MAYO CLINIC

ORIGINAL ARTICLE

Medications and Patient Factors Associated With Increased Readmission for Alcohol-Related Diagnoses

Joseph C. Osborne, II, PharmD; Susan E. Horsman, PharmD, BCPS; Kristin C. Mara, MS; Thomas C. Kingsley, MD, MPH; Robert W. Kirchoff, MD; and Jonathan G. Leung, PharmD, BCPS, BCPP

Abstract

Objective: To investigate medication factors and patient characteristics associated with readmissions following alcohol-related hospitalizations.

Patients and Methods: Adult patients admitted from September 1, 2016, through August 31, 2019, who had an alcohol-related hospitalization were identified through electronic health records. Patient characteristics and medications of interest administered during hospitalization or prescribed at discharge were identified. Medications of interest included US Food and Drug Administration–approved medications for alcohol use disorder, benzodiazepines, barbiturates, gabapentin, opioids, and muscle relaxants. The primary outcome was to identify medications and patient factors associated with 30-day alcohol-related readmission. Secondary outcomes included medications and patient characteristics associated with multiple alcohol-related readmissions within a year from the index admission (ie, two or more readmissions) and factors associated with 30-day all-cause readmission.

Results: Characteristics of the 932 patients included in this study associated with a 30-day alcohol-related readmission included younger age, severity of alcohol withdrawal, history of psychiatric disorder, marital status, and the number of prior alcohol-related admission in the previous year. Benzodiazepine or barbiturate use during hospitalization or upon discharge was associated with 30-day alcohol-related readmission (P=.006). Gabapentin administration during hospitalization or upon discharge was not associated with 30-day alcohol-related readmission (P=.079).

Conclusion: The findings reinforce current literature identifying patient-specific factors associated with 30-day readmissions. Gabapentin use was not associated with readmissions; however, there was an association with benzodiazepine/barbiturate use.

 ■ Mayo Clin Proc Inn Qual Out 2022;6(1):1-9

Chronic alcohol consumption or a diagnosis of alcohol use disorder (AUD) has a causal role in more than 200 health conditions.[1] According to the 2018 National Survey on Drug Use and Health, 9.2 million men and 5.3 million women qualified as having AUD with 88,000 yearly alcohol deaths in the United States alone.[2] Moreover, AUD in the United States is linked with a significant economic burden correlated with alcohol misuse costing $249 billion in 2010.[3] Chronic alcohol consumption has been connected to an increased risk of hospital readmission rates; thus, it is likely compounding the financial impact on health systems.[4–8]

Many studies have identified patient characteristics associated with readmission risk. Patient-specific factors such as race, age, patient reported gender, body mass index (BMI), socioeconomic status, comorbid psychiatric illness, concomitant substance or tobacco use, hospital length of stay (LOS), and medical insurance status have been recognized as significant predictors of readmission risk.[4–10] Various screening tools have also been used to classify patients at a higher readmission probability following an

From the Department of Pharmacy (J.C.O., S.E.H., J.G.L.), Division of Biomedical Statistics and Informatics (K.C.M.), and the College of Medicine (T.C.K., R.W.K.), Mayo Clinic, Rochester, MN.

alcohol-related diagnosis including the Drug Abuse Screening Test and Alcohol Use Disorders Identification Test; length of stay, acuity of admission, comorbidities, emergency department visits (LACE) index; and Charlson comorbidity index (CCI).[11−14] Despite studies examining patient demographic factors, limited data are available to assess the association between medication exposures or medications at the time discharge and readmissions following hospitalization for alcohol-related diagnoses. The present study aimed to assess specific medication factors and patient characteristics that may be associated with readmission following hospitalization for an alcohol-related diagnosis.

PATIENTS AND METHODS

Patient data used in this retrospective case-control study were collected from an electronic health record integrated into a 2000-bed academic medical center in Rochester, MN. Patients were included if they were at least 18 years of age and admitted to an internal medicine or family medicine service between September 1, 2016, and August 31, 2019, for an alcohol-related diagnosis as characterized by International Classification of Diseases, 10th revision codes (Supplemental Table, available online at http://www.mayoclinicproceedings.org). Direct psychiatric admissions were excluded from the study along with patients with an index admission resulting in any of the following dispositions: intensive residential treatment services, community behavioral health hospital, alcohol-related rehabilitation services, skilled nursing facility, hospice care, commitment to a psychiatric hospital, or death during the index LOS. Patients who revoked use of their medical record to be used for research purposes, pursuant to Minnesota statute §144.295, were also excluded. This study was found exempt by the Mayo Clinic Investigational Review Board.

The primary outcome assessed was identification of medications and patient factors associated with 30-day readmission secondary to alcohol-related diagnoses. The secondary outcomes investigated were factors associated with 30-day all-cause readmission, and factors associated with multiple alcohol-related readmissions within 1 year from index admission. The readmission period for both primary and secondary outcomes was defined as the time between the index admission discharge date and subsequent hospital admission. Patient characteristics examined were age, patient-reported gender, race, BMI, LOS, maximum and first-documented Clinical Institute Withdrawal Assessment (CIWA) score, CCI score, LACE score, history of bariatric surgery, history of a psychiatric disorder (ie, anxiety disorders, mood disorders, and psychotic disorders), marital status, and number of alcohol-related admissions in the year before the index admission. Medication exposures were also examined and defined as any medication of interest either administered at least once during the index hospitalization or prescribed at the time of discharge as indicated by the discharge summary. Medications of interest included US Food and Drug Administration−approved medications for AUD (ie, naltrexone, acamprosate, and disulfiram), topiramate, gabapentin, opioids, muscle relaxants, benzodiazepines, and barbiturates. Opioids and muscle relaxants were combined in the analyses after the initial study feasibility assessment indicated low muscle relaxant (n=18) use in this cohort and was justified given both have central nervous system−depressant properties. Benzodiazepines and barbiturates were combined for the same reason. Gabapentin was of particular interest given the increasing use of the medication for alcohol-related purposes. For assessing total exposure and exposure per day of admission, benzodiazepines were converted to lorazepam equivalents.[15,16]

Descriptive statistics were reported as means and standard deviations or medians and interquartile ranges (IQRs) for continuous data, and as frequencies and percentages for categorical data. Univariate and multivariable logistic regression were used to assess the association between patient factors, medication factors, and readmission. Least absolute shrinkage and selection operator (LASSO) was used for the variable selection for multivariable model. *P* values less than or equal to .05 were considered statistically significant. All analyses were performed using SAS version 9.4 (SAS Institute Inc., Cary, NC).

Mayo Clin Proc Inn Qual Out ■ February 2022;6(1):1-9 ■ https://doi.org/10.1016/j.mayocpiqo.2021.11.005
www.mcpiqojournal.org

TABLE 1. Patient Characteristics Associated With 30-Day Readmission[a,b]

Factor	All-cause readmission within 30 days			Alcohol-related readmission within 30 days		
	Yes (n=228)	No (n=704)	*P*	Yes (n=172)	No (n=760)	*P*
Age, mean (SD)	52.6 (13.6)	52.6 (16.2)	.90	49.9 (13.6)	53.3 (16.1)	.018
Male	163 (71.5)	497 (70.6)	.80	120 (69.8)	540 (71.1)	.74
Race			.56			.43
White	205 (89.9)	623 (88.5)		158 (91.9)	670 (88.2)	
American Indian/Alaskan Native	3 (1.3)	10 (1.4)		1 (0.6)	12 (1.6)	
Asian	0 (0.0)	8 (1.1)		0 (0.0)	8 (1.1)	
Black or African American	9 (3.9)	23 (3.3)		3 (1.7)	29 (3.8)	
Other	9 (3.9)	26 (3.7)		7 (4.1)	28 (3.7)	
Unknown	2 (0.9)	14 (2.0)		3 (1.7)	13 (1.7)	
BMI, mean (SD)	28.4 (7.9)	27.2 (6.3)	.21	27.7 (7.2)	27.5 (6.6)	.89
LOS, median (IQR)	3.3 (2.1 to 6.0)	3 (2 to 5)	.060	3.1 (2 to 5.4)	3.1 (2 to 5.1)	.89
ICU	14 (6.1)	63 (8.9)	.18	14 (8.1)	63 (8.3)	.95
Maximum CIWA			.16			.014
N	151	464		129	486	
Median (IQR)	12 (5 to 18)	10 (5 to 16)		12 (6 to 18)	9 (5 to 16)	
First CIWA			.73			.40
N	151	464		129	486	
Median (IQR)	6 (2, 11)	6 (2, 11)		6 (3, 11)	6 (2, 11)	
LACE			.064			.95
N	228	696		170	754	
Median (IQR)	58 (49 to 71)	55 (48 to 69)		55.5 (49 to 68)	55 (48 to 69)	
Charlson comorbidity index, median (IQR)	2 (1 to 4)	1 (0 to 3)	.001	2 (0 to 3)	2 (0 to 3)	.53
History of bariatric surgery	7 (3.1)	12 (1.7)	.20	6 (3.5)	13 (1.7)	.14
History of psychiatric disorder	167 (73.2)	452 (64.2)	.012	132 (76.7)	487 (64.1)	.002
Marital status			.18			.036
Single	106 (46.5)	293 (41.6)		89 (51.7)	310 (40.8)	
Married/life partner	57 (25.0)	222 (31.5)		37 (21.5)	242 (31.8)	
Widowed	5 (2.2)	27 (3.8)		4 (2.3)	28 (3.7)	
Divorced/legally separated/separated	55 (24.1)	142 (20.2)		35 (20.3)	161 (21.2)	
Unknown	5 (2.2)	20 (2.8)		6 (3.5)	19 (2.5)	
Number of alcohol related admissions in the year prior, median (IQR)	0 (0 to 2)	0 (0 to 1)	<.001	1 (0 to 2)	0 (0 to 1)	<.001
0	123 (53.9)	476 (67.6)		83 (48.3)	516 (67.9)	
1	38 (16.7)	116 (16.5)		31 (18.0)	123 (16.2)	
2	28 (12.3)	52 (7.4)		24 (14.0)	56 (7.4)	
3	11 (4.8)	30 (4.3)		11 (6.4)	30 (4.0)	
4+	28 (12.3)	30 (4.3)		23 (13.3)	35 (4.6)	
Benzodiazepine/barbiturate	132 (57.9)	381 (54.1)	.32	115 (66.9)	398 (52.4)	<.001
Opioid/muscle relaxant	108 (47.4)	264 (37.5)	.008	68 (39.5)	304 (40.0)	.91
Gabapentin	100 (43.9)	246 (34.9%)	.015	79 (45.9%)	267 (35.1%)	.008
AUD medication	8 (3.5)	29 (4.1%)	.68	9 (5.2%)	28 (3.7%)	.35
Lorazepam equivalents, median (IQR)	1 (0 to 10.3)	1 (0, 6)	.060	3 (0, 13)	0.5 (0, 5.6)	<.001
Lorazepam equivalents per day hospitalization, median (IQR)	0.3 (0, 3)	0.1 (0, 2.1)	.12	0.6 (0, 4.7)	0.1 (0, 1.9)	<.001

Continued on next page

TABLE 1. Continued

Factor	All-cause readmission within 30 days			Alcohol-related readmission within 30 days		
	Yes (n=228)	No (n=704)	*P*	Yes (n=172)	No (n=760)	*P*
Lorazepam equivalents where exposure >0 mg, median (IQR)	8.5 (3 to 23.1)[c]	5.5 (2 to 18)[d]	.055	10 (3.5 to 24)[e]	5.5 (2 to 17)[f]	.018
Lorazepam equivalents per day of hospitalization where exposure >0 mg, median (IQR)	2.3 (0.6 to 8.7)[c]	1.9 (0.6 to 5.2)[d]	.25	2.8 (0.6 to 9.3)[e]	1.8 (0.6 to 5.2)[f]	.031

[a]AUD, alcohol use disorder; BMI, body mass index; CIWA, Clinical Institute Withdrawal Assessment; ICU, intensive care unit; IQR, interquartile range; LACE, length of stay, acuity of the admission, comorbidity of the patient, emergency department use; LOS, length of stay.
[b]Values shown are n (%) unless otherwise noted.
[c]n=130.
[d]n=370.
[e]n=111.
[f]n=389.

RESULTS

The study population included 932 patients with a median age of 52.6 (SD, 15.7) years, with a majority being Caucasian (n=828, 88.8%), and men (n =660, 70.8%). Among all patients, the median LOS for the index admission was 3.1 (IQR, 2 to 5.1) days and a total of 77 (8.3%) patients were admitted to the intensive care unit at any point during the index hospitalization. Age, psychiatric diagnosis, marital status, higher maximum CIWA score, and previous alcohol-related admissions in the prior year were patient characteristics significantly associated with alcohol-related readmission within 30-days from index date. Medication administration during the index hospitalization or prescribed at the time of discharge associated with a greater likelihood of a 30-day alcohol-related readmission included gabapentin and benzodiazepines or barbiturates (Table 1). Patients with a higher total benzodiazepine exposure during hospitalization (3 mg [IQR, 0 to 13 mg] vs 0.5 mg [IQR, 0 to 5.6 mg]; $P<.001$) and higher per day of hospitalization benzodiazepine exposure (0.6 mg [IQR, 0 to 4.7 mg] vs 0.1 mg (IQR, 0 to 1.9 mg]; $P<.001$) were more likely to have an alcohol-related readmission within 30 days of the index hospitalization. Findings remained similar when investigating daily benzodiazepine exposure during hospitalization after truncating all LOSs to a maximum of 8 days. The findings also remained statistically significant for the benzodiazepine exposure variables when only including those who received greater than 0 mg of lorazepam equivalents. Opioids or muscle relaxants and AUD medications were not associated with a greater likelihood of 30-day alcohol-related readmissions. Significant factors associated with all-cause 30-day readmissions included prior hospitalizations, CCI, and history of psychiatric disorder. Significant medication factors included opioids or muscle relaxants and gabapentin exposure. Exposure to benzodiazepines or barbiturates and total lorazepam equivalents received were not significant in the analysis of 30-day all-cause readmissions.

Whereas several factors independently were associated with either 30-day alcohol-related readmissions or 30-day all-cause readmission, multivariable analyses were also conducted to assess the relationships across factors. Predictors of 30-day alcohol-related readmissions included prior alcohol-related admissions within 1 year of index (odds ratio [OR], 1.16; 95% CI, 1.07 to 1.25) and benzodiazepine or barbiturate exposure (OR, 1.65; 95% CI, 1.16 to 2.35). Gabapentin did not maintain statistical significance (Table 2). After expanding readmissions to include all-cause 30-day readmission in a multivariable model, the following factors were associated with increased risk: the number of admissions in the previous year, BMI, CCI score, and opioid or muscle relaxant exposure. Gabapentin was not associated with an increased likelihood of all-cause 30-day readmission (Table 2).

Patient factors that were associated with multiple (ie, >1) alcohol-related readmissions within 1 year of the index admission included

Mayo Clin Proc Inn Qual Out ■ February 2022;6(1):1-9 ■ https://doi.org/10.1016/j.mayocpiqo.2021.11.005
www.mcpiqojournal.org

TABLE 2. Multivariable Analysis of Risk Factors Associated With 30-Day Readmission[a]

30-day all-cause readmission	OR (95% CI)	P
BMI (per kg/m^2)	1.02 (1.00-1.05)	.038
Charlson comorbidity index (per 1)	1.07 (1.00-1.14)	.060
Number of alcohol related admissions in the year prior (per 1)	1.16 (1.07-1.25)	<.001
Opioids/muscle relaxant	1.40 (1.02-1.93)	.040
Gabapentin	1.19 (0.86-1.64)	.30
30-day alcohol-related readmission		
Number of alcohol related admissions in the year prior (per 1)	1.16 (1.07-1.25)	.002
Benzodiazepine/barbiturate	1.65 (1.16-2.35)	.006
Gabapentin	1.36 (0.96-1.92)	.079

[a]BMI, body mass index; OR, odds ratio.

LACE index score (P=.001), CCI index score (P<.001), history of psychiatric disorder (P<.001), marital status (P<.001), and number of alcohol-related admissions in the prior year (P<.001). Having higher first-documented (P=.019) or higher maximum CIWA score (P<.001) was also associated with increased risk of more than one alcohol related readmission within 1 year from the index hospitalization. Benzodiazepine or barbiturate exposure (P=.005), total benzodiazepine exposure, (P<.001), and gabapentin exposure (P=.002) were medication factors associated with a significant likelihood of multiple alcohol-related readmissions. When reviewing factors associated with more than one admission within a 1-year time from the index hospitalization, results were similar except for opioid or muscle relaxants exposure being significant (P=.045) and benzodiazepine or barbiturate exposure losing significance.

In the multivariable analysis, factors associated with multiple alcohol-related readmissions within 1 year from index admission were CCI score, psychiatric diagnosis, being single, being divorced/separated, and the number of prior alcohol-related admissions within 1 year before index date (Table 3). No medications factors were found to be associated with multiple alcohol-readmissions within 1 year from index admission in the multivariable model.

DISCUSSION

Although there are several studies assessing patient demographics associated with readmissions following hospitalization for alcohol-related diagnoses, the data are lacking regarding the impact of medication exposures on readmissions. Medications represent a critical component in the macroscopic view of patient readmission rate dynamics that requires investigation both from a substance use and medical standpoint. This study attempted to examine this by assessing medications primarily used for alcohol withdrawal syndrome (AWS) or AUD and identified that benzodiazepines or barbiturates and degree of exposure during hospitalization were risk factors for 30-day and multiple alcohol-related rehospitalizations. Benzodiazepines, and less commonly barbiturates, are recommended by guidelines for the management of AWS; thus, recognition of these medications as having a potential influence on rehospitalization is important.[17] In this study, benzodiazepines and barbiturates were combined due to the low use of barbiturates (n=11) with all patients administered, or discharged using, phenobarbital. Although benzodiazepine or barbiturate administration and the cumulative dose during hospitalization are likely markers of AWS and AUD severity, exposure may have a negative influence on cravings, anxiety, sleep, and risk of a return to drinking in early sobriety leading to a risk of rehospitalization.[17] This may be especially true when appropriate referral or follow-up for alcohol use disorder and substance use treatment is not completed. Further studies should be completed to characterize the impact of benzodiazepine or barbiturate exposure during hospitalization for alcohol-related admissions.

TABLE 3. Multivariable Analysis of Risk Factors Associated With Multiple Alcohol-Related Readmissions Within 1 Year of Index Hospitalization[a]

	Odds Ratio (95% CI)	*P*
Charlson (per 1)	1.13 (1.05-1.21)	.001
History of psychiatric disorder (yes vs no)	1.45 (1.00-2.10)	.050
Marital status		
Single	2.39 (1.56-3.65)	<.001
Married/life partner	Reference	
Widowed	0.93 (0.34-2.54)	.89
Divorced/legally separated/separated	1.93 (1.20-3.10)	.007
Unknown	2.28 (0.79-6.57)	.13
Number of alcohol related admissions in the year prior (per 1)	1.40 (1.26-1.55)	<.001
Gabapentin	1.23 (0.88-1.71)	.22

[a]Multivariable model with use of the LASSO (least absolute shrinkage and selection operator) score.

Gabapentin failed to maintain significance in the multivariable analyses for 30-day and multiple readmissions and may represent an important finding given it is increasingly being investigated for use in the management of AWS and AUD. In other studies, gabapentin has been described as a predictive factor of substance use disorders and there are data linking coprescribing of opioids or the incidence of chronic pain with an increase in morbidity and mortality.[18–20] As such, opioids (combined with muscle relaxants given the low use [n=18]) were included. In the univariate analyses, opioid or muscle relaxant exposures were not associated with either 30-day alcohol-readmissions or multiple alcohol-related readmissions within 1 year of the index hospitalization. They were associated with 30-day all-cause readmission and multiple all-cause readmissions. Pre-hospital opioid exposure or prescription at discharge has previously been reported in other studies to be associated with increased health care use and readmissions as well.[18,19] Of patients readmitted for any reason, 187 of 932 (20.1%) patients had an opioid or muscle relaxant at the time of discharge. This represents a broader safety concern for a subset of patients and should be further investigated. As it relates to medications used for AUD, it is difficult to draw conclusions because of the low exposure or prescribing rates; however, it represents an additional opportunity for improvement as it relates to evidence-based treatments for AUD. It is well described in the literature that AUD pharmacotherapy is highly underutilized.[21]

Findings from this study are congruent with other publications in that factors such as marital status, psychiatric diagnoses, and prior alcohol-related admissions were found to be associated with the risk of readmission. Yedlapati et al[5] reported that 30-day readmission following hospitalization for alcohol withdrawal was predicted by discharge against medical advice, socioeconomic status as presumed by zip code, and presence of a comorbid psychotic disorder. Hansen et al[4], as well as Yedlapati et al,[5] identified that predictors for readmission following outpatient treatment for AUD were younger age, those with longer treatment episodes in the setting of severe AUD, and history of psychiatric problems (eg, depression, psychosis). Data compiled from 2004 Medicare patients as reported by Jencks et al[8] found a higher risk of 30-day readmission with increased rehospitalizations, longer LOS, increasing age, male sex, and receiving supplemental security income. Similar risk factors for readmission in the setting of AUD were investigated in this study with results varying in agreement when compared to existing literature. There was no association found between BMI or bariatric surgery and increased risk of readmission, contrary to previous studies.[9,10] If BMI has an impact on readmission risk for alcohol-related diagnoses, it could be that this population's mean BMI of 27.5 kg/m^2 was not high enough to become sensitive to that effect.

Mayo Clin Proc Inn Qual Out ■ February 2022;6(1):1-9 ■ https://doi.org/10.1016/j.mayocpiqo.2021.11.005
www.mcpiqojournal.org

One reason for the lack of association pertaining to bariatric surgery could be the low enrollment of patients with history of bariatric surgery (n=19, or 2.4%). Age, marital status, history of psychiatric disorder, and prior readmissions were associated with increased risk of readmission. These societal aspects are postulated to indicate a poor support structure, thus resulting in higher rates of relapse and increasing dropout rates from support programs.[22,23] Depression is commonly comorbid with AUD, and social factors including marital status and psychiatric disorder directly relate to that mental health state.[24] Consideration has been given to the use of antidepressants in reducing alcohol-related readmission with comorbid depression; however, recent evidence has not found an association between antidepressant use and a decrease in alcohol-related readmission.[24,25] Clinicians should ensure that proper resource allocation is pursued to connect AUD patients with social workers and support programs. Further research is indicated to elucidate how establishing support systems and social resource provisions can attenuate readmission risk due to social factors.

Although descriptive analysis of risk factors for readmission is useful, the true value of risk factor identification lies within prescriptive implementation of existing patterns to prevent potential readmissions. One such application to reduce 30-day and beyond readmissions is the construction and implementation of artificial intelligence (AI)—based risk factor identification. Artificial intelligence has gained popularity within the scientific community given the ability to analyze large sets of data with multiple complex variables to establish statistically endorsed outcomes.[26] A common pitfall in this application lies within poorly gathered or biased data that the AI "learns" from, resulting in overfitting or other misapplication of analyzed patterns.[26] Artificial intelligence is currently being used for medication decisions to treat patients and make drug selection decisions; therefore, it can be feasibly implemented to align with risk factor identification.[26] The current data gathered from this study, although a valuable start, may incorporate bias, including the high prevalence of Caucasian men, and would require a larger pool of a diverse population in which to train an AI device to predict readmission based upon investigated factors.

Study Limitations

Limitations to this study include the retrospective design in which any association does not equate to causation. This study also is reliant on accurate coding of diagnoses and discharge medication lists. Several patient factors had limited occurrences such as a history of bariatric surgery and prescribed AUD medications which may result in improper weight of individual risk factors. As compared to other studies that used large insurance databases to find patient characteristics associated with alcohol-related hospitalization readmissions (eg, Yedlapati et al,[5] with more than 300,000 patients), this study had a much smaller sample size. However, using electronic health records allowed collection of details not reported in prior studies, such as medication exposures, total lorazepam equivalents during the index hospitalization, and discharge medications. Future studies may also wish to include medication exposures and duration of those exposures before hospitalization as well as the influence of other medications that impact the central nervous system, such as psychotropic medications. This represents a surrogate marker for the use of psychiatric medications. Another limitation was the inability to draw any conclusion about the influence of medications US Food and Drug Administration—approved for AUD given the small number (n=37). This low number, however, was important to note given the known under-prescribing of medications for AUD and need to increase initiatives that promote use of medications such as naltrexone and acamprosate. It is possible that prescribing or ordering bias was present and that benzodiazepines were more commonly used in those patients who had or were suspected to have a higher severity of AWS as compared to those prescribed gabapentin; thus, there would be a difference in risk of readmission. For this population, median first CIWA scoring was 6 (IQR, 2 to 11) and median maximum CIWA scoring was 10 (IQR, 5 to 17), which represents mild-to-moderate withdrawal. However, as this study did not aim to compare rates of readmission between agents, we are unable to discern if there is less of a concern for

readmission with gabapentin as compared to benzodiazepines or barbiturates. Also, use of medications for indications other than AWS or AUD was not censored, such as gabapentin for neuropathy. A broad approach was taken to include all indications to better capture medication exposures and readmissions regardless of the underlying diagnosis for a medication. Larger, prospective studies assessing the risks of medication exposures considering patient specific characteristics are needed.

CONCLUSION

These findings reinforce current literature reports that age, marital status, history of psychiatric disorder, and previous admissions are associated with increased 30-day readmission risk. Gabapentin use was not associated with readmission risk. Benzodiazepine and barbiturate use were associated with increased 30-day readmission risk. Given these factors, gabapentin and benzodiazepine use in the setting of AUD warrants further examination. Prescriber education and implementation of identification tools are needed to lessen patient mortality and health-system cost associated with AUD readmissions.

SUPPLEMENTAL ONLINE MATERIAL

Supplemental material can be found online at http://www.mayoclinicproceedings.org. Supplemental material attached to journal articles has not been edited, and the authors take responsibility for the accuracy of all data.

Abbreviations and Acronyms: **AI,** artificial intelligence; **AUD,** alcohol use disorder; **AWS,** alcohol withdrawal syndrome; **BMI,** body mass index; **CCI,** Charlson comorbidity index; **CIWA,** clinical institute withdrawal assessment; **LOS,** length of stay

Potential Competing Interests: The authors report no potential competing interests.

Correspondence: Address to Jonathan G. Leung, PharmD, Mayo Clinic, 200 First St SW, Rochester, MN 55905 (leung.jonathan@mayo.edu).

ORCID

Joseph C. Osborne: https://orcid.org/0000-0002-3201-7283; Susan E. Horsman: https://orcid.org/0000-0002-4572-9730; Kristin C. Mara: https://orcid.org/0000-0002-8783-0191; Thomas C. Kingsley: https://orcid.org/0000-0002-6212-8988; Robert W. Kirchoff: https://orcid.org/0000-0001-9369-2242; Jonathan G. Leung: https://orcid.org/0000-0003-3836-9375

REFERENCES

1. Rehm J, Baliunas D, Borges GL, et al. The relation between different dimensions of alcohol consumption and burden of disease: an overview. *Addiction*. 2010;105(5):817-843.
2. National Institute on Alcohol Abuse and Alcoholism (NIAAA). Alcohol facts and statistics. Accessed July 26, 2020. Available: https://www.niaaa.nih.gov/sites/default/files/AlcoholFactsAndStats.pdf
3. Sacks JJ, Gonzales KR, Bouchery EE, Tomedi LE, Brewer RD. 2010 National and state costs of excessive alcohol consumption. *Am J Prev Med*. 2015;49(5):e73-e79.
4. Hansen EM, Mejldal A, Nielsen AS. Predictors of readmission following outpatient treatment for alcohol use disorder. *Alcohol Alcohol*. 2020;55(3):291-298.
5. Yedlapati SH, Stewart SH. Predictors of alcohol withdrawal readmissions. *Alcohol Alcohol*. 2018;53(4):448-452.
6. Secombe PJ, Stewart PC. The impact of alcohol-related admissions on resource use in critically ill patients from 2009 to 2015: an observational study. *Anaesth Intensive Care*. 2018;46(1):58-66.
7. Clark BJ, Rubinsky AD, Ho PM, et al. Alcohol screening scores and the risk of intensive care unit admission and hospital readmission. Subst Abus. 37(3):466-473.
8. Jencks SF, Williams MV, Coleman EA. Rehospitalizations among patients in the Medicare fee-for-service program. *N Engl J Med*. 2009;360(14):1418-1446.
9. Weinland C, Mühle C, Kornhuber J, Lenz B. Body mass index and craving predict 24-month hospital readmissions of alcohol-dependent in-patients following withdrawal. *Prog Neuropsychopharmacology Biol Psychiatry*. 2019;90:300-307.
10. Östlund MP, Backman O, Marsk R, et al. Increased admission for alcohol dependence after gastric bypass surgery compared with restrictive bariatric surgery. *JAMA Surg*. 2013;148(4):374-377.
11. Damery S, Combes G. Evaluating the predictive strength of the LACE index in identifying patients at high risk of hospital readmission following an inpatient episode: A retrospective cohort study. *BMJ Open*. 2017;7(7):e016921.
12. Argueta PP, Salazar M, Vohra I, et al. Thirty-day readmission among patients with alcoholic acute pancreatitis. *Dig Dis Sci*. 2021;66(12):4227-4236.
13. Nguyen OK, Makam AN, Clark C, et al. Predicting all-cause readmissions using electronic health record data from the entire hospitalization: Model development and comparison. *J Hosp Med*. 2016;11(7):473-480.
14. Gerke SP, Agley JD, Wilson C, Gassman RA, Forys P, Crabb DW. An initial assessment of the utility of validated alcohol and drug screening tools in predicting 30-day readmission to adult general medicine wards. *Am J Med Qual*. 2018;33(4):397-404.
15. Barr J, Zomorodi K, Bertaccini EJ, Shafer SL, Geller E. A double-blind, randomized comparison of IV lorazepam versus midazolam for sedation of ICU patients via a pharmacologic model. *Anesthesiology*. 2001;95(2):286-298.
16. Guina J, Merrill B. Benzodiazepines II: waking up on sedatives: providing optimal care when inheriting benzodiazepine prescriptions in transfer patients. *J Clin Med*. 2018;7(2):20.
17. The ASAM Clinical Practice Guideline on Alcohol Withdrawal Management [published correction appears in J Addict Med. 2020 Sep/Oct;14(5):e280]. *J Addict Med*. 2020;14(3S Suppl 1):1-72.
18. LaRowe LR, Powers JM, Garey L, Rogers AH, Zvolensky MJ, Ditre JW. Pain-related anxiety, sex, and co-use of alcohol and prescription opioids among adults with chronic low back pain. *Drug Alcohol Depend*. 2020;214:10871.

19. Smith RV, Havens JR, Walsh SL. Gabapentin misuse, abuse, and diversion: a systematic review. *Addiction*. 2016;111(7):1160-1174.
20. Mason BJ, Quello S, Shadan F. Gabapentin for the treatment of alcohol use disorder. *Expert Opin Investig Drugs*. 2018;27(1):113-124.
21. Kranzler HR, Soyka M. Diagnosis and Pharmacotherapy of Alcohol Use Disorder: A Review. *JAMA*. 2018;320(8):815-824. https://doi.org/10.1001/jama.2018.11406.
22. NICE. Alcohol-use disorders: diagnosis, assessment and management of harmful drinking (high-risk drinking) and alcohol dependence clinical guideline. *Adv Dual Diagn*. 2011;4(1):39. www.nice.org.uk/guidance/cg115. Accessed April 17, 2021.
23. Dale V, Coulton S, Godfrey C, et al. Exploring treatment attendance and its relationship to outcome in a randomized controlled trial of treatment for alcohol problems: secondary analysis of the UK alcohol treatment trial (UKATT). *Alcohol Alcohol*. 2011;46(5):592-599.
24. Mchugh RK, Weiss RD. Alcohol use disorder and depressive disorders. *Alcohol Res*. 2019;40(1):e1-e8.
25. Chan P, Yomen K, Turcios J, Richman M. Prescription for antidepressant in reducing future alcohol-related readmission in patients suffering from depression and alcohol use disorder: a retrospective medical record review. *Subst Abus Treat Prev Policy*. 2015;10(1):48.
26. Flynn A. Using artificial intelligence in health-system pharmacy practice: finding new patterns that matter. *Am J Health Syst Pharm*. 2019;76(9):622-627.