



Published in final edited form as:

Heart Lung. 2021 ; 50(2): 244–251. doi:10.1016/j.hrtlng.2020.12.009.

National rates and trends of tobacco and substance use disorders among atrial fibrillation hospitalizations

Rajkumar Doshi, MD, MPH^{#a,*}, Mihir Dave, MD^{#a}, Monil Majmundar, MD^b, Ashish Kumar, MBBS^c, Devina Adalja, MBBS^d, Mariam Shariff, MBBS^c, Rupak Desai, MBBS^e, Boback Ziaieian, MD, PhD^{f,g}, Saraschandra Vallabhajosyula, MD, MSc^{h,i,j}

^aDepartment of Internal Medicine, University of Nevada Reno School of Medicine, 1155 Mill St, W-11, Reno, NV 89502, USA

^bDepartment of Internal Medicine, Metropolitan Medical Center, New York, NY, USA

^cDepartment of Critical Care Medicine, St John's Medical College Hospital, Bengaluru, Karnataka, India

^dDepartment of Medicine, GMERS Gotri Medical College, Vadodara, Gujarat, India

^eDepartment of Cardiology, Atlanta VA Medical Center, Decatur, GA, United States

^fDivision of Cardiology, David Geffen School of Medicine at University of California, Los Angeles, CA, USA

^gDivision of Cardiology, Veterans Affairs Greater Los Angeles Healthcare System, Los Angeles, CA, USA

^hDepartment of Cardiovascular Medicine, Mayo Clinic, Rochester, MN, USA

ⁱDivision of Pulmonary and Critical Care Medicine, Department of Medicine, Mayo Clinic, Rochester, MN, USA

^jCenter for Clinical and Translational Science, Mayo Clinic Graduate School of Biomedical Sciences, MN, USA

These authors contributed equally to this work.

Abstract

Background: Atrial Fibrillation (AF) has been associated with various behavioral risk factors such as tobacco, alcohol, and/or substances abuse.

Objective: The main objective is to describe the national trends and burden of tobacco and substance abuse in AF hospitalizations. Also, this study identifies potential population who are more vulnerable to these substance abuse among AF hospitalizations.

* Corresponding author. rdoshi@med.unr.edu (R. Doshi).

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.hrtlng.2020.12.009.

Methods: The National Inpatient Sample database from 2007 to 2015 was utilized and the hospitalizations with AF were identified using the international classification of disease, Ninth Revision, Clinical Modification code. They were stratified into without abuse, tobacco use disorder (TUD), substance use disorder (SUD), alcohol use disorder (AUD) and drug use disorder (DUD).

Results: Of 3,631,507 AF hospitalizations, 852,110 (23.46%) had TUD, 1,851,170 (5.1%) had SUD, 155,681 (4.29%) had AUD and 42,667 (1.17%) had DUD. The prevalence of TUD, SUD, AUD, and DUD was substantially increased across all age groups, races, and gender during the study period. Female sex was associated with lower odds TUD, SUD, AUD, and DUD. Among AF hospitalizations, the black race was associated with higher odds of SUD, and DUD. The younger age group (18–35 years), male, Medicare/Medicaid as primary insurance, and lower socioeconomic status were associated with increased risk of both TUD and SUDs.

Conclusion: TUD and SUD among AF hospitalizations in the United States mainly affects males, younger individuals, white more than black, and those of lower socioeconomic status which demands for the development of preventive strategies to address multilevel influences.

Keywords

Atrial fibrillation; Tobacco abuse; Substance abuse; Trends; Drug abuse

Introduction

Atrial fibrillation (AF) is one of the most common arrhythmias in the U.S. and the prevalence of AF continue to rise secondary to the increased detection rate and population aging.^{1, 2} AF is predominantly associated with hypertension, heart failure, coronary artery disease, diabetes mellitus, and valvular heart disease.³ AF has also been associated with various behavioral risk factors such as tobacco abuse,⁴ alcohol abuse^{5, 6} and substances abuse.⁶ Tobacco abuse has been shown to increase the risk of AF in the Framingham Heart Study (FHS) and Rotterdam study.^{7, 8} Alcohol has been strongly associated with the risk of AF and reducing intake was shown to be associated with reduction in AF recurrences.^{9, 10} Similarly, various substances such as cocaine, amphetamine and other illicit drugs have been shown to have cardiotoxic effects resulting in cardiac arrhythmias.^{11, 12} Furthermore, rates of tobacco, alcohol and illegal drug use in the U.S. continue to increase, especially in the young adults, which may add to the incidence and prevalence of AF.^{13–15} Prior studies on substance use and AF in the U.S. are not nationally representative. National tobacco abuse and substance abuse rates among heart failure hospitalizations have been studied.¹⁶ The national burden of tobacco and other substance use disorders among AF hospitalizations is not well described.

Nationally representative data helps to understand the prevalence and influence of tobacco and substance use disorders on health outcomes among AF hospitalizations. Identifying AF hospitalizations with tobacco, alcohol or other substance use disorders is critical in developing preventive policies. This study describes the national burden and trend of tobacco and substance abuse in AF hospitalizations. Also, this study identifies potential population who are more vulnerable to these substance abuse among AF hospitalizations.

Moreover, we stratified these trends by age, race, and sex to observe predominant group characteristics in AF hospitalizations.

Methods

Data source

The National Inpatient Sample (NIS) was used for the present analysis. The NIS is created and maintained by the Agency for Healthcare Research and Quality and is developed for the Healthcare Cost and Utilization Project (HCUP). The NIS contains data from more than 7 million unweighted hospital discharges each year and weighted, and the NIS estimates more than 35 million hospitalizations nationally. The design of the NIS was changed after the year 2012. The NIS included all inpatient discharges from a random 20% sample of hospitalizations from 2007 to 2011. From 2012 onwards, the database was built using a systematic sampling of 20% of discharges from all the hospitals. Additionally, we used “trend weights” for the database prior to the year 2011, as recommended. These trend weights help facilitate comparison of estimates from the year prior to 2012. These changes in the NIS database structure has been described previously.^{17, 18} Since, the NIS uses de-identified hospital discharges as samples with prior ethical committee approval, no additional ethical committee approval was required for the present analysis.

Study population

AF hospitalizations were identified using the international classification of disease, Ninth Revision, Clinical Modification (ICD-9-CM) code 427.31 in the primary diagnosis column. We included the database from January 2007 to September 2015 since the coding system changed to ICD-10-CM after September 2015. These codes for identifying AF hospitalizations from the NIS have been utilized in previous studies.^{19–21} Hospitalizations under 18 years of age were excluded from the present analysis. Demographic data including age, sex, race, co-morbidities, region of hospital, location of the hospital, hospital size, payment type and median household income category for hospitalization’s zip code were retrieved for each of the included hospitalizations. Tobacco, alcohol and drug use disorders were defined using ICD-9-CM codes (Supplementary Table 1), as described previously.¹⁶ Substance use disorder (SUD) was defined as any drug or alcohol use disorder excluding tobacco. This method has been utilized previously for heart failure hospitalization using the same database.¹⁶ Finally, Charlson’s comorbidity index score has been explained in the Supplementary Table 2. This was later stratified by 0, 1, 2 or 3.

Statistical analysis

AF hospitalizations were stratified into without abuse, tobacco use disorder (TUD), SUD, alcohol use disorder (AUD) and drug use disorder (DUD). Descriptive statistics of hospitalizations in each stratum with in-hospital outcomes were reported. AF hospitalizations were later stratified based on sex. All analyses in the present study accounted for NIS clustering, survey nature, stratification, and weights per recommendations (Supplementary Table 3).²² Continuous variables were expressed as mean (standard deviations [SD]) or median (interquartile range [IQR]) depending on the data distribution and analyzed using the Student *t*-test or Wilcoxon rank sum test, as appropriate. Categorical

data were expressed in frequency and percentages and analyzed using the Pearson's chi-square test. We used the Jonckheere-Terpstra trend test to analyze the trend of the frequency of substance use percentage combined, stratified into five age groups (18–35, 36–50, 51–65, 66–80 and more than 80), sex and race. Statistical significance was set at a P-value of <0.05. The cost was calculated by multiplying the total cost with the cost-to-charge ratio provided by the sponsor for each given year and adjusted for inflation to year 2011. Finally, we performed multivariable logistic regression analysis to analyze demographic factors associated with TUD, SUD, AUD and DUD. We included age, sex, race, hospital region, median household income, primary payor, hospital bedsize and hospital location in this model. SAS, version 9.4 (SAS Institute Inc.) was used for all statistical analyses.

Results

A total of 3,631,507 AF hospitalizations from 2007 - 2015 over 18 years of age were included in the present analysis. Of the hospitalizations, 852,110 (23.46%) had TUD, 1,851,170 (5.1%) had SUD, 155,681 (4.29%) had AUD and 42,667 (1.17%) had DUD. 2,689,315 (74.06%) had no documented history of any abuse.

Atrial fibrillation hospitalization without a history of abuse

Hospitalizations without a history of abuse had a mean age of 71.8 ± 30.1 years. Majority of the hospitalizations without drug abuse were between 66 and 80 years (38.7%), females (57.4%) and whites (72.6%). Hypertension (67.6%) and dyslipidemia (43.3%) were the most frequently occurring co-morbidities. Most of the AF hospitalizations without a history of drug abuse had CHA₂DS₂VASc score ≥ 3 (62%) (CHA₂DS₂VASc scores are used in AF patients to stratify the risk of stroke). The majority of the hospitalizations were at large hospitals by bed-size (60.1%) and urban teaching locations (44.3%) with Medicare/Medicaid (72.5%) being the most common primary payment type among AF hospitalizations with drug abuse (Table 1).

Tobacco use disorder in AF hospitalizations

AF hospitalizations with TUD had a mean age of 67 ± 29.5 years. The majority of the hospitalizations in TUD were between 51 and 65 years of age (41.4%), male (61%), and white (76.7%). Most of the AF hospitalizations with TUD had CHA₂DS₂VASc score ≥ 3 (48.4%). Like AF hospitalizations without drug abuse, AF hospitalizations with TUD were predominantly admitted to a large bed-sized hospital (60.1%), urban teaching hospitals (47.4%) with Medicare/Medicaid being the primary payor in AF hospitalizations with TUD (66.7%). Among AF hospitalizations, 1.1% had a stroke, 0.7% died in hospital, and 78.5% were discharged to home (Table 1). TUD was most common in age groups >50 years, the majority were whites, and Medicare/Medicaid was the primary payor for AF hospitalizations with TUD in both sexes (Table 2).

Substance use disorder in AF hospitalizations

AF hospitalizations with SUD had a mean age of 58.4 ± 29.9 years, with the majority in the age group of 51–65 (45.4%). Majority of the hospitalizations were male (82.2%) and whites (70%), at a large bed-sized hospital (58.5%) and urban teaching hospitals (47.9%) with

Medicare/Medicaid being the primary payor. Among AF hospitalization with SUD, 1% had a stroke, 0.8% died in hospital, and 77% were discharged to home. (Table 1) Among males, the most common age group was 51–65 years, while it was 66–80 years in females, with whites being majority among both sexes. (Table 2)

Alcohol use disorder in AF hospitalizations

AF hospitalizations with AUD had a mean age of 58.7 ± 28.4 years, with the majority in the age group of 51–65 years (46.7%). The majority of the hospitalizations were male (85%), whites (70.8%), at a large bed-sized hospital (58.2%), urban teaching settings (47.31%) with Medicare/Medicaid being a significant payor for AF hospitalizations with AUD. Among AF hospitalizations with AUD, 1% had a stroke, 0.75% died in the hospital, and 78.1% were discharged to home (Table 1). Among males, the most common age group was 50–65 years, while it was 66–80 years in females. (Table 2)

Drug use disorder in AF hospitalizations

AF hospitalizations with DUD had a mean age of 55 ± 34.2 years, and the majority were in the age group of 51–65 (42.8%). The majority of the hospitalizations were male (74%), whites (63.9%), at a large bed-sized hospital (59.5%), urban teaching settings (51.6%) with Medicare/Medicaid (57.8%) being the primary payor. Hypertension (57%) and chronic lung disease (28.8%) were the most prevalent comorbidities. Among AF hospitalization with DUD, 0.9% had a stroke, 1% died in the hospital, and 73.6% were discharged to home (Table 1). DUD among AF hospitalizations was most common in the 51–65 years age group in both sexes (Table 2).

Associated demographic factors

Among AF hospitalizations, compared to the age group of 18–35 years, all the other age groups had lower odds of TUD, SUD, AUD, and DUD. The exception to this was the age group of 51–65 years, which had an increased odds of TUD as compared with the age group 18–35 years (1.05 (1.03–1.07), P -value <0.001). Female sex was associated with lower odds of TUD (0.57 (0.56–0.57), P -value <0.001), SUD (0.27 (0.26–0.27), P -value <0.001), AUD (0.22 (0.22–0.22), P -value <0.001), and DUD (0.51 (0.5–0.52), P -value <0.001). Among AF hospitalizations, the black race was associated with higher odds of SUD (1.12 (1.1–1.14), P -value <0.001), and DUD (1.42 (1.38–1.47), P -value <0.001). Midwest (1.45 (1.44–1.46), P -value <0.001), south (1.16 (1.15–1.17), P -value <0.001) and west (1.34 (1.33–1.35), P -value <0.001) hospital regions had a higher odds of TUD as compared with northeast region. The hospitalizations in the lower percentile median household income category had higher odds of TUD and SUDs. Private insured patients had the lowest odds of TUD, and SUDs and self-pay/no charge patients had the highest odds of TUD and SUDs (Table 3).

The trend of tobacco, substance, alcohol and drug use disorder from 2007 to 2015 among AF hospitalizations

There was a significant increase in trend of AF hospitalizations with TUD, SUD, AUD, and DUD from 2007 to 2015 combined, stratified gender, and race (Fig. 1, Fig. 2). TUD has the highest prevalence of hospital admissions as shown in the Fig. 1. DUD has the lowest

prevalence of hospital admission for Afib as explained in the Fig. 1. In males (Fig. 2A) and in females (Fig. 2B), TUD had highest prevalence throughout the study period. The prevalence of TUD consistently increases during the study period in males and as well in females. Similarly, TUD had the highest prevalence in whites as well as African Americans (Fig. 2C and 2D). Further, TUD, SUD, AUD and DUD increased significantly in all age groups; 18–35 years, 36–50 years, 51–65 years, 66–80 years and >80 years (Fig. 3). Prevalence of TUD was highest in the younger population (below 35 years of age) as shown in Fig. 3A. Additionally, prevalence of SUD, AUD and DUD is also highest compared to other population (Fig. 3 panel B-D).

Discussion

This current nationwide research of ~3.6 million hospitalizations for AF from 2007 to 2015 demonstrated the rates and temporal trends of AF hospitalizations with TUD, AUD, DUD, or SUD. Of ~3.6 million hospitalizations with AF, 23.46% had TUD, which was the most commonly associated disorder followed by 5.1% had SUD, 4.3% had AUD, and 1.2% had DUD. Among AF hospitalizations, the prevalence of TUD, SUD, AUD, and DUD was substantially up trended across all age groups, races, and gender during the study period. The younger age group (18–35 years), male, and lower socioeconomic status were associated with increased risk of both TUD and SUDs. Patients with private insurance were associated with lower odds of all types of substance abuse compared with Medicare/Medicaid. All AF hospitalizations were more likely to be admitted to urban teaching hospitals. While white race and Midwest regional hospitals were associated with increased risk of TUD, the black race, and west regional hospitals were associated with higher rates of SUD, AUD, and DUD in AF hospitalizations.

Several former studies showed an association between tobacco and the incidence of AF.^{4, 8, 23} This study showed an increasing trend of TUD among hospitalization with AF, consistent with the most recent report by Wang et al.¹⁴ Several mechanisms may explain an association between smoking and AF. Nicotine has sympathomimetic activity leading to tachycardia and elevated blood pressure from catecholamine release.²⁴ Nicotine also has a profibrotic response leading to atrial structural and electric remodeling in the animal study.²⁵ All these point towards a causal pathway between tobacco and AF as evidenced in the former literature depicting the role of nicotine in atrial fibrosis leading to AF.²⁶ Few small studies showed that alcohol and opioid use are independently associated with AF.^{6, 12, 27, 28} Literature showed an increasing trend of alcohol use from 2000 to 2016¹⁵, opioid use disorder, opioid overdose from 2006 to 2016,²⁹ and increasing trend of AF among opioid overdose hospitalizations from 2005 to 2015, consistent with our results.²⁸ Three large observational studies documented a dose-dependent relationship between alcohol consumption and the risk of AF.^{30–32} Furthermore, as explained above, cessation of alcohol was associated with reduction in the trends of AF in a previous study.¹⁰ Several mechanism have also been proposed for a strong association between alcohol and AF which may include, but not limited to sympathetic activation, direct myocardial injury and inflammation, and increasing oxidative stress.⁹ Alcohol also has indirect effects such as increasing blood pressure, causing obstructive sleep apnea and left ventricular

cardiomyopathy which can eventually lead to AF.⁹ Additionally, substance abuse has been strongly associated with heart failure which can eventually lead to AF.^{16, 33}

In the general population, TUD and SUDs are continually on the rise without discriminating against age. Across the age strata, young adults were more predilected towards the TUD and SUDs, as shown in this study. Among the young adults, depression, peer pressure, desire to be among the ‘cool’, whereas, among old adults, psychiatric illness, stress, social factors like divorce, life events, and prescription medications misuse could be the contributing factors towards abuse.³⁴ The TUD and SUD would have a different magnitude of impact among the younger as compared with older patients with AF hospitalization due to differences in the prevalence of comorbidities. Among the AF hospitalizations, the TUD and SUDs had a high prevalence of male that goes with a similar trend of TUD and SUD in the general population.³⁵ Noticeably, the up-trend in the male was steeper as compared to the female in this study. The difference in trend and prevalence by gender could be explained by the neurobiological mechanism.³⁶

This study reported that white and black were associated with an increased risk of TUD and SUDs, respectively. A national survey reported the maximum prevalence of TUD and DUD among the American Indians and whites.³⁵ However, the authors categorized the race by white, black, and others. There is no substantial research revealing the disparity by race in the past. However, certain factors such as multiple peers, family (poor parenting), school (location), community domain (neighborhood deterioration), culture-specific risk (greater acculturation), protective correlates (cultural pride) might influence the difference.³⁷ In the general population, AUD was more prevalent among the higher socioeconomic status (SES), but TUD and DUD were more prevalent among lower SES.³⁸ Among AF hospitalizations, our study showed that the prevalence of TUD and SUDs was higher for patients with lower socioeconomic status as represented by payor status (Medicaid/Medicare, self-pay, or no other charge) and median household income quartiles. These are consistent with the results of previous studies.^{39, 40} This result can be attributed to the possible “downward drift” of substance users into disadvantaged neighborhood overtime.⁴¹ This could also explain the higher odds of TUD, SUD, AUD, and DUD reported among hospitalizations, where the primary payor was Medicare/Medicaid. The results in the study were not adjusted for other complex community factors predisposing to TUD or SUD. Geographically, the Midwest, west region stood out for high rates of TUD and SUD among AF hospitalizations, which mirror the data from NSDUH reporting a high prevalence of illicit drug use by individuals 18 years or older in the west region.³⁵

TUD and SUD in the AF hospitalizations have broader implications on the healthcare system. The REGARDS study demonstrated that environmental tobacco smoke exposure is associated with a higher prevalence of AF,⁴² and childhood second-hand smoke exposure predicts the increased risk for adulthood AF.⁴³ The Rotterdam Study reported a similar risk of AF in former smokers as it is current smokers.⁸ In general, substance use leads to increased costs from decreased productivity, healthcare expenditure, and crime.⁴⁴ SUDs have a lasting impact on social, economic, health, and legal consequences. Screening for TUD and SUDs is inadequate in primary care, emergency room, and hospital settings for a long time.⁴⁵ Considering the effect of tobacco, alcohol, and drugs (cocaine, opioids,

marijuana, amphetamine, and others) on AF and its rising trend among AF hospitalizations across the age, gender, and race demands for the development of preventive strategies to address multilevel influences. Additional education must be provided to the patients during clinic visit or hospital admission to explain the preventable behavioral risk factor, which may be contributing to their AF risk.

The limitations of this study are as following: The NIS database is prone to inherent miscoding among diagnoses and procedural codes. However, the authors used authenticated codes from literature laid out by HCUP/AHRQ to recognize the ICD-9-CM codes for diagnosis or procedure. Occasionally, patients with recent history of tobacco or substance use but presently under abstinence may not be coded as TUD and SUDs that might have led to under-coding of conditions. The authors could not quantify the amount and duration of tobacco, alcohol, or illicit substance use disorder due to the nature of the NIS dataset where such information is unavailable. However, these codes have been utilized previously.¹⁶ The unmeasured factors related to lifestyle or cardiovascular risk factors not measured may influence some of these associations, primarily as related to socioeconomic status or race. This study is only focused on hospitalized AF and did not include any patients who were diagnosed in the clinic, given the nature of the database. This affects the actual rates of substance abuse. The frequency for opioid abuse, amphetamine abuse and other drug abuse was low and hence, were not reported in this study. We have not adjusted out trend analysis with demographics. Finally, one hospitalization can have more than one substance abuse which was not accounted for in this study given the complex nature of the combinations. However, the NIS is a large and nationally representative database that allows us to generalize findings and utilize it as a reference tool for potential implications on healthcare policy.

In nationally representative data, despite these limitations, the authors highlighted the rising trend of the TUD, AUD, DUD and SUD among hospitalized AF patients. To our knowledge, this is the most extensive study of its kind that reveals that TUD and SUD among AF hospitalizations in the U.S. affects more males, younger individuals, white individuals, and those of lower socioeconomic status. An AF hospitalization is an opportunity to screen for and treat TUD, AUD or SUD. Further research on the prevalence of TUD and SUD, its impact on outcomes such as readmission, mortality, and the intervention that reduces rates of TUD or SUD among discharged AF are imminent.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Funding Source

Dr. Saraschandra Vallabhajosyula is supported by the Clinical and Translational Science Award (CTSA) Grant Number UL1 TR000135 from the National Center for Advancing Translational Sciences (NCATS), a component of the National Institutes of Health (NIH). Its contents are solely the responsibility of the authors and do not necessarily represent the official view of NIH.

Abbreviations and Acronyms:

AF	Atrial Fibrillation
AUD	Alcohol Use Disorder
DUD	Drug Use Disorder
FHS	Framingham Heart Study
HCUP	Healthcare Cost and Utilization Project
ICD-9-CM	International classification of disease, Ninth Revision, Clinical Modification
NIS	National Inpatient Sample
SUD	Substance Use Disorder
TUD	Tobacco Use Disorder
US	United States

References

1. Patel NJ, Deshmukh A, Pant S, et al. Contemporary trends of hospitalization for atrial fibrillation in the United States, 2000 through 2010: implications for healthcare planning. *Circulation*. 2014;129(23):2371–2379. [PubMed: 24842943]
2. Miyasaka Y, Barnes ME, Gersh BJ, et al. Secular trends in incidence of atrial fibrillation in Olmsted County, Minnesota, 1980 to 2000, and implications on the projections for future prevalence. *Circulation*. 2006;114(2):119–125. [PubMed: 16818816]
3. Benjamin EJ, Levy D, Vaziri SM, D'Agostino RB, Belanger AJ, Wolf PA. Independent risk factors for atrial fibrillation in a population-based cohort. The Framingham Heart Study. *JAMA*. 1994;271(11):840–844. [PubMed: 8114238]
4. Chamberlain AM, Agarwal SK, Folsom AR, et al. Smoking and incidence of atrial fibrillation: results from the Atherosclerosis Risk in Communities (ARIC) study. *Heart Rhythm*. 2011;8(8):1160–1166. [PubMed: 21419237]
5. Samokhvalov AV, Irving HM, Rehm J. Alcohol consumption as a risk factor for atrial fibrillation: a systematic review and meta-analysis. *Eur J Cardiovasc Prev Rehabil*. 2010;17(6):706–712. [PubMed: 21461366]
6. Krishnamoorthy S, Lip GY, Lane DA. Alcohol and illicit drug use as precipitants of atrial fibrillation in young adults: a case series and literature review. *Am J Med*. 2009;122(9): 851–856 e3. [PubMed: 19699381]
7. Schnabel RB, Sullivan LM, Levy D, et al. Development of a risk score for atrial fibrillation (Framingham Heart Study): a community-based cohort study. *Lancet*. 2009;373(9665):739–745. [PubMed: 19249635]
8. Heeringa J, Kors JA, Hofman A, van Rooij FJ, Witteman JC. Cigarette smoking and risk of atrial fibrillation: the Rotterdam Study. *Am Heart J*. 2008;156(6):1163–1169. [PubMed: 19033014]
9. Voskoboinik A, Prabhu S, Ling LH, Kalman JM, Kistler PM. Alcohol and atrial fibrillation: a sobering review. *J Am Coll Cardiol*. 2016;68(23):2567–2576. [PubMed: 27931615]
10. Voskoboinik A, Kalman JM, De Silva A, et al. Alcohol abstinence in drinkers with atrial fibrillation. *N Engl J Med*. 2020;382(1):20–28. [PubMed: 31893513]

11. Huang MC, Yang SY, Lin SK, et al. Risk of cardiovascular diseases and stroke events in methamphetamine users: a 10-Year Follow-Up Study. *J Clin Psychiatry*. 2016;77 (10):1396–1403. [PubMed: 27574836]
12. Doshi R, Majmundar M, Kansara T, et al. Frequency of cardiovascular events and in-hospital mortality with opioid overdose hospitalizations. *Am J Cardiol*. 2019;124(10):1528–1533. [PubMed: 31521260]
13. Mack KA, Jones CM, Ballesteros MF. Illicit drug use, illicit drug use disorders, and drug overdose deaths in metropolitan and nonmetropolitan areas-United States. *Am J Transplant*. 2017;17(12):3241–3252. [PubMed: 29145698]
14. Wang TW, Gentzke AS, Creamer MR, et al. Tobacco product use and associated factors among middle and high school students - United States, 2019. *MMWR Surveill Summ*. 2019;68(12):1–22.
15. Gruzca RA, Sher KJ, Kerr WC, et al. Trends in adult alcohol use and binge drinking in the early 21st-Century United States: a meta-analysis of 6 national survey series. *Alcohol Clin Exp Res*. 2018;42(10):1939–1950. [PubMed: 30080258]
16. Snow SC, Fonarow GC, Ladapo JA, Washington DL, Hoggatt KJ, Ziaieian B. National rate of tobacco and substance use disorders among hospitalized heart failure patients. *Am J Med*. 2019;132(4). 478–488 e4. [PubMed: 30562497]
17. Thakkar S, Majmundar M, Kumar A, et al. Comparison of management and outcomes of acute heart failure hospitalization in medicaid beneficiaries versus privately insured individuals. *Am J Cardiol*. 2020;125(7):1063–1068. [PubMed: 32146925]
18. Khera R, Cram P, Lu X, et al. Trends in the use of percutaneous ventricular assist devices: analysis of national inpatient sample data, 2007 through 2012. *JAMA Intern Med*. 2015;175(6):941–950. [PubMed: 25822170]
19. Shah J, Kumar A, Majmundar M, et al. Prevalence of cardiovascular risk factors and financial burden in younger adults hospitalized with atrial fibrillation. *Heart Lung*. 2020.
20. Doshi R, Al-Khafaji JF, Dave M, et al. Comparison of baseline characteristics and in-hospital outcomes in medicaid versus private insurance hospitalizations for atrial fibrillation. *Am J Cardiol*. 2019;123(5):776–781. [PubMed: 30558759]
21. Doshi R, Pisipati S, Taha M, et al. Incidence, 30-day readmission rates and predictors of readmission after new onset atrial fibrillation who underwent transcatheter aortic valve replacement. *Heart Lung*. 2020;49(2):186–192. [PubMed: 31690493]
22. Khera R, Angraal S, Couch T, et al. Adherence to methodological standards in research using the national inpatient sample. *JAMA*. 2017;318(20):2011–2018. [PubMed: 29183077]
23. Staerk L, Sherer JA, Ko D, Benjamin EJ, Helm RH. Atrial fibrillation: epidemiology, pathophysiology, and clinical outcomes. *Circ Res*. 2017;120(9):1501–1517. [PubMed: 28450367]
24. Haass M, Kubler W. Nicotine and sympathetic neurotransmission. *Cardiovasc Drugs Ther*. 1997;10(6):657–665. [PubMed: 9110108]
25. Shan H, Zhang Y, Lu Y, et al. Downregulation of miR-133 and miR-590 contributes to nicotine-induced atrial remodelling in canines. *Cardiovasc Res*. 2009;83(3):465–472. [PubMed: 19398468]
26. Goette A. Nicotine, atrial fibrosis, and atrial fibrillation: do microRNAs help to clear the smoke? *Cardiovasc Res*. 2009;83(3):421–422. [PubMed: 19502283]
27. Qureshi WT, O'Neal WT, Khodneva Y, et al. Association between opioid use and atrial fibrillation: the reasons for geographic and racial differences in stroke (REGARDS) study. *JAMA Intern Med*. 2015;175(6):1058–1060.
28. Doshi R, Shah J, Desai R, Gullapalli N. Burden of arrhythmia in hospitalizations with opioid overdose. *Int J Cardiol*. 2019;286:73–75. [PubMed: 30674434]
29. Wei YJ, Chen C, Fillingim R, Schmidt SO, Winterstein AG. Trends in prescription opioid use and dose trajectories before opioid use disorder or overdose in US adults from 2006 to 2016: a cross-sectional study. *PLoS Med*. 2019;16:(11)e1002941. [PubMed: 31689302]
30. Ruigomez A, Johansson S, Wallander MA, Rodriguez LA. Incidence of chronic atrial fibrillation in general practice and its treatment pattern. *J Clin Epidemiol*. 2002;55(4):358–363. [PubMed: 11927203]

31. Djousse L, Levy D, Benjamin EJ, et al. Long-term alcohol consumption and the risk of atrial fibrillation in the Framingham Study. *Am J Cardiol.* 2004;93(6):710–713. [PubMed: 15019874]
32. Krahn AD, Manfreda J, Tate RB, Mathewson FA, Cuddy TE. The natural history of atrial fibrillation: incidence, risk factors, and prognosis in the Manitoba Follow-Up Study. *Am J Med.* 1995;98(5):476–484. [PubMed: 7733127]
33. Nishimura M, Bhatia H, Ma J, et al. The impact of substance abuse on heart failure hospitalizations. *Am J Med.* 2020;133(2). 207–213 e1. [PubMed: 31369724]
34. Kuerbis A, Sacco P, Blazer DG, Moore AA. Substance abuse among older adults. *Clin Geriatr Med.* 2014;30(3):629–654. [PubMed: 25037298]
35. Results from the 2017 National Survey on Drug Use and Health: Detailed Tables <https://www.samhsa.gov/data/sites/default/files/cbhsq-reports/NSDUHDetailedTabs2017/NSDUHDetailedTabs2017.pdf> Accessed on June 1, 2020.
36. Becker JB, Hu M. Sex differences in drug abuse. *Front Neuroendocrinol.* 2008;29(1):36–47. [PubMed: 17904621]
37. Wu LT, Woody GE, Yang C, Pan JJ, Blazer DG. Racial/ethnic variations in substance-related disorders among adolescents in the United States. *Arch Gen Psychiatry.* 2011;68(11):1176–1185. [PubMed: 22065533]
38. Patrick ME, Wightman P, Schoeni RF, Schulenberg JE. Socioeconomic status and substance use among young adults: a comparison across constructs and drugs. *J Stud Alcohol Drugs.* 2012;73(5):772–782. [PubMed: 22846241]
39. Galea S, Ahern J, Tracy M, Vlahov D. Neighborhood income and income distribution and the use of cigarettes, alcohol, and marijuana. *Am J Prev Med.* 2007;32(6 Suppl):S195–S202. [PubMed: 17543711]
40. Karriker-Jaffe KJ. Neighborhood socioeconomic status and substance use by U.S. adults. *Drug Alcohol Depend.* 2013;133(1):212–221. [PubMed: 23726978]
41. Buu A, Mansour M, Wang J, Refior SK, Fitzgerald HE, Zucker RA. Alcoholism effects on social migration and neighborhood effects on alcoholism over the course of 12 years. *Alcohol Clin Exp Res.* 2007;31(9):1545–1551. [PubMed: 17635420]
42. O’Neal WT, Qureshi WT, Judd SE, et al. Environmental Tobacco Smoke and Atrial Fibrillation: the REasons for Geographic And Racial Differences in Stroke (REGARDS) Study. *J Occup Environ Med.* 2015;57(11):1154–1158. [PubMed: 26539762]
43. Groh CA, Vittinghoff E, Benjamin EJ, Dupuis J, Marcus GM. Childhood tobacco smoke exposure and risk of atrial fibrillation in adulthood. *J Am Coll Cardiol.* 2019;74(13):1658–1664. [PubMed: 31558248]
44. Bouchery EE, Harwood HJ, Sacks JJ, Simon CJ, Brewer RD. Economic costs of excessive alcohol consumption in the U.S., 2006. *Am J Prev Med.* 2011;41(5):516–524. [PubMed: 22011424]
45. Pilowsky DJ, Wu LT. Screening for alcohol and drug use disorders among adults in primary care: a review. *Subst Abuse Rehabil.* 2012;3(1):25–34. [PubMed: 22553426]

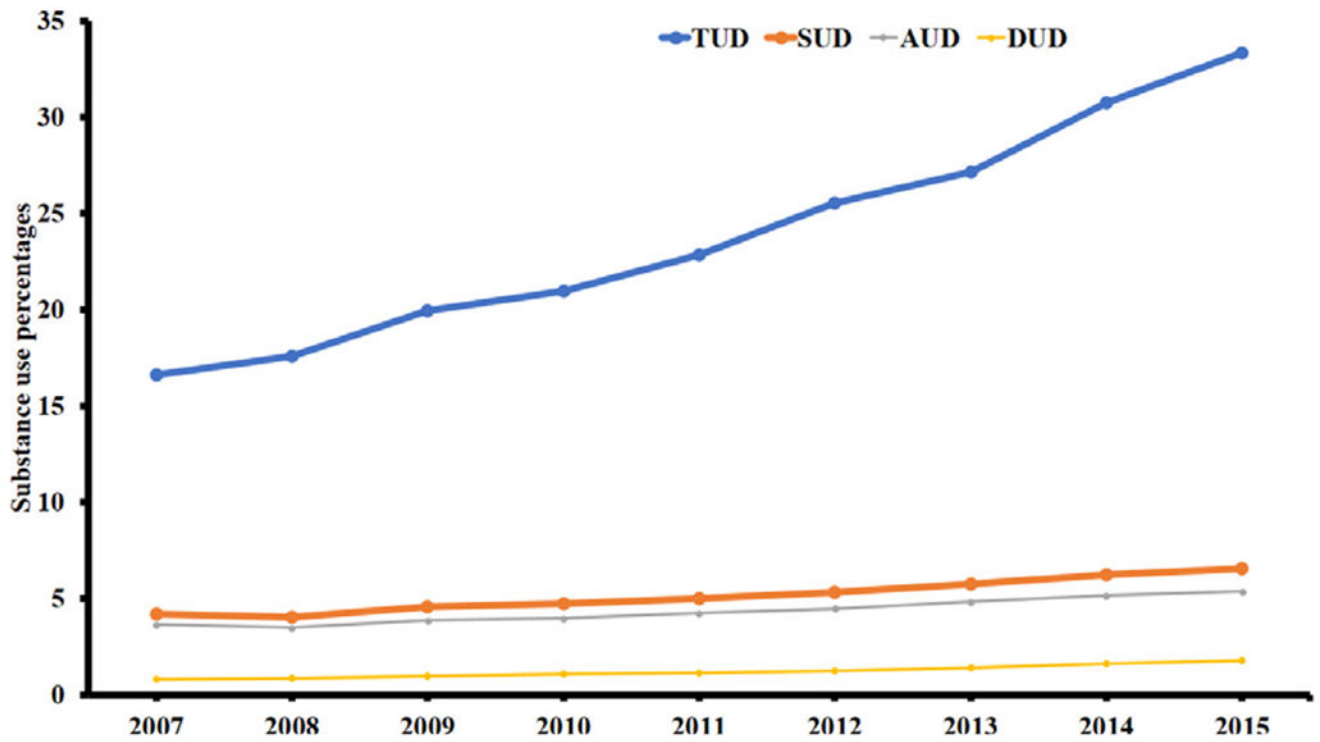


Fig. 1.

Temporal trend of TUD, SUD, AUD and DUD.

Panel A represent overall hospitalizations included in the study. X-axis represents timeline in years, and Y-axis represents frequency of substance use disorder in percentages.

Abbreviations: TUD: Tobacco Use Disorder; SUD: Substance Use Disorder; AUD: Alcohol Use Disorder; and DUD: Drug Use Disorder.

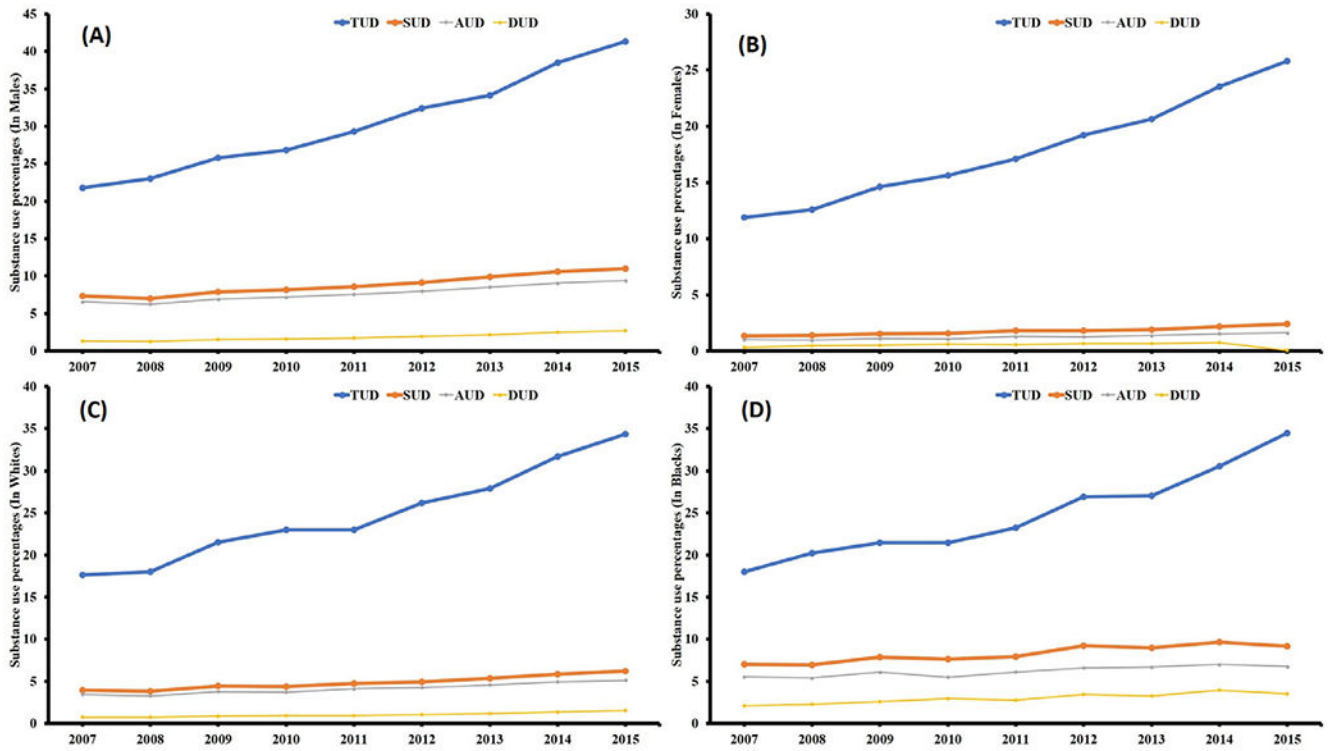


Fig. 2. Trend plots for TUD, SUD, AUD and DUD stratified based on gender and race. Panel A represents temporal trends in males and Panel B represented temporal trends in females. Panel C represents temporal trends in white race and Panel D represents temporal trends in black race. X-axis represents timeline in years, and Y-axis represents frequency of substance use disorder in percentages. Abbreviations: TUD: Tobacco Use Disorder; SUD: Substance Use Disorder; AUD: Alcohol Use Disorder; and DUD: Drug Use Disorder.

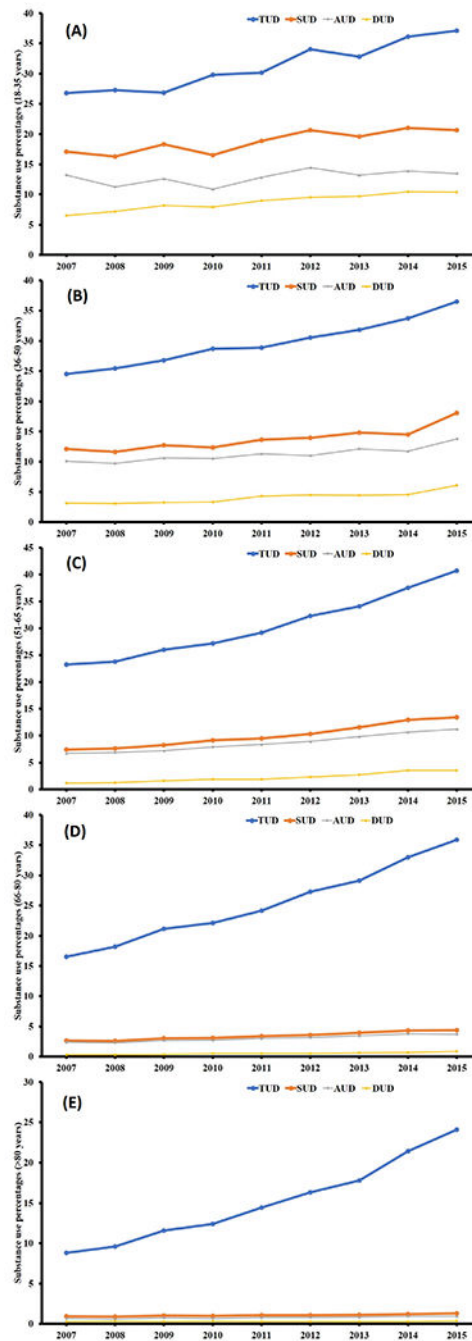


Fig. 3. Trend plots for TUD, SUD, AUD and DUD stratified based on age groups. (Panel A is for 18–35 years, Panel B is for 36–50 years, Panel C is for 51–65 years, Panel D is for 66–80 and Panel E is for >80 years). X-axis represents timeline in years and Y-axis represents frequency of substance use disorder. Abbreviations: TUD: Tobacco Use Disorder; SUD: Substance Use Disorder; AUD: Alcohol Use Disorder; and DUD: Drug Use Disorder.

Demographics, baseline characteristics and in-hospital outcomes of patients admitted with atrial fibrillation and substance abuse.

Table 1

Variable	Without Abuse (2,689,315)	TUD (852,110)	SUD (185,170)	AUD (155,681)	DUD (42,667)
Age, years (Mean±SD)	71.8 ± 30.1	67±29.5	58.4 ± 29.9	58.7 ± 28.4	55±34.2
18–35	36,563 (1.4)	18,501 (2.2)	11,213 (6.1)	7717 (5)	5194 (12.17)
36–50	145,669 (5.4)	655,012 (7.7)	30,297 (16.4)	24,838 (16)	8833 (20.7)
51–65	558,193 (20.8)	256,048 (30.1)	84,068 (45.4)	72,562 (46.7)	18,261 (42.8)
66–80	1,040,383 (38.7)	353,048 (41.4)	48,255 (26.1)	42,391 (27.2)	7121 (16.7)
>80	908,560 (33.8)	159,011 (18.7)	11,338 (6.1)	8172 (5.3)	3258 (7.6)
Sex					
Male	1,146,283 (42.6)	519,812 (61)	152,287 (82.2)	132,378 (85)	31,569 (74)
Female	1,543,032 (57.4)	332,290 (39)	32,880 (17.8)	23,299 (15)	11,098 (26)
Race					
White	1,952,137 (72.6)	653,703 (76.7)	129,093 (70)	110,263 (70.8)	27,259 (63.9)
Black	168,472 (6.3)	58,933 (6.9)	19,759 (10.7)	14,708 (9.5)	7200 (16.9)
Other	568,498 (21.1)	139,428 (16.36)	36,319 (20)	30,710 (19.7)	8208 (19.2)
Comorbidities					
Hypertension	1,817,966 (67.6)	582,136 (68.32)	112,540 (60.8)	95,368 (61.3)	24,327 (57)
Diabetes Mellitus	675,975 (25.1)	209,941 (24.64)	30,737 (16.6)	24,325 (15.6)	8106 (19)
Chronic Lung Disease	465,053 (17.3)	314,874 (40)	49,966 (30)	41,160 (26.4)	12,284 (28.8)
Congestive Heart Failure	10,335 (0.38)	2422 (0.28)	727 (0.4)	565 (0.4)	192 (0.45)
Dyslipidemia	1,164,022 (43.3)	409,553 (48)	55,868 (30.2)	46,912 (30.1)	11,811 (27.7)
Chronic Kidney Disease	355,061 (13.2)	102,391 (12)	13,632 (7.4)	9965 (6.4)	4351 (10.2)
Chronic Liver Disease	27,935 (1)	20,258 (2.38)	19,619 (10.6)	18,184 (11.7)	3387 (7.9)
Cancer with or without metastasis	103,601 (3.9)	46,776 (5.5)	4586 (2.5)	3578 (2.3)	1195 (2.8)
Obesity	355,338 (13.2)	143,394 (16.8)	27,414 (14.8)	22,128 (14.2)	7153.2 (16.8)
Thyroid Dysfunction	495,453 (18.4)	121,424 (14.25)	14,882 (8)	11,480 (7.4)	4149 (9.72)
Obstructive sleep apnea	195,427 (7.3)	84,731.2 (9.9)	14,430 (7.8)	11,565 (7.4)	3673 (8.6)
Electrical cardioversion	386,458 (14.4)	132,616 (15.6)	22,537 (12.2)	19,051 (12.2)	4837 (11.3)
CHA2DS2VASc Score					
0	168,234 (6.3)	80,497 (9.5)	41,160 (22.2)	34,745 (22.3)	10,941 (25.6)

Variable	Without Abuse (2,689,315)	TUD (852,110)	SUD (185,170)	AUD (155,681)	DUD (42,667)
1	354,086 (13.2)	160,896 (18.9)	62,612 (33.8)	54,124 (34.8)	13,722 (32.16)
2	499,746 (18.6)	198,084 (23.3)	42,936 (23.2)	36,650 (23.5)	8705 (20)
>=3	1,667,302 (62)	412,633 (48.4)	38,463 (20.8)	30,161 (19.4)	9299 (21.8)
Charlson's Comorbidity Index					
0	998,579 (37.1)	239,955 (26.2)	70,618 (38.1)	60,977 (39.2)	15,332 (36)
1	755,457 (28.1)	248,203 (29.1)	55,835 (30.2)	47,664.3 (30.6)	12,117 (28.4)
2	436,110 (16.2)	167,244 (19.6)	30,350 (16.4)	24,944.3 (16.0)	7315 (17.1)
>=3	499,221 (18.6)	196,707 (23.1)	28,368 (15.3)	22,096 (14.2)	7903 (18.5)
Hospital-level Characteristics					
Region of the Hospital					
Northeast	588,634 (21.9)	157,460 (18.5)	40,140 (21.7)	34,797 (22.3)	8036 (18.8)
Midwest	661,976 (24.6)	230,076 (27)	40,074 (21.6)	34,048 (21.9)	8734 (20.4)
South	1,045,666 (38.9)	328,662 (38.6)	67,163 (36.3)	56,466 (36.2)	15,208 (35.6)
West	392,903 (14.6)	135,787 (15.9)	37,773 (20.4)	30,350 (20)	10,690 (25)
Hospital Bed Size					
Small	398,144 (14.9)	117,024 (13.8)	26,754 (14.5)	22,727 (14.7)	5933 (14)
Medium	668,824 (25)	220,502 (26)	49,723 (27)	42,011 (27.1)	11,278 (26.6)
Large	1,607,656 (60.1)	510,336 (60.1)	107,666 (58.5)	90,071 (58.2)	25,263 (59.5)
Location of the Hospital					
Rural	389,364 (14.6)	106,388 (12.6)	20,677 (11.2)	17,624 (11.4)	4346 (10.2)
Urban, Nonteaching	1,100,741 (41.2)	339,788 (40.1)	75,276 (40.9)	63,937 (41.3)	16,231 (38.2)
Urban, Teaching	1,184,520 (44.3)	401,685 (47.4)	88,190 (47.9)	73,247 (47.31)	21,895 (51.6)
Median household income category for patient's zip code					
1. 0–25th percentile	669,952 (25.4)	228,195 (27.3)	54,488 (30.5)	44,264 (29.4)	14,866 (36.1)
2. 26–50th percentile	709,693 (27)	224,826 (27)	45,751 (25.6)	38,426 (25.5)	10,650 (25.9)
3. 51–75th percentile	651,437 (25)	207,050 (24.9)	42,771 (23.9)	36,452 (24.2)	9168 (22.3)
4. 76–100th percentile	604,831 (23)	175,363 (22)	35,913 (20.1)	31,320 (20.8)	6452 (15.7)
Payment Type					
Medicare/Medicaid	1,947,167 (72.5)	567,002 (66.7)	98,681 (53.4)	80,383 (51.8)	24,598 (57.8)
Private insurance	630,849 (23.5)	215,899 (25.4)	52,650 (28.5)	46,832 (30.2)	8830 (20.8)
Self pay/no charge/others	107,154 (4)	67,743 (8)	33,317 (18)	28,005 (18)	9131 (21.5)

Variable	Without Abuse (2,689,315)	TUD (852,110)	SUD (185,170)	AUD (155,681)	DUD (42,667)
In-hospital Outcomes					
Stroke	35,355 (1.3)	8924 (1.1)	1762 (1)	1472 (1)	374 (0.9)
In-hospital Mortality	26,753 (1)	5953 (0.7)	1530 (0.8)	1166 (0.75)	438 (1.0)
Discharge to Home	1,971,907 (73.4)	668,381 (78.5)	142,544 (77)	121,483 (78.1)	31,368 (73.6)
Length of Stay (Median, IQR)	3 (1–4)	3 (1–4)	3 (2–5)	3 (2–5)	3 (1–5)
Cost, \$\$ (Median, IQR)	5409 (3366–9363)	5637 (3551–9532)	6037 (3855–9920)	6008 (3848–9790)	6083 (3871–10,226)

SD-Standard Deviation; IQR: Interquartile range; TUD-tobacco use disorder; SUD-substance use disorders; AUD-alcohol use disorders, DUD-drug use disorders.

Table 2

Atrial fibrillation patient characteristics by substance abuse disorders stratified by sex.

Variable	MALE			
	TUD (519,812)	SUD (152,287)	AUD (132,378)	DUD (31,486)
18–35	15,617 (3)	10,136 (6.7)	7118 (5.3)	4601 (14.6)
36–50	51,076 (9.8)	26,902 (17.7)	22,563 (17.0)	7295 (23.1)
51–65	179,858 (34.6)	73,038 (48)	64,416 (48.7)	14,687 (46.5)
66–80	200,661 (38.6)	36,078 (23.7)	33,038 (24.9)	4032 (12.8)
>80	72,601 (13.8)	6132 (4)	5241 (4)	953 (3)
Race				
White	393,822 (75.8)	105,250 (69.1)	93,178 (70.4)	19,597 (62)
Black	35,107 (6.8)	15,916 (10.5)	12,152 (9.2)	5561 (17.6)
Other	90,870 (17.5)	31,121 (20.4)	27,049 (20.4)	6410 (20.3)
Hospital-level Characteristics				
Region of the Hospital				
Northeast	95,692 (18.4)	33,139 (21.8)	29,390 (22.2)	6104 (19.3)
Midwest	139,362 (26.8)	33,261 (21.8)	29,170 (22)	6504 (20.6)
South	202,783 (39)	55,542 (36.5)	48,474 (36.6)	11,056 (35)
West	81,910 (15.8)	30,324 (20)	25,324 (19.1)	7903 (25)
Hospital Bed Size				
Small	69,796 (13.5)	22,019 (14.5)	19,286 (14.7)	4422 (14)
Medium	132,635 (25.7)	40,772 (26.9)	35,641 (27.1)	8344 (26.5)
Large	314,700 (60.9)	88,646 (58.5)	76,692 (58.3)	18,679 (59.4)
Location of the Hospital				
Rural	64,939 (12.6)	16,848 (11.1)	14,946 (11.4)	3053 (9.7)
Urban, Nonteaching	204,953 (39.6)	61,447 (40.6)	54,055 (41.1)	11,726 (37.3)
Urban, Teaching	247,239 (47.8)	73,142 (48.3)	62,618 (47.6)	16,666 (53)
Median household income category for patient’s zip code				
1. 0–25th percentile	138,746 (27.3)	45,111 (30.7)	38,041 (29.8)	11,155 (36.8)
2. 26–50th percentile	137,480 (27.1)	37,570 (25.6)	32,768 (25.7)	7726 (25.5)
3. 51–75th percentile	125,988 (24.8)	35,178 (24)	30,968 (24.2)	6721 (22.1)

MALE					
Variable	TUD (519,812)	SUD (152,287)	AUD (132,378)	DUD (31,486)	
4. 76–100th percentile	106,077 (20.9)	28,932 (20)	25,859 (20.3)	4740 (15.6)	
Payment Type					
Medicare/Medicaid	312,469 (60.2)	75,498 (49.7)	64,836 (49.13)	16,070 (51)	
Private insurance	154,280 (29.7)	46,218 (30.4)	41,520 (31.5)	7458 (23.7)	
Self-pay/no charge/others	52,010 (10)	30,107 (19.8)	25,600 (19.4)	7957 (25.3)	
FEMALE					
Variable	TUD (332,290)	SUD (32,880)	AUD (23,299)	DUD (11,074)	
18–35	2884 (0.9)	1077 (3.3)	599 (2.6)	593 (5.4)	
36–50	14,426 (4.3)	3395 (10.3)	2275 (9.8)	1539 (13.9)	
51–65	76,190 (23)	11,025 (33.5)	8142 (35)	3573 (32.2)	
66–80	152,383 (45.9)	12,177 (37)	9353 (40.1)	3088 (27.8)	
>80	86,406 (26)	5205 (15.8)	2931 (12.6)	2304 (20.8)	
Race					
White	259,881 (78.2)	23,843 (72.5)	17,085 (73.3)	7661 (69)	
Black	23,828 (7.2)	3843 (11.7)	2556 (11)	1639 (14.8)	
Other	48,550 (14.6)	5194 (15.8)	3657 (15.7)	1797 (16.2)	
Hospital-level Characteristics					
Region of the Hospital					
Northeast	61,768 (18.6)	7001 (21.3)	5408 (23.2)	1931 (17.4)	
Midwest	90,706 (27.3)	6808 (20.7)	4874 (21)	2229 (20.1)	
South	125,879 (37.9)	11,621 (35.3)	7991 (34.3)	4152 (37.4)	
West	53,877 (16.2)	7449 (22.3)	5026 (21.6)	2786 (25.1)	
Hospital Bed Size					
Small	47,219 (14.30)	4731 (14.5)	3437 (14.8)	1511 (13.7)	
Medium	87,867 (26.6)	8951 (27.4)	6370 (27.5)	2934 (26.6)	
Large	195,655 (59.2)	19,020 (58.2)	13,379 (57.7)	6584 (59.7)	
Location of the Hospital					
Rural	41,449 (12.5)	3829 (11.7)	2678 (11.6)	1293 (11.7)	
Urban, Nonteaching	134,827 (40.8)	13,825 (42.3)	9878 (42.6)	4506 (40.8)	

MALE					
Variable	TUD (519,812)	SUD (152,287)	AUD (132,378)	DUD (31,486)	
Urban, Teaching	154,446 (46.7)	15,048 (46)	10,629 (45.8)	5229 (47.4)	
Median household income category for patient's zip code					
1. 0–25th percentile	89,445 (27.3)	9377 (29.2)	6223 (27.2)	3711 (34.4)	
2. 26–50th percentile	87,342 (26.7)	8177 (25.5)	5653 (24.8)	2923 (27.1)	
3. 51–75th percentile	81,062 (24.8)	7593 (23.6)	5484 (24)	2446 (22.7)	
4. 76–100th percentile	69,285 (21.2)	6980 (21.7)	5460 (24)	1712 (15.9)	
Payment Type					
Medicare/Medicaid	254,525 (76.7)	23,179 (70.6)	15,544 (66.8)	8528 (77)	
Private insurance	61,620 (18.6)	6432 (19.6)	5311 (22.8)	1372 (12.4)	
Self-pay/no charge/others	15,733 (4.7)	3210 (9.8)	2404 (10.3)	1174 (10.6)	

Table 3
Demographic factors associated with Tobacco or Substance use disorders Among Hospitalized Atrial Fibrillation Patients.

	TUD	SUD	AUD	DUD
Variable				
Age groups				
18–35	Reference	Reference	Reference	Reference
36–50	0.96 (0.94–0.98) [#]	0.74 (0.72–0.75) [#]	0.93 (0.9–0.95) [#]	0.46 (0.44–0.48) [#]
51–65	1.05 (1.03–1.07) [#]	0.59 (0.57–0.6) [#]	0.8 (0.78–0.82) [#]	0.27 (0.26–0.28) [#]
66–80	0.76 (0.75–0.78) [#]	0.17 (0.16–0.17) [#]	0.25 (0.25–0.26) [#]	0.04 (0.04–0.05) [#]
>80	0.42 (0.42–0.44) [#]	0.06 (0.06–0.06) [#]	0.08 (0.07–0.08) [#]	0.03 (0.01–0.01) [#]
Female vs. Male	0.57 (0.56–0.57) [#]	0.27 (0.26–0.27) [#]	0.22 (0.22–0.22) [#]	0.51 (0.5–0.52) [#]
Black vs. White	0.85 (0.84–0.86) [#]	1.12 (1.1–1.14) [#]	1 (0.99–1.02) ^{\$}	1.42 (1.38–1.47) [#]
Region of the Hospital				
Northeast	Reference	Reference	Reference	Reference
Midwest	1.45 (1.44–1.46) [#]	0.88 (0.87–0.9) [#]	0.86 (0.84–0.87) [#]	1.01 (0.98–1.04) [£]
South	1.16 (1.15–1.17) [#]	0.83 (0.82–0.85) [#]	0.81 (0.8–0.83) [#]	0.93 (0.9–0.96) [#]
West	1.34 (1.33–1.35) [#]	1.36 (1.34–1.38) [#]	1.22 (1.2–1.23) [#]	2.05 (1.99–2.1) [#]
Median household income category for patient’s zip code				
1. 0–25th percentile	Reference	Reference	Reference	Reference
2. 26–50th percentile	0.93 (0.92–0.93) [#]	0.85 (0.84–0.86) [#]	0.87 (0.85–0.88) [#]	0.8 (0.78–0.83) [#]
3. 51–75th percentile	0.91 (0.91–0.92) [#]	0.85 (0.83–0.86) [#]	0.87 (0.86–0.89) [#]	0.75 (0.73–0.77) [#]
4. 76–100th percentile	0.84 (0.83–0.85) [#]	0.78 (0.77–0.79) [#]	0.82 (0.8–0.83) [#]	0.63 (0.61–0.65) [#]
Payment Type				
Medicare/Medicaid	Reference	Reference	Reference	Reference
Private insurance	0.71 (0.71–0.71) [#]	0.45 (0.45–0.46) [#]	0.52 (0.51–0.52) [#]	0.27 (0.26–0.27) [#]
Self-pay/no charge/others	1.2 (1.19–1.2) [#]	1.36 (1.34–1.38) [#]	1.46 (1.43–1.48) [#]	1.03 (1.01–1.06) [#]
Hospital Bed Size				

Variable	TUD	SUD	AUD	DUD
	Reference	Reference	Reference	Reference
Age groups				
Small	Reference	Reference	Reference	Reference
Medium	1.08 (1.07–1.09) #	0.99 (0.97–1) β	0.99 (0.97–1) $\&$	0.99 (0.96–1.02) $\&$
Large	1.02 (1.02–1.04) #	0.85 (0.84–0.86) #	0.84 (0.83–0.85) #	0.89 (0.87–0.92) #
Location of the Hospital				
Rural	Reference	Reference	Reference	Reference
Urban, Nonteaching	1.15 (1.14–1.16) #	1.19 (1.17–1.21) #	1.17 (1.15–1.2) #	1.22 (1.18–1.27) #
Urban, Teaching	1.25 (1.24–1.26) #	1.15 (1.13–1.17) #	1.09 (1.08–1.12) #	1.39 (1.34–1.44) #

#: $P < 0.001$.

β : $P = 0.124$.

$\$$: $P = 0.034$.

$\&$: $P = 0.1$.

\mathcal{L} : $P = 0.521$.

\mathcal{F} : $P = 0.078$.