The Canadian Journal of Neurological Sciences (2024), **51**, 767–777
doi:10.1017/cjn.2024.10

Canadian Journal of Neurological Sciences
Journal Canadien des Sciences Neurologiques

Original Article

Alcohol Use Disorder in Patients with Chronic Migraine: A Retrospective, Observational Study

Leon S. Moskatel and Niushen Zhang
Department of Neurology and Neurological Sciences, Stanford University, Palo Alto, CA, USA

ABSTRACT: ***Objective:*** The relationship between migraine and alcohol consumption is unclear. We assessed the association between chronic migraine and alcohol use disorder(AUD), relative to chronic disease controls, and in conjunction with common comorbidities. ***Methods:*** We conducted a retrospective, observational study. The primary outcome was the odds ratio for AUD in patients with chronic migraine or with chronic migraine and additional comorbidities relative to controls. ***Results:*** A total of 3701 patients with chronic migraine, 4450 patients with low back pain, and 1780 patients with type 2 diabetes mellitus met inclusion criteria. Patients with chronic migraine had a lower risk of AUD relative to both controls of low back pain (*OR* 0.37; 95% CI: 0.29–0.47, $p < 0.001$) and type 2 diabetes mellitus (*OR* 0.39; 95% CI: 0.29–0.52, $p < 0.001$). Depression was associated with the largest OR for AUD in chronic migraine (*OR* 8.62; 95% CI: 4.99–14.88, $p < 0.001$), followed by post-traumatic stress disorder (*OR* 6.63; 95% CI: 4.13–10.64, $p < 0.001$) and anxiety (*OR* 3.58; 95% CI: 2.23–5.75, $p < 0.001$). ***Conclusion:*** Patients with chronic migraine had a lower odds ratio of AUD relative to controls. But in patients with chronic migraine, those with comorbid depression, anxiety, or PTSD are at higher risk of AUD. When patients establish care, comorbid factors should be assessed and for those at higher risk, AUD should be screened for at every visit.

RÉSUMÉ : Troubles liés à la consommation d'alcool chez des patients souffrant de migraine chronique : une étude rétrospective et observationnelle. ***Objectif :*** La relation qui existe entre la migraine et la consommation d'alcool n'est pas claire. À cet égard, nous avons cherché à évaluer l'association entre la migraine chronique et les troubles liés à la consommation d'alcool (TCA) en comparaison avec des témoins atteints de maladies chroniques et en conjonction avec des comorbidités communes. ***Méthodes :*** Nous avons mené une étude rétrospective et observationnelle dont le principal résultat évalué était le rapport de cotes (RC) pour les TCA chez des patients souffrant de migraine chronique ou de migraine chronique et de comorbidités supplémentaires en comparaison avec des témoins. ***Résultats :*** Au total, 3 701 patients souffrant de migraine chronique, 4 450 patients souffrant de lombalgie et 1 780 patients atteints de diabète de type 2 ont répondu à nos critères d'inclusion. À noter que les patients souffrant de migraine chronique ont présenté un risque plus faible de TCA par rapport aux témoins atteints de lombalgie (RC 0,37 ; IC 95 % : 0,29-0,47; $p < 0,001$) et de diabète de type 2 (RC 0,39 ; IC 95 % : 0,29-0,52 ; $p < 0,001$). Ajoutons aussi que la dépression a été associée à un RC plus important pour les TCA associés à la migraine chronique (RC 8,62 ; IC 95 % : 4,99-14,88 ; $p < 0,001$) ; elle a été suivie par le trouble de stress post-traumatique (TSPT) (RC 6,63 ; IC 95 % : 4,13-10,64 ; $p < 0,001$) et l'anxiété (RC 3,58 ; IC 95 % : 2,23-5,75 ; $p < 0,001$). ***Conclusion :*** Les patients souffrant de migraine chronique ont présenté un RC des TCA inférieur à celui des témoins. Cela dit, les patients souffrant de migraine chronique ainsi que ceux qui présentent une comorbidité telle que la dépression, l'anxiété ou le TSPT ont donné à voir un risque plus élevé de souffrir de TCA. Ainsi donc, lorsque des patients commencent à recevoir des soins, ces facteurs de comorbidité devraient être évalués. De plus, pour ceux qui présentent un risque plus élevé, les TCA devraient faire l'objet d'un dépistage à chaque visite.

Keywords: Chronic migraine; Alcohol; Alcohol use disorder; Depression; Anxiety; Post-traumatic stress disorder

(Received 31 October 2023; final revisions submitted 15 January 2024; date of acceptance 17 January 2024; First Published online 25 January 2024)

Introduction

The association between migraine and alcohol consumption continues to generate mixed and unclear results. In the Head-HUNT study from Norway, an association was found between increased alcohol consumption and migraine while in a Danish population study, the risk of migraine with aura was reduced in patients with weekly alcohol consumption.[1,2] In a 12-month prevalence of alcohol dependence, rates were similar between patients with migraine and those without.[3]

The reasons for potentially decreased alcohol consumption stem from widely held beliefs that alcohol can trigger or exacerbate migraine, with one study reporting that 35.6% of its 2197 participants noted alcoholic beverages to be a "trigger" of migraine, with red wine being most commonly implicated.[4] A 2022

Corresponding author: L. S. Moskatel; Email: moskatel@stanford.edu
Cite this article: Moskatel LS and Zhang N. (2024) Alcohol Use Disorder in Patients with Chronic Migraine: A Retrospective, Observational Study. *The Canadian Journal of Neurological Sciences* **51**: 767–777, https://doi.org/10.1017/cjn.2024.10

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prospective study conversely suggested that there was no significant effect on the likelihood of a migraine attack in the 24 hours after drinking, and a slightly lower chance from 24 to 48 hours after ingestion.[5] A 2020 prospective study showed that in adults with episodic migraine, ingestion of five or more drinks was associated with a twofold increase in headache the next day but there was no increase with one to two drinks.[6] More recently, a 2023 meta-analysis incorporating 22 studies suggested that alcohol consumption and migraine are inversely correlated but such a study utilized a heterogenous group of patients.[7]

Within the migraine population, it is also unclear what factors could potentially affect the risk of alcohol consumption for patients with migraine. The National Comorbidity Survey Replication (NCSR) found that the odds ratio for 12-month prevalence of alcohol use disorder was not higher for patients with chronic daily headache relative to those without headache, after demographics were controlled for, suggesting this was possibly due to comorbid post-traumatic stress disorder or depression.[8] Similarly, the previous literature has suggested a strong relationship between depression, anxiety, post-traumatic stress disorder, and alcohol use disorder.[9]

We sought to build on these studies by assessing the association between chronic migraine and alcohol use disorder relative to chronic disease controls and to analyze the impact of comorbid depression, anxiety, and post-traumatic stress disorder on this association.

Methods

All data were obtained through the Stanford Research Repository (STARR) and approved by the Stanford Institutional Review Board. Cohorts for assessment were built on different criteria for each but were drawn from the baseline group of patients seen in the Stanford Headache Clinic of the Department of Neurology, a tertiary headache center, or the Pain Management Clinic in the Department of Anesthesia between January 1, 2017 and December 31, 2019, and were older than 18 at the time of visit. Demographics for each group were determined include sex, race, ethnicity, and average age.

Patient groups were then built based on one of these International Classification of Disease, Tenth Edition (ICD-10) codes that were assigned during the observed time period: G43.7 chronic migraine; M54.5 low back pain; E11 type 2 diabetes mellitus (T2DM). Low Back Pain served as a non-headache chronic pain control. T2DM acted as the chronic non-pain condition control. Subgroups were then built for these disease states based on the presence or absence of: F32 Depressive episode or F33 Major depressive disorder, recurrent; F41 Other anxiety disorders; F43.1 Post-traumatic stress disorder.

Smaller subgroups were then built to include patients meeting these previous criteria and ever receiving a diagnosis of alcohol use disorder stemming from the ICD-10 codes: F10.1 Alcohol Abuse or F10.2 Alcohol Dependence.

The primary outcome was the odds ratio for alcohol use disorder in patients with chronic migraine or with chronic migraine and additional factors relative to controls. Secondary outcomes included differences in demographics between these groups including sex, race, ethnicity, and age. This is the primary analysis of this data.

Statistical Analysis

All data were analyzed in Microsoft Excel. Descriptive statistics were used to assess for demographics of each cohort. Due to the small number, or absence of patients entirely, in certain disease and demographic combinations, tests for statistical significance were not conducted for race and ethnicity. Odds ratios with 95% confidence intervals were used to assess for differences in rates of alcohol use disorder between groups. A two-sided, students *T*-test was used to assess for statistically significant differences in ages between groups. Statistical significance was set at $p < 0.05$.

Results

A total of 3701 patients with chronic migraine, 4450 patients with low back pain, and 1780 patients with type 2 diabetes mellitus met inclusion criteria. The full demographics of each cohort are available in Table 1, Table 2, and Table 3. In patients with chronic migraine, male sex was not associated with a higher risk of alcohol use disorder relative to women (*OR* 1.38; 95% CI: 0.87–2.21, $p = 0.173$). When looking at men and women with chronic migraine, separately, relative to their controls of male or female patients with LBP or T2DM, respectively, the risk of alcohol use disorder was statistically significantly lower in those with chronic migraine relative to the comparators (Fig. 1a,b). A portion of the subsets of patients with alcohol use disorder and chronic migraine, with or without additional factors, were statistically significantly older than the cohort-at-large (4/9 with an average age difference of $+ 5.1 \pm 0.9$ years). Fewer of the subset of patients with alcohol use disorder and LBP, with or without additional factors, had statistically significant age differences (2/9 with an average age difference of $+ 2.6 \pm 1.4$ years). This is in contrast to the patients with alcohol use disorder and T2DM, with or without additional factors, in whom the age difference relative to the cohorts-at-large, was younger (3/9 with an average age difference of -2.7 ± 2.3 years).

Patients with chronic migraine had a lower risk of alcohol use disorder relative to both controls of LBP (*OR* 0.37; 95% CI: 0.29–0.47, $p < 0.001$) and T2DM (*OR* 0.39; 95% CI: 0.29–0.52, $p < 0.001$) (Fig. 2).

Given that they are often comorbid with chronic migraine, we assessed the prevalence of receiving a diagnosis of depression, anxiety, or PTSD at any point. Anxiety was most commonly present in 1607/3701 (43.4%) of patients, followed by depression with 1311/3701 (35.4%) of patients, and PTSD with 253/3701 (6.8%) of patients.

Indeed, anxiety, depression, and PTSD were all associated with increased OR of alcohol use disorder for patients with chronic migraine (Fig. 3). Depression was associated with the largest OR for alcohol use disorder in chronic migraine (*OR* 8.62; 95% CI: 4.99–14.88, $p < 0.001$), followed by PTSD (*OR* 6.63; 95% CI: 4.13–10.64, $p < 0.001$), and anxiety (*OR* 3.58; 95% CI: 2.23–5.75, $p < 0.001$). When patients had both depression and anxiety, the OR for alcohol use disorder increased further (*OR* 13.92; 95% CI: 6.44–30.08, $p < 0.001$). Patients with depression, anxiety, and PTSD had the highest OR for alcohol use disorder (*OR* 27.6; 95% CI: 12.58–60.73, $p < 0.001$).

When depression, anxiety, PTSD, and sex were controlled for individually, the risk of alcohol use disorder in patients with chronic migraine was significantly lower relative to LBP and T2DM, excluding PTSD (Fig. 4); the risk of alcohol use disorder in patients with chronic migraine and PTSD was not statistically significantly different from that of LBP and PTSD (*OR* 0.64, 95% CI: 0.39–1.05, $p = 0.076$) and T2DM (*OR* 0.55, 95% CI: 0.28–1.07, $p = 0.077$).

https://doi.org/10.1017/cjn.2024.10 Published online by Cambridge University Press

Table 1: Sex for each group

	Screened Inclusion/Exclusion of Factor									
Primary diagnosis	Depression	Anxiety	PTSD	Sex	Alcohol use	Number	Female	%	Male	%
Chronic migraine						3701	2942	79.5%	759	20.5%
Chronic migraine					Included	86	64	74.4%	22	25.6%
Chronic migraine	Excluded					2389	1850	77.4%	539	22.6%
Chronic migraine	Excluded				Included	16	10	62.5%	6	37.5%
Chronic migraine	Included					1311	1091	83.2%	220	16.8%
Chronic migraine	Included				Included	72	55	76.4%	17	23.6%
Chronic migraine		Excluded				2094	1599	76.4%	495	23.6%
Chronic migraine		Excluded			Included	24	15	62.5%	9	37.5%
Chronic migraine		Included				1607	1343	83.6%	264	16.4%
Chronic migraine		Included			Included	64	50	78.1%	14	21.9%
Chronic migraine			Excluded			3448	2718	78.8%	730	21.2%
Chronic migraine			Excluded		Included	61	42	68.9%	19	31.1%
Chronic migraine			Included			253	224	88.5%	29	11.5%
Chronic migraine			Included		Included	27	23	85.2%	4	14.8%
Chronic migraine				Male		759			759	100.0%
Chronic migraine				Male	Included	23			23	100.0%
Chronic migraine				Female		2943	2943	100.0%		0.0%
Chronic migraine				Female	Included	65	65	100.0%		0.0%
Low back pain						4450	2906	65.3%	1544	34.7%
Low back pain					Included	271	139	51.3%	132	48.7%
Low back pain	Excluded					2296	1371	59.7%	925	40.3%
Low back pain	Excluded				Included	77	29	37.7%	48	62.3%
Low back pain	Included					2154	1535	71.3%	619	28.7%
Low back pain	Included				Included	194	110	56.7%	84	43.3%
Low back pain		Excluded				2247	1305	58.1%	942	41.9%
Low back pain		Excluded			Included	78	33	42.3%	45	57.7%
Low back pain		Included				2203	1601	72.7%	602	27.3%
Low back pain		Included			Included	193	106	54.9%	87	45.1%
Low back pain			Excluded			4100	2636	64.3%	1464	35.7%
Low back pain			Excluded		Included	216	104	48.1%	112	51.9%
Low back pain			Included			350	270	77.1%	80	22.9%
Low back pain			Included		Included	55	35	63.6%	20	36.4%
Low back pain				Male		1544		0.0%	1544	100.0%
Low back pain				Male	Included	132		0.0%	132	100.0%
Low back pain				Female		2906	2906	100.0%		
Low back pain				Female	Included	139	139	100.0%		
Type 2 diabetes						1780	921	51.7%	859	48.3%
Type 2 diabetes					Included	102	38	37.3%	64	62.7%
Type 2 diabetes	Excluded					1070	473	44.2%	597	55.8%
Type 2 diabetes	Excluded				Included	34	9	26.5%	25	73.5%
Type 2 diabetes	Included					711	448	63.0%	263	37.0%
Type 2 diabetes	Included				Included	68	29	42.6%	39	57.4%
Type 2 diabetes		Excluded				1082	480	44.4%	602	55.6%
Type 2 diabetes		Excluded			Included	41	10	24.4%	31	75.6%

(*Continued*)

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Table 1: (*Continued*)

Primary diagnosis	Screened Inclusion/Exclusion of Factor					Number	Female	%	Male	%
	Depression	Anxiety	PTSD	Sex	Alcohol use					
Type 2 diabetes		Included				699	441	63.1%	258	36.9%
Type 2 diabetes		Included			Included	494	327	66.2%	167	33.8%
Type 2 diabetes			Excluded			1691	866	51.2%	825	48.8%
Type 2 diabetes			Excluded		Included	86	30	34.9%	56	65.1%
Type 2 diabetes			Included			90	55	61.1%	35	38.9%
Type 2 diabetes			Included		Included	16	8	50.0%	8	50.0%
Type 2 diabetes				Male		860			860	100.0%
Type 2 diabetes				Male	Included	64			64	100.0%
Type 2 diabetes				Female		921	921	100.0%		0.0%
Type 2 diabetes				Female	Included	38	38	100.0%		0.0%

Discussion

The previous studies have sought to look at alcohol consumption in patients with migraine relative to patients without migraine; however, that may be a suboptimal control as patients with chronic conditions may have different utilization of alcohol relative to healthy controls. Consequently, we elected to use patients with low back pain and T2DM as the controls to represent a control with a pain condition and chronic, non-pain condition, respectively. We found that compared to both of these controls, patients with chronic migraine had a lower OR for alcohol use disorder, consistent with the studies suggesting that alcohol use can exacerbate migraine or is perceived to worsen migraine to the extent that patients avoid it by reputation alone. This comparison held true not only for chronic migraine overall, but for chronic migraine with comorbid depression and anxiety, but not PTSD. This suggests that similar to the NCSR, alcohol use disorder is driven by PTSD to the same extent in these populations.[8]

However, for patients with chronic migraine, comorbid depression, anxiety, and PTSD are drivers of increased alcohol use disorder, particularly when in combination with each other, as suggested by the exceptionally high OR of 27.6 for alcohol use disorder in chronic migraine patients with depression, anxiety, and PTSD relative to those with none of these comorbid conditions.

This relationship is especially important given that these comorbidities frequently present with chronic migraine; the observed rates of depression, anxiety, and PTSD in our patients with chronic migraine were consistent with what has been previously reported in literature.[10] The relationship between depression and chronic migraine has been suggested to be bidirectional, and that depression can be a risk factor for being refractory to treatment and medication-overuse headache.[11] With anxiety and chronic migraine, each is a risk factor for the other; patients with generalized anxiety disorder are at increased risk of migraine and vice versa.[12] PTSD has also been found to have a higher prevalence in patients with migraine than in the general population and a cross sectional study of patients with and without migraine found that PTSD could be a predictor of migraine.[13,14]

The association of these psychiatric comorbidities with alcohol use disorder has been well reported. Depression and alcohol use disorder have been shown in a 14-year longitudinal study to be highly comorbid and with those patients at higher risk for downstream sequelae including life dissatisfaction and suicide attempts.[15] Alcohol use disorder has also been shown to be higher in patients with a current anxiety disorder than in those without.[16] Patients with PTSD have also been shown to develop alcohol use disorder at rates of 4.5–6.5 times higher than patients without PTSD.[17–19]

Additionally, the effect of sex on risk of alcohol use disorder in chronic migraine was minimal; there was no increase in OR for alcohol use disorder in men relative to women and both sexes with chronic migraine had a lower risk of alcohol use disorder relative to the LBP and T2DM controls. This is in contrast to the previous studies using NHANES and Swedish data to associate alcohol consumption and female sex and in agreement to the NHANES study suggesting no association between heavy alcohol use and migraine in men.[20,21]

While there are no previous studies identifying specific treatments for patients with chronic migraine and alcohol use disorder, many of the typical preventive medications can be applied for either this use directly, or towards the depression, anxiety, or PTSD which may be comorbid. For example, topiramate, which is commonly used for the prevention of chronic migraine, has also been shown to be effective for reducing alcohol consumption, including greater abstinence and decreased heavy drinking.[22] Gabapentin has also been proposed as a treatment for alcohol use disorder but with mixed evidence.[23] Beyond these medications, anti-depressants such as venlafaxine or amitriptyline may be helpful in treating patients with chronic migraine, depression, and alcohol use disorder, with the aim of indirectly treating the alcohol use by directly treating the comorbid depression.[24]

Taken together, when patients establish care, it is the opportune time to not only assess for alcohol use disorder itself but also the comorbid factors that can impact not only their headache burden but also increases the risk for alcohol use disorder. To achieve this, validated alcohol screening tools, such as the Cut down, Annoyed, Guilty, and Eye-opener screener (CAGE) can be integrated into the patient intake paperwork to assess for alcohol use disorder.[25] Alternatively, screening patients with the 11 questions asked in the DSM-5 criteria for alcohol use disorder could allow for longitudinal and quantitative monitoring.[26] Similarly, validated

https://doi.org/10.1017/cjn.2024.10 Published online by Cambridge University Press

https://doi.org/10.1017/cjn.2024.10 Published online by Cambridge University Press

Table 2: Racial demographics for each group

	Screened inclusion/exclusion of factor					Race													
Primary diagnosis	Depression	Anxiety	PTSD	Sex	Alcohol use	Asian	%	Black	%	Native american	%	Other	%	Pacific islander	%	Unknown	%	White	%
Chronic migraine						339	9.2%	94	2.5%	22	0.6%	761	20.6%	23	0.6%	207	5.6%	2255	60.9%
Chronic migraine					Included	1	1.2%	4	4.7%	1	1.2%	8	9.3%		0.0%	2	2.3%	70	81.4%
Chronic migraine	Excluded					223	9.3%	50	2.1%	13	0.5%	493	20.6%	14	0.6%	172	7.2%	1424	59.6%
Chronic migraine	Excluded				Included	1	6.3%	1	6.3%		0.0%		0.0%		0.0%	1	6.3%	13	81.3%
Chronic migraine	Included					116	8.8%	43	3.3%	9	0.7%	267	20.4%	9	0.7%	36	2.7%	831	63.4%
Chronic migraine	Included				Included	3	4.2%		0.0%	1	1.4%	8	11.1%		0.0%	1	1.4%	59	81.9%
Chronic migraine		Excluded				190	9.1%	46	2.2%	12	0.6%	446	21.3%	14	0.7%	152	7.3%	1234	58.9%
Chronic migraine		Excluded			Included	1	4.2%		0.0%	1	4.2%	1	4.2%		0.0%	1	4.2%	20	83.3%
Chronic migraine		Included				150	9.3%	47	2.9%	11	0.7%	310	19.3%	9	0.6%	55	3.4%	1025	63.8%
Chronic migraine		Included			Included		0.0%	4	6.3%		0.0%	7	10.9%		0.0%	1	1.6%	52	81.3%
Chronic migraine			Excluded			318	9.2%	77	2.2%	21	0.6%	717	20.8%	21	0.6%	203	5.9%	2091	60.6%
Chronic migraine			Excluded		Included	1	1.6%	2	3.3%	1	1.6%	6	9.8%		0.0%	2	3.3%	49	80.3%
Chronic migraine			Included			22	8.7%	16	6.3%	2	0.8%	39	15.4%	2	0.8%	4	1.6%	168	66.4%
Chronic migraine			Included		Included		0.0%	2	7.4%		0.0%	2	7.4%		0.0%		0.0%	23	85.2%
Chronic migraine				Male		62	8.2%	15	2.0%	7	0.9%	130	17.1%	8	1.1%	43	5.7%	494	65.1%
Chronic migraine				Male	Included	1	4.3%	1	4.3%	1	4.3%	2	8.7%		0.0%		0.0%	18	78.3%
Chronic migraine				Female		278	9.4%	78	2.7%	16	0.5%	626	21.3%	15	0.5%	164	5.6%	1766	60.0%
Chronic migraine				Female	Included		0.0%	3	4.6%		0.0%	6	9.2%	2	3.1%		0.0%	54	83.1%
Low back pain						492	11.1%	309	6.9%	33	0.7%	828	18.6%	32	0.7%	114	2.6%	2642	59.4%
Low back pain					Included	10	3.7%	25	9.2%	2	0.7%	43	15.9%		0.0%	3	1.1%	188	69.4%
Low back pain	Excluded					291	12.7%	148	6.4%	16	0.7%	434	18.9%	21	0.9%	74	3.2%	1312	57.1%
Low back pain	Excluded				Included	2	2.6%	6	7.8%	2	2.6%	11	14.3%		0.0%		0.0%	56	72.7%
Low back pain	Included					201	9.3%	161	7.5%	17	0.8%	394	18.3%	11	0.5%	40	1.9%	1330	61.7%
Low back pain	Included				Included	8	4.1%	19	9.8%		0.0%	32	16.5%		0.0%	3	1.5%	132	68.0%
Low back pain		Excluded				291	13.0%	156	6.9%	12	0.5%	428	19.0%	19	0.8%	67	3.0%	1274	56.7%
Low back pain		Excluded			Included	3	3.8%	9	11.5%	2	2.6%	12	15.4%		0.0%	1	1.3%	51	65.4%
Low back pain		Included				201	9.1%	153	6.9%	21	1.0%	400	18.2%	13	0.6%	47	2.1%	1368	62.1%
Low back pain		Included			Included	7	3.6%	16	8.3%		0.0%	31	16.1%		0.0%	2	1.0%	137	71.0%
Low back pain			Excluded			465	11.3%	286	7.0%	31	0.8%	760	18.5%	31	0.8%	106	2.6%	2421	59.0%
Low back pain			Excluded		Included	6	2.8%	24	11.1%	2	0.9%	30	13.9%		0.0%	2	0.9%	152	70.4%
Low back pain			Included			29	8.3%	24	6.9%	3	0.9%	67	19.1%		0.0%	7	2.0%	220	62.9%
Low back pain			Included		Included	4	7.3%	1	1.8%		0.0%	13	23.6%		0.0%	1	1.8%	36	65.5%

(*Continued*)

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Table 2: (*Continued*)

	Screened inclusion/exclusion of factor					Race												
Primary diagnosis	Depression	Anxiety	PTSD	Sex	Alcohol use	Asian	%	Black	%	Native american	%	Other	%	Pacific islander	%	Unknown	%	White	%
Low back pain				Male		175	11.3%	94	6.1%	9	0.6%	260	16.8%	16	1.0%	36	2.3%	954	61.8%
Low back pain				Male	Included	5	3.8%	13	9.8%	1	0.8%	22	16.7%		0.0%	1	0.8%	90	68.2%
Low back pain				Female		317	10.9%	215	7.4%	24	0.8%	568	19.5%	16	0.6%	78	2.7%	1688	58.1%
Low back pain				Female	Included	5	3.6%	12	8.6%	1	0.7%	21	15.1%		0.0%	2	1.4%	98	70.5%
Type 2 diabetes						322	18.1%	123	6.9%	14	0.8%	431	24.2%	30	1.7%	35	2.0%	825	46.3%
Type 2 diabetes					Included	2	2.0%	11	10.8%	1	1.0%	20	19.6%	3	2.9%	2	2.0%	63	61.8%
Type 2 diabetes	Excluded					228	21.3%	70	6.5%	8	0.7%	251	23.5%	19	1.8%	26	2.4%	468	43.7%
Type 2 diabetes	Excluded				Included	2	5.9%	4	11.8%		0.0%	5	14.7%	2	5.9%	1	2.9%	20	58.8%
Type 2 diabetes	Included					95	13.4%	53	7.5%	6	0.8%	180	25.3%	11	1.5%	9	1.3%	357	50.2%
Type 2 diabetes	Included				Included		0.0%	7	10.3%	1	1.5%	15	22.1%	1	1.5%	1	1.5%	43	63.2%
Type 2 diabetes		Excluded				217	20.1%	77	7.1%	11	1.0%	258	23.8%	20	1.8%	24	2.2%	475	43.9%
Type 2 diabetes		Excluded			Included	2	4.9%	5	12.2%		0.0%	9	22.0%	2	4.9%	1	2.4%	22	53.7%
Type 2 diabetes		Included				105	15.0%	46	6.6%	3	0.4%	173	24.7%	10	1.4%	11	1.6%	351	50.2%
Type 2 diabetes		Included			Included	64	13.0%	37	7.5%	3	0.6%	126	25.5%	9	1.8%	4	0.8%	251	50.8%
Type 2 diabetes			Excluded			317	18.7%	115	6.8%	15	0.9%	406	24.0%	29	1.7%	33	2.0%	776	45.9%
Type 2 diabetes			Excluded		Included	2	2.3%	8	9.3%	1	1.2%	17	19.8%	3	3.5%	2	2.3%	53	61.6%
Type 2 diabetes			Included			5	5.6%	8	8.9%		0.0%	21	23.3%	1	1.1%	1	1.1%	54	60.0%
Type 2 diabetes			Included		Included		0.0%	3	18.8%		0.0%		0.0%	3	18.8%		0.0%	10	62.5%
Type 2 diabetes				Male		155	18.0%	44	5.1%	8	0.9%	185	21.5%	17	2.0%	15	1.7%	436	50.7%
Type 2 diabetes				Male	Included	2	3.1%	4	6.3%		0.0%	13	20.3%	3	4.7%		0.0%	42	65.6%
Type 2 diabetes				Female		167	18.1%	79	8.6%	6	0.7%	242	26.3%	13	1.4%	21	2.3%	393	42.7%
Type 2 diabetes				Female	Included		0.0%	7	18.4%	1	2.6%	7	18.4%		0.0%	2	5.3%	21	55.3%

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Table 3: Ethnicity demographics and age for each group

	Screened inclusion/exclusion of factor						Ethnicity						Age	
Primary diagnosis	Depression	Anxiety	PTSD	Sex	Alcohol use	Number	Hispanic/latino	%	Non-hispanic	%	Unknown	%	Average	St. Dev
Chronic migraine						3701	538	14.5%	2952	79.8%	211	5.7%	45.3	15.0
Chronic migraine					Included	86	12	14.0%	72	83.7%	2	2.3%	49.5	14.7
Chronic migraine	Excluded					2389	329	13.8%	1892	79.2%	168	7.0%	44.8	15.1
Chronic migraine	Excluded				Included	16	2	12.5%	13	81.3%	1	6.3%	49.5	17.0
Chronic migraine	Included					1311	209	15.9%	1059	80.8%	43	3.3%	46.1	14.9
Chronic migraine	Included				Included	72	10	13.9%	61	84.7%	1	1.4%	48.8	14.8
Chronic migraine		Excluded				2094	290	13.8%	1655	79.0%	149	7.1%	46.0	15.3
Chronic migraine		Excluded			Included	24	3	12.5%	21	87.5%		0.0%	52.3	13.6
Chronic migraine		Included				1607	251	15.6%	1294	80.5%	62	3.9%	44.4	14.8
Chronic migraine		Included			Included	64	9	14.1%	53	82.8%	2	3.1%	47.7	15.6
Chronic migraine			Excluded			3448	501	14.5%	2742	79.5%	205	5.9%	45.5	15.2
Chronic migraine			Excluded		Included	61	9	14.8%	50	82.0%	2	3.3%	50.2	17.0
Chronic migraine			Included			253	40	15.8%	207	81.8%	6	2.4%	42.9	12.3
Chronic migraine			Included		Included	27	3	11.1%	24	88.9%		0.0%	46.0	9.5
Chronic migraine				Male		759	89	11.7%	620	81.7%	50	6.6%	46.3	16.2
Chronic migraine				Male	Included	23	2	8.7%	21	91.3%		0.0%	46.9	14.1
Chronic migraine				Female		2943	452	15.4%	2330	79.2%	161	5.5%	45.1	14.8
Chronic migraine				Female	Included	65	10	15.4%	53	81.5%	2	3.1%	49.6	15.5
Low back pain						4450	671	15.1%	3654	82.1%	125	2.8%	57.8	16.4
Low back pain					Included	271	48	17.7%	217	80.1%	6	2.2%	58.3	13.6
Low back pain	Excluded					2296	319	13.9%	1896	82.6%	81	3.5%	58.4	17.0
Low back pain	Excluded				Included	77	11	14.3%	66	85.7%		0.0%	62.0	13.2
Low back pain	Included					2154	352	16.3%	1758	81.6%	44	2.0%	57.2	15.8
Low back pain	Included				Included	194	37	19.1%	151	77.8%	6	3.1%	56.8	13.6
Low back pain		Excluded				2247	313	13.9%	1863	82.9%	71	3.2%	59.3	16.6
Low back pain		Excluded			Included	78	16	20.5%	60	76.9%	2	2.6%	60.9	12.8
Low back pain		Included				2203	358	16.3%	1791	81.3%	54	2.5%	56.2	16.1
Low back pain		Included			Included	193	32	16.6%	157	81.3%	4	2.1%	57.2	13.9
Low back pain			Excluded			4100	610	14.9%	3372	82.2%	118	2.9%	58.4	16.4
Low back pain			Excluded		Included	216	35	16.2%	176	81.5%	5	2.3%	60.1	13.2
Low back pain			Included			350	63	18.0%	281	80.3%	6	1.7%	50.8	15.4
Low back pain			Included		Included	55	13	23.6%	41	74.5%	1	1.8%	51.1	13.2

(*Continued*)

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Table 3: (*Continued*)

	Screened inclusion/exclusion of factor						Ethnicity						Age	
Primary diagnosis	Depression	Anxiety	PTSD	Sex	Alcohol use	Number	Hispanic/latino	%	Non-hispanic	%	Unknown	%	Average	St. Dev
Low back pain				Male		1544	206	13.3%	1297	84.0%	41	2.7%	58.6	16.4
Low back pain				Male	Included	132	25	18.9%	104	78.8%	3	2.3%	60.4	13.2
Low back pain				Female		2906	465	16.0%	2357	81.1%	84	2.9%	57.4	16.4
Low back pain				Female	Included	139	23	16.5%	113	81.3%	3	2.2%	56.3	13.8
Type 2 diabetes						1780	354	19.9%	1383	77.7%	43	2.4%	63.7	14.6
Type 2 diabetes					Included	102	25	24.5%	75	73.5%	2	2.0%	61.0	12.9
Type 2 diabetes	Excluded					1070	200	18.7%	842	78.7%	28	2.6%	64.8	14.4
Type 2 diabetes	Excluded				Included	34	8	23.5%	26	76.5%		0.0%	66.1	13.3
Type 2 diabetes	Included					711	154	21.7%	542	76.2%	15	2.1%	62.0	14.7
Type 2 diabetes	Included				Included	68	17	25.0%	49	72.1%	2	2.9%	58.4	11.9
Type 2 diabetes		Excluded				1082	210	19.4%	842	77.8%	30	2.8%	65.4	14.1
Type 2 diabetes		Excluded			Included	41	10	24.4%	31	75.6%		0.0%	65.7	13.1
Type 2 diabetes		Included				699	144	20.6%	542	77.5%	13	1.9%	60.9	14.8
Type 2 diabetes		Included			Included	494	107	21.7%	379	76.7%	8	1.6%	60.8	14.7
Type 2 diabetes			Excluded			1691	336	19.9%	1316	77.8%	39	2.3%	64.2	14.3
Type 2 diabetes			Excluded		Included	86	22	25.6%	62	72.1%	2	2.3%	63.6	11.7
Type 2 diabetes			Included			90	19	21.1%	70	77.8%	1	1.1%	53.3	15.9
Type 2 diabetes			Included		Included	16	3	18.8%	13	81.3%		0.0%	46.6	9.7
Type 2 diabetes				Male		860	145	16.9%	701	81.5%	14	1.6%	65.2	13.7
Type 2 diabetes				Male	Included	64	14	21.9%	49	76.6%	1	1.6%	63.0	12.3
Type 2 diabetes				Female		921	210	22.8%	683	74.2%	28	3.0%	62.3	15.2
Type 2 diabetes				Female	Included	38	11	28.9%	26	68.4%	1	2.6%	57.8	13.2

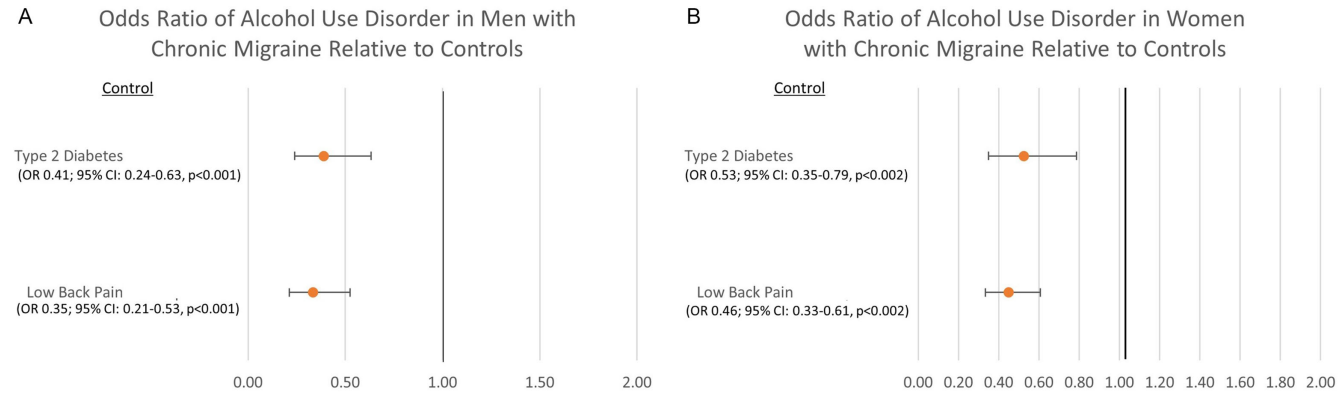


Figure 1: Odds ratio of alcohol use disorder in patients with chronic migraine relative to controls by sex: 1***a***. Men. 1***b***. Women.

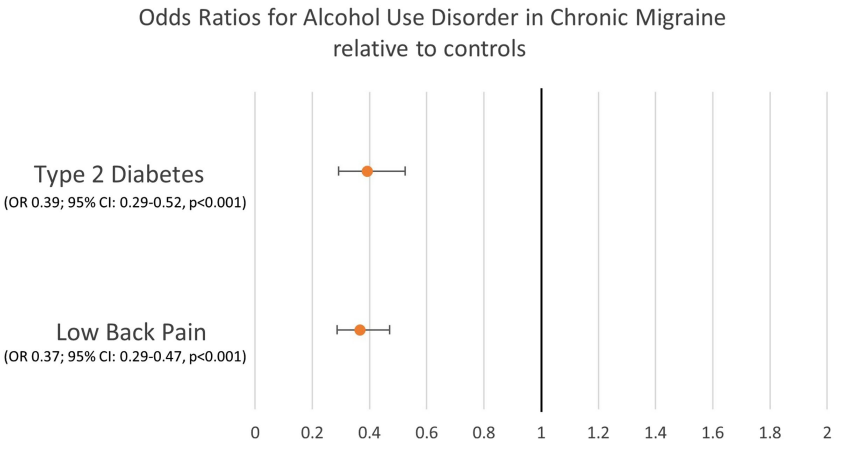


Figure 2: Odds ratios for alcohol use disorder in chronic migraine relative to disease controls.

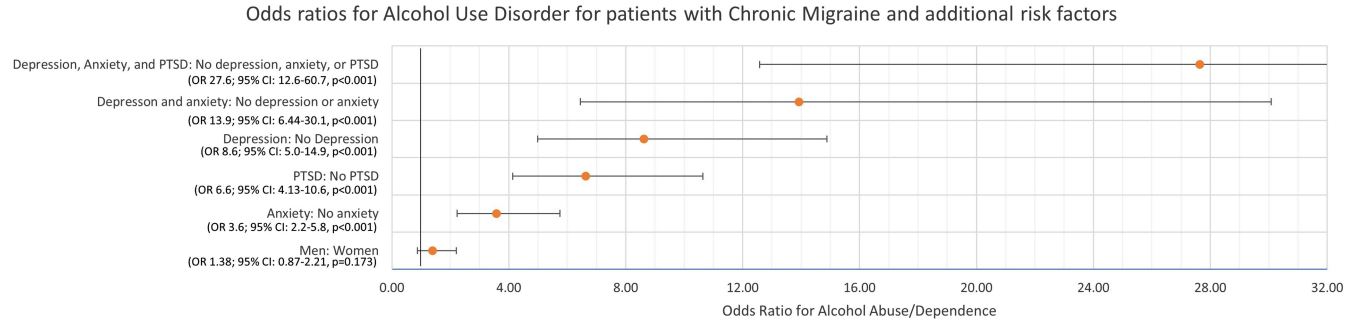


Figure 3: Odds ratios for alcohol use disorder in patients with chronic migraine by additional factors.

questionnaires for anxiety, depression, and PTSD can help alert the clinician to these comorbidities.[25] However, simply assessing for alcohol use disorder, anxiety, depression, and PTSD alone are insufficient if not then treated; comprehensive headache management requires treating not only the primary headache disorder but also underlying contributing conditions and factors, often best performed with a team approach including physicians, psychologists, physical therapists, and social workers.

Our study is limited by the size of the data and nature of using large retrospective data. While the groups of patients are generally in the hundreds or thousands of patients, with the introduction of multiple additional factors, the size of the groups frequently

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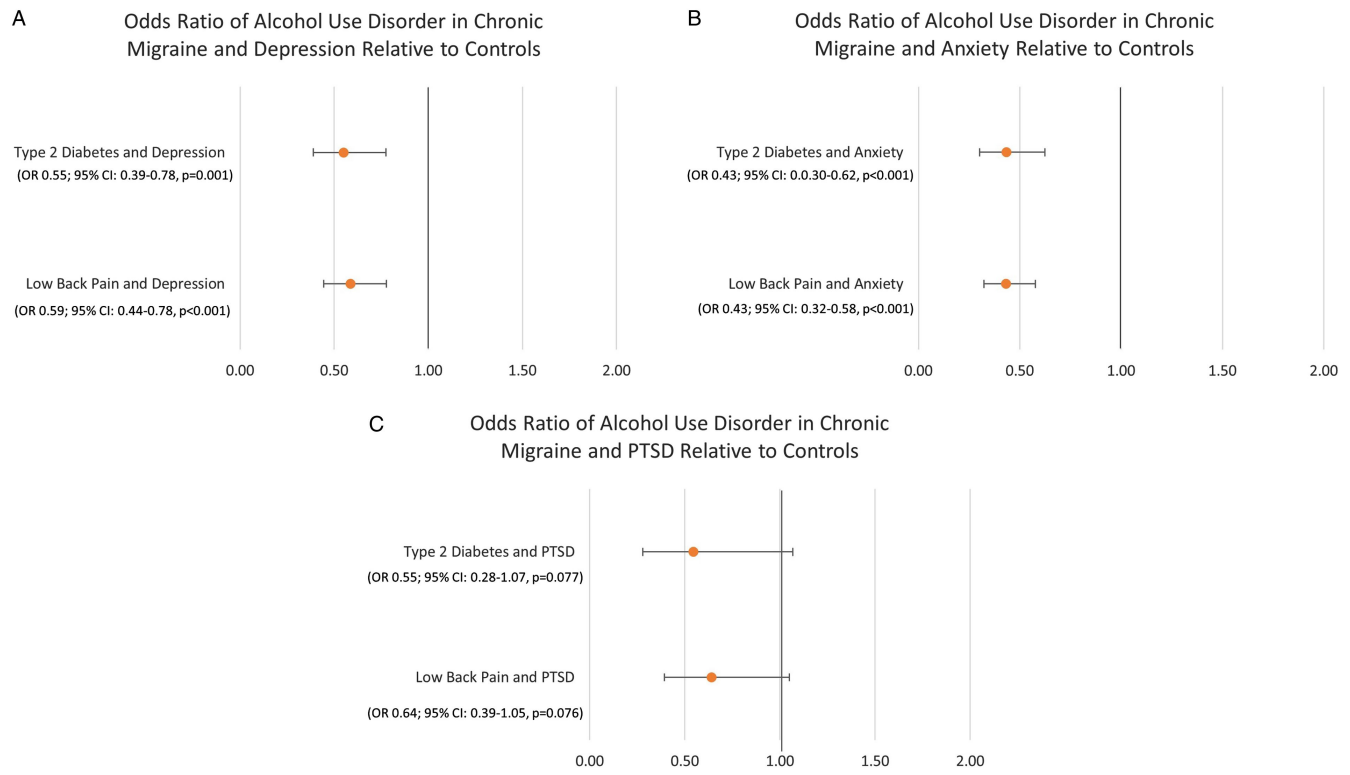


Figure 4: Odds ratios for alcohol use disorder in patients with chronic migraine relative to disease controls for 3A: depression. 3B: anxiety. 3C: PTSD.

dropped to fewer than 100 or 50 patients such that demographic analysis was limited. Given that alcohol consumption can be driven by cultural norms, determining the impact of these factors could not be performed due to the often singular or absent representation of a specific racial or ethnic group in many of the subgroups.[27] Additionally, due to the data abstraction system, it was necessary to use International Classification of Disease, Tenth Edition, codes to define these groups and not exact criteria; consequently, though we derived our chronic migraine group from patients seen exclusively by board-certified headache specialists, it is possible that a subset do not meet International Classification of Headache Disorders, Third Edition criteria for chronic migraine; with similar caveats for depression, anxiety, and PTSD and their Diagnostic and Statistical Manual of Mental Disorders criteria. Indeed, the prior studies assessing alcohol and migraine looked at either patient reported and quantified consumption of alcohol or DSM-5 diagnoses of alcohol use disorder and not ICD-10 codes, but the previous literature supports that there is acceptable agreement between DSM-5 diagnoses of alcohol use disorder and ICD-10 code diagnoses of alcohol abuse and alcohol dependence such that this could be an appropriate proxy.[28]

Future prospective trials for chronic migraine and alcohol use disorder could use ICHD-3 and DSM-5 criteria to more appropriately define study populations and then longitudinally track patients to determine if treating a patient's alcohol use disorder can positively impact their headache burden.

Conclusion

Patients with chronic migraine had a lower odds ratio of AUD relative to controls. But in patients with chronic migraine, those with comorbid depression, anxiety, or PTSD are at higher risk of AUD. When patients establish care, comorbid factors should be assessed and for those at higher risk, AUD should be screened for at every visit.

Acknowledgements. None.

Funding. None.

Competing interests. None.

Statement of authorship. Study concept and design: LSM, NZ. Acquisition of Data: LSM. Analysis and interpretation of data: LSM. Drafting of the manuscript: LSM. Revising it for intellectual content: LSM, NZ. Final approval of the completed manuscript: LSM, NZ.

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