to earlier age (>10 years difference) of decompensation requiring hospital admission.[40] Quitting smoking may be as effective a treatment as prescribing ACE inhibitors, beta-blockers, and aldosterone inhibitors in improving survival.[42,43]

Drug use disorder was uncommon among older heart failure patients. The etiology of heart failure in advanced age is well established,[28] largely due to coronary artery disease and poorly controlled hypertension. However, the pathogenesis of heart failure in patients under 40 years is less clear, with many patients diagnosed with idiopathic cardiomyopathy.[29–31] Untreated drug use disorder may be responsible for heart failure in these young patients where the etiology remains unclassified, as we found high rates of drug use disorder in this population. Because high rates of cocaine and methamphetamine use have been noted among younger heart failure patients[4,11,32] and heart failure due to stimulant use may have a reversible component,[12,33] targeted preventive and treatment efforts for young patients with drug use disorder may reduce the burden of heart failure.

There is a paucity of literature investigating tobacco and substance use disorders in heart failure patients especially amongst racial/ethnic subgroups. While Native American race was

associated with increased risk of alcohol use disorder, these patients also had high rates of tobacco and drug use disorders. Recent data from the National Survey on Drug Use and Health (NSDUH) shows that American Indians or Alaska Natives have higher prevalence of tobacco use and cigarette smoking than all other racial/ethnic groups.[38] Black race was associated with substance, alcohol, and drug use disorder. Cocaine use disorder was highest among black heart failure hospitalizations, while amphetamine use disorder was highest for Asian/PI heart failure hospitalizations. A prior study of 11,258 heart failure patients from the ADHERE-EM database found that self-reported illicit drug use with cocaine or methamphetamines was associated with black race compared to Caucasian.[32] Black men and women present with heart failure at a younger age and have the highest age-standardized hospitalization rates compared to other race/ethnicities in the US.[34] Addressing underlying substance use disorders in black patients may reduce the burden of heart failure attributed to substances and reduce hospitalizations. Conversely, Asian/PI males and females have the lowest hospitalization rates for heart failure compared to other races in the US.[34] However, the Asian/PI population in the US is rapidly growing[35] with high rates of amphetamine use, [36,37] which may contribute to future heart failure hospitalizations.

Geographically, the Pacific region stands out for high rates of substance use disorder, especially drug use disorder. Data from NSDUH reports high prevalence of past-month illicit drug use by individuals 18 years or older within Pacific states.[39] Patterns of use in heart failure patients may mirror those of the general population. Providers should be aware of types of substance use prevalent in their region.

Rates of tobacco and substance use disorders were higher for patients of lower socioeconomic status as represented by payer status (Medicaid, self-pay, or no charge) and

median household income quartiles. Socioeconomic factors mediate differences in tobacco and substance use disorders based on race/ethnicity. While we cannot adjust for complex community stressors predisposing to tobacco or substance use disorders, evaluating community risk factors for tobacco and substance use disorders, such as density of tobacco stores,[16] and identifying vulnerable groups may help develop preventive and treatment strategies, reducing observed disparities.

Tobacco and substance use disorders in heart failure patients have implications for the broader health system. Substance use leads to increased costs from decreased productivity, healthcare costs, and crime.[44] Tobacco,[45,46] alcohol,[45] and cocaine[47] use are associated with increased readmission risk in heart failure patients. Screening for tobacco and substance use disorders has historically been deficient in primary care, emergency room, and hospital settings;[48] despite efforts to improve screening, rates are likely under-appreciated. Heart failure patients who actively smoke but are attempting to quit may be coded with a different ICD-9-CM code than tobacco use disorder, further underestimating numbers.[49] Tobacco and substance use disorders may have even larger negative effects on the healthcare system than currently reported.

Limitations

The NIS does not use unique patient identifiers; a hospitalization may represent a new patient or a patient already captured in the sample being readmitted, which may increase rates. We are unable to account for geographic or provider coding variation in ICD-9-CM coding. Some conditions, notably tobacco use disorder, may be under-coded. Due to constraints within ICD-9-CM codes, we could not quantify amount or duration of tobacco or substance use disorders. Heavier or prolonged tobacco or substance use may have more detrimental cardiotoxic effects, but even substance use that does not qualify for a diagnosis may contribute to heart

failure. Many hospitalized heart failure patients with drug use disorder used “other drugs,” illustrating the complexity of coding for specific drug use. Finally, unmeasured confounding, related to other lifestyle or cardiovascular risk factors not measured, may influence some of these associations, especially as related to socioeconomic status or race/ethnicity.

Conclusions

Comorbid tobacco or substance use disorder among hospitalized heart failure patients in the US particularly affects males, younger individuals, and those of lower socioeconomic status. A heart failure hospitalization is an opportunity to screen for and treat tobacco or substance use disorders. To effectively manage heart failure, better recognition of comorbidities portending worse outcomes should be included in full assessments of patients. Further research on interventions that reduce rates of tobacco or substance use disorders among discharged heart failure patients are needed.

References

1. Pfuntner A, Wier LM, Stocks C. *Most Frequent Conditions in U.S. Hospitals, 2011*. Rockville, Maryland; 2013.

2. Schocken DD, Benjamin EJ, Fonarow GC, et al. Prevention of heart failure: a scientific statement from the American Heart Association Councils on Epidemiology and Prevention, Clinical Cardiology, Cardiovascular Nursing, and High Blood Pressure Research; Quality of Care and Outcomes Research Interdisc. *Circulation*. 2008;117(19):2544-2565. doi:10.1161/CIRCULATIONAHA.107.188965.

3. Whitman IR, Agarwal V, Nah G, et al. Alcohol Abuse and Cardiac Disease. *J Am Coll Cardiol*. 2017;69(1):13-24. doi:10.1016/j.jacc.2016.10.048.

4. Yeo KK, Wijetunga M, Ito H, et al. The Association of Methamphetamine Use and Cardiomyopathy in Young Patients. *Am J Med*. 2007;120(2):165-171. doi:10.1016/j.amjmed.2006.01.024.

5. He J, Ogden LG, Bazzano LA, Vupputuri S, Loria C, Whelton PK. Risk Factors for Congestive Heart Failure in US Men and Women. *Arch Intern Med*. 2001;161(7):996. doi:10.1001/archinte.161.7.996.

6. Piano MR, Phillips SA. Alcoholic cardiomyopathy: pathophysiologic insights. *Cardiovasc Toxicol*. 2014;14(4):291-308. doi:10.1007/s12012-014-9252-4.

7. Urbano-Marquez A, Estruch R, Navarro-Lopez F, Grau JM, Mont L, Rubin E. The Effects of Alcoholism on Skeletal and Cardiac Muscle. *N Engl J Med*. 1989;320(7):409-415. doi:10.1056/NEJM198902163200701.

3258. Schwartz BG, Rezkalla S, Kloner RA. Cardiovascular effects of cocaine. *Circulation*. 326 2010;122(24):2558-2569. doi:10.1161/CIRCULATIONAHA.110.940569.

3279. Havakuk O, Rezkalla SH, Kloner RA. The Cardiovascular Effects of Cocaine. *J Am Coll* 328 *Cardiol*. 2017. doi:10.1016/j.jacc.2017.05.014.

32910. Schürer S, Klingel K, Sandri M, et al. Clinical Characteristics, Histopathological Features, 330 and Clinical Outcome of Methamphetamine-Associated Cardiomyopathy. *JACC Hear* 331 *Fail*. 2017;5(6):435-445. doi:10.1016/j.jchf.2017.02.017.

33211. Neeki MM, Kulczycki M, Toy J, et al. Frequency of Methamphetamine Use as a Major 333 Contributor Toward the Severity of Cardiomyopathy in Adults ≤50 Years. *Am J Cardiol*. 334 2016. doi:10.1016/j.amjcard.2016.05.057.

33512. Won S, Hong RA, Shohet R V, Seto TB, Parikh NI. Methamphetamine-associated 336 cardiomyopathy. *Clin Cardiol*. 2013;36(12):737-742. doi:10.1002/clc.22195.

33713. Ray WA, Chung CP, Murray KT, Hall K, Stein CM. Prescription of Long-Acting Opioids 338 and Mortality in Patients With Chronic Noncancer Pain. *JAMA*. 2016;315(22):2415. 339 doi:10.1001/jama.2016.7789.

34014. Solomon DH, Rassen JA, Glynn RJ, Lee J, Levin R, Schneeweiss S. The Comparative 341 Safety of Analgesics in Older Adults With Arthritis. *Arch Intern Med*. 2010;170(22):1968-342 1978. doi:10.1001/archinternmed.2010.391.

34315. Hedegaard H, Warner M, Minino AM. *Drug Overdose Deaths in the United States, 1999-344 2016*.; 2017. https://www.cdc.gov/nchs/data/databriefs/db294.pdf. Accessed December 26, 345 2017.

16. Karriker-Jaffe KJ, Liu H, Johnson RM. Racial/ethnic differences in associations between neighborhood socioeconomic status, distress, and smoking among U.S. Adults. *J Ethn Subst Abuse*. 2016;15(1):73-91. doi:10.1080/15332640.2014.1002879.

17. Roux AVD, Merkin SS, Arnett D, et al. Neighborhood of Residence and Incidence of Coronary Heart Disease. *N Engl J Med*. 2001;345(2):99-106. doi:10.1056/NEJM200107123450205.

18. Karriker-Jaffe KJ, Org K. Neighborhood Socioeconomic Status and Substance Use by U.S. Adults. *Drug Alcohol Depend*. 2013;133(1):212-221. doi:10.1016/j.drugalcdep.2013.04.033.

19. Healthcare Cost and Utilization Project (HCUP). *Introduction to the HCUP National Inpatient Sample (NIS) 2014*. Vol 4287. Rockville, Maryland; 2016.

20. Blecker S, Paul M, Taksler G, Ogedegbe G, Katz S. Heart failure-associated hospitalizations in the United States. *J Am Coll Cardiol*. 2013;61(12):1259-1267. doi:10.1016/j.jacc.2012.12.038.

21. Chen J, Dharmarajan K, Wang Y, Krumholz HM. National trends in heart failure hospital stay rates, 2001 to 2009. *J Am Coll Cardiol*. 2013;61(10):1078-1088. doi:10.1016/j.jacc.2012.11.057.

22. Elixhauser A, Steiner C, Palmer L. *Clinical Classifications Software (CCS), 2014*. Rockville, Maryland; 2014.

23. Ahrnsbrak R, Bose J, Hedden SL, Lipari RN, Park-Lee E, Tice P. Key Substance Use and Mental Health Indicators in the United States: Results from the 2016 National Survey on

Drug Use and Health. 2017;7(1):877-726. https://store.samhsa.gov/shin/content//SMA17-5044/SMA17-5044.pdf. Accessed December 11, 2017.

24. Klein RJ, Schoenborn CA. *Age Adjustment Using the 2000 Projected U.S. Population*. Hyattsville, Maryland; 2001.

25. Binder H, Sauerbrei W, Royston P. Comparison between splines and fractional polynomials for multivariable model building with continuous covariates: A simulation study with continuous response. *Stat Med*. 2013;32(13):2262-2277. doi:10.1002/sim.5639.

26. Royston P, Sauerbrei W. *Multivariable Model-Building: A Pragmatic Approach to Regression Analysis Based on Fractional Polynomials for Modelling Continuous Variables*. (Balding DJ, Cressie NAC, Fitzmaurice GM, et al., eds.). Chichester, West Sussex: John Wiley & Sons, 2008; 2008.

27. Groenwold RHH, Klungel OH, Altman DG, et al. Adjustment for continuous confounders: an example of how to prevent residual confounding. *CMAJ*. 2013;185(5):401-406. doi:10.1503/cmaj.120592.

28. Ziaeian B, Fonarow GC. Epidemiology and aetiology of heart failure. *Nat Rev Cardiol*. 2016;13(6):368-378. doi:10.1038/nrcardio.2016.25.

29. Wong CM, Hawkins NM, Petrie MC, et al. Heart failure in younger patients: The meta-analysis global group in chronic heart failure (MAGGIC). *Eur Heart J*. 2014;35(39):2714-2721. doi:10.1093/eurheartj/ehu216.

30. Wong CM, Hawkins NM, Jhund PS, et al. Clinical characteristics and outcomes of young and very young adults with heart failure: The CHARM programme (candesartan in heart

failure assessment of reduction in mortality and morbidity). *J Am Coll Cardiol*. 2013;62(20):1845-1854. doi:10.1016/j.jacc.2013.05.072.

31. Andersson C, Vasan RS. Epidemiology of cardiovascular disease in young individuals. *Nat Rev Cardiol*. 2017. doi:10.1038/nrcardio.2017.154.

32. Diercks DB, Fonarow GC, Kirk JD, et al. Illicit Stimulant Use in a United States Heart Failure Population Presenting to the Emergency Department (from the Acute Decompensated Heart Failure National Registry Emergency Module). *Am J Cardiol*. 2008;102(9):1216-1219. doi:10.1016/j.amjcard.2008.06.045.

33. Sliman S, Waalen J, Shaw D. Methamphetamine-Associated Congestive Heart Failure: Increasing Prevalence and Relationship of Clinical Outcomes to Continued Use or Abstinence. *Cardiovasc Toxicol*. 2016;16(4):381-389. doi:10.1007/s12012-015-9350-y.

34. Ziaeian B, Kominski GF, Ong MK, Mays VM, Brook RH, Fonarow GC. National Differences in Trends for Heart Failure Hospitalizations by Sex and Race/Ethnicity. *Circ Cardiovasc Qual Outcomes*. 2017;10(7). doi:10.1161/CIRCOUTCOMES.116.003552.

35. Humes KR, Jones NA, Ramirez RR. Overview of Race and Hispanic Origin: 2010 2010 Census Briefs. 2010. https://www.census.gov/prod/cen2010/briefs/c2010br-02.pdf. Accessed December 10, 2017.

36. Fong TW, Tsuang J. Asian-americans, addictions, and barriers to treatment. *Psychiatry (Edgmont)*. 2007;4(11):51-59. http://www.ncbi.nlm.nih.gov/pubmed/20428303. Accessed December 10, 2017.

37. Wu LT, Blazer DG. Substance use disorders and co-morbidities among Asian Americans

and Native Hawaiians/Pacific Islanders. *Psychol Med*. 2015;45(3):481-494. doi:10.1017/S0033291714001330.

38. Odani S, Armour BS, Graffunder CM, Garrett BE, Agaku IT. Prevalence and Disparities in Tobacco Product Use Among American Indians/Alaska Natives — United States, 2010–2015. *MMWR Morb Mortal Wkly Rep*. 2017;66(50):1374-1378. doi:10.15585/mmwr.mm6650a2.

39. Center for Behavioral Health Statistics S, International R. 2015-2016 National Survey on Drug Use and Health: Model-Based Prevalence Estimates (50 States and the District of Columbia). https://www.samhsa.gov/data/sites/default/files/NSDUHsaePercents2016/NSDUHsaePercents2016.pdf. Accessed December 11, 2017.

40. Fonarow GC, Abraham WT, Albert NM, et al. A smoker's paradox in patients hospitalized for heart failure: findings from OPTIMIZE-HF. 2008.

41. Galvao M, Kalman J, Demarco T, et al. Gender differences in in-hospital management and outcomes in patients with decompensated heart failure: Analysis from the acute decompensated heart failure national registry (ADHERE). *J Card Fail*. 2006;12(2):100-107. doi:10.1016/j.cardfail.2005.09.005.

42. Lightwood J, Fleischmann KE, Glantz SA. Smoking cessation in heart failure: it is never too late. *J Am Coll Cardiol*. 2001;37(6):1683-1684. doi:10.1016/S0735-1097(01)01188-3.

43. Critchley JA, Capewell S. Mortality risk reduction associated with smoking cessation in patients with coronary heart disease: a systematic review. *JAMA*. 2003;290(1):86-97. doi:10.1001/jama.290.1.86.

43144. Bouchery EE, Harwood HJ, Sacks JJ, Simon CJ, Brewer RD. Economic Costs of
432 Excessive Alcohol Consumption in the U.S., 2006. *Am J Prev Med*. 2011;41(5):516-524.
433 doi:10.1016/j.amepre.2011.06.045.

43445. Evangelista LS, Doering L V., Dracup K. Usefulness of a history of tobacco and alcohol
435 use in predicting multiple heart failure readmissions among veterans. *Am J Cardiol*.
436 2000;86(12):1339-1342. doi:10.1016/S0002-9149(00)01238-8.

43746. Kociol RD, Greiner MA, Hammill BG, et al. Long-Term Outcomes of Medicare
438 Beneficiaries With Worsening Renal Function During Hospitalization for Heart Failure.
439 *Am J Cardiol*. 2010;105(12):1786-1793. doi:10.1016/j.amjcard.2010.01.361.

44047. Amarasingham R, Moore BJ, Tabak YP, et al. An automated model to identify heart failure
441 patients at risk for 30-day readmission or death using electronic medical record data. *Med*
442 *Care*. 2010;48(11):981-988. doi:10.1097/MLR.0b013e3181ef60d9.

44348. Pilowsky DJ, Wu L-T. Screening for alcohol and drug use disorders among adults in
444 primary care: a review. *Subst Abuse Rehabil*. 2012;3(1):25-34. doi:10.2147/SAR.S30057.

44549. Wiley LK, Shah A, Xu H, Bush WS. ICD-9 tobacco use codes are effective identifiers of
446 smoking status. *J Am Med Informatics Assoc*. 2013. doi:10.1136/amiajnl-2012-001557.

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