



Clinical Review

The effect of alcohol on subsequent sleep in healthy adults: A systematic review and meta-analysis

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ABSTRACT

Alcohol is commonly consumed prior to bedtime with the belief that it facilitates sleep. This systematic review and meta-analysis investigated the impact of alcohol on the characteristics of night-time sleep, with the intent to identify the influence of the dose and timing of alcohol intake. A systematic search of the literature identified 27 studies for inclusion in the analysis. Changes in sleep architecture were observed, including a delay in the onset of rapid eye movement (REM) sleep and a reduction in the duration of REM sleep. A dose-response relationship was identified such that disruptions to REM sleep occurred following consumption of a low dose of alcohol ($\leq 0.50 \text{ g} \cdot \text{kg}^{-1}$ or approximately two standard drinks) and progressively worsened with increasing doses of alcohol. Reductions in sleep onset latency and latency to deep sleep (i.e., non-rapid eye movement stage three (N3)) were only observed following the consumption of a high dose of alcohol ($\geq 0.85 \text{ g} \cdot \text{kg}^{-1}$ or approximately five standard drinks). The effect of alcohol on the remaining characteristics of sleep could not be determined, with large uncertainty observed in the effect on total sleep time, sleep efficiency, and wake after sleep onset. The results of the present study suggest that a low dose of alcohol will negatively impact (i.e., reduce) REM sleep. It appears that high doses of alcohol may shorten sleep onset latency, however this likely exacerbates subsequent REM sleep disruption. Future work on personal and environmental factors that affect alcohol metabolism, and any differential effects of alcohol due to sex is encouraged.

1. Introduction

It is estimated that 20–40 % of the global population fail to meet the current recommendations of seven to 9 h of sleep per night [1–5]. Given the health and economic repercussions of insufficient sleep, a ‘sleep loss’ epidemic has been identified as an emerging public health concern [6]. The prevalence of sleep insufficiency may be attributed to the 24/7 ideology of modern society, where excessive work hours and regular social interactions are often prioritised at the expense of sleep [7,8]. With the demands of daily life restricting the ability to ‘switch off’ [9],

sleep aids may be employed to enhance the transition to sleep [7]. Alcohol is one ‘over the counter’ sleep aid used by approximately 10–28 % of the population given the common belief that consumption prior to bedtime facilitates sleep initiation and maintenance [10–13].

Alcohol is a psychoactive substance that can be easily accessed given it is engrained in many social and cultural contexts [14]. The ingestion of alcohol results in a biphasic response relative to changes in blood alcohol concentration over time [15]. With the initial intake of alcohol, blood alcohol concentration begins to rise with associated feelings of euphoria and relaxation. However, as blood alcohol concentration accumulates, alcohol acts as a central nervous system depressant and

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Abbreviations	
ADH	alcohol dehydrogenase
CI	confidence interval
GABA	gamma-aminobutyric acid
PI	prediction interval
N1	non-rapid eye movement stage one
N2	non-rapid eye movement stage two
N3	non-rapid eye movement stage three
N4	non-rapid eye movement stage four
NREM	non-rapid eye movement
REM	rapid eye movement

Table 1
Search strategy.

	Population or Problem	Intervention	Comparison	Outcome
Keywords	"sleep" NOT "dependence" NOT "withdrawal" NOT "syndrome" NOT "disorder" NOT "review" NOT "meta-analysis" NOT "COVID-19" NOT "depression" NOT "anxiety" NOT "adolescent" NOT "children" NOT "cross-sectional" NOT "heart disease" NOT "heart failure" NOT "mice" NOT "rat" NOT "animal" NOT "stroke" NOT "mortality" NOT "illness"	"alcohol" OR "ethanol"	N/A	"sleep quality" OR "quality of sleep" OR "sleep quantity" OR "sleep duration" OR "sleep time" OR "sleep duration" OR "time in bed" OR "sleep efficiency" OR "sleep latency" OR "sleep onset" OR "sleep stage" OR "sleep architecture" OR "slow wave" OR "non rapid eye movement" OR "NREM" OR "rapid eye movement" OR "REM" OR "sleep-wake" OR "sleep maintenance" OR "sleep satisfaction" OR "wake after sleep" OR "sleep arousal" OR "sleep disturbance" OR "awakening from sleep" OR "EEG" OR "electroencephalogram"

typically exerts a sedative effect [16]. By altering the activity of select neurochemicals, including gamma-aminobutyric acid (GABA), glutamate, and adenosine, alcohol promotes neural inhibition with reductions in cerebral cortex activity [17]. The sedative properties of alcohol may increase the perception of sleepiness and can shorten the time to sleep onset [18], leading to the belief that alcohol is an effective sleep aid.

Despite the potential to reduce sleep onset latency, alcohol may disrupt the maintenance of subsequent sleep [11,18]. In most experimental trials investigating the effect of alcohol on subsequent sleep, the dose of alcohol administered is between 0.16 and 1.20 g•kg⁻¹ within 3 h of the scheduled sleep opportunity [18]. Given this timeframe of ingestion, peak blood alcohol concentration coincides with the onset of sleep and the subsequent metabolism of alcohol occurs across the sleep bout [19]. As blood alcohol concentration falls, the sedative effect of alcohol subsides as alcohol is eliminated from the body, with a tendency for greater sleep disruptions to occur in the second half of the sleep opportunity [20]. In addition, the scientific evidence indicates that larger doses of alcohol have a greater effect on sleep [18]. However, the magnitude of this effect remains unclear as the impact of dose and timing of alcohol ingestion has yet to be quantified using a systematic approach [21]. Therefore, the aims of this systematic review and meta-analysis are to: 1) establish the level of evidence for the effect of alcohol intake on the characteristics of subsequent sleep (i.e., sleep onset latency, total sleep time, rapid eye movement (REM) sleep onset latency, latency to non-rapid eye movement (NREM) stage three (N3) sleep, wake after sleep onset, sleep efficiency, sleep architecture, and subjective sleep quality; 2) quantify the effect of alcohol intake on the characteristics of subsequent sleep; 3) quantify the influence of the dose and timing of alcohol intake on the characteristics of subsequent sleep; and 4) quantify the influence of sex on the characteristics of subsequent sleep.

2. Methods

The systematic review and meta-analysis were conducted in accordance with the Preferred Reporting Items for Systematic Reviews and

Meta-Analysis (PRSIMA) 2020 guidelines. The protocol was registered with the Open Science Framework (OSF) registry (Registration DOI: 10.17605/OSF.IO/EJX5Q).

2.1. Databases and search strategy

The search strategy was structured using the PICO framework (Table 1). Search terms within each component were combined using the Boolean operator “OR” with search terms across each component combined using the Boolean operator “AND”. The search was executed using the PubMed, Scopus, and Web of Science databases. The results were limited to peer-reviewed journal articles, published in the English language, investigating human populations only. The results of the search were uploaded to the Covidence systematic review software (Veritas Health Innovation, Melbourne, Australia).

2.2. Study screening and selection

Duplicate results were removed automatically by Covidence and two independent reviewers (CG and JW) screened the remaining articles. The title and abstract of each article was screened, and those articles outside the scope of the review were removed. For the remaining articles, full-text versions were located for screening. Studies were included if they: 1) employed a healthy adult population aged 18–70 years; 2) used a controlled experimental design; 3) administered a measured alcohol dose; and 4) implemented a protocol in which sleep was assessed during a subsequent night-time sleep opportunity (i.e., sleep was initiated in the evening and was terminated the following morning). Studies were excluded if: 1) the duration of the subsequent sleep opportunity was <90 min (defined as a napping protocol); 2) the alcohol dose was administered >18 h prior to the scheduled sleep opportunity; 3) the alcohol dose was administered after the onset of the scheduled sleep opportunity; or 4) measures of sleep were not reported.

2.3. Assessment of reporting quality

The Cochrane Risk of Bias Tool (RoB2) for crossover trials [22] was employed to assess the methodological reporting quality of the studies included in the analysis. Two authors (CG and JW) independently completed the tool with any discrepancies resolved through discussion. For each study, signalling questions were answered across six domains, including randomisation process (domain one), period and carryover effects (domain S), deviations from the intended intervention (domain two), missing outcome data (domain three), measurement of the outcomes (domain four), and selection of the reported results (domain five). Potential bias for each domain was assessed through a pre-defined algorithm with outcomes of “low risk”, “some concern”, or “high risk”. The overall risk of bias for a study was determined by the highest risk of bias recorded across each domain.

2.4. Data extraction and coding of outcomes

For studies that met the inclusion criteria, two researchers (CG and

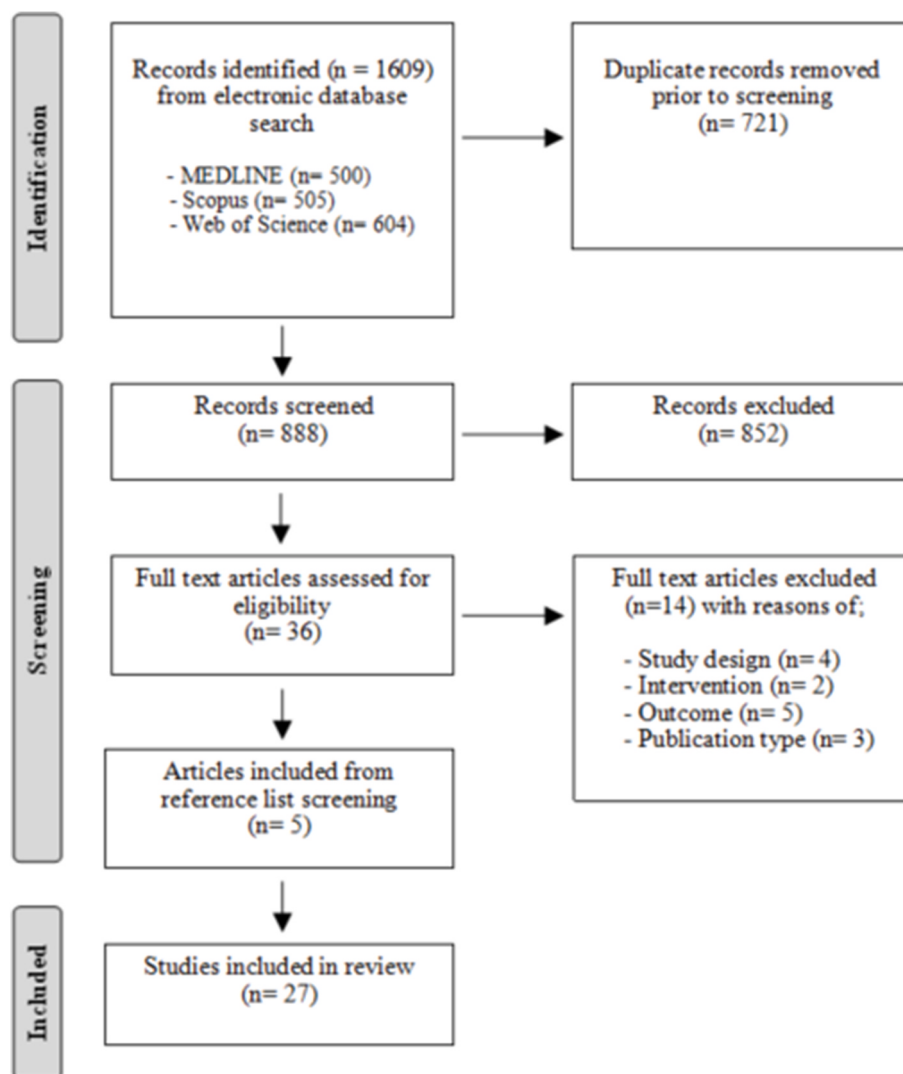


Fig. 1. Preferred Reporting Items for Systematic Reviews and Meta Analyses flow diagram outlining the process for selection of studies.

JW) independently coded the data into a pre-defined Microsoft Excel (V2201, Microsoft, Washington, USA) template for the following variables: authors, title, year of publication, sample size, sex, weight, height, alcohol dose, proximity of consumption to sleep opportunity, objective sleep measurement tools, subjective sleep measurement tools, objective sleep outcomes, and subjective sleep outcomes. Coding was cross-checked between reviewers, with any discrepancies resolved by mutual consensus.

For the studies meeting the criteria for inclusion, each measured objective sleep outcomes using polysomnography and subjective sleep outcomes using self-report diaries and questionnaires. In the present review, time in bed was defined as the period between lights off and lights on with total sleep time defined as the time spent asleep during this period. Sleep efficiency was calculated as the percentage of time in bed spent asleep. Sleep onset latency was accepted as the time from lights out to the first epoch of sleep, except where the author defined this to occur with three consecutive epochs of NREM stage one (N1) sleep [23,24] or to the first epoch of NREM stage two (N2) sleep [25]. REM sleep onset latency was accepted as the time from sleep onset to the first occurrence of REM sleep, except in one study where it was defined as the first occurrence of REM sleep from the first occurrence of N2 sleep [26]. Latency to N3 sleep was accepted as the time from sleep onset to the first occurrence of N3 sleep, except in one study where it was defined as the first occurrence of N3 sleep from the first occurrence of N2 sleep [27].

Wake after sleep onset was defined as the duration of time spent awake after sleep onset and before final awakening. Outcome data reported as N3 and NREM stage four (N4) sleep [28–32], slow wave sleep [23,24,26,27,33–37], or deep sleep [38] were classified as N3 sleep in line with the current American Academy of Sleep Medicine guidelines [39], except for three studies [40–42] where N3 and N4 sleep were reported independently.

Data were extracted as the mean and standard deviation for control and alcohol conditions. For studies where mean data were reported with the standard error of the mean [26,36,38,42] or coefficient of variability [32], calculations were performed to transform these measures into standard deviations. If a measure of variance for total sleep time [43], sleep onset latency [27], or latency to N3 sleep [27] was not reported, the data for these outcomes were excluded from the quantitative synthesis. Outcome data reported as a combination of distinctively different sleep stages, including light sleep [38] and stage 1-REM [43,44], were also excluded from the quantitative synthesis. In two studies [23,35], sleep outcomes from the same data set were reported – the study [23] in which the outcome data for alcohol dose were reported was included in the quantitative synthesis. Sleep outcome data from one study [42] were excluded due to unclear reporting of the outcome definitions, and the sleep staging data from another study [38] were excluded due to the implausible measures of variance that were substantially smaller than expected in comparison to the included studies. Outcome data that were

Table 2

Summary characteristics of the included studies.

Study	Sample (n)	Age (years)	Weight (kg)	Method of alcohol administration	Alcohol dose (g·kg ⁻¹)	Proximity to bedtime	Method of sleep measurement	Reported sleep outcomes of interest	Significant findings (compared to control for entire night)
Arnedt et al., 2011 [23]	34M; 59F	24.4 ± 2.7	Undisclosed	1.20 g·kg ⁻¹ for M & 1.10 g·kg ⁻¹ for F of alcohol to achieve a peak BrAC of 0.10 %	M: 1.20 F: 1.10	150 min with 90 min to consume	PSG Questionnaire	TST, SE, SOL, ROL, LN3, WASO, sleep stages Subjective TST, SOL, WASO, quality	↓ SOL, LN3, SE, REM ↑ ROL, WASO, N2, N3 ↓ Quality
Bazil et al., 2005 [33]	3M; 9F	30.8*	Undisclosed	4 ounces of 40 % alcohol (vodka) in orange juice	Undisclosed	60 min with 15 min to consume	PSG	TST, SE, sleep stages	No significant change
Block & Hellard, 1987 [40]	13M; 4F	43.6 ± 14.7	78.6 ± 6.9	1.00 ml·lb ⁻¹ of 100-proof scotch or vodka	0.87 [^]	~90 min	PSG	TST, sleep stages	↓ TST, REM
Block et al., 1985 [41]	18F	58.0*	62.60*	2.00 ml·kg ⁻¹ of 100-proof vodka in orange juice	0.79 [^]	~90 min	PSG	TST, sleep stages	↓ TST, REM
Feige et al., 2006 [25]	5M; 5F	29.7 ± 7.4	Undisclosed	Vodka and orange juice consumed to reach a BAC of 0.03 % or 0.1 %	0.35 [^] 1.15 [^]	60 min	PSG Questionnaire	SE, SOL, ROL, sleep stages Subjective quality	No significant change No significant change
Finnigan et al., 1998 [46]	40M	25.6*	75.0*	37.5 % vodka mixed with orange juice and water to achieve peak BAC of approximately 100 mg/100 ml of body water	0.59 [^]	60 min	Sleep Diary	Subjective SOL	↓ SOL
Kido et al., 2016 [42]	3M; 3F	28.8 ± 9.5	61.2 ± 8.2	40 g of alcohol as either beer, shochu, or sake	0.65 [^]	120 min with 30 min to consume	PSG	TST, SE, SOL, ROL, sleep stages	↓ ROL (<i>shochu and sake</i>)
Knowles et al., 1968 [43]	1M	Undisclosed (adult)	Undisclosed	~3.5 oz and ~6.0 oz of alcohol to induce BAC of ~0.06–0.08 % and ~0.10–0.15 % respectively	Undisclosed	Within ~220 min of bedtime	PSG	TST, sleep stages	No significant change
Kobayashi et al., 2002 [28]	10M	22.5 ± 0.6	Undisclosed	Each subject drank the equivalent of 0.8 g·kg ⁻¹ of alcohol	0.80	15 min	PSG	TST, SOL, ROL, sleep stages	↑ ROL
Landolt et al., 1996 [26]	10M	61.6 ± 2.9	Undisclosed	Drinks contained 0.55 g·kg ⁻¹ body weight vodka (40 % alcohol per volume unit) mixed with mineral water	0.22	360 min with 15 min to consume	PSG Questionnaire	TST, SE, SOL, ROL, WASO, sleep stages Subjective SOL, WASO	↓ TST, SE, N1, REM ↑ WASO, N2 No significant change
MacLean & Cairns, 1982 [34]	10M	23.6*	Undisclosed	Beverage which consisted of either 0, 0.25, 0.50, 0.75 or 1.00 g·kg ⁻¹ of 95 % alcohol and 3 ml of tincture of gentian with orange juice added for a total volume of 500 ml	0.24 0.48 0.71 0.95	47 min	PSG	TST, SOL, ROL, LN3, sleep stages	↓ SOL
Miyata et al., 2004 [29]	13F	21.1 ± 0.7	Undisclosed	Participants ingested 0, 0.28, or 0.69 g·kg ⁻¹ of alcohol	0.28 0.69	~60 min with 30 min to consume	PSG	TST, SE, SOL, ROL, sleep stages	No significant change
Pabon et al., 2022 [51]	11M; 11F	25.3 ± 6.1	78.9 ± 13.9	1.0 g·kg ⁻¹ for M and 0.85 g·kg ⁻¹ for F mixed in a 1:3 ratio of 95 % alcohol to desired volume using fruit juice	M: 1.00 F: 0.85	Half 180 min & half 120 min with 15 min to consume	PSG	TST, SE, SOL, sleep stages	↓ TST, SE, REM ↑ N2
Payseur et al., 2020 [38]	17M	21.7 ± 2.1	78.8 ± 15.7	100-proof vodka mixed in a 1:4 ratio with tonic water and normalized to 2 ml·kg ⁻¹	0.79 [^]	Between 17:00–19:00 with 15 min to consume ^b	Partial PSG	TST, SOL, sleep stages	↓ SOL ↑ TST, Light Sleep, REM

(continued on next page)

Table 2 (continued)

Study	Sample (n)	Age (years)	Weight (kg)	Method of alcohol administration	Alcohol dose (g·kg ⁻¹)	Proximity to bedtime	Method of sleep measurement	Reported sleep outcomes of interest	Significant findings (compared to control for entire night)
Prinz et al. (1980) [45]	5M	21–25 ^a	Undisclosed	0.80 g·kg ⁻¹ alcohol in a mixer	0.80	Within 60 min	PSG	Sleep stages	No significant change
Roehrs et al., 1999 [30]	6M; 3F	26.1 ± 3.7	Undisclosed	0.50 g·kg ⁻¹ alcohol (80-proof vodka) mixed in a 1:4 ratio with tonic water	0.50	60 min with 45 min to consume	PSG	SE, SOL, ROL, WASO, sleep stages	↓ REM
Roehrs et al., 1991 [31]	5M	21–34 ^a	Undisclosed	0.80 g·kg ⁻¹ alcohol (80-proof vodka) mixed in a 1:4 ratio with tonic water	0.80	60 min with 30 min to consume	PSG	SE, SOL, ROL, WASO, sleep stages	↓ N1, REM ↑ N2
Rohsenow et al., 2010 [35]	37M; 58F	24.5 ± 2.8	Undisclosed	Bourbon or vodka mixed with chilled caffeine-free cola to reach a BrAC of 0.10 % (1.20 g·kg ⁻¹ for M & 1.10 g·kg ⁻¹ for F)	M: 1.20 F: 1.10	150 min with 90 min to consume	PSG Questionnaire	TST, SE, SOL, WASO, sleep stages Subjective quality	↓ SE, REM ↑ WASO, N3 ↓ Quality
Rohsenow et al., 2006 [54]	25M; 6F (Alcohol group) 25M; 5F (Control group)	21.8 ± 1.2 21.8 ± 1.3	Undisclosed	Beer containing 5.9 % alcohol sufficient to yield 0.10 % BrAC (1.20 g·kg ⁻¹ for M & 1.00 g·kg ⁻¹ for F)	M: 1.20 F: 1.00	150 min with 90 min to consume	Questionnaire	Subjective TST, SOL, quality	↓ SOL ↑ Quality
Rundell et al., 1972 [27]	10M (Experiment 1) 7M (Experiment 2)	21–30 ^a 21–27 ^a	Undisclosed	0.90 g·kg ⁻¹ of 95 % alcohol mixed with 750 ml ginger ale and divided into 3 drinks	0.86	~90 min with 60 min to consume	PSG	SOL, LN3, sleep stages	↓ SOL, LN3
Sagawa et al., 2011 [36]	10M	21.6 ± 3.5	66.4 ± 8.5	Japanese sake was consumed so that subjects received alcohol dosages of 0, 0.50 or 1.00 g·kg ⁻¹	0.50 1.00	100 min with 30 min to consume	PSG	TST, SE, SOL, ROL, WASO, sleep stages	↓ REM ↑ N1, ROL (1.00)
Scrima et al., 1982 [55]	4M; 2F	27 ± 2.9	67.3 ± 11.5	0.8 g·kg ⁻¹ of alcohol (80-proof vodka) mixed with orange juice	0.80	30 min with 30 min to consume	PSG	TST, SE, SOL, ROL, sleep stages	↑ ROL
Smith & Smith, 2003 [53]	2M; 13F	29–24 ^a	Undisclosed	Given 3–4 oz. of vodka (alcohol dosage of 0.7 g·kg ⁻¹ body weight) in 200 ml of orange juice per 1 oz. of drink	0.70	Undisclosed	PSG	TST, SOL, WASO, sleep stages	No significant change
Stone, 1980 [32]	6M	20–31 ^a	Undisclosed	A flavoured 18 % solution of alcohol in doses of 0.16, 0.32 and 0.64 g·kg ⁻¹	0.16 0.32 0.64	30–60 min	PSG VAS	TST, SE, SOL, ROL, LN3, sleep stages Subjective SOL quality	↑ TST (0.16), SE (0.16, 0.32) ↓ SOL (0.32, 0.64)
Van Reen et al., 2006 [24]	7F	23.5 ± 1.0	Undisclosed	0.49 g·kg ⁻¹ vodka mixed with tonic water to achieve a BrAC of 0.05 %	0.49	90 min with 30 min to consume	PSG	TST, SE, SOL, ROL, LN3, WASO, sleep stages	↓ REM
Williams et al., 1983 [37]	11F	19.50*	Undisclosed	Beverage which consisted of either 0, 0.50 or 0.75 of 95 % g·kg ⁻¹ of alcohol & 2 drops of tincture of gentian with orange juice added for a total volume of 400 ml	0.48 0.71	~90 min with 30 min to consume	PSG	TST, SOL, ROL, LN3, sleep stages	↓ SOL ↑ N1
Yules et al., 1966 [44]	3M	Undisclosed (adult)	Undisclosed	1.00 g·kg ⁻¹ mixed into orange juice	1.00	Consumption finished 15 min prior to bedtime	PSG	ROL, sleep stages	No significant change

Abbreviations: BAC- blood alcohol concentration; BrAC: breath alcohol concentration; LN3: latency to non-rapid eye movement (NREM) stage 3 sleep; PSG- polysomnography; N1- NREM stage 1 sleep; N2- NREM stage 2 sleep; N3- NREM stage 3 sleep; N4- NREM stage 4 sleep; REM-rapid eye movement (REM) sleep; ROL- REM sleep onset latency; SE-sleep efficiency; SOL-sleep onset latency; TST-total sleep time; VAS- visual analogue scale; WASO- wake after sleep onset.

^a Mean not reported, *Standard deviation not reported, ^Alcohol dose calculated from data provided, ~Approximate timing reported.

^b Proximity to bedtime not reported.

Table 3
Results of the cochrane risk of bias (RoB2) Tool.

Study	D1	DS	D2	D3	D4	D5	Overall Bias
Arnedt et al., 2011 [23]	+	+	+	+	+	+	+
Bazil et al., 2005 [33]	+	+	+	+	+	+	+
Block & Hellard, 1987 [40]	+	-	+	+	+	+	-
Block et al., 1985 [41]	+	-	+	+	+	+	-
Feige et al., 2006 [25]	+	+	+	+	+	+	+
Finnigan et al., 1998 [46]	+	+	+	+	+	!	!
Kido et al., 2016 [42]	!	+	+	+	-	+	-
Knowles et al., 1968 [43]	!	-	+	!	-	!	-
Kobayashi et al., 2002 [28]	!	+	+	+	+	!	!
Landolt et al., 1996 [26]	!	+	+	+	+	+	!
MacLean & Cairns, 1982 [34]	+	+	+	+	+	-	-
Miyata et al., 2004 [29]	!	+	+	+	+	+	!
Pabon et al., 2022 [51]	+	+	+	+	+	+	+
Payseur et al., 2020 [38]	!	+	+	+	+	-	-
Prinz et al., 1980 [45]	!	+	+	+	+	-	-
Roehrs et al., 1999 [30]	+	!	+	+	+	+	!
Roehrs et al., 1991 [31]	+	+	+	+	+	+	+
Rohsenow et al., 2010 [35]	+	+	+	+	+	!	!
Rohsenow et al., 2006 [54]	+	+	+	+	+	+	+
Rundell et al., 1972 [27]	!	+	+	+	+	!	!
Sagawa et al., 2011 [36]	!	+	+	+	+	+	!
Scrima et al., 1982 [55]	+	-	+	+	+	!	-
Smith & Smith, 2003 [53]	+	+	+	+	+	!	!
Stone, 1980 [32]	+	+	+	+	+	-	-
Van Reen et al., 2006 [24]	!	+	+	+	+	+	!
Williams et al., 1983 [37]	+	+	+	+	+	-	-
Yuiles et al., 1966 [44]	!	-	+	+	-	!	-

D1: Randomisation process, DS: Period and carryover effects, D2: Deviations from intended interventions, D3: Missing outcome data, D4: Measurement of outcome, D5: Selection of reported result

+

 Low risk

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 Some concerns

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 High risk

not obtained from an entire sleep opportunity (i.e., first half of a sleep opportunity) [45] were excluded from the quantitative synthesis. Finally, manual calculations were performed for six studies [25,38,40–42,46] where the alcohol dose was not explicitly reported but could be calculated from the data reported using the standard density of alcohol (0.79 g•mL⁻¹) [47]. Where necessary, corresponding authors were contacted for further information.

2.5. Meta-analysis and meta-regression

Meta-analysis was performed using the “metafor” [48] and “club-Sandwich” [49] packages in the R programming language (R Core Team,

2023). For each outcome variable and sample, we calculated the mean difference effect size and sampling variance. Since none of the studies directly reported the correlation between the alcohol and control conditions (which is required to account for the cross-over design employed by studies [50]), we relied on contact with authors to determine appropriate correlations, with chosen values typically sourced from Pabon et al., 2022 [51] and Bazil et al., 2005 [33]. As correlation data were not obtained for all samples, we also conducted a sensitivity analysis to ensure our results were robust to uncertainty around the chosen value. The sensitivity analysis showed conclusions to be robust when using a low (r = 0.1) and high (r = 0.9) correlation value for all outcomes except latency to N3 sleep. Further details of handling of

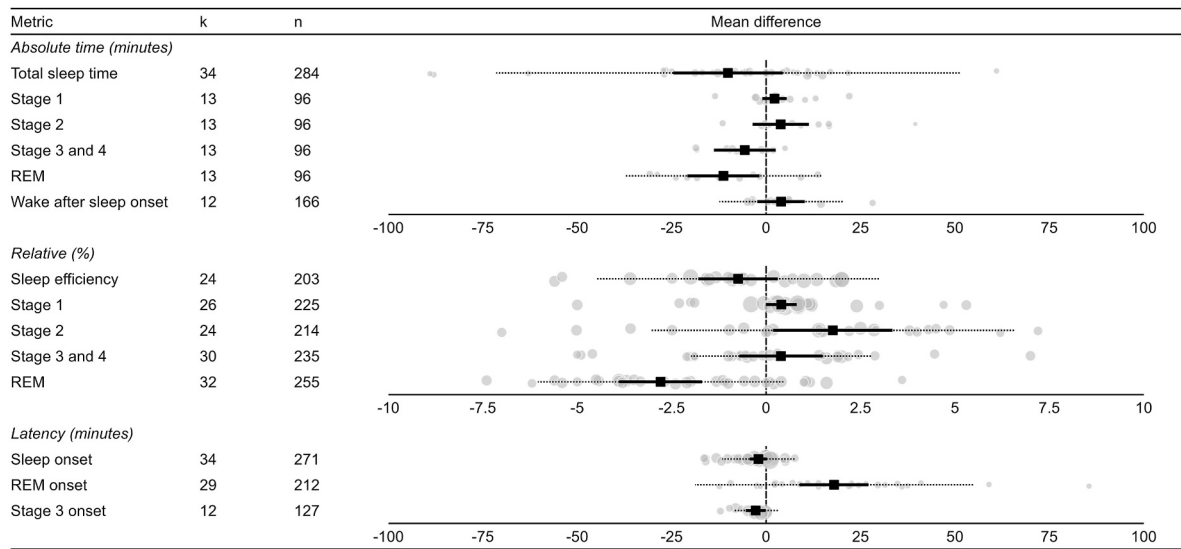


Fig. 2. Forest plot displays the duration (min) of total sleep time, non-rapid eye movement (NREM) stage one (N1) sleep, NREM stage two (N2) sleep, NREM stage three (N3) sleep, rapid eye movement (REM) sleep, and wake after sleep onset; the proportion (%) of sleep efficiency, N1 sleep, N2 sleep, N3 sleep, and REM sleep; and the latency (min) to sleep onset, REM sleep onset, and N3 sleep onset. The number of effect sizes (k) and participants (n) included in each meta-analytic model are reported and each circle represents the mean difference between the control and alcohol condition, with the size of the circle representing the statistical weight of the effect size. A negative effect size indicates a reduction in the outcome with the alcohol condition compared to the control condition. The solid black lines represent the 95 % confidence interval and the dotted grey lines represent the 95 % prediction interval.

correlation data and the sensitivity analysis can be found in [Supplementary Fig. S1](#) and [Supplementary Table S1](#).

Effect sizes were pooled using a multi-level mixed-effects meta-analysis to account for the hierarchical structure of the data. Specifically, dependency between effect sizes from the same sample was accounted for by imputing block-diagonal covariance-matrices with an assumed correlation of $r = 0.50$. Owing to uncertainty around this correlation value, we used robust inference methods with an adjustment for small samples, so that our interpretation of fixed effects were unbiased [52]. We reported the pooled mean difference and 95 % confidence interval (CI) for each outcome variable, including sleep onset latency, total sleep time, REM sleep onset latency, latency to N3 sleep, wake after sleep onset, sleep efficiency, and both absolute (i.e., min) and relative (i.e., expressed as a percentage of total sleep time) sleep architecture (N1, N2, N3 (and N4), and REM sleep). To support interpretation of these data, we also report the number of effect sizes (k) and participants (n) included in each meta-analytic model, and the 95 % prediction intervals (PI) to support clinical interpretation of heterogeneity. Where additional data related to the amount and timing of alcohol consumption were available, we performed moderator (meta-regression) analysis to assess the impact of these potential effect modifiers on sleep outcomes. Additionally, we assessed whether sex (represented as % of sample that was female) moderated the effect size for each outcome variable. A full summary of all meta-analytical models is provided in [Supplementary Tables S2–S4](#).

3. Results

3.1. Study selection and characteristics

Following the screening process, 27 studies were identified for inclusion in the review (Fig. 1). All included studies employed a controlled crossover design except for two [35,53] in which a controlled experimental design without a crossover was employed. Across the included studies, 37 alcohol conditions were administered with 12 [24–26,29,30,32,34,36,37,43] classified as a low dose ($\leq 0.50 \text{ g}\cdot\text{kg}^{-1}$), eight [29,32–34,37,42,46,53] classified as a moderate dose (>0.50 to $<0.75 \text{ g}\cdot\text{kg}^{-1}$), and 17 [23,25,27,28,31,34–36,38,40,41,43–45,51,54,55]

classified as a high dose ($\geq 0.75 \text{ g}\cdot\text{kg}^{-1}$) [18]. Based off an average adult mass of 62 kg [56] and one standard drink containing 10 g of alcohol [57], the dose classifications can be approximated as follows: a low dose of alcohol as less than or equal to three standard drinks, a moderate dose of alcohol between three and five standard drinks, and a high dose of alcohol as greater than or equal to five standard drinks. The intervention was administered as an acute daily dose on the day of the measured sleep opportunity in all studies except for four where administration was sustained across two [30], three [25,27], or nine nights [45]. The key characteristics of each study are presented in [Table 2](#).

3.2. Assessment of reporting quality

A summary of the risk of bias assessment is displayed in [Table 3](#). In domain one, 11 studies [24,26–29,36,38,42–45] were deemed to be of “some concern” as participants were exposed to the intervention in the same sequence rather than being randomised into a condition sequence. In domain S, five studies [40,41,43,44,55] were deemed “high risk” due to the absence of an appropriate washout period, while one study [30] was considered to be of “some concern” as the washout period was not clearly defined. There were no notable concerns in domain two or domain three. In domain four, three studies [42–44] was deemed “high risk” due to an unclear protocol description and absence of sleep outcome definitions. Five studies were deemed to be “high risk” in domain five, in four of these studies [32,34,37,45] sleep staging data was reported for the first portion of the sleep bout only, and in one study [38] implausibly small measures of variance were reported for the sleep staging data. Additionally, eight studies [27,28,35,43,44,46,53,55] were deemed to be of “some concern” in domain five due to the lack of a clear statistical analysis protocol.

3.3. Objective sleep outcomes

3.3.1. Sleep onset latency

Measures of objective sleep onset latency were reported in 19 studies [23–32,34–38,42,51,53,55]. Sleep onset latency was not different between the alcohol condition and the control condition (Fig. 2; mean difference = -2.0 min , 95%CI = -4.3 to 0.2 min , 95%PI = -11.6 to 7.5

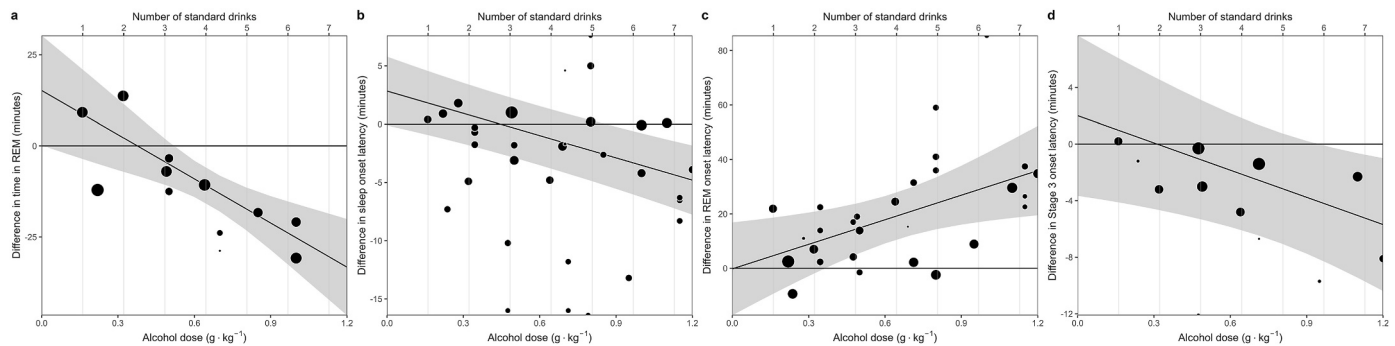


Fig. 3. Meta-analytic model accounting for the dose of alcohol ($\text{g} \cdot \text{kg}^{-1}$) with standard drink equivalents (x-axis) based on the assumption of one standard drink containing 10 g of alcohol [57] and a standard body mass of 62 kg [56]. Each circle represents the mean difference (y-axis) between the control and alcohol condition, with the size of the circle proportional to the statistical weight of the effect size. The 95 % confidence interval (CI) is represented by the banded shading. For panel a, b, and d (negative slope), when looking at the zero reference line, any value below indicates the alcohol group exhibited a reduction in the sleep outcome, with a significant effect occurring when the upper 95 % CI crosses the zero reference line. For panel c (positive slope), any value above the zero reference line indicates the alcohol group exhibited an increase in the sleep outcome, with a significant effect occurring when the lower 95 % CI crosses the zero reference line. As such, the estimated dose cut-off occurs for a) absolute rapid eye movement (REM) sleep (min) at a dose of alcohol of $0.50 \text{ g} \cdot \text{kg}^{-1}$ which equates to approximately three standard drinks; b) sleep onset latency (min) at a dose of alcohol of $0.85 \text{ g} \cdot \text{kg}^{-1}$ which equates to approximately five standard drinks; c) REM sleep onset latency at a dose of alcohol $0.35 \text{ g} \cdot \text{kg}^{-1}$ which equates to approximately two standard drinks; and d) latency to non-rapid eye movement stage three (N3) sleep at a dose of alcohol of $0.95 \text{ g} \cdot \text{kg}^{-1}$ which equates to approximately six standard drinks.

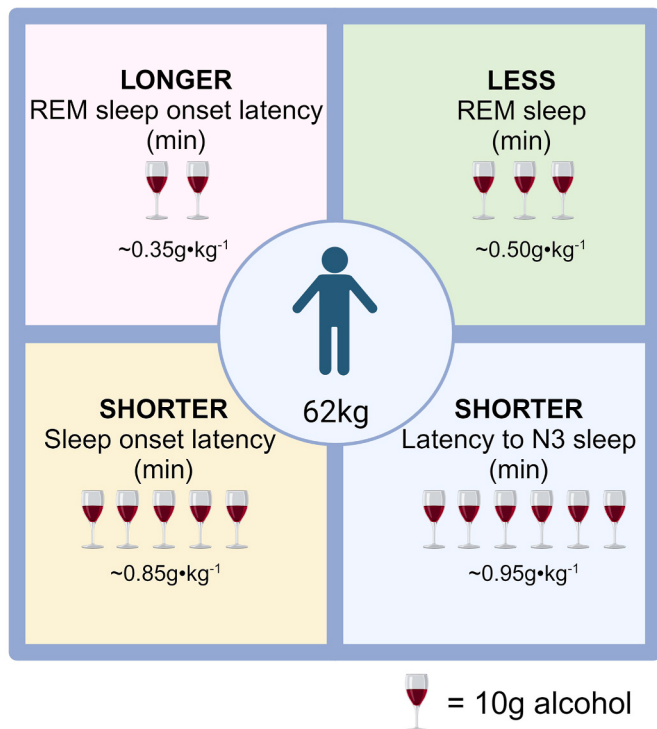


Fig. 4. Summary of the meta-regression findings with the dose-thresholds for rapid eye movement (REM) sleep onset latency (min), REM sleep duration (min), sleep onset latency (min), and latency to non-rapid eye movement stage three (N3) sleep modelled for a 62 kg individual.

min, $k = 34$, $n = 271$, $p = 0.074$). For every $1 \text{ g} \cdot \text{kg}^{-1}$ increase in alcohol dose, sleep onset latency in the alcohol condition was shortened by 6.4 min (Fig. 3; 95%CI = -9.3 to -3.5 min, $k = 30$, $n = 222$, $p = 0.004$) compared to the control condition, with a significantly shorter sleep onset latency identified with a high dose of alcohol (Fig. 3; $\sim 0.85 \text{ g} \cdot \text{kg}^{-1}$). The effect of alcohol on sleep onset latency was not moderated by the timing of intake ($k = 30$, $n = 222$, $p = 0.684$).

3.3.2. Total sleep time

Measures of objective total sleep time were reported in 18 studies

[23,24,26,28,29,32–38,40–42,51,53,55]. Total sleep time was not different between the alcohol condition and the control condition (Fig. 2; mean difference = -10.1 min, 95%CI = -24.6 to 4.4 min, 95%PI = -71.5 to 51.3 min, $k = 34$, $n = 284$, $p = 0.160$). The effect of alcohol on total sleep time was not moderated by the dose of alcohol ($k = 30$, $n = 235$, $p = 0.701$) or the timing of intake ($k = 30$, $n = 235$, $p = 0.488$).

3.3.3. REM sleep onset latency

Measures of objective REM sleep onset latency were reported in 14 studies [23–26,28–32,34,36,37,42,55]. REM sleep onset latency was 18.0 min longer in the alcohol condition compared to the control condition (Fig. 2; 95%CI = 8.8 – 27.1 min, 95%PI = -18.8 to 54.8 min, $k = 29$, $n = 212$, $p = 0.001$). For every $1 \text{ g} \cdot \text{kg}^{-1}$ increase in alcohol dose, REM sleep onset latency in the alcohol condition was delayed by 30.1 min (Fig. 3; 95%CI = 6.4 – 53.8 min, $k = 28$, $n = 200$, $p = 0.024$) compared to the control condition, with a significantly longer REM sleep onset latency identified with a low dose of alcohol (Fig. 3; $\sim 0.35 \text{ g} \cdot \text{kg}^{-1}$). The effect of alcohol on REM sleep onset latency was not moderated by the timing of intake ($k = 28$, $n = 200$, $p = 0.657$).

3.3.4. Latency to N3 sleep

Measures of objective latency to N3 sleep were reported in six studies [23,24,27,32,34,37]. Latency to N3 sleep was 2.8 min shorter in the alcohol condition compared to the control condition (Fig. 2; 95%CI = -5.4 to -0.1 min, 95%PI = -8.7 to 3.1 min, $k = 12$, $n = 127$, $p = 0.044$). For every $1 \text{ g} \cdot \text{kg}^{-1}$ increase in alcohol dose, latency to N3 sleep in the alcohol condition was shortened by 6.4 min (Fig. 3; 95%CI = -12.0 to -0.8 min, $k = 12$, $n = 127$, $p = 0.037$) compared to the control condition, with a significantly shorter latency to N3 sleep identified with a high dose of alcohol (Fig. 3; $\sim 0.95 \text{ g} \cdot \text{kg}^{-1}$). The effect of alcohol on latency to N3 sleep was not moderated by the timing of intake ($k = 12$, $n = 127$, $p = 0.400$).

3.3.5. Wake after sleep onset

Measures of objective wake after sleep onset were reported in eight studies [23,24,26,30,31,35,36,53]. Wake after sleep onset was not different between the alcohol condition and the control condition (Fig. 2; mean difference = 4.0 min, 95%CI = -2.3 to 10.3 min, 95%PI = -12.4 to 20.3 min, $k = 12$, $n = 166$, $p = 0.187$). The effect of alcohol on wake after sleep onset was not moderated by the dose of alcohol ($k = 9$, $n = 134$, $p = 0.661$) or the timing of intake ($k = 9$, $n = 134$, $p = 0.058$).

3.3.6. Sleep efficiency

Measures of objective sleep efficiency were reported in 14 studies [23–26,29–33,35,36,42,51,55]. Sleep efficiency was not different between the alcohol condition and the control condition (Fig. 2; mean difference = -0.7% , 95%CI = -1.8 to 0.3% , 95%PI = -4.5 to 3.0% , $k = 24$, $n = 203$, $p = 0.147$). The effect of alcohol on sleep efficiency was not moderated by the dose of alcohol ($k = 23$, $n = 191$, $p = 0.815$) or the timing of intake ($k = 23$, $n = 191$, $p = 0.125$).

3.3.7. Absolute sleep architecture

Measures of absolute sleep architecture were reported in 10 studies [24,26,30,32,34,36–38,42,53]. Compared to the control condition, alcohol consumption reduced the duration of REM sleep by 11.3 min (Fig. 2; 95%CI = -20.8 to -1.8 min, 95%PI = -37.2 to 14.6 min, $k = 13$, $n = 96$, $p = 0.026$). For every $1 \text{ g}\cdot\text{kg}^{-1}$ increase in alcohol dose, REM sleep duration in the alcohol condition was reduced by 40.4 min (Fig. 3; 95%CI = -60.0 to -20.8 min, $k = 10$, $n = 64$, $p = 0.009$) compared to the control condition, with a significant reduction in REM sleep identified with a low dose of alcohol (Fig. 3; $\sim 0.50 \text{ g}\cdot\text{kg}^{-1}$). For every additional hour that alcohol was consumed prior to bedtime, REM sleep duration in the alcohol condition was increased by 0.06 min (95%CI = -0.1 to 0 min, $k = 10$, $n = 64$, $p = 0.049$) compared to the control condition.

Compared to the control condition, alcohol consumption had no effect on the duration of N1 sleep (Fig. 2; mean difference = 2.2 min, 95%CI = -1.0 to 5.5 min, 95%PI = -1.0 to 5.5 min, $k = 13$, $n = 96$, $p = 0.130$), the duration of N2 sleep (Fig. 2; mean difference = 3.9 min, 95%CI = -3.6 to 11.3 min, 95%PI = -3.6 to 11.3 min, $k = 13$, $n = 96$, $p = 0.241$), or the duration of N3 and N4 sleep (Fig. 2; mean difference = -5.7 min, 95%CI = -13.8 to 2.5 min, 95%PI = -13.8 to 2.5 min, $k = 13$, $n = 96$, $p = 0.135$). The effects of alcohol consumption on the duration of NREM sleep were not moderated by the dose of alcohol or the timing of intake (Supplementary Table 2; $p > 0.050$).

3.3.8. Relative sleep architecture

Measures of relative sleep architecture were reported in 19 studies [23,25–29,31–35,37,40,41,43,45,51,53,55]. Compared to the control condition, alcohol consumption reduced the proportion of REM sleep by 2.8 % (Fig. 2; 95%CI = -3.9 to -1.7% , 95%PI = -6.1 to 0.5% , $k = 32$, $n = 255$, $p < 0.001$). The effect of alcohol on the proportion of REM sleep was not moderated by the dose of alcohol ($k = 29$, $n = 223$, $p = 0.424$) or the timing of intake ($k = 29$, $n = 223$, $p = 0.664$).

Compared to the control condition, alcohol consumption had no effect on the proportion of N1 sleep (Fig. 2; mean difference = 0.4 %, 95%CI = 0.0 – 0.8% , 95%PI = 0.0 – 0.8% , $k = 26$, $n = 225$, $p = 0.052$), increased (+1.8 %) the proportion of N2 sleep (Fig. 2; 95%CI = 0.18 – 3.4% , 95%PI = -3.0 to 6.6% , $k = 24$, $n = 214$, $p = 0.032$), and had no effect on the proportion of N3 and N4 sleep (Fig. 2; mean difference = 0.4 %, 95%CI = -0.7 to 1.5% , 95%PI = -2.0 to 2.8% , $k = 30$, $n = 235$, $p = 0.450$). The effects of alcohol consumption on the proportion of NREM sleep were not moderated by the dose of alcohol or the timing of intake (Supplementary Table 2; $p > 0.050$).

3.3.9. Subjective sleep outcomes

Measures of subjective sleep were reported in eight studies [23,25,26,32,33,35,46,54] using varying self-report tools detailed in Table 2. Due to a lack of homogeneity in the outcomes measured, a meta-analysis was not performed for subjective sleep. Measures of subjective total sleep time were reported in two studies [23,54], with no significant difference between the alcohol and control condition. Measures of subjective sleep onset latency were reported in five studies, with a significant reduction in the perceived time to fall asleep in the alcohol condition reported in three studies [32,46,54] and no significant difference between the alcohol condition and control condition reported in two studies [23,26]. Measures of subjective wake after sleep onset were reported in two studies [23,26], with no significant difference between

the alcohol and control condition. Measures of subjective sleep quality were reported in five studies, with a significant reduction in perceived sleep quality in the alcohol condition reported in two studies [23,35], a significant increase in perceived sleep quality in the alcohol condition reported in one study [54], and no significant difference between the alcohol condition and control condition reported in two studies [25,32].

3.3.10. Sex differences

No moderating effect of sex was observed on objective sleep outcomes (Supplementary Table 4; $p > 0.050$). Study cohorts were comprised of males only in 12 studies [26–28,31,32,34,36,38,43–46], females only in four studies [24,29,37,41], and a mix of males and females (45.3 % males; 54.7 % females) in 11 studies [23,25,30,33,35,40,42,51,53–55]. Of the 11 studies with a mixed cohort, the effect of sex on sleep outcomes was investigated in one study [23], with a dose of $1.2 \text{ g}\cdot\text{kg}^{-1}$ administered to males ($n = 34$) and $1.1 \text{ g}\cdot\text{kg}^{-1}$ administered to females ($n = 59$). Compared to the control condition, significant effects of alcohol were observed on objective outcomes in the female cohort with a reduction in total sleep time (-18.8 min; $p < 0.050$), a reduction in sleep efficiency (-3.6% ; $p < 0.010$), an increase in wake after sleep onset ($+14.5$ min; $p < 0.010$), and a shortening in latency to N3 sleep (-2.3 min; $p < 0.050$). No significant effects of alcohol were observed on these sleep outcomes in the male cohort. Furthermore, no significant effect by sex was observed for sleep onset latency, REM sleep onset latency, or the proportion of N1, N2, N3, or REM sleep despite significant condition effects being observed.

4. Discussion

In the present review, the impact of alcohol consumption on subsequent sleep in healthy adults was quantified. The main findings are: 1) low doses of alcohol delay the onset of REM sleep ($0.35 \text{ g}\cdot\text{kg}^{-1}$) and reduce the duration of REM sleep ($0.50 \text{ g}\cdot\text{kg}^{-1}$) in a dose-dependent manner; 2) high doses of alcohol ($0.85 \text{ g}\cdot\text{kg}^{-1}$) shorten sleep onset latency and latency to N3 sleep ($0.95 \text{ g}\cdot\text{kg}^{-1}$) in a dose-dependent manner; 3) alcohol consumption has no significant effect on total sleep time, sleep efficiency, or wake after sleep onset, although it is important to note that there is large uncertainty in these findings as evidenced by the wide 95 % prediction intervals. Furthermore, the ability to discern the impact of timing was limited given the administration of alcohol predominantly occurred within 3 h of the scheduled bedtime. The influence of sex could not be determined given the limited number of studies providing sex-specific data. The findings demonstrate a shorter sleep onset latency with alcohol consumption but only when consumed at a high dose. Beyond the impact on sleep onset, the findings highlight the disruption to subsequent sleep, with reductions in REM sleep occurring at low doses and progressively worsening with consumption of higher doses.

4.1. Objective sleep outcomes

4.1.1. Sleep onset latency

Alcohol significantly shortened sleep onset latency in five studies [23,27,34,37,38], with three of these studies reporting a sleep onset latency in the control condition above 20 min. This is an important consideration given 82 % of control latencies reported across studies were within a normal range of less than 20 min [58], which may limit the potential for a significant reduction with alcohol administration. For example, when the control latency was short (6.9 ± 1.9 min), a dose of alcohol of $0.50 \text{ g}\cdot\text{kg}^{-1}$ (3.8 ± 1.1 min) or $1.00 \text{ g}\cdot\text{kg}^{-1}$ (2.2 ± 0.8 min) did not significantly reduce sleep onset latency. The findings suggest alcohol may have a more pronounced effect on sleep onset latency in individuals experiencing delays in sleep initiation. The dose-response relationship between alcohol consumption and sleep onset latency was investigated in six studies [25,29,32,34,36,37], with shorter latencies (ranging from 1.6 to 8.7 min) when larger doses of alcohol were

consumed. As no study has investigated the effects of a fixed dose of alcohol administered at varying time points, there is no clear evidence to determine the influence of timing of alcohol consumption on sleep onset latency.

Based on the current analysis, the effect of alcohol on sleep onset latency (-2.0 min) was not significant. However, reductions in sleep onset latency were dependent on the amount of alcohol consumed (i.e., larger doses resulted in shorter latencies). Specifically, a significantly shorter sleep onset latency was identified with a dose of alcohol of approximately $0.85 \text{ g}\cdot\text{kg}^{-1}$, which equates to approximately five standard drinks [56]. It is proposed that alcohol may shorten sleep onset latency by altering the action of neurotransmitter systems to depress central nervous system function [17], with an increase in the action of GABA and a reduction in the action of glutamate to promote a state of sedation [11]. Recently, it has been suggested that alcohol may also facilitate the action of adenosine, a neuromodulator suggested to heighten sleep pressure [59]. By facilitating the formation of adenosine and preventing the reuptake of adenosine into the cell, alcohol may increase the propensity for sleep with a subsequent shortening of sleep onset latency [59]. However, the findings of the present review suggest the consumption of high doses of alcohol are required to elicit a shorter sleep onset latency. It remains unclear whether the shortening of sleep onset latency is affected by the timing of alcohol consumption.

4.1.2. Total sleep time

Total sleep time was significantly reduced in five studies [23,26,40,41,51] and significantly increased in two studies [32,38] with the consumption of alcohol. Notably, a large proportion of studies did not control for time in bed between the control and alcohol conditions, making it difficult to ascertain the true effect of alcohol on total sleep time. The dose-response relationship between alcohol consumption and total sleep time was investigated in five studies, with four [29,32,34,36] demonstrating greater reductions in total sleep time (ranging from 12.8 to 27.7 min) with larger doses of alcohol. In one study [32], total sleep time significantly increased ($+14.9$ min) with the lowest dose of alcohol ($0.16 \text{ g}\cdot\text{kg}^{-1}$) compared to the control condition (431.1 ± 8.6 min), suggesting that a low dose of alcohol may increase total sleep time. There were no data available regarding the effect of a fixed dose of alcohol on subsequent sleep when consumed at varying time points prior to the sleep opportunity. Therefore, it is difficult to draw conclusions on the relationship between the timing of alcohol consumption and the subsequent effect on total sleep time.

The results of this analysis revealed a non-significant effect of alcohol on total sleep time (-10.1 min). The reduction in total sleep time was not moderated by the amount of alcohol or the timing of alcohol intake. Importantly, the findings in the present systematic review suggest that low doses of alcohol may increase total sleep time, potentially leading to a misrepresentation in the effect of alcohol on total sleep time when results are pooled without consideration of the dose of alcohol administered. Alcohol is largely metabolised by the alcohol dehydrogenase (ADH) enzyme, which becomes saturated at low doses [60]. Therefore, even with the consumption of larger doses, the rate of alcohol metabolism remains constant and blood alcohol concentration rises [61]. Given the cessation of alcohol upon sleep commencement, blood alcohol concentration will fall across the sleep period as a function of metabolism. With this, the sedative effect of alcohol will lessen and the concentration of metabolites will increase. Such metabolites, including acetaldehyde and acetate, can increase physiological arousal and body temperature which may disrupt sleep [62,63]. However, the effect of alcohol on total sleep time remains uncertain, as evidenced by the wide 95 % prediction interval ranging from substantial reductions (-71.5 min) to substantial increases ($+51.3$ min) in duration. The influence of the amount and timing of alcohol intake on total sleep time could not be determined.

4.1.3. REM sleep onset latency

REM sleep onset latency was significantly longer in four studies [23,28,36,55] with the consumption of alcohol. The dose-response relationship was investigated in six studies [25,29,32,34,36,37] with a tendency for longer latencies (ranging from 2.6 to 85.8 min) when larger doses of alcohol were consumed. For example, in one study [36], a non-significant effect on REM sleep onset latency was reported with a dose of alcohol of $0.50 \text{ g}\cdot\text{kg}^{-1}$ (86.8 ± 13.8 min) compared to the control condition (88.3 ± 14.9 min). When the dose was increased to $1.00 \text{ g}\cdot\text{kg}^{-1}$ (173.8 ± 18.9 min), REM sleep onset latency was 86 min longer. From the current evidence, it appears that larger doses of alcohol are associated with longer REM sleep onset latencies. However, no data were available on the timing of alcohol intake and it is unclear whether the effect of alcohol on REM sleep onset latency is influenced by the timing of consumption relative to bedtime.

REM sleep onset latency was 18 min longer following the consumption of alcohol. The increase in REM sleep onset latency was dependent on the dose of alcohol consumed (i.e., larger doses resulted in longer latencies). Specifically, a significantly longer REM sleep onset latency was identified with a dose of alcohol of approximately $0.35 \text{ g}\cdot\text{kg}^{-1}$, which equates to approximately two standard drinks [56]. The consumption of alcohol may delay REM sleep onset latency by influencing REM-on and REM-off neural groups within the brainstem [17]. Activity of the REM-off neural group is facilitated by GABAergic interneurons [64], and it is proposed that alcohol may facilitate activity of these neural groups to suppress REM sleep during the initial sleep opportunity [17]. Given NREM sleep typically precedes the onset of REM sleep, REM sleep onset latency can be viewed as the length of the first NREM sleep cycle [65]. In line with the recently proposed theory that alcohol may facilitate the action of adenosine [59], an increase in sleep pressure is associated with greater N3 sleep in the first cycle of NREM sleep [66], which may occur at the expense of REM sleep. The findings of the present review indicate that a low dose of alcohol will delay REM sleep onset latency, with longer latencies occurring with larger doses. However, it remains unclear if the effect of alcohol on REM sleep onset latency is influenced by the timing of consumption.

4.1.4. Latency to N3 sleep

Alcohol significantly shortened latency to N3 sleep in two studies [23,27]. No clear dose-dependent effect was observed across the three studies [32,34,37] that investigated more than one dose. For instance, there was no effect with a dose of alcohol of $0.48 \text{ g}\cdot\text{kg}^{-1}$ (10.3 ± 3.0 min) or $0.71 \text{ g}\cdot\text{kg}^{-1}$ (9.2 ± 3.0 min) compared to the control (10.6 ± 2.4 min), [37]. Minimal change occurred with a $0.24 \text{ g}\cdot\text{kg}^{-1}$ dose of alcohol (31.3 ± 17.5 min) compared to the control condition (32.5 ± 23.5 min), with a non-significant trend for a shorter latency to N3 sleep when the dose was increased to $0.95 \text{ g}\cdot\text{kg}^{-1}$ (22.8 ± 13.7 min) [34]. From the current evidence, there appears to be no clear relationship between the dose of alcohol and the latency to N3 sleep. Additionally, there exists a lack of evidence investigating the timing relationship and further research is needed to clarify the influence of both the amount and timing of alcohol consumption on the latency to N3 sleep.

Latency to N3 sleep was shortened by 2.8 min with the consumption of alcohol. The reduction in latency to N3 sleep was dependent on the dose of alcohol consumed (i.e., larger doses resulted in shorter latencies). Specifically, a significantly shorter latency to N3 sleep was identified with a dose of alcohol of approximately $0.95 \text{ g}\cdot\text{kg}^{-1}$, which equates to approximately six standard drinks [56]. Within the studies included in the analysis of latency to N3 sleep, the bedtime was reported to be consistent across the alcohol condition and control condition in two [23,27]. As the expression of N3 sleep is suggested to be under homeostatic control, where pressure for N3 sleep builds with prior wakefulness, a delay in bedtime in the alcohol condition may shorten the latency to N3 sleep [67]. Additionally, N3 sleep is characterised by high amplitude, low frequency delta waves that reflect the synchronous shift of membrane potentials between cortical neurons [68]. Alcohol is

suggested to enhance the function of GABA_A receptors that facilitate the hyperpolarisation of cortical neurons [17]. Consequently, alcohol consumption may increase the occurrence of delta activity, which is a key characteristic of N3 sleep [17]. Furthermore, alcohol may facilitate the action of adenosine to promote the earlier occurrence of N3 sleep [11]. However, the observed reduction in latency to N3 sleep is modest and the findings indicate that the consumption of a high dose of alcohol is required to shorten the latency to N3 sleep. It remains unclear how the effect of alcohol on latency to N3 sleep is influenced by the timing of consumption.

4.1.5. Wake after sleep onset

Alcohol significantly increased wake after sleep onset in three studies [23,26,35], with two of these studies stemming from the same data set and analysed by sex [23] or beverage type [35]. Interestingly, in the remaining study [26], a 28.2-min increase in wake after sleep onset was reported following the administration of a low dose ($0.22 \text{ g} \cdot \text{kg}^{-1}$) of alcohol 6 h prior to bedtime, despite the presence of alcohol in the breath being undetectable immediately prior to bedtime [26]. A potential effect of alcohol metabolites, including acetaldehyde and acetate, could explain this finding and warrants further research [17]. Only one study investigated the dose relationship between alcohol and wake after sleep onset, with no significant effect of a dose of alcohol of $0.50 \text{ g} \cdot \text{kg}^{-1}$ ($24.6 \pm 40.2 \text{ min}$) or $1.00 \text{ g} \cdot \text{kg}^{-1}$ ($23.5 \pm 19.0 \text{ min}$) compared to the control condition ($21.3 \pm 18.3 \text{ min}$). Collectively, there is no clear evidence of a dose-response relationship between alcohol and wake after sleep onset. Given the lack of available data, it is unclear whether the timing of alcohol consumption has an impact on wake after sleep onset.

Based on the current analysis, the effect of alcohol on wake after sleep onset was not significant ($+4.0 \text{ min}$). The increase in wake after sleep onset was not moderated by the amount of alcohol or the timing of alcohol intake. It is proposed that alcohol may initially enhance sleep pressure by facilitating the action of adenosine, resulting in greater sleep disruption across the night due to a subsequent reduction in sleep pressure [59]. In addition, the consumption of alcohol can cause diuresis which may increase periods of wake throughout the night [69]. An important consideration is that time in bed was standardised in four of the studies [23,26,30,31] included in the analysis, reported as comparable in two of the studies [24,36], and uncontrolled in one study [53]. When uncontrolled, the differences in time in bed between the control and alcohol conditions could influence the observed effect on wake after sleep onset. Overall, the wide 95 % prediction interval (-12.4 to 20.3 min) observed in the present review highlights large uncertainty in the effect of alcohol on wake after sleep onset [70]. The influence of the amount and timing of alcohol consumption on wake after sleep onset remains unclear.

4.1.6. Sleep efficiency

Sleep efficiency was significantly reduced in four studies [23,26,35,51] and increased in one study [32] with alcohol consumption. The dose-response relationship was investigated in four studies [25,29,32,36], with three [25,29,32] demonstrating a tendency for greater reductions in sleep efficiency (ranging from 0.8 to 4 %) with larger doses of alcohol. In one study [32], a significant increase in sleep efficiency of 2.0 % was reported in the two low dose conditions (0.16 and $0.32 \text{ g} \cdot \text{kg}^{-1}$) compared to the control condition, suggesting that low doses of alcohol may reduce sleep efficiency. However, this finding is not supported across studies and further research is needed to determine the effect of alcohol on sleep efficiency. The available evidence does not allow clear conclusions to be drawn on whether sleep efficiency is influenced by the amount or timing of alcohol consumption relative to bedtime.

No significant effect of alcohol was observed on sleep efficiency (-0.7%). This effect was not moderated by the amount of alcohol or the timing of alcohol intake. Sleep efficiency represents the time spent asleep as a proportion of the time in bed, recognising that not all time in

bed is spent asleep [71]. Given the systematic review findings supported an improvement in total sleep time at low doses, it is feasible to conclude that sleep efficiency may improve in a similar manner. Therefore, the pooled effect across varying doses may underestimate the impact of larger doses of alcohol on sleep efficiency. The uncertainty in the effect of alcohol on sleep efficiency is underscored by the 95 % prediction interval ranging from a potential reduction (-4.5%) to a potential increase ($+3.0 \%$) in efficiency. Further research is required to better understand the influence of the amount and timing of alcohol consumption on sleep efficiency.

4.1.7. Absolute sleep architecture

Alcohol consumption did not significantly affect N3 sleep duration across the sleep period but N3 sleep duration was significantly increased in the two studies [34,37] that analysed the first 3 h of the sleep period. This increase in N3 sleep occurred in a dose-dependent manner, with larger doses of alcohol resulting in greater increases (ranging from 6.4 to 9.6 min) [34,37]. However, within the second half of the sleep opportunity, a dose-dependent reduction in N3 sleep was observed along with a concurrent reduction in REM sleep, with larger doses of alcohol resulting in greater reductions in N3 sleep (ranging from 5.2 to 6.4 min) and REM sleep (ranging from 11.0 to 17.4 min) [34,37]. Only one study [36] investigated the dose-response relationship across the entire sleep opportunity, with a significant reduction in REM sleep duration occurring in a dose-dependent manner. Further research is needed to investigate the influence of timing of consumption on absolute sleep architecture.

No significant effect was observed on the duration of NREM sleep in the current analysis. However, a significant reduction of 11.3 min was observed in the duration of REM sleep. The reduction in REM sleep was dependent on the dose consumed (i.e., larger doses resulted in less REM sleep). Specifically, a significant reduction in the duration of REM sleep was identified at a dose of alcohol of approximately $0.50 \text{ g} \cdot \text{kg}^{-1}$, which equates to approximately two standard drinks [56]. The largest disruption to sleep typically occurs in the second half of sleep when alcohol has been metabolised and concentrations of acetaldehyde and acetate are increased [17]. Given this latter period of sleep is typically REM sleep dominant, the reduction in alcohol's sedative effects and accumulation of metabolites can increase arousal with a subsequent reduction in REM sleep [62,63]. Despite suggestions of a REM sleep rebound, whereby the occurrence of REM sleep is increased to compensate for the alcohol-induced suppression of REM sleep in the first half of the sleep opportunity [44], the current findings suggest the overall duration of REM sleep will be reduced following alcohol consumption. It's important to note that among the studies analysed, time in bed between the control condition and alcohol condition was standardised in two studies [26,30], reported to be comparable in two studies [24,36], and uncontrolled in the remaining studies. Given REM sleep predominantly occurs in the second half of the sleep opportunity, a shortened time in bed in the alcohol condition may reduce the duration of REM sleep [72]. The findings of the present review suggest the duration of REM sleep will be reduced with the consumption of a low dose of alcohol, with greater reductions observed when larger doses of alcohol are consumed. The influence of timing of alcohol intake on the duration of REM sleep remains unclear.

4.1.8. Relative sleep architecture

Alcohol consumption significantly increased the proportion of N3 sleep in two studies [23,35] and reduced the proportion of REM sleep in seven studies [23,31,35,37,40,41,51]. The dose-response relationship was investigated in six studies [25,29,32,34,37,43] with four [32,34,37,43] demonstrating a tendency for greater reductions in REM sleep (ranging 2.1 %–8.0 %) with larger doses of alcohol. Furthermore, one study [25] investigated the effect of varying doses of alcohol on relative sleep architecture in the first and second half of the sleep opportunity. With the high alcohol dose condition (blood alcohol concentration 1.0

Practice Points

1. The impact of alcohol consumption on total sleep time, sleep efficiency, and wake after sleep onset remains unclear. Determining the effect of alcohol on these sleep outcomes requires further investigation.
2. A low dose ($\leq 0.50 \text{ g}\cdot\text{kg}^{-1}$) of alcohol consumed prior to bedtime (within $\sim 3 \text{ h}$) can delay the onset of REM sleep and reduce the duration of REM sleep with greater disruptions at larger doses of alcohol. Individuals seeking to protect the quality of their REM sleep should be mindful of alcohol intake, particularly with larger doses.
3. A high dose ($\geq 0.85 \text{ g}\cdot\text{kg}^{-1}$) of alcohol consumed prior to bedtime (within $\sim 3 \text{ h}$) may reduce sleep onset latency and reduce the time to the first occurrence of deep sleep (i.e., N3). However, the use of alcohol as an aid to promote sleep is not an appropriate strategy. While a high dose may shorten the time to sleep initiation, larger doses of alcohol increase subsequent sleep disruption which outweighs any potential benefit.

%), there was a 7.9 % increase in the proportion of N3 sleep and a 2.0 % reduction in the proportion of N1 sleep in the first half of the sleep opportunity. Conversely, in the second half of the sleep opportunity, there was a 3.0 % increase in the proportion of N1 sleep [25]. In accordance with these findings, a dose of alcohol of $0.80 \text{ g}\cdot\text{kg}^{-1}$ increased N3 sleep in the first half of the sleep opportunity [31,45] and increased N1 sleep in the second half of the sleep opportunity [31]. The current evidence suggests that alcohol may initially promote sleep by increasing the occurrence of deep sleep (i.e., N3). However, this improvement appears to be transient, with an increase in the occurrence of lighter sleep (i.e., N1) in the latter portion of the sleep opportunity. In addition to the alterations in the structure of NREM sleep, the consumption of alcohol may reduce the overall proportion of REM sleep. These effects appear to be greater with larger doses of alcohol. With a lack of evidence investigating the timing relationship, it is not clear how relative sleep architecture is influenced by the timing of alcohol consumption.

An increase in the proportion of N2 sleep (+1.8 %) and reduction in the proportion of REM sleep (−2.8 %) occurred with the consumption of alcohol. The effects on relative sleep architecture were not moderated by the amount of alcohol or the timing of alcohol intake. The findings suggest alcohol may increase the occurrence of NREM sleep at the expense of REM sleep. However, given the sleep architecture of a healthy adult is comprised of approximately 21–30 % of REM sleep, the observed changes may not elicit clinically meaningful change [58]. Further investigation is required to understand the influence of the amount and timing of intake on relative sleep architecture.

4.1.9. Subjective sleep outcomes

There was no clear effect of alcohol on perceived total sleep time, sleep onset latency, wake after sleep onset, or sleep quality [23,25,26,32,35,46,54]. The most common trend observed was a reduction in the perceived time to fall asleep [32,46,54], although this effect was not consistent across studies [23,26]. One study [32] investigated the dose-response relationship with a reduction in perceived sleep onset latency with $0.32 \text{ g}\cdot\text{kg}^{-1}$ and $0.64 \text{ g}\cdot\text{kg}^{-1}$ of alcohol compared to the control condition. There was no significant effect observed for the low dose ($0.16 \text{ g}\cdot\text{kg}^{-1}$) and no effect on sleep quality with any dose of

alcohol compared to the control [32]. This was the only study to report both objective and subjective measures of sleep onset latency. Interestingly, despite no significant change in the objective measurement, a reduction in the perceived time to fall asleep was observed, suggesting the benefit of alcohol may be subjective in nature with minimal effect when evaluated objectively [32]. However, further research is needed to support this notion. Across studies, there was no effect on perceived sleep onset latency with a dose of alcohol of $0.22 \text{ g}\cdot\text{kg}^{-1}$ [26] or $1.20 \text{ g}\cdot\text{kg}^{-1}$ [23] indicating a lack of a clear dose-response relationship. Due to the limited investigations into subjective outcomes, it is challenging to draw firm conclusions on the effect of alcohol on subjective sleep outcomes.

4.1.10. Sex differences

Of the studies included in this review, the influence of sex on the effects of alcohol on subsequent sleep was investigated in one study [23]. Given the unique physiological profiles of males and females, including potential differences in ADH activity and distribution of alcohol within the body [73], there is a need to specifically investigate potential sex differences. Furthermore, in females, fluctuations in estradiol and progesterone across the menstrual cycle may be of importance given these sex hormones hold potential to mediate the acute effects of alcohol by interacting with neurotransmitters including GABA and dopamine [74]. An adapted protocol in consideration of the menstrual cycle was reported in three studies, with sleep evaluation undertaken during specific days of the menstrual cycle in two studies (days 25–32 [51] and days 4–21 [37]) and during the follicular phase in one study [29], although it was not outlined how this phase was determined. Additionally, the absence of a protocol that accounted for the menstrual cycle phase in female participants was cited as a limitation in three studies [24,37,51], with the authors of one study [51] emphasising the need for further research to address the known sex and hormone-related differences in response to alcohol [51]. Given the reported physiological differences between females using hormonal contraception and those who are naturally menstruating [75], research which investigates both endogenous and exogenous hormonal concentrations is warranted. In addition, menopausal and postmenopausal women experience high rates of sleep disturbance attributed largely to

Research Agenda

1. Employ controlled experimental designs to investigate the effect of alcohol on the characteristics of subsequent sleep with consideration of individual factors that may influence the effect of alcohol as well as the temporal influence of alcohol across the sleep opportunity.
2. Investigate the influence of the dose and the timing of alcohol intake to establish cut-off times for a range of standard alcoholic drinks aimed at minimising the negative effect of alcohol on the characteristics of subsequent sleep.

vasomotor symptoms and mood disorders, meaning they may be susceptible to greater alcohol induced sleep disruptions [76]. Future research should consider the potential influence of hormonal fluctuations that occur across the female lifespan to allow practical recommendations that account for the potential influence of sex.

4.1.11. Practical significance

The present review could not determine the influence of alcohol on total sleep time, sleep efficiency, or wake after sleep onset. The large uncertainty in the influence of alcohol was underpinned by the wide 95 % prediction interval displayed for each of these outcomes. Given the administration of alcohol occurred primarily within 3 h of bedtime, the impact of timing could not be established but dose dependent relationships were identified for alcohol consumption and subsequent sleep architecture (summarised in Fig. 4). The clearest effect of alcohol was on REM sleep, with a low dose of alcohol ($\leq 0.50 \text{ g} \cdot \text{kg}^{-1}$) delaying the first occurrence of REM sleep and reducing the duration of REM sleep across the sleep opportunity. This reduction in REM sleep was observed at approximately two standard drinks, with greater disruptions occurring with the consumption of larger doses of alcohol. Disruptions to REM sleep are suggested to impair memory consolidation, cognitive function, and emotional regulation, highlighting the negative effect alcohol-induced sleep disruption may have on wellbeing [77]. Interestingly, a shortening of sleep onset latency and the time to the first occurrence of deep sleep (i.e., N3) was observed only with a high dose of alcohol ($\geq 0.85 \text{ g} \cdot \text{kg}^{-1}$). This is an important finding that raises concern around the use of alcohol to initiate sleep. Although there may be a benefit to sleep onset latency, the high dose required to achieve this poses a challenge to subsequent REM sleep, which is reduced in a dose-dependent manner. Therefore, any potential benefit of using alcohol as an 'over the counter' sleep aid to initiate sleep is likely outweighed by greater sleep disruptions to REM sleep across the sleep opportunity.

4.2. Limitations

The present review synthesises current evidence to provide novel insights into the effect of alcohol on subsequent sleep. However, there are limitations that must be considered when interpreting the findings. The quality of the included evidence limits the strength of the conclusions, with 21 of the 27 studies presenting a risk of bias. To address this, further randomised controlled trials are required with the inclusion of a clear outline of the randomisation process, implementation of appropriate washout periods, and a pre-registered statistical analysis plan. Without a standardised unit of measure for alcohol dose, it was necessary to calculate the dose in $\text{g} \cdot \text{kg}^{-1}$ when not reported. Although calculations were made in accordance with standard units for the density of alcohol, there are a myriad of factors that may influence the standardisation of alcohol dose relative to mass that could not be taken into account. Additionally, rather than pure ethanol, the alcohol condition was administered in a variety of beverage types across studies which may introduce a confounding influence. Across the included studies, the methodologies employed largely involved the administration of alcohol within 3 h of bedtime. Consequently, there exists limited data regarding the effect of afternoon alcohol consumption on subsequent sleep, which limits the ability to assess the influence of the timing of alcohol intake on subsequent sleep. Given the limited number of studies reporting outcomes for the first and second half of the sleep opportunity, the temporal influence of alcohol on sleep could not be determined using the quantitative synthesis. With the systematic review findings identifying greater sleep disruption in the second half of the sleep opportunity, the temporal influence of alcohol warrants further investigation. Importantly, the dose thresholds are based on statistical significance with the assumption that changes identified are equivalent to clinically significant alterations in sleep outcomes. There also exists large variability in the pharmacokinetics of alcohol attributed to a combination of

environmental and genetic factors that deserve consideration when evaluating the effect of alcohol on subsequent sleep [78]. A key factor to consider is the rate of gastric emptying, with the ingestion of alcohol in a fed state attenuating the rise in blood alcohol concentration [79]. Alternative factors that may influence the rate of metabolism include the rate of alcohol consumption, beverage ingredients (e.g., glucose), and co-ingestion with smoking or other drugs [78]. Additionally, functional genetic polymorphisms in genes encoding the ADH enzyme may result in individual variation in the pharmacokinetics of alcohol [80]. Furthermore, the review could not discriminate between males and females, which may be an important consideration with suggestions that the effect of a fixed dose of alcohol may be greater in females given an increase in blood alcohol concentration resulting from a reduced volume of total body water and a reduction in ADH activity [73]. However, impact of sex remains uncertain given the limited investigations available. Lastly, the review included healthy adult populations aged between 18 and 70 years, and therefore the results may not generalise to alternative populations including adolescents, older adults (>70 years), or individuals with alcohol use disorder or sleep disorders. In addition, consideration should be given to the effect of alcohol within the included population given the wide age range. For example, older adults experience age-related declines in N3 sleep and may have greater susceptibility to the effect of alcohol [81].

5. Conclusion

Currently, there is considerable uncertainty regarding the effect of alcohol on the outcomes of subsequent sleep, including total sleep time, sleep efficiency, and wake after sleep onset. The findings suggest that the consumption of a low dose of alcohol will suppress the initial occurrence of REM sleep with a reduction in the duration of REM sleep across the sleep opportunity. The observed impairments in REM sleep are greater with larger doses of alcohol. Despite the belief that alcohol facilitates sleep onset, a shorter sleep onset latency and latency to deep sleep are only observed following consumption of larger doses of alcohol. Larger doses of alcohol will result in greater REM sleep disruptions, highlighting a concern for the potential use of alcohol as an 'over the counter' sleep aid. There is a need for further well-controlled experimental trials to provide evidence-based guidelines for the consumption of alcohol with regard to subsequent night-time sleep. Individual factors including the effect of sex on these responses require careful investigation.

Conflicts of interest

The authors do not have any conflicts of interest to disclose.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.smrv.2024.102030>.

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