



## Review

## Preoperative alcohol use disorders and adverse outcomes in surgical patients: A systematic review and meta-analysis

Nethmi Rajapakse<sup>a</sup>, Eric Rubenzahl<sup>a</sup>, Aparna Saripella<sup>b</sup>, Jun Won Lee<sup>c</sup>, Sara Mansouri<sup>a</sup>, Shirley Fan<sup>d</sup>, Marina Englesakis<sup>e</sup>, Frances Chung<sup>a,b,f,\*</sup>

<sup>a</sup> Temerty Faculty of Medicine, University of Toronto, Toronto, ON, Canada

<sup>b</sup> Department of Anesthesia and Pain Management, Toronto Western Hospital, University Health Network, University of Toronto, Toronto, ON, Canada

<sup>c</sup> Faculty of Medicine, University of Saskatchewan, Saskatoon, SK, Canada

<sup>d</sup> Schulich School of Medicine & Dentistry, Western University, London, ON, Canada

<sup>e</sup> Library & Information Services, University Health Network, Toronto, ON, Canada

<sup>f</sup> Institute of Medical Science, Temerty Faculty of Medicine, University of Toronto, ON, Canada

## HIGHLIGHTS

- Surgical patients with unhealthy alcohol use (UAU) had almost 3x more respiratory and 2x more greater infection/wound complications.
- Surgical patients with UAU showed 70% higher in-hospital mortality and almost 1-day longer length of stay.
- Males had over 2.5x higher odds of UAU, while females had ~60% lower odds; UAU patients were consistently younger overall.
- Routine preoperative alcohol screening may support integration of alcohol-focused risk assessment and perioperative care.

## ARTICLE INFO

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## ABSTRACT

**Objective:** To evaluate the association between preoperative unhealthy alcohol use (UAU), including alcohol use disorder and hazardous/risky alcohol use, and postoperative outcomes in adult surgical patients.

**Methods:** The Ovid MEDLINE, Embase, and Cochrane databases were searched for English-language studies involving adults undergoing surgery. Eligible studies compared patients with preoperative UAU to those with no UAU and reported at least one postoperative outcome within 12 months. Preoperative alcohol exposure was determined using validated assessment tools or self-reported alcohol use disorder. Random-effects meta-analyses were conducted to calculate risk ratios (RRs) or mean differences (MDs) with 95% confidence intervals (CIs).

**Results:** Thirty-five studies ( $n = 18,472,205$ ) met inclusion criteria, and 35 studies were included in the meta-analyses. Preoperative alcohol use disorder was associated with a higher risk of respiratory complications (RR 2.59, 95% CI 1.51–4.45;  $P = 0.0005$ ), infections/wound complications (RR 1.71, 95% CI 1.37–2.15;  $P < 0.0001$ ), longer length of hospital stay (mean difference 0.76 days, 95% CI 0.24–1.29;  $P = 0.004$ ), and higher in-hospital mortality (RR 1.67, 95% CI 1.21–2.29;  $P = 0.002$ ).

**Conclusion:** Surgical patients with alcohol use disorder were associated with worse postoperative outcomes, including higher rates of respiratory complications and infections, longer length of hospital stay and increased in-hospital mortality. These findings support screening for alcohol use and preoperative optimization including cessation support and postoperative monitoring.

## 1. Introduction

Alcohol consumption is a major global health concern and is

recognized by the World Health Organization (WHO) as one of the leading preventable causes of non-communicable diseases [1]. Harmful alcohol use contributes to approximately 3 million deaths annually and

\* Corresponding author at: Department of Anesthesia and Pain Medicine, Toronto Western Hospital, University Health Network, University of Toronto, 399 Bathurst Street, Toronto, ON, M5T 2S8, MCL 2-405, Canada.

E-mail address: [frances.chung@uhn.ca](mailto:frances.chung@uhn.ca) (F. Chung).

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accounts for 5.3% of all global mortality [2]. Alcohol use disorder (AUD) is defined by the Diagnostic and Statistical Manual of Mental Disorders-5 (DSM-5) as “a problematic pattern of alcohol use leading to clinically significant impairment or distress” [3].

Preoperative alcohol consumption has been associated with an increased risk of postoperative complications [1,4]. Despite its known adverse impact on health and the high prevalence of harmful alcohol use among surgical patients, it remains under-recognized and undertreated in clinical settings, particularly within surgical care [5]. As a modifiable behavioral risk factor, preoperative unhealthy alcohol use (UUA) represents a clinically relevant target for preoperative intervention to reduce adverse outcomes.

The biological mechanisms linking alcohol use to postoperative risk are of clinical importance. Chronic alcohol consumption impairs wound healing and heightens susceptibility to infection through reduced neutrophil and macrophage function, altered cytokine production, and impaired cell-mediated immunity [6]. Alcohol also disrupts the hypothalamic-pituitary-adrenal axis and stress hormone regulation, diminishing the body's capacity to respond to the physiological stress of surgery [6]. Together, these effects increase patient vulnerability to surgical complications.

Despite the availability of validated screening tools, such as the Alcohol Use Disorders Identification Test (AUDIT) [7], the abbreviated Alcohol Use Disorders Identification Test–Consumption (AUDIT-C) [8], diagnostic tools of Diagnostic and Statistical Manual of Mental Disorders-3/4 (DSM 3/4) [9,10], and International Classification of Diseases 9th/10th Revision (ICD 9/10) [11,12], alcohol use is not consistently assessed in preoperative evaluations [13]. Furthermore, there is a lack of evidence-based guidelines for the perioperative management of patients with UUA, contributing to significant variability in clinical practice and missed opportunities for intervention [14,15].

An updated synthesis of the literature is warranted to reflect the current data and guide perioperative care as a previous systematic review was published over ten years ago [4]. This systematic review and meta-analysis aims to (1) evaluate the association between excessive preoperative UUA and the risk of postoperative complications, and (2) explore differences in complication rates across the types of surgery and UUA definitions.

## 2. Methods

### 2.1. Study protocol and registration

The protocol for this systematic review and meta-analysis was registered with the International Prospective Register of Systematic Reviews (PROSPERO; registration number: 420251010380). Additionally, the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist was fully completed.

### 2.2. Literature search methodology

The following databases were searched by the information specialist (ME) from inception via the Ovid platform: MEDLINE, MEDLINE ePubs and In-Process Citations (daily), Embase Classic+Embase, Cochrane Central Register of Controlled Trials, and the Cochrane Database of Systematic Reviews. All the databases were searched on, March 11, 2025. Preliminary searches were conducted, and full text literature was mined for potential keywords and appropriate controlled vocabulary terms (such as Medical Subject Headings for MEDLINE and Emtree descriptors for Embase). The Yale MeSH Analyser was used to facilitate the MeSH and text word analysis [16]. The search strategy concept blocks were built on the topics of: Preoperative and Alcohol Use Disorder and (Surgery or Perioperative) and (Prevalence or Outcomes or Complications); using both controlled vocabularies and text word searching for each component. Searches were limited to English language, humans, and adults. Conference abstracts and/or non-journal materials were

removed from results at source, where possible. The Ovid MEDLINE search strategy is provided in S-Appendix A.

### 2.3. Study selection and data extraction

Following the removal of duplicates, four independent reviewers working in pairs (NR, ER, JL, SM) screened titles and abstracts using the Covidence platform. Full-text assessments were similarly conducted independently. Discrepancies at any stage were resolved through consultation with a fifth reviewer (SF).

The primary outcomes of interest were postoperative complications and healthcare utilization within 12 months of surgery. Postoperative complications included: respiratory (pneumonia, respiratory failure, mechanical ventilation/prolonged intubation), cardiac (arrhythmias, myocardial ischemia/infarction, heart failure, venous thromboembolism), neurologic (stroke/TIA, new focal deficit, encephalopathy/delirium), urological, infections (surgical-site infection, wound dehiscence, etc.), bleeding (hemorrhage and/or transfusion), and others. Also, length of hospital stay (LOS), mortality (in-hospital, 30-day, 90-day, and 1-year), ICU admission, 30–90-day readmission, emergency department (ED) visit, and reoperation were included.

The inclusion criteria encompassed: (1) adult surgical patients ( $\geq 18$  years) undergoing elective or emergency procedures; (2) preoperative alcohol use measured using: diagnostic criteria, validated instruments, screening tools, or self-reported; (3) at least one reported postoperative outcome within 12 months; and (4) prospective cohort or retrospective cohort studies or cross-sectional cohorts. The exclusion criteria included: (1) study population  $< 18$  years old; (2) local anesthesia, monitored anesthesia care, sedation; (3) case reports, case-controls, case-series; (4) non-English language; (5) non-primary research; and (6) studies focused on liver disease or liver transplantation.

Data from eligible studies were independently extracted by four reviewers working in pairs (NR, ER, JL, SM). Discrepancies were resolved through discussion. Extracted data included study characteristics (e.g., author, year, study design, country, surgical type), patient demographics, detailed information regarding alcohol exposure (e.g., exposure type, assessment method, threshold, timing preoperatively, categorization of consumption groups), and postoperative outcomes. In keeping with prior methodological standards, we classified alcohol-exposure definitions into three categories: (1) validated screening or diagnostic tools (AUDIT, AUDIT-C, or DSM-III/IV), with DSM used as the primary classification when applied following any screening instrument; (2) ICD-9/10 alcohol-related diagnostic codes; and (3) self-report or custom thresholds, which included non-validated measures such as patient- or clinician-reported number of drinks per day, usual alcohol intake, or study-specific quantity-frequency cut-offs (e.g.,  $\geq 2$  drinks/day or  $\geq 60$  g ethanol/day). Outcome data included both binary and continuous measures, along with effect estimates.

### 2.4. Quality appraisal

Two independent reviewers (JL, SM) appraised the methodological quality of the included studies, with disagreements resolved through discussion or consultation with a third reviewer (NR). The Newcastle-Ottawa Scale (NOS) and the Meta-Analyses of Observational Studies in Epidemiology (MOOSE) checklist were employed [17,18]. The NOS, adapted for prospective and retrospective cohort studies, evaluated cohort selection, comparability, and outcome assessment. For prospective cohorts, scores of 8–9 indicated high quality, 6–7 moderate quality, and  $< 6$  low quality. For retrospective cohorts, scores of 5–6 were considered high quality, 4 moderate quality, and  $< 4$  low quality. For the cross-sectional study, scores of 7–8 were considered high quality, 5–6 moderate quality, and  $< 5$  low quality. The MOOSE checklist was used to assess study design, statistical analysis, population selection, outcome definition and measurement, follow-up completeness, and control of confounding factors.

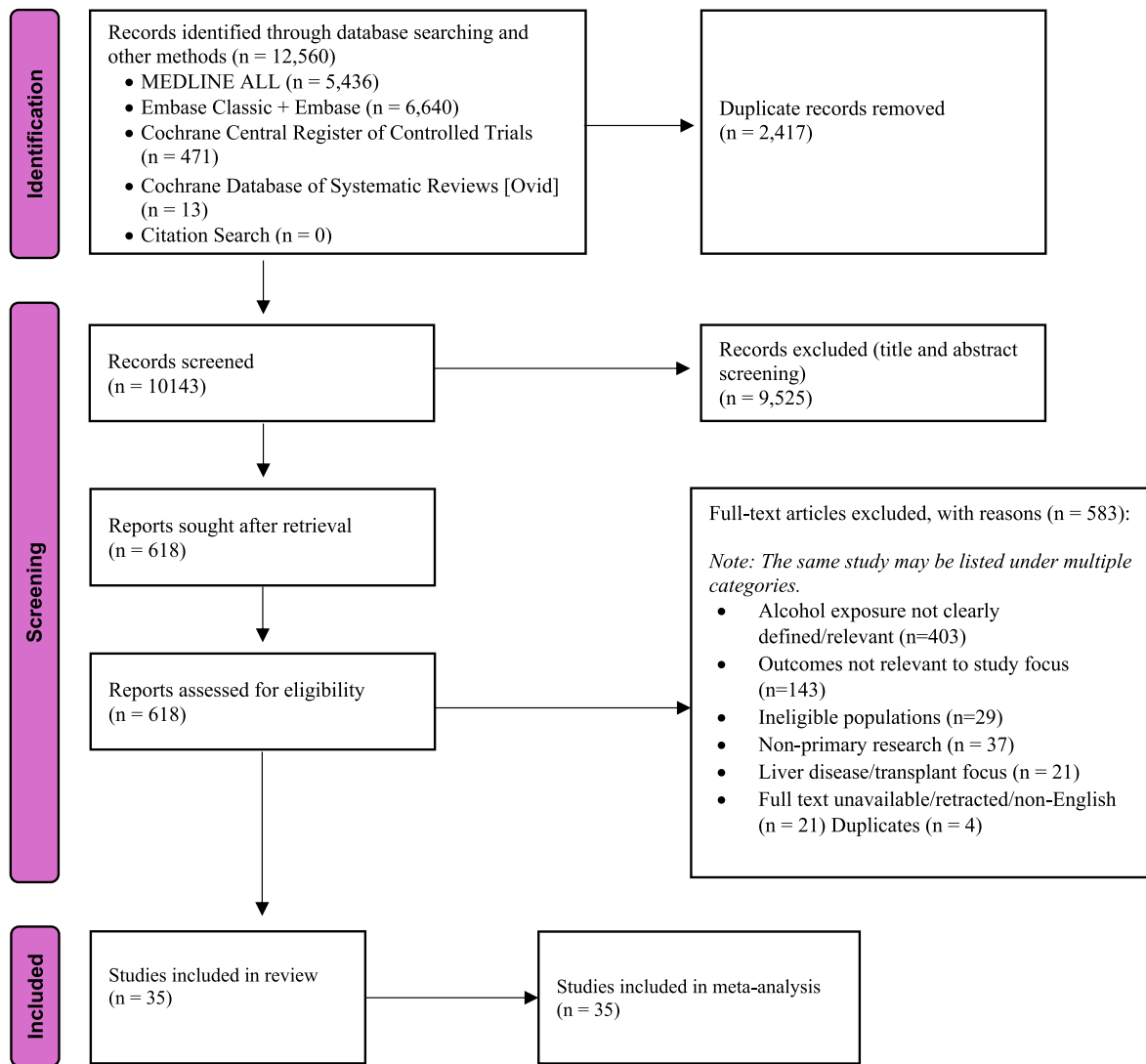


Fig. 1. PRISMA flow diagram. PRISMA, Preferred Reporting Items for Systematic Review and Meta-Analyses.

### 2.5. Statistical analysis

We generated a descriptive summary of study characteristics (sample size, study design, surgery type), patient demographics (age, female sex, AUD exposure), and clinical (postoperative complications including respiratory, cardiac, neurological, urological complications LOS, mortality, etc.). UAU was defined using different instruments across studies (AUDIT/AUDIT-C, DSM-III/IV diagnostic criteria, ICD-9/10 diagnostic codes, and self-reported alcohol use). We pre-specified subgroup analyses by AUD definition and conducted sensitivity analyses restricted to studies using validated screening or diagnostic tools (AUDIT/AUDIT-C or DSM-III/IV).

Factorial data was reported as frequencies and percentages and continuous data was described as mean and standard deviations. Data reported as median and interquartile range was converted to mean and standard deviations for pooled calculations and analysis [19]. Quantitative analyses were completed using R version 4.4.2 (R Foundation for Statistical Computing, Vienna, Austria) and Cochrane Review Manager Version 5.4.

Random-effects model was used for meta-analysis and a  $P \leq 0.05$  was considered statistically significant. For dichotomous outcomes, risk ratio (RR) with 95% confidence intervals (CI) and restricted maximum likelihood (REML) estimation of between study variance and Mantel Haenszel (MH) method was used. For continuous outcomes, mean

difference (MD) and 95% CI with Inverse Variance method was used. We conducted meta-analysis when there were 3 or more studies for a particular outcome. All calculated estimates are presented in the form of a forest plot. Statistical heterogeneity was assessed using Cochran's Q statistic and  $I^2$  statistic, with 95% prediction intervals. Publication bias and meta-regression were conducted when there were 10 or more studies reporting the same outcome.

Publication bias was completed both visually using funnel plots and quantitatively using linear regression test or Egger's test [20]. Univariable meta-regression was conducted to examine the effect of covariates such as sample size, age, study design, female sex, surgery type and UAU definition on clinical outcomes. Sample size, mean age, and percentage of female participants were examined as continuous covariates, whereas study design, surgery type, and the definition of UAU were treated as categorical factors.

Subgroup analysis was performed to explore the effect of clinically significant variables on the pooled estimates of important outcomes. We conducted subgroup analyses by type of surgery, UAU definition, type of self-reported AUD assessment, age ( $\geq 60$  years vs  $< 60$  years) and sex (female vs male). Sensitivity analysis was conducted to assess the effect of each individual study on the pooled estimate by excluding one study at a time and recalculating the heterogeneity ( $I^2$ ). We conducted the sensitivity analyses excluding studies with converted values to evaluate the strength of the findings. We noted that the results were not influenced by

**Table 1**  
Demographic and characteristics by unhealthy alcohol use status in non-cardiac surgery.

Study <sup>Year</sup>	Country	Study design; Patient No.	UAU No.	Non-UAU No.	Surgery type	UAU Age (mean ± SD)	Non-UAU Age (mean ± SD)	UAU Female %	Non-UAU Female %	Definition of alcohol exposure
Ashraf <sup>2022</sup>	USA	RC; 32,845	5479	27,367	TSA	NR	NR	40.9	40.9	ICD-9
Best <sup>2015</sup>	USA	RC; 8,372,232	50,861	8,321,371	TKA THA	62 ± 12.1	67 ± 11.7	38.3	61.6	ICD-9
Chiu <sup>2024</sup>	USA	RC; 59,261	1522	57,739	TSA	62	68	34.3	53.6	ICD-9/10
DelgadoRodriguez <sup>2003</sup>	Spain	RC; 1505	193	1312	Mixed	NR	NR	34.9	76.5	Self-Report
deMenezes <sup>2020</sup>	Brazil	PC; 486	101	385	Breast Ca	54 ± 8.1	56 ± 8.1	100	100	Self-Report
deWit <sup>2013</sup>	USA	RC; 24,041	12,081	11,960	CS*	NR	NR	50.2	49.8	ICD-9
Fernandez <sup>2023</sup>	USA	RC; 200,816	5692	195,124	Mixed	NR	NR	22.1	55.4	Self-Report
Gold <sup>2020</sup>	USA	RC; 11,403	71	11,312	TKA	67 ± 9.6	66 ± 9.6	NR	NR	ICD-9/10
Graf <sup>2018</sup>	USA	RC; 4715	630	4085	Lung resection	64 ± 7.7	66 ± 8.9	0.8	3.5	Self-Report
Han <sup>2021</sup>	USA	CS 3,132,192	35,833	3,096,355	Spinal fusion	55 ± 0.18	56 ± 0.09	26.3	55.2	ICD-9
Khan <sup>2025</sup>	USA	RC; 4,896,757	97,565	4,799,192	Spinal fusion	56 ± 0.125	57 ± 0.075	12.3	12.3	ICD-9/10
Klasen <sup>2004</sup>	Germany	RC; 1794	897	897	Mixed	52 ± 12.7	52 ± 12.7	11.5	17.3	Self-Report
Kudoh <sup>2007</sup>	Japan	PC; 81	31	50	THA TKA	72 ± 4.4	72 ± 3.8	0	0	Self-Report
Ladjevic <sup>2021</sup>	Serbia	PC; 80	4	76	Prostatectomy	NR	NR	0	0	Self-Report
Paull <sup>2004</sup>	USA	RC; 56	19	37	Lung resection	62 ± 2.3	67 ± 1.5	5.3	0	DSM-IV
Ponce <sup>2014</sup>	USA	RC; 422,371	5658	416,713	TSA/ HA	62 ± 11	69 ± 11	37.0	61.0	ICD-9
Rolfzen <sup>2022</sup>	USA	RC; 603,730	17,308	586,422	Colectomy	NR	NR	NR	NR	ICD-10
Rotevatn <sup>2017</sup>	Denmark	RC; 30,799	1958 high; 2463 excessive	26,378	Partial HA/KA	NR	NR	24.3 high; 72.9 excessive	41.3	Self-Report
Rubinsky <sup>2012</sup>	USA	RC; 5171	879	4292	Mixed	62 ± 9	66 ± 10	0	0	AUDIT-C
Rubinsky <sup>2013</sup>	USA	RC; 8811	626	8185	Mixed	62 ± 9	64 ± 11	0	0	AUDIT-C
Sander <sup>2002</sup>	Germany	PC; 45	25	20	GI tumor	60 ± 6.00	62 ± 9.75	12.0	20.0	DSM-III
Schoenfeld <sup>2010</sup>	Germany	PC; 25	12	13	TKA THA	63 ± 3	61 ± 2.75	25.0	46.0	Self-Report
Spies <sup>2004</sup>	Germany	PC; 54	31	23	GI Tumor	56 ± 3.0	55 ± 2.25	12.9	13.0	DSM-IV
Stearns <sup>2009</sup>	Scotland	RC; 78	37	41	Internal Fixation/ THA	54 ± 7.28	52 ± 8.50	24.0	68.0	Self-Report
White <sup>2023</sup>	USA	RC; 164,527	501	164,026	TSA	65 ± 9.2	69 ± 9.5	34.7	56.1	ICD-10
Williams <sup>2008</sup>	AUS	PC; 153	47	106	Ortho	NR	NR	2.0	45.0	AUDIT-C
Wu, <sup>2023</sup>	China	PC; 252	114	138	TKA THA	NR	NR	NR	NR	Self-Report

Abbreviations: AUD: Alcohol Use Disorder; AUDIT-C: Alcohol Use Disorders Identification Test – Consumption; CABG: Coronary Artery Bypass Grafting; CS: Cross Section; CS\*: Caesarian Section; DSM-IV: *Diagnostic and Statistical Manual of Mental Disorders*, 4th Edition; F: Female; GI: Gastrointestinal; HA: Hemiarthroplasty; ICD-9/10: *International Classification of Diseases*, 9th/10th Revision; IQR: Interquartile Range; M: Male; Mixed: Multiple surgical specialties included, excluding cardiac and orthopedic surgery; NR: Not Reported; PC: Prospective Cohort; RC: Retrospective Cohort; SD: Standard Deviation; Self Report: non-validated measures such as patient- or clinician-reported number of drinks per day, usual alcohol intake, or study-specific quantity–frequency cut-offs (e.g., ≥2 drinks/day or ≥ 60 g ethanol/day);TAAD: Type A Aortic Dissection; THA: Total Hip Arthroplasty; TKA: Total Knee Arthroplasty; TSA: Total Shoulder Arthroplasty.

the conversion of summary statistics.

**2.6. GRADE (Grading of Recommendations Assessment, Development, and Evaluation)**

We assessed the certainty of evidence of each postoperative outcome using Grading of Recommendations Assessment, Development, and Evaluation method (GRADE) [21]. This consisted of five domains: risk of bias, imprecision, inconsistency, indirectness, and publication bias. The evidence was downgraded by one level for serious and two levels for very serious concerns which were identified in any domain. The RCTs are considered high quality with a baseline rating of four while observational studies are considered low quality and the rating starts at two. GRADE results are presented in the summary of findings table (S-Table E.1).

**3. Results**

**3.1. Study selection**

Comprehensive literature searching yielded 12,560 citations. After removal of duplicates and title/abstract screening, 618 articles were included in full-text screening. Of these, 583 articles were excluded. Finally, 35 studies were included in the quantitative analysis (Fig. 1).

**3.2. Study characteristics**

The study characteristics and demographic data are summarized in Tables 1 and 2. There were 35 studies (n = 18,472,205) with mean age 62 ± 10 years and 46% female. Eleven were prospective cohort [22–32], one cross-sectional [33], and 23 retrospective cohort studies [34–56]. Studies were mostly from USA (n = 20) [33–51,56], with five from Germany (n = 5) [27–30,52], and one each from other countries. The

**Table 2**  
Demographic and characteristics by unhealthy alcohol use status in cardiac surgery.

Study <sup>Year</sup> Country	Study design; Patient No.	UAU No.	Non- UAU No.	Surgery type	UAU Age (mean ± SD)	Non- UAU Age (mean ± SD)	UAU Female %	Non- UAU Female %	Definition of alcohol exposure
Azarasa <sup>2009</sup> Iran	PC; 600	49	551	CABG ± valve repair	AA 523 ± 9 /49 CE ± 9	55 ± 14	0	35.6	DSM-IV
Li <sup>2024</sup> USA, CABG	RC; 23,009	5694	17,315	CABG	NR	NR	6.8	24.9	ICD-10
Li, <sup>2024</sup> USA, TAAD	Propensity Matching RC; 4282	220	4062	Aortic dissection	NR	NR	13.2	11.3	ICD-10
Maheshwari <sup>2010</sup> USA	RC; 13,065	2235	10,830	CABG	65 ± 11	67 ± 11	8.9	31.7	Self-Report
Nath <sup>2010</sup> USA	RC; 309,625	7631	301,994	Mixed	NR	NR	23.5	59.7	Self-Report
Nissila <sup>2024</sup> Finland	RC; 758	107	651	Cardiac	59.0 ± 3.75	69.0 ± 2.75	6.5	28.1	AUDIT-C
Sander <sup>2005</sup> Germany	PC; 44	10	34	Cardiac	64.83 ± 6.08	67 ± 2.75	10.0	20.6	DSM-IV
Stombaugh <sup>2024</sup> USA	RC; 1338	170 2–7 d/wk; 110 8+ d/wk	1058	CABG	66 ± 10, 2–7 d/ wk 65 ± 10; 8+ d/wk	65 ± 10	12.3 2–7 d/w, 7.3 ≥ 8d/w	27.1	Self-Report

Abbreviations: AA: Alcohol Abuse; AD: Alcohol Dependence; AUD: Alcohol Use Disorder; AUDIT-C: Alcohol Use Disorders Identification Test – Consumption; CABG: Coronary Artery Bypass Grafting; Cardiac (mult.): Multiple cardiac surgeries; DSM-IV: *Diagnostic and Statistical Manual of Mental Disorders*, 4th Edition; F: Female; ICD-9/10: *International Classification of Diseases*, 9th/10th Revision; IQR: Interquartile Range; Mixed: Cardiac and Non Cardiac Surgery; M: Male; NR: Not Reported; PC: Prospective Cohort; RC: Retrospective Cohort; SD: Standard Deviation; Self Report: non-validated measures such as patient- or clinician-reported number of drinks per day, usual alcohol intake, or study-specific quantity–frequency cut-offs (e.g., ≥2 drinks/day or ≥ 60 g ethanol/day); TAAD: Type A Aortic Dissection;

types of surgery included non-cardiac ( $n = 27$ ) [22–29,31,32,34–56] and cardiac surgeries ( $n = 8$ ) [24,29,48–51,54,56]. Definitions of UAU varied: AUDIT-C scores ( $n = 4$ ) [26,45,46,54]; DSM-III/IV criteria ( $n = 5$ ) [24,27,29,30,47]; ICD-9/10 codes ( $n = 12$ ) [33–42,48,49]; and self-reported thresholds ( $n = 14$ ) [22,23,25,28,31,32,43,44,50–53,55,56].

### 3.3. Quality assessment

Using the cohort-adapted Newcastle-Ottawa Scale, methodological quality was moderate to good. Among prospective cohorts ( $n = 11$ ), NOS scores ranged from 6 to 8 [22–32]. Among retrospective cohorts ( $n = 23$ ), scores ranged from 4 to 7 [34–56]. Most studies met items for selection of the non-exposed cohort, ascertainment of exposure, assessment of outcomes, and sufficient follow-up length. In prospective cohorts, adequacy of follow-up and confirmation that outcomes were absent at baseline were consistently met. Representativeness of the exposed cohort was the weakest domain overall, with 0 of 11 prospective studies meeting this item and 17 of 23 retrospective studies meeting it. Comparability was adequate in most but not all studies.

On the MOOSE checklist (cohort studies;  $n = 34$ ), all studies specified study design and study population, clearly defined outcomes and outcome assessment, and reported no selective loss to follow-up. Important confounders or prognostic factors were identified in 28 of 34 studies (82%). The cross-sectional database study was appraised with the modified NOS and scored 7/7; its MOOSE assessment likewise indicated clear population/outcome definitions, no selective loss, and identification of confounders [33]. Individual NOS item ratings and MOOSE responses for each study are provided in S-Table A.1–6.

### 3.4. Association between preoperative alcohol use/exposure and postoperative outcomes

Meta-analyses were performed to examine the association between UAU and adverse postoperative outcomes (Figs. 2,3). All included studies contributed to at least one quantitative synthesis; not all outcomes had sufficient studies for pooling. For **respiratory complications**, eight studies ( $n = 436,845$ ) showed a significantly higher risk in patients with UAU (RR 2.59, 95% CI 1.51–4.45;  $P = 0.0005$ ;  $I^2 =$

96%) (Fig. 2) [24,27,29,30,38,47,49,50]. There was no significant association between UAU and **cardiac complications** [25,39,48–53,58], **neurological complications** [24,26,32,36,48–50], or **urological complications** (Fig. 2) [38,48–51].

Meta-analysis on twelve studies ( $n = 383,024$ ) reporting for infections/wound complications demonstrated increased risk in the UAU group (RR 1.71, 95% CI 1.37–2.15;  $P < 0.00001$ ;  $I^2 = 79%$ ) (Fig. 3) [27,29,30,35,39,40,47–50,54–56]. Among ten studies ( $n = 3,346,845$ ), LOS was longer in patients with UAU (MD 0.76 days, 95% CI 0.24–1.29;  $P = 0.004$ ;  $I^2 = 100%$ ) (Fig. 3) [28,29,33,39,40,48,49,51,54]. In-hospital mortality was higher in the UAU group (10 studies;  $n = 4,198,798$ , RR 1.67, 95% CI 1.21–2.29;  $P = 0.002$ ;  $I^2 = 96%$ ) (Fig. 3) [24,29,33,38,41,48–52]. Data on postoperative bleeding, ICU admission, 30–90-day readmission, ED visits, and reoperation were insufficient to permit meta-analysis.

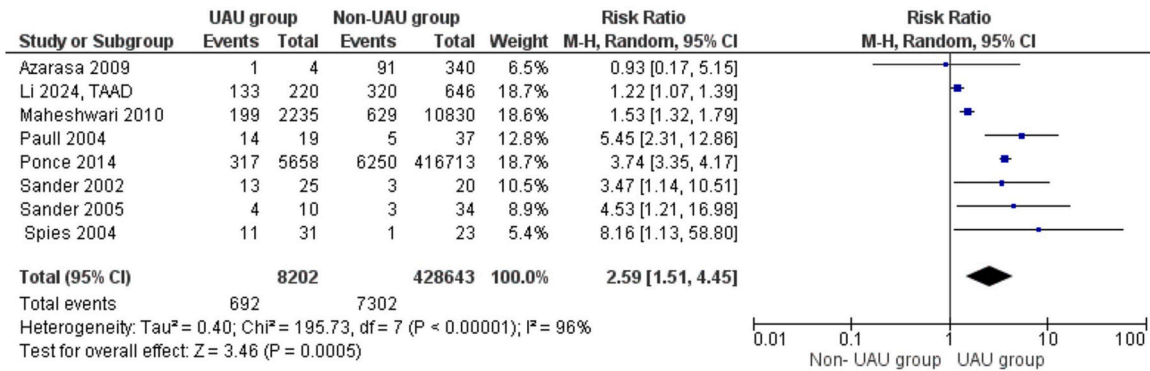
### 3.5. Subgroup and sensitivity analysis

Tests for subgroup differences were not significant by the type of surgery ( $P = 0.52$ ) when non-cardiac surgeries were compared with cardiac surgeries. (Fig. 4A). When comparing orthopedic vs mixed surgeries (non-cardiac surgical cohorts without orthopedic), we observed that mixed surgeries had a higher prevalence than orthopedic surgeries (0.17 [0.14, 0.19] vs 0.05 [0.04, 0.05],  $P = 0.52$ ) (Fig. 4A).

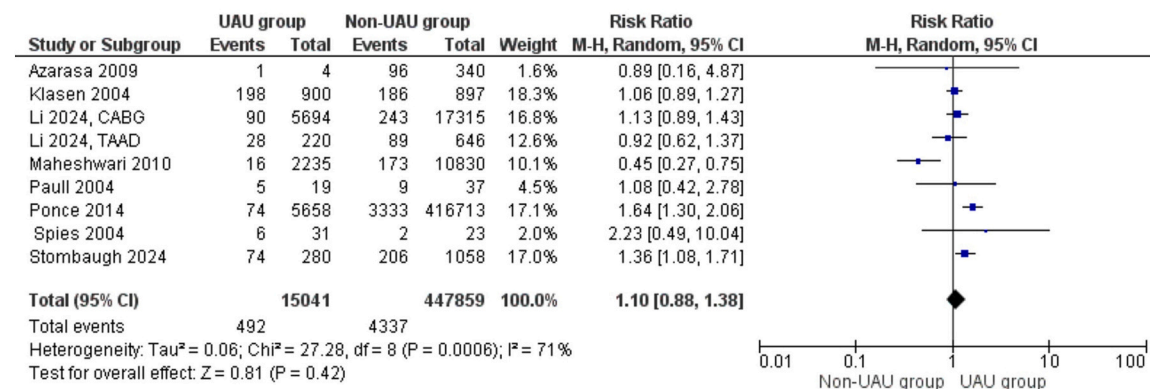
UAU group was associated with a higher risk among males (RR = 1.28, 95% CI 1.17, 1.40) and lower risk among females (RR = 0.56, 95% CI 0.47, 0.66). The test of subgroup differences was significant with a  $P$  value  $< 0.001$  (Fig. 4B). For age group  $\geq 60$  years, the UAU group was almost 2.5 years younger than non-UAU group with a mean difference of  $-2.49$  [ $-3.56, -1.41$ ]. Similarly, for age group  $< 60$  years, the UAU group was 1 year younger than non-UAU group with a mean difference of  $-1.01$  [ $-1.03, -0.98$ ]. The test for subgroup differences was significant for subgroup age ( $\geq 60$  years vs  $< 60$  years) [ $P = 0.007$ ] (Fig. 4B).

By UAU definition, the tests for subgroup differences were significant ( $P < 0.001$ ) with DSM 3 and 4 showing the highest prevalence [0.35 (0.13–0.57)] than other UAU assessment tools like AUDIT-C (0.16 [0.09, 0.23]), self-reported (0.14 [0.12, 0.16] and ICD-9 and 10 (0.07 [0.06, 0.08]) (S-Fig. A1). We further analyzed the self-reported UAU definition

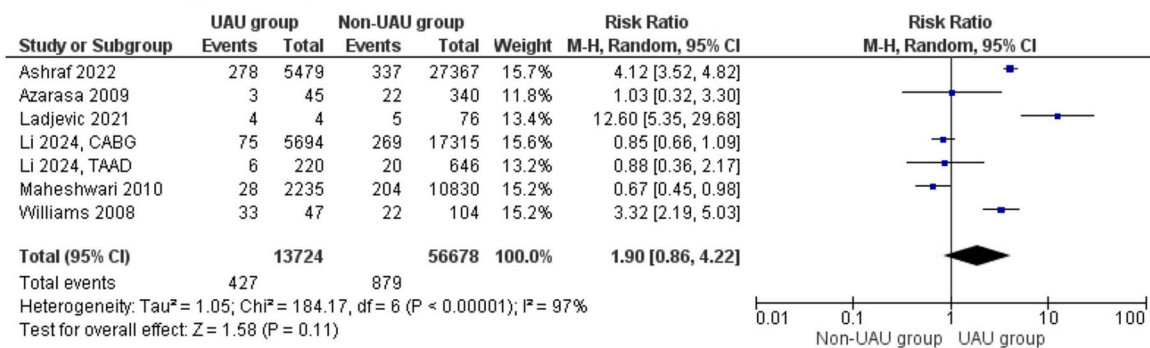
### Respiratory complications



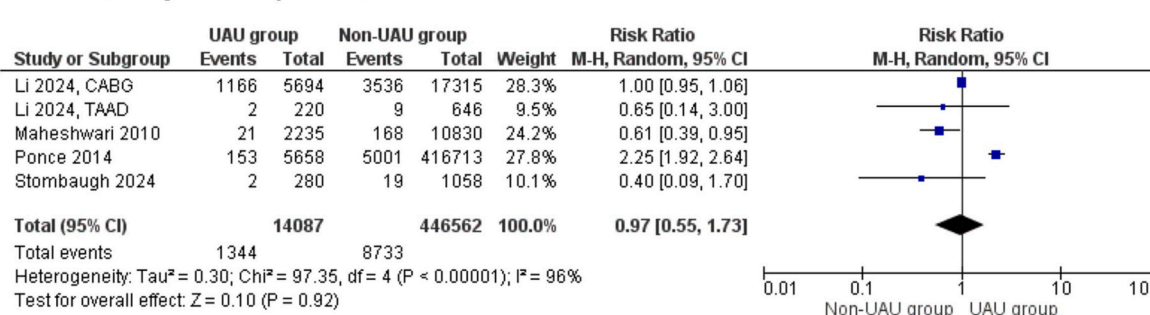
### Cardiac complications



### Neurological complications



### Urological complications



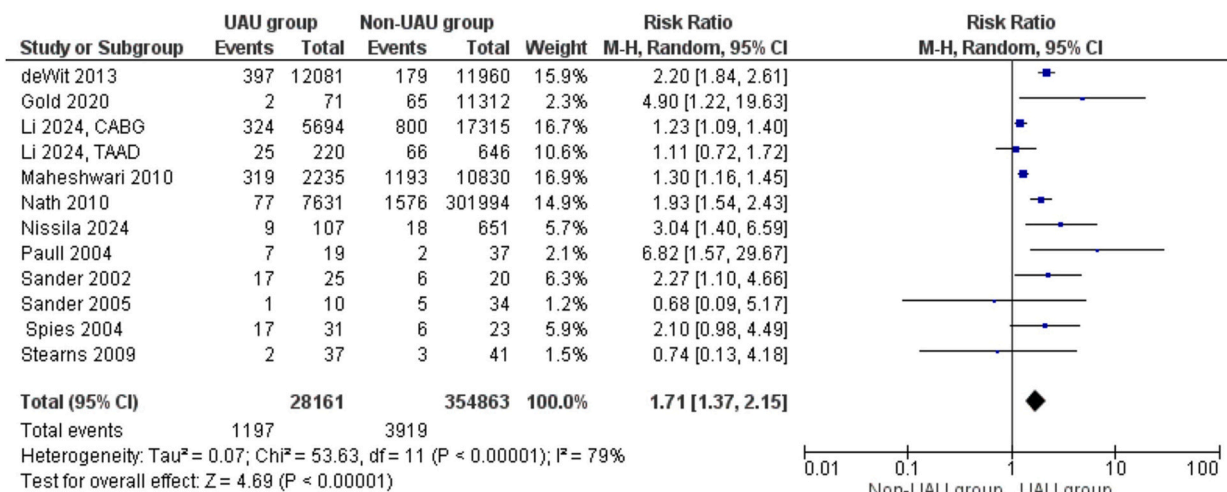
### UAU: Unhealthy Alcohol Use

Fig. 2. Postoperative complications in unhealthy alcohol use and non-alcohol use group.

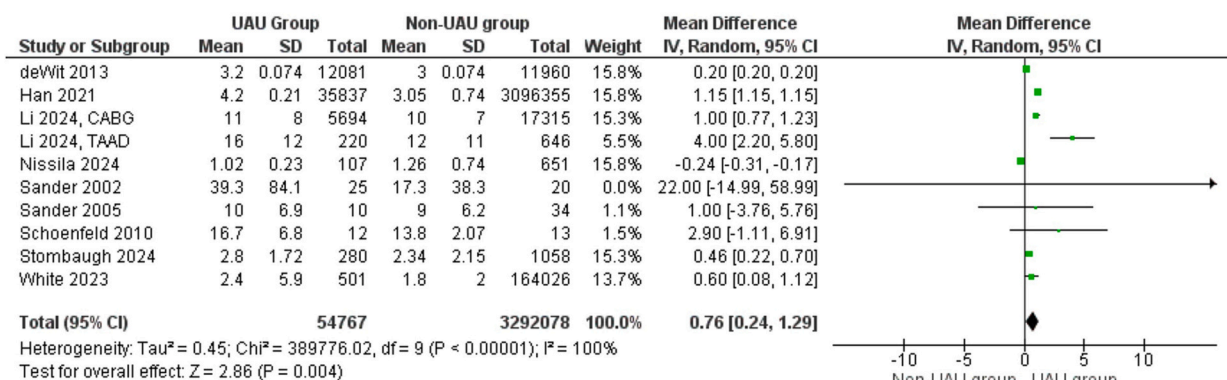
tools into two groups: simple binary single cutoff versus multi-level quantitative self-reports. Multi-level version gave a higher prevalence than that the simple binary cut-off (0.23 [0.18, 0.28] vs 0.09 [0.07, 0.10], P < 0.0001) (S-Fig. A2).

We conducted sensitivity analysis for key clinical outcomes. The heterogeneity in respiratory and urological complications decreased from 96% to 76% and 96% to 54% when Ponce 2014 was excluded [38]. The cardiac complications heterogeneity decreased from 71% to 45%

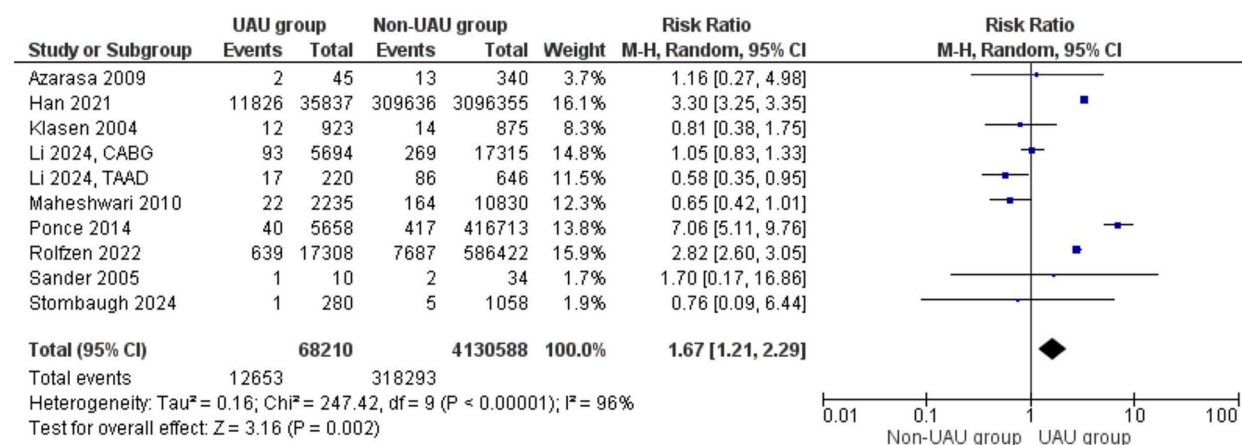
### Infections/wound complications



### Length of hospital stay



### In-hospital mortality



### UAU:Unhealthy Alcohol Use

Fig. 3. Postoperative outcomes in unhealthy alcohol use and non-alcohol use group.

when Maheshwari 2010 was removed from the analysis [50]. Leave-one-study-out analysis for other outcomes of neurological complications, infections, in-hospital mortality and LOS showed that removing any individual study did not alter the heterogeneity. I<sup>2</sup> values consistently remained high for these postoperative outcomes. We performed sensitivity analysis within all subgroups to observe the effect of omission of

any individual study on heterogeneity. The sequential exclusion of individual studies did not affect the high heterogeneity and was observed to be contributed by all included studies. We noticed that the results were not driven by any single study as the association remained statistically significant in all iterations.

Subgroup analysis of non-cardiac vs cardiac surgeries

Subgroup analysis of orthopedic vs mixed surgeries

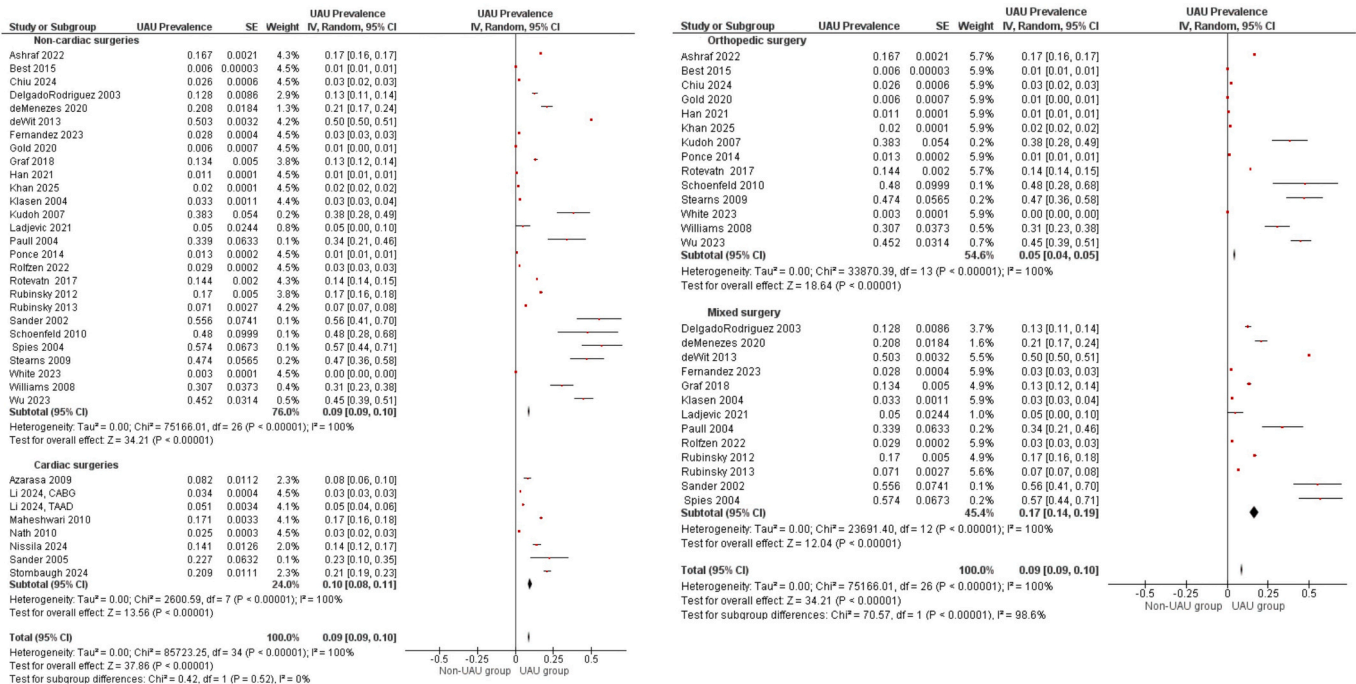


Fig. 4A. Subgroup analysis based on types of surgeries.

3.6. Meta-regression and publication bias

We conducted univariable meta-regression analysis for the postoperative outcomes of in-hospital mortality, infections/ wound complications and LOS. We could not conduct regression analysis for the outcomes of respiratory, cardiac, neurological and urological complications as there were not enough studies to explain the true moderator effect. The covariates sample size, age, study design, female sex and UAU definition had no significant association with in-hospital mortality. With cardiac surgery as a reference, orthopedic surgery showed a positive association with in-hospital mortality ( $P < 0.001$ ) while mixed surgery showed no significant association. We did not observe a positive relationship between any of the covariates and infection/ wound complications. There was a significant association between only age and LOS ( $P = 0.05$ ). Publication bias was assessed visually by funnel plot which showed marginal asymmetry for in-hospital mortality. Egger's test was nearly significant for the outcome of in-hospital mortality ( $P = 0.054$ ) but not for infections/ wound complications ( $P = 0.29$ ) and LOS (0.42).

3.7. GRADE summary of findings

GRADE evaluation was completed for all postoperative outcomes (respiratory, cardiac, neurologic, urologic complications, infections/ wound complications, LOS, and in-hospital mortality). The study design for all the studies were observational cohorts, and the quality of evidence was rated very low due to inconsistency and imprecision (S-Table E.1).

4. Discussion

The objective of this systematic review and meta-analysis was to clarify the association between preoperative UAU and adverse postoperative outcomes across different types of surgeries. Compared with non-AUD patients, patients with UAU had almost 3-fold respiratory complications and 2-fold infection/wound complications. Importantly,

patients with UAU showed 70% higher in-hospital mortality and almost 1-day longer LOS than non-UAU patients. The precise effect sizes are uncertain as the study heterogeneity was substantial. Nevertheless, the direction of effect consistently favored non-UAU patients, supporting the finding that alcohol use is a significant surgical risk factor that warrants attention in preoperative assessment.

Respiratory complications were notably 3-fold more common in patients with preoperative UAU, aligning with evidence that alcohol impairs pulmonary defense and predisposes to acute lung injury [58]. Alcohol-related suppression of mucociliary clearance, alveolar macrophage activity, and immune responses likely contributes to higher rates of postoperative pneumonia and respiratory compromise [59,60]. Despite alcohol's known links to hypertension and arrhythmias, we did not find a consistent association with cardiac complications, suggesting that procedure-specific cardiac risk may require further study [61]. This may reflect heterogeneity in cardiac risk across surgical populations, confounding by comorbidities, and a possibly predominant mechanistic role for immune dysfunction rather than direct cardiac injury in the perioperative period [62,63].

Excessive preoperative alcohol use was significantly associated with a 71% higher risk of infections/wound complications. This is consistent with experimental data showing alcohol impairs tissue repair by reducing fibroblast proliferation and collagen synthesis [62,63]. It also reflected the suppression of innate and adaptive immunity by alcohol [57,58]. Trials of perioperative alcohol-reduction programs suggest reduced infection rates in heavy drinkers, reinforcing alcohol-use assessment and management as key modifiable immunologic risk factors [59].

Crucially, in-hospital mortality was almost 70% higher in patients with UAU than those without UAU. Prior studies showed mixed effects on 30-day mortality, with two reporting increased risk [1,4] and one reporting no difference [6]. This difference in findings is likely due to variation in patient mix, definitions of alcohol exposure, and follow up period. Aligned with previous reviews, preoperative UAU was associated with almost 1-day longer LOS [4,41,64]. Alcohol related

Subgroup analysis of females vs males

Subgroup analysis of patients with age ≥60 years vs <60 years

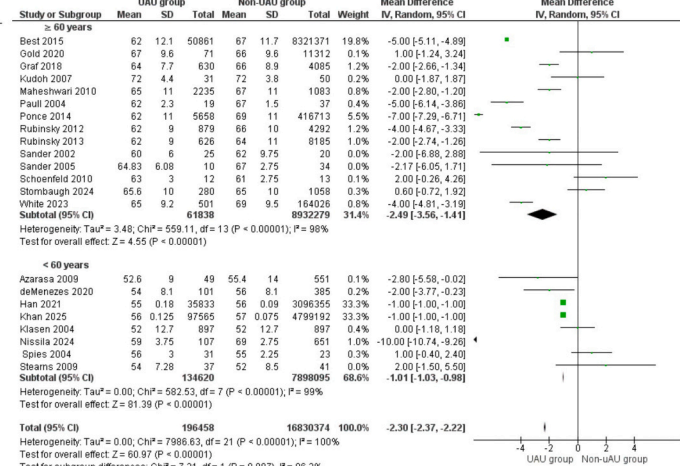
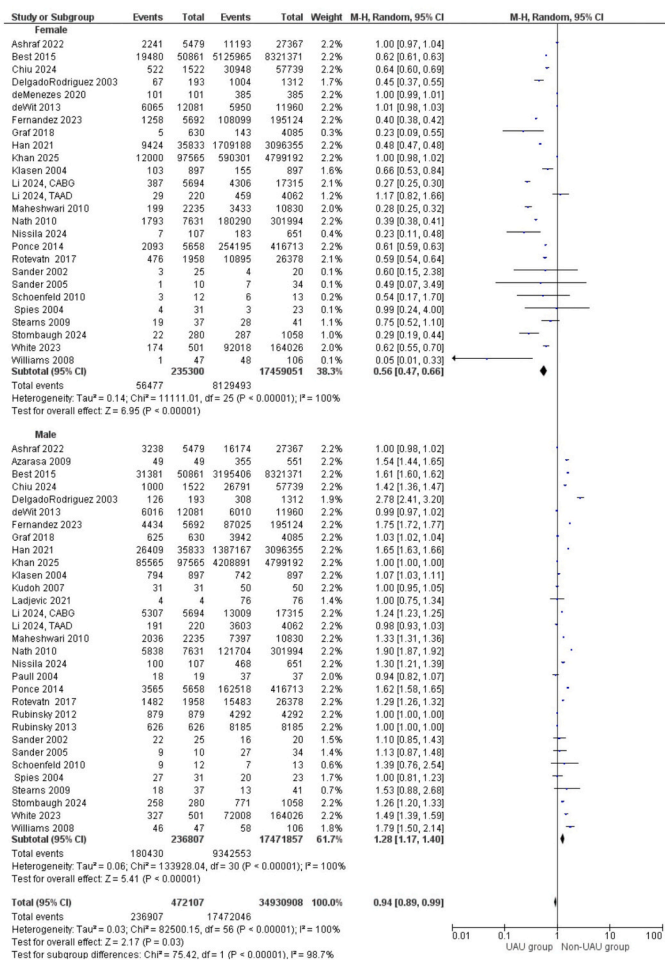


Fig. 4B. Subgroup analysis based on age and sex.

complications delayed wound healing, immune dysfunction and withdrawal syndromes all contributed to increased LOS. These adverse outcomes added greatly to health care utilization.

Although prior studies have reported alcohol-related postoperative cognitive decline in older patients [65] and a higher frequency of neurologic complications with alcohol exposure in the critically ill [60], our findings do not support an increased neurologic risk in patients with UAU [66]. Although a urologic ERAS guidance advised at least four weeks of preoperative abstinence to reduce the surgical stress response [67], we did not show a higher urological complication with meta-analysis of five studies. Variation in procedures, exposure definitions, and outcome measurement probably explain these inconsistencies.

We showed that surgical patients with UAU were younger and predominantly male, reflecting the known epidemiologic patterns of alcohol use. Males had over 2.5-fold higher odds of UAU while females had ~60% lower odds. Also, we demonstrated that patients with UAU were consistently younger than their non-UAU counterparts across both age groups. This pattern may suggest that UAU may be associated with earlier surgical presentation, particularly in older adults. Together, these demographic differences may partially influence perioperative risk profiles and underscore the importance of age- and sex-adjusted risk assessment models in surgical patients with UAU.

From a clinical perspective, these findings support targeted preoperative alcohol screening strategies focused on high-risk populations, while recognizing that UAU often coexists with other behavioral and medical comorbidities that may contribute to postoperative risk. The observed demographic variability and reliance on heterogeneous

exposure definitions also highlight the potential for residual confounding, which should be considered when interpreting the magnitude of observed associations.

4.1. Limitations and strengths

Most included studies were observational and retrospective, limiting causal inference and introducing the potential for systematic bias. We acknowledge our meta-analysis of retrospective cohorts may amplify limitations of the primary studies. There is considerable heterogeneity across the effects of primary outcome, reflecting differences in exposure definitions, surgical populations, and covariate adjustment. Subgroup analyses stratified by clinical characteristics, including age, sex and surgery type further explain the observed heterogeneity and highlight the complexity of isolating alcohol-related risk across diverse clinical contexts. The remaining variables (i.e. demographics, AUD severity and duration of use) lacked sufficient data to support additional analyses. Nevertheless, this systematic review and meta-analysis is the most updated and comprehensive literature highlighting the association between UAU and adverse postoperative outcomes and health care utilization. Preoperative alcohol screening, prehabilitation, and closer postoperative monitoring may shorten stays in high-risk drinkers and reduce healthcare costs. Further research with prospective studies with standardized, validated exposure measures and control of confounders are needed.

## 5. Conclusion

In summary, our systematic review and meta-analysis showed that patients with UAU had almost 3-fold respiratory complications, 2-fold infection/wound complications, 70% higher in-hospital mortality and almost 1-day longer LOS than non-UAU patients. We demonstrate that high preoperative alcohol exposure is a modifiable risk factor with clear implications for adverse outcomes across diverse surgical settings. Targeted prehabilitation and postoperative monitoring protocols may help mitigate the elevated risk of complications associated with preoperative alcohol use.

## CRedit authorship contribution statement

**Nethmi Rajapakse:** Writing – review & editing, Writing – original draft, Visualization, Validation, Methodology, Investigation, Data curation, Conceptualization. **Eric Rubenzahl:** Writing – review & editing, Methodology, Investigation, Data curation, Conceptualization. **Aparna Saripella:** Writing – review & editing, Visualization, Formal analysis. **Jun Won Lee:** Writing – review & editing, Validation, Investigation, Data curation. **Sara Mansouri:** Writing – review & editing, Investigation, Data curation. **Shirley Fan:** Writing – review & editing, Validation, Investigation, Data curation. **Marina Englesakis:** Writing – review & editing, Resources, Methodology, Conceptualization. **Frances Chung:** Writing – review & editing, Supervision, Project administration, Methodology, Conceptualization.

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## Declaration of competing interest

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## Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.jclinane.2026.112194>.

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## Glossary

- AUD:** DSM-defined alcohol use disorder or ICD-coded alcohol-related diagnoses (i.e., a disorder-level diagnosis)
- AUDIT:** Alcohol Use Disorders Identification Test
- AUDIT-C:** Alcohol Use Disorders Identification Test-Consumption
- CI:** Confidence interval
- Cochran's Q:** Statistical test used to assess heterogeneity across studies in meta-analysis
- Covidence:** Web-based platform used for screening and managing systematic review records
- DSM-III:** Diagnostic and Statistical Manual of Mental Disorders, 3rd edition
- DSM-IV:** Diagnostic and Statistical Manual of Mental Disorders, 4th edition
- DSM-5:** Diagnostic and Statistical Manual of Mental Disorders, 5th edition
- ED:** Emergency department
- Egger's test:** Linear regression test used to assess funnel plot asymmetry (possible publication bias)
- Emtree:** Controlled vocabulary used to index Embase records
- GRADE:** Grading of Recommendations Assessment, Development, and Evaluation (framework for rating certainty of evidence)
- Heterogeneity:** Variation in study results beyond what would be expected by chance
- ICD-9:** International Classification of Diseases, 9th Revision
- ICD-10:** International Classification of Diseases, 10th Revision
- ICU:** Intensive care unit
- I<sup>2</sup>:** Percentage of variability across studies attributable to heterogeneity rather than chance
- Inverse variance method:** Meta-analysis weighting approach that gives more weight to more precise studies
- LOS:** Length of hospital stay
- MD:** Mean difference (effect measure for continuous outcomes)
- MeSH:** Medical Subject Headings (controlled vocabulary used for MEDLINE indexing/ searching)
- MH:** Mantel-Haenszel method (approach for pooling effect estimates for dichotomous outcomes)
- Meta-analysis:** Statistical pooling of results across studies
- Meta-regression:** Analysis examining whether study-level factors explain differences in effect estimates across studies
- MOOSE:** Meta-Analyses of Observational Studies in Epidemiology (reporting guidance/ checklist)
- NOS:** Newcastle-Ottawa Scale (tool for assessing quality/risk of bias in nonrandomized studies)
- Ovid:** Literature search platform used to access databases such as MEDLINE and Embase
- Prediction interval:** Estimated range in which the true effect of a future study is expected to lie
- UAU:** Any preoperative alcohol exposure above low-risk levels, including AUD and hazardous/risky use, measured by validated tools, ICD codes, DSM criteria, or study-defined thresholds
- PRISMA:** Preferred Reporting Items for Systematic Reviews and Meta-Analyses (reporting guideline).
- PROSPERO:** International Prospective Register of Systematic Reviews (protocol registration database)
- Random-effects model:** Meta-analysis model that allows true effects to vary between studies
- RCT:** Randomized controlled trial
- REML:** Restricted maximum likelihood (estimator for between-study variance in random-effects meta-analysis)
- RevMan:** Review Manager software (Cochrane tool used for systematic reviews/meta-analyses).
- RR:** Risk ratio (relative risk of an outcome in exposed versus unexposed groups)
- Sensitivity analysis:** Analysis testing robustness of results to changes in assumptions or included studies
- Subgroup analysis:** Analysis comparing results across predefined categories
- TIA:** Transient ischemic attack
- WHO:** World Health Organization