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**1National rate of tobacco and substance use disorders among hospitalized heart failure  
2patients**

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39

## 40Abstract

41**Background:** Several cardiotoxic substances impact heart failure incidence. The burden of  
42comorbid tobacco or substance use disorders among heart failure patients is under-characterized.  
43We describe the burden of tobacco and substance use disorders among hospitalized heart failure  
44patients in the U.S.

45**Methods:** We calculated the proportion of primary heart failure hospitalizations in the 2014  
46National Inpatient Sample with tobacco or substance use disorders accounting for demographic  
47factors.

48**Results:** Of 989,080 heart failure hospitalizations, 15.5% (n=152,965) had documented tobacco  
49(n= 119,285, 12.1%) or substance (n=61,510, 6.2%) use disorder. Female sex was associated  
50with lower rates of tobacco (OR 0.72; 95% CI, 0.70 to 0.74) and substance (OR 0.37; 95% CI,  
510.36 to 0.39) use disorder. Tobacco and substance use disorder rates were highest for  
52hospitalizations <55 years of age. Native American race was associated with increased risk of  
53alcohol use disorder (OR 1.67; 95% CI, 1.27 to 2.20) and Black race with alcohol (OR 1.09; 95%  
54CI, 1.02 to 1.16) or drug (OR 1.63; 95% CI, 1.53 to 1.74) use disorder. Medicaid insurance or  
55income in the lowest quartile were associated with increased risk of tobacco and substance use  
56disorders.

57**Conclusions:** Tobacco and substance use disorders affect vulnerable heart failure populations,  
58including those of male sex, younger age, lower socioeconomic status, and racial/ethnic  
59minorities. Enhanced screening for tobacco and substance use disorders in hospitalized heart  
60failure patients may reveal opportunities for treatment and secondary prevention.

## 61Introduction

62 Heart failure is the fourth overall principal diagnosis and first among cardiovascular  
63conditions as the reason for hospitalization in the U.S.<sup>1</sup> Heart failure is a prevalent condition with  
64several preventable etiologies including uncontrolled hypertension or ischemic heart disease.<sup>2</sup>  
65Behavioral risk factors such as tobacco, alcohol, and drug use are known to contribute to heart  
66failure incidence.<sup>3-5</sup> Alcohol,<sup>6,7</sup> cocaine,<sup>8,9</sup> and amphetamines<sup>10-12</sup> have cardiotoxic effects. Drug  
67overdose death rates in the U.S. are rising, especially in younger persons.<sup>15</sup> The burden of active  
68tobacco and substance use disorders among hospitalized heart failure patients in the U.S. has not  
69been well described.

70 Nationally representative administrative data facilitates understanding the burden of  
71tobacco and substance use disorders among heart failure patients and its potential influence on  
72health outcomes. Vulnerable populations, including patients from racial/ethnic minorities or  
73lower socioeconomic status, may be at increased risk of developing tobacco or substance use  
74disorders for multiple reasons including social stressors, lack of economic opportunity, and  
75community factors.<sup>16-18</sup> Identifying heart failure patients with tobacco or substance use disorders  
76is critical to developing treatment strategies to address observed cardiovascular health disparities.

77 We describe the national burden of heart failure and comorbid tobacco or substance use  
78disorder among hospitalized patients in the U.S. We used data from the 2014 National Inpatient  
79Sample (NIS) to describe diagnosis rates of tobacco and substance use disorders among  
80hospitalized heart failure patients and examined demographic groups that may be at higher risk  
81for these disorders.

## 82Methods

### 83 **Data Source**

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

### 92 **Study Cohort**

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

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

105relievers, tranquilizers, stimulants, and sedatives), hallucinogen, and other use disorder  
106categories (eTable 3).<sup>23</sup>

### 107**Statistical Analysis**

108 Overall and for each tobacco and substance use disorder category, we estimated the  
109national proportion of hospitalized heart failure patients and provided descriptive statistics for  
110patient characteristics, select comorbidities, hospital length of stay, and inpatient mortality. We  
111next stratified heart failure hospitalizations by sex and other demographic factors (age,  
112race/ethnicity, geographic Census division, payer source, and median household income of  
113patient's zip code). For each stratum, we reported the percent of patients in each tobacco or  
114substance use disorder category.

115 Tobacco and substance use disorder rates were age-standardized (by single year of life for  
116ages between 18 and 90 or greater) using the 2000 US Standard Population, per Center for  
117Disease Control and Prevention recommendations.<sup>24</sup> To evaluate demographic factors (sex,  
118race/ethnicity, region, health insurance, and median household income) associated with each co-  
119morbid tobacco or substance use disorder category, we used logistic regression models  
120accounting for clustering (region and hospital level) and non-linear age-adjustment using  
121multivariable fractional polynomials.<sup>25</sup> Selection of best-fit multivariable fractional polynomial  
122models used a closed-test algorithm.<sup>26</sup> This curvilinear adjustment was used to reduce residual  
123confounding that may arise secondary to model misspecification using age as a single linear  
124term.<sup>27</sup>

125 All estimation procedures were performed with appropriate NIS survey weights to  
126account for sampling design, and all results are presented as the weighted national 2014

127hospitalized population. Analyses were performed in STATA 15.1 (StataCorp, College Station,  
128TX). Institutional IRB provided an exemption for this research.

## 129Results

130 There were 989,080 heart failure hospitalizations in the U.S. in 2014 (Table 1) of which  
13115.5% (n=152,965) had documented tobacco or substance use disorder. Tobacco use disorder  
132was found in 12.1% (n=119,285), substance use disorder in 6.2% (n=61,510), alcohol use  
133disorder in 3.5 % (n=34,285) and drug use disorder in 3.5% (n=34,600). Both tobacco and  
134substance use disorder were documented on 2.8% (n=27,830) of heart failure hospitalizations,  
135while both alcohol and drug use disorder were found in 0.7% (n=7,375).

136 In the overall heart failure cohort, mean patient age was 72.0 (SD 14.2), and females  
137comprised almost half (48.5%) of the hospitalizations. The majority of heart failure  
138hospitalizations were for patients age 65 or older (71.2%), of white race/ethnicity (64.3%), and  
139with payer source of Medicare (74.2%). The most common comorbidities were hypertension  
140(81.8%) and coronary artery disease (55.3%). Demographic patterns of the cohort with no  
141tobacco or substance use disorder mirrored that of the overall heart failure cohort.

### 142Tobacco use disorder and heart failure hospitalizations

143 Tobacco use disorder patients were younger (mean age 61.2, SD 12.7) than the overall  
144heart failure cohort and 36.0% female (Table 1). Tobacco use disorder was more common among  
145males than females across demographic subcategories (Table 2). Rates were highest for both  
146sexes between ages 45 and 55 (30.8% males, 26.6% females). Native American males had  
147highest age-adjusted rates (31.4%), while white and Native American females had highest age-  
148adjusted rates (21.8% and 21.1% respectively). Tobacco use disorder rates were highest in the



149East South Central region (17.5% males, 11.3% females) and for payer status of no charge  
150(34.8% males, 19.5% females), self-pay (33.5% males, 24.5% females), or Medicaid (32.8%  
151males, 23.1% females). Rates of tobacco use disorder increased as median household income  
152decreased.

### 153*Substance use disorder and heart failure hospitalizations*

154 Heart failure hospitalizations with documented substance use disorder represented  
155younger patients (mean age 57.6, SD 13.0) than the overall or tobacco use disorder cohorts and  
156were 22.9% female (Table 1). Substance use disorder diagnosis rates were highest for males 45  
157to 55 years of age (25.1%) and females <45 years of age (13.9%) (Table 2). Native Americans  
158had highest rates of substance use disorder when age-adjusted (31.2% males, 13.1% females).  
159Substance use disorder was highest for heart failure hospitalizations in the Pacific region, payer  
160status of Medicaid, self-pay or no-charge, and for lower income quartiles.

### 161*Alcohol use disorder and heart failure hospitalizations*

162 Alcohol use disorder was less common among female heart failure hospitalizations  
163relative to tobacco and drug use disorder (Table 1). Heart failure hospitalizations for those age 45  
164to 55 years had highest rates of alcohol use disorder (13.2% males, 3.7% females) (Table 2).  
165Alcohol use disorder rates were highest among Native Americans (23.8% males, 8.3% females,  
166age-adjusted), the Pacific region (8.1% males, 1.6% females), payer status of no charge (16.6%  
167males, 4.1% females), Medicaid (14.0% males, 3.4% females) or self-pay (13.6% males, 3.1%  
168females), and the lowest income quartile.

### 169*Drug use disorder and heart failure hospitalizations*

170 Heart failure hospitalizations with drug use disorder were the youngest cohort (mean age  
171 53.9, SD 12.3) and 29.1% female (Table 1). Racial/ethnic minorities had higher representation  
172 among drug use disorder hospitalizations, as 44.9% of drug use disorder hospitalizations were  
173 for black race/ethnicity. Medicaid insurance (43.3%) and lowest quartile income (47.3%) was  
174 more prevalent among heart failure hospitalizations with drug use disorder compared to no use,  
175 tobacco, or alcohol use disorder (Table 1).

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

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

### 189 ***Associated Demographic Factors***

190 Black race ethnicity was associated with substance (OR 1.30; 95% CI, 1.24 to 1.36),  
191 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.

192 Native American race/ethnicity was associated with alcohol use disorder (OR 1.67; 95% CI, 1.27  
193 to 2.20). All census divisions when compared to New England were associated with tobacco use  
194 disorder. The Pacific region was associated with substance (OR 1.81; 95% CI, 1.63 to 2.02),  
195 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,  
196 while the Mountain region was associated with drug use disorder (OR 1.44; 95% CI, 1.20 to  
197 1.73). Payer status of Medicaid was associated with tobacco (OR 1.50; 95% CI, 1.44 to 1.57),  
198 substance (OR 1.98; 95% CI, 1.88 to 2.09), alcohol (OR 1.75; 95% CI, 1.63 to 1.88), and drug  
199 (OR 2.15; 95% CI, 2.01 to 2.30) use disorder. Payer status of self-pay, no charge, or other was  
200 also associated with each use disorder. The lowest income quartile was associated with substance  
201 use disorder (OR 1.25; 95% CI, 1.17 to 1.33), while all income quartiles were associated with  
202 tobacco or drug use disorder when compared to the highest income quartile. Curvilinear  
203 relationships are noted between age and risk of tobacco, alcohol, and drug use disorder (eFigure  
204 1-3).

205 Female sex was associated with lower odds of tobacco (OR 0.72; 95% CI, 0.70 to 0.74),  
206 substance (OR 0.37; 95% CI, 0.36 to 0.39), alcohol (OR 0.23; 95% CI, 0.22 to 0.25), and drug  
207 (OR 0.58; 95% CI, 0.55 to 0.62) use disorder. All racial/ethnic groups had decreased risk of  
208 tobacco use disorder when compared to whites except for Native Americans. Hispanic  
209 race/ethnicity was associated with less substance (OR 0.80; 95% CI 0.74 to 0.86) or drug (OR  
210 0.76; 95% CI, 0.69 to 0.83) use disorder, and Asian/PI race/ethnicity was associated with less  
211 substance (OR 0.65; 95% CI, 0.57 to 0.75), alcohol (OR 0.53; 95% CI, 0.43 to 0.65), and drug  
212 (OR 0.83; 95% CI, 0.70 to 0.97) use disorder. Private insurance was associated with less tobacco  
213 (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;  
214 95% CI, 0.54 to 0.65) use disorder.

## 215 Discussion

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

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

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

238associated with increased risk of alcohol use disorder, these patients also had high rates of  
239tobacco and drug use disorders. Recent data from the National Survey on Drug Use and Health  
240(NSDUH) shows that American Indians or Alaska Natives have higher prevalence of tobacco use  
241and cigarette smoking than all other racial/ethnic groups.<sup>38</sup> Black race was associated with  
242substance, alcohol, and drug use disorder. Cocaine use disorder was highest among black heart  
243failure hospitalizations, while amphetamine use disorder was highest for Asian/PI heart failure  
244hospitalizations. A prior study of 11,258 heart failure patients from the ADHERE-EM database  
245found that self-reported illicit drug use with cocaine or methamphetamines was associated with  
246black race compared to Caucasian.<sup>32</sup> Black men and women present with heart failure at a  
247younger age and have the highest age-standardized hospitalization rates compared to other  
248race/ethnicities in the US.<sup>34</sup> Addressing underlying substance use disorders in black patients may  
249reduce the burden of heart failure attributed to substances and reduce hospitalizations.  
250Conversely, Asian/PI males and females have the lowest hospitalization rates for heart failure  
251compared to other races in the US.<sup>34</sup> However, the Asian/PI population in the US is rapidly  
252growing<sup>35</sup> with high rates of amphetamine use,<sup>36,37</sup> which may contribute to future heart failure  
253hospitalizations.

254 Geographically, the Pacific region stands out for high rates of substance use disorder,  
255especially drug use disorder. Data from NSDUH reports high prevalence of past-month illicit  
256drug use by individuals 18 years or older within Pacific states.<sup>39</sup> Patterns of use in heart failure  
257patients may mirror those of the general population. Providers should be aware of types of  
258substance use prevalent in their region.

259 Rates of tobacco and substance use disorders were higher for patients of lower  
260socioeconomic status as represented by payer status (Medicaid, self-pay, or no charge) and

261median household income quartiles. Socioeconomic factors mediate differences in tobacco and  
262substance use disorders based on race/ethnicity. While we cannot adjust for complex community  
263stressors predisposing to tobacco or substance use disorders, evaluating community risk factors  
264for tobacco and substance use disorders, such as density of tobacco stores,<sup>16</sup> and identifying  
265vulnerable groups may help develop preventive and treatment strategies, reducing observed  
266disparities.

267 Tobacco and substance use disorders in heart failure patients have implications for the  
268broader health system. Substance use leads to increased costs from decreased productivity,  
269healthcare costs, and crime.<sup>44</sup> Tobacco,<sup>45,46</sup> alcohol,<sup>45</sup> and cocaine<sup>47</sup> use are associated with  
270increased readmission risk in heart failure patients. Screening for tobacco and substance use  
271disorders has historically been deficient in primary care, emergency room, and hospital settings;<sup>48</sup>  
272despite efforts to improve screening, rates are likely under-appreciated. Heart failure patients  
273who actively smoke but are attempting to quit may be coded with a different ICD-9-CM code  
274than tobacco use disorder, further underestimating numbers.<sup>49</sup> Tobacco and substance use  
275disorders may have even larger negative effects on the healthcare system than currently reported.

### 276**Limitations**

277 The NIS does not use unique patient identifiers; a hospitalization may represent a new  
278patient or a patient already captured in the sample being readmitted, which may increase rates.  
279We are unable to account for geographic or provider coding variation in ICD-9-CM coding.  
280Some conditions, notably tobacco use disorder, may be under-coded. Due to constraints within  
281ICD-9-CM codes, we could not quantify amount or duration of tobacco or substance use  
282disorders. Heavier or prolonged tobacco or substance use may have more detrimental cardiotoxic  
283effects, but even substance use that does not qualify for a diagnosis may contribute to heart

284failure. Many hospitalized heart failure patients with drug use disorder used “other drugs,”  
285illustrating the complexity of coding for specific drug use. Finally, unmeasured confounding,  
286related to other lifestyle or cardiovascular risk factors not measured, may influence some of these  
287associations, especially as related to socioeconomic status or race/ethnicity.

### 288**Conclusions**

289 Comorbid tobacco or substance use disorder among hospitalized heart failure patients in  
290the US particularly affects males, younger individuals, and those of lower socioeconomic status.  
291A heart failure hospitalization is an opportunity to screen for and treat tobacco or substance use  
292disorders. To effectively manage heart failure, better recognition of comorbidities portending  
293worse outcomes should be included in full assessments of patients. Further research on  
294interventions that reduce rates of tobacco or substance use disorders among discharged heart  
295failure patients are needed.

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