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The association between alcohol use, all-cause, and cardiovascular disease-related hospitalizations or death in older, high-risk Veterans

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Abstract

Background: The prevalence of alcohol misuse among older adults has dramatically grown in the past decade, yet little is known about the association between alcohol misuse and hospitalization and death in this patient population.

Methods: We examined the association between alcohol use (measured by a screening instrument in primary care) and 6-month hospitalization or death (all-cause and cardiovascular disease (CVD)-related) via electronic health records (EHR) in a nationally representative sample of older, high-risk Veterans. Models were adjusted for sociodemographic and clinical characteristics, including frailty and comorbid conditions.

Results: The all-cause hospitalization or death rate at 6 months was 14.9%, and the CVD-related hospitalization or death rate was 1.8%. In adjusted analyses, all-cause hospitalization or death was higher in older Veterans that were non-drinkers or harmful use drinkers compared to moderate use drinkers, but CVD-related hospitalization or death was similar in all categories of drinking.

Conclusions: These findings suggest that the complex association between alcohol and allcause acute care utilization found in the broader population is similar in older, high-risk Veteran

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patients. These findings did not support any association between alcohol and CVD-specific hospitalizations.

Keywords

Veterans; alcohol; screening; hospitalizations; cardiovascular disease

INTRODUCTION

Alcohol misuse refers to hazardous drinking that ranges from consumption above recommended limits to maladaptive patterns of consumption and dependence associated with alcohol use disorder (AUD; Friedman, 2013; Schuckit, 2009). Alcohol misuse is the third leading cause of preventable deaths in the U.S., and accounts for over \$25 billion per year in annual health care related expenses (Stahre, Roeber, Kanny, Brewer, & Zhang, 2014; Bouchery, Harwood, Sacks, Simon, & Brewer, 2011).

The association between alcohol use, misuse, and healthcare utilization has been demonstrated in numerous settings, including Veterans Administration (VA) hospitals. Severe alcohol misuse has been associated with increased risk of gastrointestinal-related hospitalizations (Au, Kivlahan, Bryson, Blough, & Bradley, 2007; Lembke, Bradley, Henderson, Moos, & Harris, 2011) and trauma-related hospitalizations (Harris, Bryson, Sun, Blough, & Bradley, 2009; Williams, Bryson, Sun, Chew, Chew et al., 2012). Severe alcohol misuse has also been associated with longer and more complicated post-operative hospital stays in patients admitted for major noncardiac operations (Bradley, Harwood, Sacks, Simon, & Brewer, 2011; Rubinsky, Sun, Blough, Maynard, Bryson et al., 2012), intensive care unit admission and readmission (Clark, Rubinsky, Ho, Au, Chavez et al., 2016), and ambulatory care sensitive hospitalizations (Chew, Bryson, Au, Maciejewski, & Bradley, 2011).

Much of this work on the association between alcohol use, misuse, and healthcare utilization includes a large proportion of older adults, who represent the fastest growing demographic of people engaging in alcohol use, alcohol misuse, binge drinking, and diagnosis of AUD (Grant, Chou, Saha, Pickering, Kerridge et al., 2017; Han, Moore, Ferris, & Palamar, 2019). Older adults also have the highest rate of hospital admissions and deaths (the two outcomes used to define "high-risk"), so it is important to determine how alcohol use and misuse may contribute to all-cause hospitalization and death specifically in those who are at high risk for those outcomes. Additionally, severe alcohol misuse is associated with increased cardiovascular disease (CVD)-related mortality two-fold (Roerecke & Rehm, 2014), whereas moderate alcohol use may be associated with reduced CVD risk (Wood, Kaptoge, Butterworth, Willeit, Warnakula et al., 2018; Zhao, Stockwell, Roemer, Naimi, & Chikritzhs, 2017). However, the association between alcohol use, misuse, and CVD-related hospitalizations is unknown despite CVD being the number one cause of mortality in the U.S. and the leading cause of hospital admission (Mozaffarian, Benjamin, Go, Arnett, Blaha et al., 2015).

The Veterans Health Administration (VHA), the largest integrated health care system, has implemented yearly alcohol use screenings via the three-item Alcohol Use Disorders

Identification Test (AUDIT-C) since 2004 (Williams, Johnson, Lapham, Caldeiro, Chew et al., 2011). The current study leverages these data by examining the association between different levels of alcohol use (including varying degrees of misuse) and both all-cause and CVD-related hospitalization or death in a population of Veterans at high risk for hospitalization or death.

Specifically, examination of alcohol use in the current high-risk sample is important for four reasons: 1) this high-risk sample provides an exceptionally high prevalence of a rare, but important outcome of 6-month hospitalization or death; 2) the increasing number of health conditions in older adults (i.e., the conditions that define our "high risk" sample) put older adults at disproportionately greater risk for problems due to alcohol misuse, 3) the prevalence of alcohol use and misuse in older adults is growing more quickly than any other demographic (Grant, Chou, Saha, Pickering, Kerridge et al., 2017; Han, Moore, Ferris, & Palamar, 2019, cited in the manuscript).; and 4) older adults are rarely a focus of alcohol-related research, and no work has investigated the increased risk of alcohol misuse across the spectrum of patients considered "high risk." Examining the association between alcohol use, misuse, and CVD-related health care utilization will begin to provide evidence about the strength of this association. Further, examining the association between patient-reported alcohol use, misuse, and all-cause acute care utilization in a high-risk population can help inform the degree to which effective alcohol misuse interventions may reduce such utilization.

METHODS

Study Design and Population

As part of a larger survey project focusing on "high-risk" VA patients in partnership with VA's Office of Primary Care (Zulman, Maciejewski, Grubber, Weidenbacher, Blalock et al., 2020), we created a nationally-representative sample of 10,000 Veterans from 18 VA Veterans Integrated Services Networks (VISNs). Each Veteran in the sample had at least one VA outpatient visit from 3/20/17-3/18/18, and were considered "high risk," as defined by a 1-year risk of hospitalization or death on 3/16/18 that was 75th percentile based on the VA's Care Assessment Need (CAN) score (Wang, Porter, Maynard, Evans, Bryson et al., 2013). The CAN score estimates probability of hospitalization or death within one year and is calculated based on demographics, medical conditions, vital signs, prior vear Veteran Health Administration (VHA) health services utilization, medications dispensed, and laboratory results. PROC SURVEYSELECT in SAS v9.4 was used to obtain this nationally representative sample by randomly sampling within each VA Medical Center (using sta3n) proportional to the number of Veterans in that VA Medical Center with CAN score 75. The analytic sample for this paper comprises the 9,794 individuals (97.9% of the full sample) with an EHR-documented AUDIT-C.(required annually in VA) in the two years prior to the index date.

For analyses regarding CVD-related hospitalization or death, we excluded Veterans who died in the 6-month period for whom we were unable to determine a cause of death (n = 34). These were Veterans who died outside of a VA hospital; their VA data revealed that they

had died, but data from the Master Death Index which details the cause of death was not yet available.

Measures

Independent Variable – Alcohol Screening Categories via the AUDIT-C—All Veterans who receive care within the VHA system are supposed to be screened annually for alcohol use with the 3 question AUDIT-C. The AUDIT-C is a validated screen for alcohol misuse that asks about past year drinking. It contains one question assessing drinking frequency, one question assessing the number of drinks per typical drinking occasion, and one question assessing frequency of drinking 6 or more drinks on one occasion (Bush, Kivlahan, McDonell, Fihn, & Bradley, 1998; Bradley, Bush, Epler, Dobie, Davis et al., 2003).

The three items have scores 0–4 that are summed to produce a total score ranging from 0 to 12 points. A score of 0 denotes abstinence in the past year. Prior research has established scores of 1-3 (for men) and 1-2 (for women) to represent moderate use, scores of 4-7 (for men) and 3-7 (for women) to represent hazardous use, and scores of 8-12 to represent harmful use (Dawson, Grant, Stinson, & Zhou, 2005).

An AUDIT-C does not distinguish former drinkers who quit more than one year prior from lifetime abstainers, who may differ markedly in the number and severity of their medical comorbidities (Au et al., 2007). To account for this, we examined the interaction between AUDIT-C and presence of AUD diagnosis in Veterans' electronic health records (EHR). The most recent AUDIT-C scores for each Veteran in the two-year period prior to the data pull date of 3/17/18 were obtained from the EHR.

Outcome Variables – All-cause and CVD-related hospitalization or death—The primary outcome was a composite variable of 6-month hospitalization or death. From a health system policy standpoint, a 6-month outcome window (or shorter) represents a period of time in which outcomes may be more modifiable, and changes in outcomes can be more clearly linked to specific interventions and programs. All-cause hospitalizations also represent a high-cost, high-impact services utilization metric for all healthcare organizations. To additionally capture the risk of severe outcomes from the patient side, as opposed to just a measure of healthcare utilization alone, the most severe outcome of death is also incorporated into the primary outcome.

VHA EHR data, accessed through the VA corporate data warehouse (CDW), was used to identify all-cause VA inpatient hospitalizations within 180 days after the AUDIT-C pull date of 3/17/18. All-cause death was identified via the presence of a death date during this same time period in the EHR.

Consistent with previous investigations (Sidney, Sorel, Quesenberry Jr, DeLuise, Lanes et al., 2005; Krumolz, Normand, & Wang, 2014), CVD-related hospitalization or death was indicated if primary diagnosis associated with an inpatient stay or inpatient death was any of the following codes: ventricular tachycardia (VT)/ ventricular fibrillation (VF)/cardiac arrest (International Classification of Diseases, 10th revision [ICD-10] codes I46.2 and I49.0),

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Covariates—Age, race, gender, and marital status at the time of sampling; and smoking status and AUD diagnosis in the year prior to sampling date were obtained from VA CDW data for purpose of descriptive information and adjustment for potential confounding. Because of our older, high risk sample of Veterans, three additional covariates associated with hospitalization and death were captured: 1-year risk of hospitalization or death via the CAN score (as described earlier), past year JEN frailty index (a composite of diagnostic codes related to frailty or frailty risk that predict the need for long-term institutionalization or support; JFI; Kinosian, Wieland, Gu, Stallard, Phibbs et al., 2018), and the presence of chronic conditions included in the past year Gagne comorbidity score (a comorbidity score that considers both Charlson and Elixhauser comorbidity scores with improved predictive capability; Gagne, Glynn, Avorn, Levin, & Schneeweiss, 2011). We calculated the overall Gagne comorbidity score from these 37 conditions, including other drug use disorders (see Appendix for complete list of comorbidities and weight), removing AUD as it is accounted for separately in our models. All covariates were pulled from EHR.

Statistical Analysis

All analyses were conducted using SAS version 9.4 (SAS Institute, 2015). Demographic and clinical characteristics were examined overall, and by the AUDIT-C category as described above (Dawson et al., 2005). Unadjusted and adjusted logistic regression models were used to estimate odds ratios and 95% confidence intervals for the association between AUDIT-C and our composite outcome of hospitalization or death within 6 months of index date (vs. no hospitalization or death within 6 months of index date). Inferences from the models are limited to results that do not include 1.00 in the 95% confidence intervals. Models predicting all-cause hospitalization or death and CVD-related hospitalization or death within 6 months were run separately, controlling for age, race, gender, marital status, smoking status, AUD diagnosis, 1-year CAN score, JFI score, and Gagne score. Patients with hospitalization or death due to non-CVD causes were removed from the reference group in the CVD-related models to prevent the potential for competing risks to impact the associations of interest. We evaluated the continuous variables for non-linear associations with the logit of hospitalization or death using the PSPLINET macro and included variables with non-linear associations in the models as cubic splines (Harrell, 1985). A non-linear association was only observed with age, so age was included as a cubic spline in all adjusted models.

A sensitivity analysis was conducted, modifying the AUDIT-C strata to those of the 2015 VHA/DoD Clinical Practice Guidelines for the Treatment of Substance Use Disorders. For VHA, scores of 1–4 (irrespective of sex) denote moderate alcohol use, 5–7 hazardous

alcohol use, and 8–12 harmful alcohol use, providing a comparison between VHA-related and non-VHA cutoffs.

An additional sensitivity analysis was run to determine whether results changed due to EHR diagnostic data that conflicted with self-reported alcohol use (i.e., EHR indication of an active AUD diagnosis, but AUDIT-C score indicative of no or minimal alcohol use). This was done to explore the potential influence of the "sick quitter" effect where some Veterans reporting an AUDIT-C of 0 may have recently become abstinent due to medical complications (Shaper, Wannamethee, & Walker, 1988). Because evidence on "sick quitters" is complex in terms of effects on utilization (Bares & Kennedy, 2020; Gordon, McGinnis, Dao, Rentsch, Small et al., 2020), this sensitivity analysis was aimed at first determining *if* a distinction needed to be made, followed by examining results across levels of this distinction. Models were run including an interaction term (AUDIT-C*AUD) to assess whether AUD (presence vs. absence) was an effect modifier of the association between 6-month hospitalization or death and AUDIT-C score to determine if separate models would be needed for Veterans with an active AUD diagnosis. This interaction term was null, so Veterans with an active AUD diagnosis were retained in the results.

RESULTS

As shown in Table 1, 59.1% of the sample were non-drinkers (AUDIT-C=0), 27.7% were moderate use drinkers (Mean AUDIT-C=1.60, SD=0.76), 8.3% were hazardous use drinkers (Mean AUDIT-C=4.58, SD=1.00), and 2.8% were harmful use drinkers (Mean AUDIT-C=10.08, SD=1.48). Mean AUDIT-C across the entire sample was 1.13 (SD=2.11). Across all drinking groups, Veterans were predominantly male, white non-Hispanic, and older (>65 years old, except for the most severe drinking category).

Within 6 months of the index date, 14.9% (n=1459) of Veterans had an all-cause hospitalization or death and 1.8% (n=184) had a CVD-related hospitalization or death. Specifically, 11.2% (n=1096) were hospitalized and 3.7% (n=363) died within 180 days. Unadjusted all-cause hospitalization or death resembled a "J-Curve" across drinking categories (see Figure 1), with 15.9% of non-drinkers, 12.2% of moderate use drinkers, 13.8% of hazardous use drinkers, and 22.7% of harmful use drinkers having an all-cause hospitalization or death. CVD-related hospitalization or death rates were low and did not exhibit a distinguishable curve. At 6 months, 2.1% of non-drinkers, 1.5% of moderate use drinkers had a CVD-related hospitalization or death.

Compared to moderate use drinkers (Table 2), non-drinkers (OR=1.36, 95% C.I.[1.19, 1.55]) and harmful use drinkers (OR=2.10, 95% C.I.[1.55, 2.85]) had higher odds of 6-month all-cause hospitalization or death in unadjusted analyses. In adjusted analyses, non-drinkers (OR=1.19, 95% C.I.[1.03, 1.37]) and harmful use drinkers (OR=1.57, 95% C.I.[1.12, 2.19]) continued to have higher odds of 6-month all-cause hospitalization or death than moderate use drinkers.

Compared to moderate use drinkers, non-drinkers had higher odds (*OR*=1.50, *95% C.I.* [1.05, 2.15]) of 6-month CVD-related hospitalization or death in unadjusted analyses. In adjusted analyses, odds of 6-month CVD-related hospitalization or death were similar in all AUDIT-C groups.

Adjusted results from the sensitivity analysis that applied VA-related AUDIT-C cutoffs were consistent with the primary results using lower, gender-specific AUDIT-C cutoffs (Table 3).

DISCUSSION

In an analysis of the association between 6-month all-cause and CVD-related hospitalization or death and alcohol use screening scores, we found that older Veterans who were at high risk for hospitalization or death but with no current alcohol use or hazardous alcohol use had higher odds of 6-month all-cause hospitalization or death compared to moderate use drinkers. We found no association between alcohol use and 6 month CVD-related hospitalization or death.

These data in older, high-risk Veterans complement previous findings in the general VA population among Veterans with specific causes of hospitalization. In particular, when compared to moderate use drinkers, non-drinkers and harmful use drinkers have exhibited decreased risk of ambulatory care hospitalizations in a sample of younger, lower-risk Veterans (Chew et al., 2011). Two other samples of non-drinkers and harmful use drinkers have also exhibited increased risk of hospital readmission in intensive care unit Veterans at 30 days and 1 year compared to moderate use drinkers (Clark et al., 2016), and increased risk of GI-related hospitalization compared to moderate use drinkers (Lembke et al., 2011).

This extension to previous work predicting hospitalization or death from different levels of alcohol use is important for two reasons: 1) as alcohol use and misuse continues to increase in older adults, it is important to determine how alcohol contributes to their increased risk of hospitalization and death, and 2) CVD is a prominent contributor to health problems in older adults, and so any evidence about the association between increased alcohol use or misuse in this population and CVD-related health outcomes is particularly important.

The reduced risk of all-cause hospitalization or death in moderate use drinkers is consistent with prior epidemiological evidence suggesting a "protective" association between low/ moderate levels of alcohol consumption and mortality (Di Castelnuovo, Costanzo, Bagnardi, Donati, Iacoviello et al., 2006; Rehm, Shield, Roerecke, & Gmel, 2016). This "J-Curve" effect has also been more recently observed in an older adult sample in Europe (van den Brandt & Brandts, 2020). It is important to note, however, that much recent work has questioned the validity of any "protective" effects inferred from epidemiological data due to methodological biases such as immortal time bias and poor study designs(Stockwell, Zhao, Panwar, Roemer, Naimi et al., 2016; Zhao et al., 2017). Even still, zero alcohol consumption is still the most universally recommended threshold to minimize all risks (e.g., cancer, stroke) associated with alcohol consumption (GBD 2016 Alcohol Collaborators, 2018).

Our failure to observe an association between any level of drinking and CVD-related hospitalization or death is particularly surprising given the increased risk for CVD and

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CVD-related health problems in older adults. In the general population, harmful alcohol use is a risk factor for CVD-related mortality, increasing risk up to two-fold (Roerecke & Rehm, 2014). Additionally, CVD is the most proximate cause for over 26% of alcoholattributable deaths (Rehm et al., 2016). It may be that the specific high-risk nature of this older adult sample (CAN score 75) was associated with increased prevalence of other competing health problems, decreasing the relative importance of CVD as a risk factor in this particular population. Some evidence for this decreased relative importance can be seen in the relatively low percentage of 6-month hospitalizations that were attributable to CVD-related causes.

There are several limitations to this study. First, these results may not be generalizable outside of the sample of older, high-risk and predominantly male Veterans. It is possible that either the combination of being older and low risk (i.e., CAN Score < 75), or the combination of being high-risk and younger, may lead to findings different from ours; however, the two classifications of age and risk of hospitalization or death share a high degree of overlap. The low number of women Veterans in the current sample also precluded examination of sex-related hospitalization risk estimates. Future examinations would benefit from over-sampling of women Veterans. Second, the limited number of observations in CVD-related hospitalizations and potential for the comparisons presented to still include patients whose hospitalization or death was due to competing risks may minimize our ability to draw inferences about both the magnitude and significance of the association between hospitalization or death and different levels of alcohol use. Third, while our high-risk sample is likely to have more instances of hospitalization or death in a shorter timeframe, longerterm follow-up would provide additional relevant information about risk. Fourth, evaluation of the "sick quitters" hypothesis with EHR data was limited to active AUD diagnosis, which is likely an imperfect metric to evaluate lifetime alcohol misuse due to substantial variability in how clinicians assign diagnoses and the persistence of AUD diagnoses in EHR after AUD remission. Future studies should seek to corroborate this information with additional data on lifetime prevalence of alcohol misuse or AUD. Finally, the association between no current alcohol use and increased all-cause hospitalization or death in comparison to moderate alcohol use may still be subject to some residual confounding, as noted in some arguments against any protective effects of alcohol consumption, since several negative health outcomes (e.g., cancer and stroke) are at increased risk with any level of alcohol consumption (Keyes, Calvo, Ornstein, Rutherford, Fox, et al., 2019; Stott, 2020).

Conclusions

Taken together, this study provides evidence that increased risk for all-cause hospitalization or death in older, high-risk Veterans who report no current drinking or harmful alcohol use may be higher than those who report a range of drinking behaviors that are typically combined under the category of "moderate alcohol use." Importantly, however, the current study design is not able to determine if this association is causal. This association also represents risk estimates across a range of low, moderate, and high drinking behaviors that are typically combined but may confer differing amounts of risk themselves. As the proportion of older adults who use and misuse alcohol continues to grow, it will become increasingly important to attend to associated risks (or lack thereof) in this group. It will also

be important to continue to explore the comparisons driving these risks (such as comparing harmful use drinkers to non-drinkers instead of moderate use drinkers). These associations may inform the urgency of impressing population-level interventions for alcohol misuse on older adults, or the potential need for targeted alcohol intervention in older adults within certain risk stratifications (Blalock, Calhoun, Crowley, & Dedert, 2019).

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure 1.

Unadjusted All-Cause (n=9794) and CVD-related (n=8521) VA Hospitalization or Death Rates by Audit-C Drinking Category

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| Misuse Category |
|--------------------|
| Alcohol |
| Recent |
| ' Most |
| Characteristics by |
| Sample |

| | | | | | AUDIT-0 | C Alcoho | l Use Ca | $\operatorname{ategory}^{b}$ | | | | |
|--------------------------------------|----------------------|---------|------|--------------|-------------|----------------|-------------|------------------------------|------------|--------------|------------|--------------|
| Patient Characteristics | Total ^a (| N=9794) | ĭ≡N) | one 5911) | Σ=N) poM | erate 2772) | Haza (N= | rdous 833) | Har (N= | mful 278) | Unk (N= | nown 206) |
| | N | (%) | Ν | (%) | N | (%) | N | (%) | N | (%) | N | (%) |
| Demographic | | | | | | | | | | | | |
| Age (mean, (SD)) | 67.4 | (13.7) | 69.2 | (13.1) | 65.3 | (14.1) | 65.3 | (14.2) | 57.1 | (13.6) | 71.0 | (13.9) |
| Sex | | | | | | | | | | | | |
| Female | 802 | (8.2) | 470 | (8.0) | 254 | (9.2) | 99 | (0.7) | 12 | (4.3) | 13 | (6.3) |
| Male | 8992 | (91.8) | 5441 | (92.0) | 2518 | (90.8) | 767 | (92.1) | 266 | (95.7) | 193 | (93.7) |
| Race | | | | | | | | | | | | |
| White Non-Hispanic | 6573 | (67.1) | 3979 | (67.3) | 1856 | (67.0) | 549 | (62.9) | 189 | (68.0) | 151 | (73.3) |
| Nonwhite | 2780 | (28.4) | 1653 | (28.0) | 803 | (29.0) | 244 | (29.3) | 80 | (28.8) | 47 | (22.8) |
| Unknown | 441 | (4.5) | 279 | (4.7) | 113 | (4.1) | 40 | (4.8) | 6 | (3.2) | 8 | (3.9) |
| Married | | | | | | | | | | | | |
| Yes | 4393 | (44.9) | 2756 | (46.6) | 1219 | (44.0) | 334 | (40.1) | 84 | (30.2) | 106 | (51.5) |
| No | 5395 | (55.1) | 3153 | (53.3) | 1550 | (55.9) | 498 | (59.8) | 194 | (69.8) | 100 | (48.5) |
| Missing | 9 | (0.1) | 2 | (0.0) | 3 | (0.1) | 1 | (0.1) | 0 | (0.0) | 0 | (0.0) |
| Clinical | | | | | | | | | | | | |
| Alcohol Use Disorder (AUD) Diagnosis | | | | | | | | | | | | |
| Yes | 1308 | (13.4) | 456 | (7.7) | 336 | (12.1) | 303 | (36.4) | 213 | (76.6) | 15 | (7.3) |
| No | 8486 | (86.6) | 5455 | (92.3) | 2436 | (87.9) | 530 | (63.6) | 65 | (23.4) | 191 | (92.7) |
| Smoking Status | | | | | | | | | | | | |
| Current | 2275 | (23.2) | 1168 | (19.8) | 707 | (25.5) | 268 | (32.2) | 132 | (47.5) | 27 | (13.1) |
| Former | 2082 | (21.3) | 1314 | (22.2) | 584 | (21.1) | 152 | (18.2) | 32 | (11.5) | 42 | (20.4) |
| Never Smoker/Non-smoker | 2696 | (27.5) | 1779 | (30.1) | 693 | (25.0) | 175 | (21.0) | 46 | (17.6) | 50 | (24.3) |
| No Smoking Health Factor | 1803 | (18.4) | 1103 | (18.7) | 504 | (18.2) | 167 | (20.0) | 29 | (10.4) | 75 | (36.4) |
| Unknown ^c | 938 | (9.6) | 547 | (9.3) | 284 | (10.2) | 71 | (8.5) | 36 | (12.9) | 12 | (5.8) |

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| | | | | | AUDIT | C Alcoho | l Use C | ategory ^b | | | | |
|--|-----------------------|---------|-------------|--------------|-------------|----------------|-------------|----------------------|------------|--------------|------------|--------------|
| Patient Characteristics | Total ^a (1 | V=9794) | Σ Σ Υ | one (911) | Mod (N=X | erate 2772) | Haza (N= | rdous 833) | Har (N= | mful 278) | Unk (N= | nown 206) |
| | N | (%) | N | (%) | N | (%) | N | (%) | N | (%) | N | (%) |
| JEN Frailty Index (JFI) ^d (mean, (SD) | 4.4 | (1.8) | 4.5 | (1.9) | 4.2 | (1.8) | 4.0 | (1.8) | 4.4 | (1.9) | 4.0 | (2.0) |
| Gagne Score ^e (mean, (SD)) | 1.5 | (2.0) | 1.7 | (2.0) | 1.3 | (1.8) | 1.0 | (1.7) | 0.8 | (1.5) | 1.6 | (1.8) |
| 1-Year CAN Score (mean, (SD)) | 85.5 | (7.7) | 86.0 | (7.8) | 84.5 | (7.4) | 84.7 | (7.5) | 87.9 | (8.0) | 85.0 | (7.3) |

 a Total patients with non-missing AUDIT-C values

^bAUDIT-C categorization based on most recent AUDIT-C score available in the two years prior to data sampling date: None (0); Moderate (female 1-2, male 1-3); Hazardous (female 3-7, male 4-7); Harmful (8-12).

^c"Unknown" refers to patients with a smoking-related Health Factor where Current, Former, or Never Smoker status was unable to be coded.

 $d_{\rm A}$ dditional missing values for JFI: none (n=49); low (n=22); moderate (n=7); severe (n=2); missing (n=2).

e Gagne comorbidity score calculated from 37 conditions, removing AUD as it is accounted for separately in our models. All covariates were pulled from EHR.

Table 2.

6-Month Hospitalization or Death Odds Ratios by Alcohol Use Category

| | Unadjusted Model (n=9794) | Adjusted Model (n=9708) |
|--|--------------------------------------|--------------------------------------|
| 6-month All-Cause Hospitalization or Death | Odds Ratio [95% confidence interval] | Odds Ratio [95% confidence interval] |
| Alcohol Use | | |
| AUDIT-C = Non-Drinker | 1.36 [1.19, 1.55] | 1.19 [1.03, 1.37] |
| AUDIT-C = Moderate Use | 1.00 (Ref) | 1.00 (Ref) |
| AUDIT-C = Hazardous Use | 1.15 [0.92, 1.44] | 1.15 [0.91, 1.47] |
| AUDIT-C = Harmful Use | 2.10 [1.55, 2.85] | 1.57 [1.12, 2.19] |
| AUD Diagnosis $^{\dot{\tau}}$ (vs. no Diagnosis) | — | 1.07 [0.89, 1.28] |
| Age | _ | Cubic Spline [‡] |
| Male (vs. Female) | _ | 1.18 [0.92, 1.51] |
| White (vs. Non-White) | _ | 0.93 [0.83, 1.05] |
| Married (vs. Not Married) | _ | 0.98 [0.87, 1.11] |
| Smoking Status | | |
| Never Smoker | _ | 1.00 (Ref) |
| Former Smoker | — | 1.05 [0.89, 1.25] |
| Current Smoker | — | 1.35 [1.14, 1.60] |
| No Smoking Status | — | 1.17 [0.97, 1.40] |
| Unknown | — | 1.26 [1.02, 1.55] |
| JFI | — | 1.12 [1.08, 1.17] |
| Gagne (Without AUD Diagnosis) | — | 1.06 [1.03, 1.10] |
| 1-Year CAN Score | _ | 1.07 [1.06, 1.08] |
| | C Statistic = 0.54 | C Statistic = 0.70 |
| | Unadjusted Model (n=8521) | Adjusted Model (n=8440) |
| 6-month CVD-related Hospitalization or Death | Odds Ratio [95% confidence interval] | Odds Ratio [95% confidence interval] |
| Alcohol Use | | |
| AUDIT-C= Non-Drinker | 1.50 [1.05, 2.15] | 1.25 [0.87, 1.80] |
| AUDIT-C= Moderate Use | 1.00 (Ref) | 1.00 (Ref) |
| AUDIT-C= Hazardous Use | 1.16 [0.63, 2.14] | 1.42 [0.76, 2.66] |
| AUDIT-C= Harmful Use | 0.83 [0.25, 2.70] | 1.10 [0.32, 3.81] |
| AUD Diagnosis (vs. no Diagnosis) | _ | 0.61 [0.34, 1.10] |
| Age | — | Cubic Spline ## |
| Male (vs. Female) | _ | 3.40 [1.06, 10.87] |
| White (vs. Non-White) | — | 0.83 [0.62, 1.11] |
| Married or Cohabitating (vs. Not) | — | 0.91 [0.67, 1.24] |
| Smoking Status | | |
| Never Smoker | _ | 1.00 (Ref) |

| | Unadjusted Model (n=9794) | Adjusted Model (n=9708) |
|--|--------------------------------------|--------------------------------------|
| 6-month All-Cause Hospitalization or Death | Odds Ratio [95% confidence interval] | Odds Ratio [95% confidence interval] |
| Former Smoker | - | 1.44 [0.96, 2.17] |
| Current Smoker | - | 1.08 [0.68, 1.74] |
| No Smoking Status | - | 1.21 [0.75, 1.95] |
| Unknown | - | 1.45 [0.87, 2.42] |
| JFI | _ | 1.07 [0.97, 1.18] |
| Gagne (Without AUD Diagnosis) | - | 1.12 [1.04, 1.20] |
| 1-Year CAN Score | | 1.07 [1.04, 1.10] |
| | C Statistic = 0.55 | C Statistic = 0.74 |

Notes. Adjusted model controls for age, race, gender, marital status, smoking status, JFI, Gagne, and 1-Year CAN. Age entered into model as cubic spline due to non-linear association with hospitalization or death logit. "Unknown" refers to patients with a smoking-related Health Factor where Current, Former, or Never Smoker status was unable to be coded. 95% Confidence Intervals in parentheses.

 $^{\neq}$ Wald χ^2 =14.49, p<.01.

^{##}Wald χ^2 =4.38, p=.22.

 † Interaction between AUD diagnosis and Audit-C category was not significantly associated with hospitalization or death; analyses were not stratified by AUD diagnosis.

Table 3.

Odds of 6-Month All-Cause or CVD-related VA Admission Based on VA-related Audit-C Cutoffs

| | Unadjusted Model (n=9794) | Adjusted Model (n=9708) |
|--|--------------------------------------|--------------------------------------|
| 6-month All-Cause Hospitalization or Death | Odds Ratio [95% confidence interval] | Odds Ratio [95% confidence interval] |
| Alcohol Use | | |
| AUDIT-C = 0 | 1.35 [1.19, 1.53] | 1.17 [1.03, 1.34] |
| AUDIT-C = 1-4 | 1.00 (Ref) | 1.00 (Ref) |
| AUDIT-C = 5-7 | 1.37 [0.99, 1.90] | 1.28 [0.91, 1.81] |
| AUDIT-C = 8-12 | 2.10 [1.55, 2.83] | 1.56 [1.12, 2.17] |
| | C Statistic = 0.54 | C Statistic = 0.70 |
| | | |
| | Unadjusted Model (n=8521) | Adjusted Model (n=8440) |
| 6-month CVD-related Hospitalization or Death | Odds Ratio [95% confidence interval] | Odds Ratio [95% confidence interval] |
| Alcohol Use | | |
| AUDIT-C = 0 | 1.47 [1.06, 2.04] | 1.19 [0.85, 1.67] |
| AUDIT-C = 1-4 | 1.00 (Ref) | 1.00 (Ref) |
| AUDIT-C = 5-7 | 1.14 [0.45, 2.87] | 1.47 [0.56, 3.83] |
| AUDIT-C = 8-12 | 0.81 [0.25, 2.61] | 1.05 [0.31, 3.59] |
| | C Statistic $= 0.55$ | C Statistic $= 0.74$ |

Notes. Adjusted model controls for age, race, gender, marital status, smoking status, JFI, Gagne, and 1-Year CAN in the same manner as models reported in Table 2. Age entered into model as cubic spline due to non-linear association with hospitalization or death logit. 95% Confidence Intervals in parentheses.