The Association of Alcohol Use Disorder with Perioperative Complications following Primary Total Hip Arthroplasty

Andrew R. Horn, MD, Keith B. Diamond, MD, Mitchell K. Ng, MD, Rushabh M. Vakharia, MD, Michael A. Mont, MD*, Orry Erez, MD

Department of Orthopaedic Surgery, Maimonides Medical Center, Brooklyn, NY, USA
Department of Orthopaedic Surgery, Lenox Hill Hospital, Northwell Health, New York, NY, USA*

Purpose: Alcohol use disorder is a leading mental health disorder in the United States. Few studies evaluating the association of alcohol use disorder following primary total hip arthroplasty (THA) have been reported. Therefore, the purpose of this study was to determine whether patients with alcohol use disorder undergoing primary THA have higher rates of: 1) in-hospital lengths of stay (LOS); 2) complications (medical/implant-related); and 3) costs.

Materials and Methods: Using a nationwide claims database from January 1st, 2005 to March 31st, 2014, patients with alcohol use disorder undergoing primary THA were identified and matched to a comparison group according to age, sex, and various comorbidities, resulting in 230,467 patients who were included in the study (n=38,416) and a matched-cohort (n=192,051). Outcomes of interest included comparison of LOS, 90-day medical and 2-year implant-related complications, and costs. A P-value less than 0.002 was considered statistically significant.

Results: Patients with alcohol use disorder had longer in-hospital LOS (4 days vs 3 days; P<0.0001) as well as higher frequency and odds ratio (OR) of 90-day medical (45.94% vs 12.25%; OR, 2.89; P<0.0001) and 2-year implant-related complications (17.71% vs 8.46%; OR, 1.97; P<0.0001). Patients in the study group incurred higher 90-day costs of care ($17,492.63 vs $14,921.88; P<0.0001).

Conclusion: With the growing prevalence of alcohol use disorder in the United States, the current investigation can be utilized to evaluate the need for interventions prior to THA which can potentially minimize the rates of morbidity and mortality within this population.

Key Words: Alcohol use disorder, Total hip arthroplasty, Postoperative complications, Cost and costs analysis
INTRODUCTION

Alcohol use disorder has been reported as one of the most highly prevalent mental health disorders\(^1\). Depending on the study source, the lifetime prevalence of alcohol use disorder ranges from 18.8% to 30.3% with the highest prevalence generally in men, Caucasians and Native American respondents, and previously married or unmarried individuals\(^2\). DSM-V (The Diagnostic and Statistical Manual of Mental Health Disorders, Fifth Edition) defines alcohol use disorder as a constellation of symptoms consisting of dependence and abuse, with the addition of cravings, leading to psycho-social and interpersonal functioning\(^6\). The negative association of alcohol use disorder following primary total hip arthroplasty (THA) has been demonstrated in previous studies\(^7\)\(^-\)\(^11\).

Gold et al.\(^7\) demonstrated that alcohol use disorder is a significant risk factor for development of peri-prosthetic joint infections (PJIs) and deep vein thromboses following primary total knee arthroplasty. Lavernia and Villa\(^9\) demonstrated that patients with alcohol use disorder had a negative impact on patient reported outcome measurements compared to moderate drinkers or non-drinkers following primary THA. However, limitations to the aforementioned study and other studies include coalescence of other psychiatric comorbidities into the study cohort causing difficulty in understanding the relationship of alcohol use disorder following primary THA. Another limitation is that there was no adjusting for additional covariates, which could potentially overestimate the results of analysis of the dependent variables, or that the results are not generalizable to the orthopaedic community\(^7\)\(^-\)\(^9\)\(^,\)\(^12\)\(^-\)\(^13\). Thus, with the growing incidence and prevalence of alcohol use disorder with a concomitant exponential increase in the frequency of performance of primary THA procedures worldwide, conduct of studies evaluating the disorder following primary THA is warranted\(^14\)\(^-\)\(^13\).

Therefore, the purpose of this study was to conduct a case-matched study through analysis of the Medicare claims database to determine whether patients with alcohol use disorder have worse outcomes. Specifically, the study compared: 1) in-hospital lengths of stay (LOS); 2) complications (medical/implant-related); and 3) costs of care.

MATERIALS AND METHODS

1. Data Source

A retrospective level III case-control study query from January 1st, 2005 to March 31st, 2014 of the 100% Medicare Standard Analytical Files (SAF) from the PearlDiver (PearlDiver Technologies, Fort Wayne, IN, USA) platform was performed. The supercomputer houses the records of more than 150 million patients between a private payor database and the Medicare claims database. The time frame provided within the Medicare claims of the PearlDiver platform is analyzed; it has been utilized in other studies using the same database\(^14\)\(^-\)\(^19\). Due to the number of patient records available within the database, PearlDiver has been used extensively for orthopaedic-related research within all disciplines of orthopaedic surgery. The supercomputer uses a syntax-based language which is reliant on International Classification of Disease, Ninth Revision (ICD-9) and Current Procedural Terminology (CPT) coding for query and identification of cohorts of interest. Deidentified information is subsequently aggregated and downloaded as a comma separated value (.csv) spreadsheet for further analyses. The current investigation was determined to be exempt from review by our institutional review boards because the information provided from the administrative database is does not include patient identifiers.

2. Cohorts

A query of patients undergoing primary THA was performed using CPT and ICD-9 procedural codes 27130 and 81.51. Patients with a diagnosis of alcohol use disorder were identified using the codes comprising alcohol abuse (ICD-9: 305.01 and 305.02) and alcohol dependence (ICD-9: 303.91 and 303.92). These codes were chosen because they have been used in previously published studies\(^2\)\(^-\)\(^20\). In addition, when combined accurately these codes represent alcohol use disorder per the DSM-5\(^6\). Not including these codes in the current study could potentially introduce a selection bias. Patients with osteoarthritis of the hip were identified using ICD-9 diagnostic codes 715.15, 715.25, 715.35, and 715.95. These codes were chosen because they were utilized in a previously published study\(^21\). The “FIRST_COMMAND” syntax function was utilized to ensure that patients were not double counted to prevent overestimation regarding the association of alcohol use disorder on the dependent
variables being measured within the study. Using Boolean command syntax language, all patients undergoing primary THA for osteoarthritis of the hip with a concomitant diagnosis of alcohol use disorder were included in the study group, while patients without the diagnosis were included in the comparison group.

The two cohorts were subsequently matched by a predefined set of parameters within the database to eliminate any potential confounding. The two groups of patients were matched in a 1:5 ratio according to age, sex, and the following medical comorbidities commonly found within the orthopaedic community—chronic obstructive pulmonary disease (COPD), diabetes mellitus, hyperlipidemia, hypertension, obesity—defined as a body mass index (BMI>30 kg/m²) and tobacco use. Ratio matching was performed to increase the overall power of the study, which has been done in prior investigations utilizing the same database. A total of 230,467 patients within the study (n=38,416) and matched-cohort (n=192,051) were identified using the matching process. No statistical difference was observed between the aforementioned matching parameters, therefore the matching process was successful (Table 1).

3. Study Endpoints

The primary endpoint of the study was to compare perioperative outcomes among patients with alcohol use disorder to a matched cohort. Specifically, the study compared in-hospital LOS, 90-day medical complications, 2-year implant-related complications, day of surgery and total global 90-day episode of care costs. Ninety-day medical complications assessed included: acute kidney injuries, cerebrovascular accidents, deep vein thromboses, ileus episodes, myocardial infarctions, pneumoniae, pulmonary emboli, respiratory failures, transfusion of blood products, urinary tract infections, and venous thromboemboli.

Two-year implant-related complications analyzed included dislocation of prostheses, mechanical loosenings, periprosthetic fractures, PJIs, and THA revisions. Analysis of costs of care was performed by comparing reimbursements between the cohorts, which was done in previously published investigations. Reimbursements are provided for the entire cohort per the investigator’s time period of interest, in this case 90-days. The cost includes the reimbursements paid by the insurance provider for diagnostic tests, clinic visits, any procedures performed during the time interval, prescription medications, and other medical associated costs.

4. Data Analyses

Statistical analyses were performed using the open programming language R (R Foundation for Computational Statistics, Vienna, Austria). Pearson’s chi-square analyses

| Demographics          | Alcohol use disorder | Matched-cohort | P-value |
|-----------------------|----------------------|----------------|---------|
| Age (yr)              |                      |                |         |
| <64                   | 12,068 (25.6)        | 60,333 (25.6)  | 0.99    |
| 65-69                 | 13,985 (29.7)        | 69,919 (29.7)  |         |
| 70-74                 | 9,516 (20.2)         | 47,573 (20.2)  |         |
| 75-79                 | 6,834 (14.5)         | 34,162 (14.5)  |         |
| 80-84                 | 3,484 (7.4)          | 17,419 (7.4)   |         |
| >85                   | 1,240 (2.6)          | 6,197 (2.6)    |         |
| Sex                   |                      |                | 0.99    |
| Female                | 19,492 (41.4)        | 97,455 (41.4)  |         |
| Male                  | 27,635 (58.6)        | 138,148 (58.6) |         |
| Comorbidities         |                      |                |         |
| COPD                  | 2,129 (4.5)          | 10,621 (4.5)   | 0.93    |
| Diabetes mellitus     | 15,799 (33.5)        | 78,981 (33.5)  | 0.99    |
| Hyperlipidemia        | 31,934 (67.8)        | 159,656 (67.8) | 0.94    |
| Hypertension          | 41,771 (88.6)        | 208,836 (88.6) | 0.98    |
| Obesity               | 4,997 (10.6)         | 24,955 (10.6)  | 0.98    |
| Tobacco               | 19,205 (40.8)        | 95,998 (40.7)  | 0.98    |

Values are presented as number (%).
P-value by Pearson’s chi-square analyses.
COPD: chronic obstructive pulmonary disease.
were used for comparison of baseline demographics of the matched cohorts. While age has been compared as a continuous variable, the database provides age as a categorical variable with an age distribution from less than 64 to greater than 84 years of age with five-year increments. Welch’s t-tests were used for comparison of in-hospital LOS and costs of care following the index procedure between the matched cohorts. To determine the association of alcohol use disorder on medical- and implant-related complications, multivariate logistic regression analyses were performed for calculation of the odds ratio (OR) and 95% confidence interval (95% CI) adjusting for age, sex, geographic region, and Elixhauser Comorbidity Index (ECI)\(^27\).

Due to the ease of finding statistical differences with large administrative datasets, a Bonferroni-correction was performed to minimize the probability of a type I error. As such, a \(P\)-value less than 0.002 was the threshold utilized in this study to determine statistical significance. This value was attained by dividing 0.05 by the number of comparisons performed within the study (\(n=18\))\(^{28,29}\).

**RESULTS**

1. **In-Hospital Lengths of Stay and Medical Complications**

In-hospital LOS (4 days vs 3 days, \(P<0.0001\)) was significantly longer for patients with alcohol use disorder undergoing primary THA. In addition, the study cohort had higher rates of medical complications (45.94% vs 12.25%; OR, 2.89; 95% CI, 2.74-3.03; \(P<0.0001\)) such as respiratory failures (5.79% vs 1.09%; OR, 3.41; 95% CI,
3.22-3.61; \( P<0.0001 \)), cerebrovascular accidents (4.40\% vs 0.90\%; OR, 3.39; 95\% CI, 3.18-3.62; \( P<0.0001 \)), acute kidney injuries (7.04\% vs 1.33\%; OR, 3.33; 95\% CI, 3.16-3.51; \( P<0.0001 \)), pneumonias (6.61\% vs 1.39\%; OR, 3.12; 95\% CI, 2.96-3.29; \( P<0.0001 \)), ileus episodes (1.23\% vs 0.27\%; OR, 2.95; 95\% CI, 2.62-3.32; \( P<0.0001 \)), urinary tract infections (12.03 vs 3.63\%; OR, 2.56; 95\% CI, 2.47-2.66; \( P<0.0001 \)) and other medical complications within 90-days following the index procedure (Fig. 1).

2. Implant-Related Complications and Costs of Care

In addition, patients with alcohol use disorder had higher incidence and odds of 2-year implant-related complications (17.71\% vs 8.46\%; OR, 1.97; 95\% CI, 1.85-2.09; \( P<0.0001 \)) such as peri-prosthetic fractures (1.67\% vs 0.61\%; OR, 2.06; 95\% CI, 1.88-2.26; \( P<0.0001 \)), dislocations of the prostheses (4.78\% vs 2.17\%; OR, 1.66; 95\% CI, 1.58-1.76; \( P<0.0001 \)), revisions (6.15\% vs 3.07\%; OR, 1.58; 95\% CI, 1.51-1.66; \( P<0.0001 \)) and other implant-related complications within two-years following the index procedure.
well-powered studies evaluating the association of alcohol use disorder following primary THA, the study demonstrated that patients in the study group incurred significantly higher costs than controls ($13,201.80 vs $11,908.17; \textit{P}<0.0001) and total global 90-day episode of care costs ($17,492.63 vs $14,921.88; \textit{P}<0.0001).

DISCUSSION

In the United States, approximately one-third of adults will meet the criteria for alcohol use disorder at some point during their lives, and approximately 15.1 million adults currently meet the criterion for alcohol use disorder\textsuperscript{30,31}. With the continually rising prevalence of alcohol use disorder, well-powered studies evaluating the association of alcohol use disorder following primary THA are limited\textsuperscript{12,29}. Therefore, the aim of this study was to perform an analysis by identifying patients with alcohol use disorder and determining its impact on certain dependent variables. After adjusting for covariates, the study demonstrated an association between alcohol use disorder and longer in-hospital LOS, higher rates of medical and implant-related complications, and increased healthcare expenditure following primary THA.

While the large sample size provides power to the study, the current study is not without limitations, most of which are inherent to the use of large administrative claim registries. A single insurance claims database was analyzed in this study, and the results may not be a true cross-sectional representation on the impact of alcohol use disorder following primary THA\textsuperscript{32}. Additionally, it is possible that patients in the control cohort may not have been formally diagnosed with alcohol use disorder, potentially underestimating the true relationship of this condition on the outcomes assessed within the study. Furthermore, the validity and accuracy of the study is dependent on accurate diagnostic and procedural coding and, according to an estimate the Medicare claims database contains up to 1.3% coding errors\textsuperscript{15}. In addition, while we found that certain variables showed statistical significance (i.e., LOS) this may not correlate to clinical significance, due to the ease of finding statistical significance with large datasets. Due to restrictions within the PearlDiver database, the frequency and amount of alcohol intake could not be adjusted for within the study, and this could potentially skew the results of the study; but can certainly serve as the basis for future studies by stratifying severity and frequency and determining its relationship on outcomes following total joint arthroplasty (TJA). Similarly, while our cohorts were matched on various comorbid conditions, due to further restrictions, the cohorts could not be matched according to height and weight; which could potentially have impacted the results of the study. Despite these limitations, this is a large study to assess and quantify the relationship of alcohol use disorder with various dependent variables in patients exclusively undergoing primary THA.

The results of this study are consistent with findings from the literature\textsuperscript{11,12,23-35}. We demonstrated an association between alcohol use disorder and a longer hospital course following primary THA. In a retrospective study utilizing the Nationwide Inpatient Sample (NIS) database, Best et al.\textsuperscript{12} demonstrated significantly longer in-hospital LOS following primary TJA in patients with alcohol misuse. Nath et al.\textsuperscript{11} reported results similar to those of the aforementioned study in an analysis of the National Surgical Quality Improvement Program (NSQIP) database by demonstrating that alcohol users had significantly longer LOS (5 days vs 3 days; \textit{P}<0.05) compared to controls. In an analysis of their own institution’s data of 191 patients (218 primary hips), Lavermia et al.\textsuperscript{9} stratified patients into three separate cohorts based on the frequency of alcohol consumption and demonstrated no statistical significance between the LOS of the three cohorts. However, a significant limitation to the aforementioned study potentially explaining the disparities between the results of this study could be due to the study being underpowered with only 218 primary hips. In addition, the results compared LOS between all three cohorts together, but it is possible that a significant difference could have been observed between the control and occasional users cohort of the study\textsuperscript{9}. In addition to longer in-hospital LOS, the findings of the study showed higher frequency and odds of developing medical and implant-related complications following primary THA.

Patients in the study group had higher cardiopulmonary related complications, most notably respiratory failures (OR, 3.49), cerebrovascular accidents (OR, 3.39), and pneumonia (OR, 3.12). Best et al.\textsuperscript{12} found that alcohol misuse significantly increased the odds of developing pulmonary insufficiency (OR, 5.23; \textit{P}<0.0001) following primary TJA. Higher results were reported for their study compared with the results of this study, which can be attributed to lack of adjusting for covariates within their investigation, unlike the current study. Luo et al.\textsuperscript{33} reported similar results; cardiopulmonary manifestations were the leading medical complications. Studies have shown alcohol-induced changes in hemodynamic parameters of clot formation, stability, and...
alteration of sensitivity to fibrinolysis, which could explain the higher rates of cerebrovascular accidents found in this study\textsuperscript{36}.

As such, education of these patients and insisting on the importance of proper optimization prior to their elective procedure is critical, similar to when great care is taken to educate patients on the effects of nicotine and smoking during the perioperative period. Alcohol use should additionally be discussed in depth with patients undergoing primary THA. Treatment options demonstrating the greatest efficacy for patients with alcohol use disorder include brief interventions such as motivational interviewing approaches, operant conditioning approaches, utilizing a community reinforcement approach, and cognitive behavioral therapy\textsuperscript{37}. Mutual support group attendance and programs such as alcoholics anonymous have been associated with recovery from alcohol use disorder, even in the absence of formal treatment\textsuperscript{38}.

**CONCLUSION**

The prevalence of alcohol use disorder continues to increase in the United States; the condition is one of the leading mental health disorders nationwide. Well-powered studies investigating the impact of alcohol use disorder in patients exclusively undergoing primary THA are limited. Therefore, the aim of this study was to analyze a large comprehensive nationwide database to determine the association of the condition in patients undergoing primary THA. After adjusting for covariates, the study demonstrated an association between alcohol use disorder and longer in-hospital LOS in addition to higher rates of adverse events and healthcare expenditures. Future investigations should stratify the severity of the condition with regard to outcomes following the procedure as this could provide clarity as to which patients would be at the greatest risk for complications. The current study can be used by orthopaedists and other healthcare professionals to educate potential patients on outcomes following their elective procedure.

**CONFLICT OF INTEREST**

The authors declare that there is no potential conflict of interest relevant to this article.

**REFERENCES**

1. Rehm J, Anderson P, Barry J, et al. *Prevalence of and potential influencing factors for alcohol dependence in Europe*. Eur Addict Res. 2015;21:6-18.
2. Wittchen HU, Jacobi F, Rehm J, et al. *The size and burden of mental disorders and other disorders of the brain in Europe 2010*. Eur Neuropsychopharmacol. 2011;21:655-79.
3. Kessler RC, Chiu WT, Demler O, Merikangas KR, Walters EE. *Prevalence, severity, and comorbidity of 12-month DSM-IV disorders in the National Comorbidity Survey Replication*. Arch Gen Psychiatry. 2005;62:617-27.
4. Kessler RC, Berglund P, Demler O, Jin R, Merikangas KR, Walters EE. *Lifetime prevalence and age-of-onset distributions of DSM-IV disorders in the National Comorbidity Survey Replication*. Arch Gen Psychiatry. 2005;62:593-602.
5. Hasin DS, Stinson FS, Ogburn E, Grant BF. *Prevalence, correlates, disability, and comorbidity of DSM-IV alcohol abuse and dependence in the United States: results from the National Epidemiologic Survey on Alcohol and Related Conditions*. Arch Gen Psychiatry. 2007;64:830-42.
6. Grant BF, Goldstein RB, Saha TD, et al. *Epidemiology of DSM-5 alcohol use disorder: results from the National Epidemiologic Survey on Alcohol and Related Conditions III*. JAMA Psychiatry. 2015;72:757-66.
7. Gold PA, Garbarino LJ, Anis HK, et al. *The cumulative effect of substance abuse disorders and depression on postoperative complications after primary total knee arthroplasty*. J Arthroplasty. 2020;35(6S):S151-7.
8. Best MJ, Buller LT, Klika AK, Barsoum WK. *Outcomes following primary total hip or knee arthroplasty in substance misusers*. J Arthroplasty. 2015;30:1137-41.
9. Lavernia CJ, Villa JM, Contreras JS. *Alcohol use in elective total hip arthroplasty: risk or benefit?* Clin Orthop Relat Res. 2013;471:504-9.
10. Bradley KA, Rubinsky AD, Sun H, et al. *Prevalence of alcohol misuse among men and women undergoing major noncardiac surgery in the Veterans Affairs health care system*. Surgery. 2012;152:69-81.
11. Nath B, Li Y, Carroll JE, Szabo G, Tseng JF, Shah SA. *Alcohol exposure as a risk factor for adverse outcomes in elective surgery*. J Gastrointest Surg. 2010;14:1732-41.
12. Best MJ, Buller LT, Gosthe RG, Klika AK, Barsoum WK. *Alcohol misuse is an independent risk factor for poorer postoperative outcomes following primary total hip and total knee arthroplasty*. J Arthroplasty. 2015;30:1293-8.
13. Sloan M, Premkumar A, Sheth NP. *Projected volume of primary total joint arthroplasty in the U.S., 2014 to 2030*. J Bone Joint Surg Am. 2018;100:1455-60.
14. Cancienne JM, Dempsey JJ, Holzgreve RE, Brockmeier SF, Werner BC. *Is hepatitis C infection associated with a higher risk of complications after total shoulder arthroplasty?* Clin Orthop Relat Res. 2016;474:2664-9.
15. Cancienne JM, Patel KJ, Browne JA, Werner BC. *Narcotic use and total knee arthroplasty*. J Arthroplasty. 2018;33:113-8.
16. Casp AJ, Montgomery SR Jr, Cancienne JM, Brockmeier SF, Werner BC. *Osteoporosis and implant-related complications after anatomic and reverse total shoulder arthroplasty*. J Am Acad Orthop Surg. 2020;28:121-7.
17. Swiggett SJ, Mannino A, Vakharia RM, et al. *Impact of biological sex on complications, lengths of stay, readmission rates,
and costs of care following primary total knee arthroplasty. J Knee Surg. Published online February 5 2021; doi: 10.1055/s-0041-1723014.

18. Swiggett SJ, Vakharia AM, Ehiorobo JO, et al. Impact of depressive disorders on primary total shoulder arthropalsties: a matched control analysis of 113,648 Medicare patients. Shoulder Elbow. 2021;13:181-7.

19. Vakharia RM, Sodhi N, Anis HK, Ehiorobo JO, Mont MA, Roche MW. Patients who have cannabis use disorder have higher rates of venous thromboemboli, readmission rates, and costs following primary total knee arthroplasty. J Arthroplasty. 2020;35:997-1002.

20. Passias PG, Bortz C, Alas H, et al. Alcoholism as a predictor for pseudarthrosis in primary spine fusion: an analysis of risk factors and 30-day outcomes for 52,402 patients from 2005 to 2013. J Orthop. 2018;46:36-40.

21. Malahias MA, Gu A, Richardson SS, De Martino I, Sculco PK, McLawhorn AS. Hip arthroscopy for hip osteoarthritis is associated with increased risk for revision after total hip arthroplasty. Hip Int. 2021;31:656-62.

22. LeBrun DG, Tran T, Wypij D, Kocher MS. How often do orthopaedic matched case-control studies use matched methods? A review of methodological quality. Clin Orthop Relat Res. 2019;477:655-62.

23. Sabeh KG, Rosas S, Buller LT, Freiberg AA, Emory CL, Roche MW. The impact of medical comorbidities on primary total knee arthroplasty reimbursements. J Knee Surg. 2019;32:475-82.

24. Cancienne JM, Gwathmey FW, Miller MD, Werner BC. Tobacco use is associated with increased complications after anterior cruciate ligament reconstruction. Am J Sports Med. 2016;44:99-104.

25. Vakharia RM, Ehiorobo JO, Sodhi N, Swiggett SJ, Mont MA, Roche MW. Effects of depressive disorders on patients undergoing primary total knee arthroplasty: a matched-control analysis. J Arthroplasty. 2020;35:1247-51.

26. Martin CT, D’Oro A, Buser Z, et al. Trends and costs of anterior cervical discectomy and fusion: a comparison of inpatient and outpatient procedures. Iowa Orthop J. 2018;38:167-76.

27. Maron SZ, Neifert SN, Ranson WA, et al. Elkhassar Comorbidity measure is superior to Charlson Comorbidity Index in predicting hospital complications following elective posterior cervical decompression and fusion. World Neurosurg. 2020;138:e26-34.

28. Yoshihara H, Yoneoka D. Understanding the statistics and limitations of large database analyses. Spine (Phila Pa 1976). 2014;39:1311-2.

29. Chen SY, Feng Z, Yi X. A general introduction to adjustment for multiple comparisons. J Thorac Dis. 2017;9:1725-9.

30. Hasin DS, Sardar VA, Meyers J, et al. Epidemiology of adult DSM-5 major depressive disorder and its specifiers in the United States. JAMA Psychiatry. 2018;75:336-46.

31. Center for Behavioral Health Statistics and Quality. Results from the 2013 national survey on drug use and health: summary of national findings [Internet]. Rockville: Center for Behavioral Health Statistics and Quality; 2014 Sep [cited 2019 Sep 8]. Available from: https://www.samhsa.gov/data/sites/default/files/NSDUHresultsPDFWHTML2013/Web/NSDUHresults2013.pdf.

32. Cancienne JM, Brockmeier SF, Carson EW, Werner BC. Risk factors for infection after shoulder arthroscopy in a large Medicare population. Am J Sports Med. 2018;46:809-14.

33. Luo TD, Vakharia RM, Gwam CU, Zuskov A, Plate JF, Roche MW. A matched control analysis on the effects of alcohol use disorder after primary total knee arthroplasty in Medicare patients. J Am Acad Orthop Surg. 2021;29:e593-600.

34. Gandhi JA, Ekhar VV, Asplund MB, et al. Alcohol enhances Acinetobacter baumannii-associated pneumonia and systemic dissemination by impairing neutrophil antimicrobial activity in a murine model of infection. PloS One. 2014;9:e95707.

35. Karavitis J, Kovacs EJ. Macrophage phagocytosis: effects of environmental pollutants, alcohol, cigarette smoke, and other external factors. J Leukoc Biol. 2011;90:1065-78.

36. Drieu A, Lanquetin A, Levard D, et al. Alcohol exposure-induced neurovascular inflammatory priming impacts ischemic stroke and is linked with brain perivascular macrophages. JCI Insight. 2020;5:e129226.

37. Witkiewitz K, Litten RZ, Leggio L. Advances in the science and treatment of alcohol use disorder. Sci Adv. 2019;5:eaaax4043.

38. Kelly JF, Bergman B, Hoepnner BB, Vilsaint C, White WL. Prevalence and pathways of recovery from drug and alcohol problems in the United States population: implications for practice, research, and policy. Drug Alcohol Depend. 2017;181:162-9.