‘High’ Risk? A Systematic Review of the Acute Outcomes of Mixing Alcohol with Energy Drinks

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Abstract

Aims: Alcohol mixed with energy drinks (AmED) is a relatively new consumption trend generating increasing concern regarding potential adverse effects. Despite the political and health imperative, there has been no systematic and independent synthesis of the literature to determine whether AmED offers additional harms relative to alcohol. The aim of this study was to review the evidence about whether co-consumption of energy drinks and alcohol, relative to alcohol alone, alters: (i) physiological, psychological, cognitive, and psychomotor outcomes, (ii) hazardous drinking practices, and (iii) risk-taking behaviour.

Methods: Pubmed, PsycInfo, and Embase databases were searched up until May 2013 for articles outlining descriptive, observational analytic, and human experimental studies which compared target outcomes for AmED versus alcohol consumers (between-subjects), or AmED versus alcohol consumption (within-subjects). Odds ratios were calculated for target outcomes following screening, data extraction, and quality assessment.

Results: Data were extracted from 19 articles. Analyses typically revealed increased odds of self-reported stimulation-based outcomes and decreased odds of sedation-based physiological and psychological outcomes relative to when alcohol was consumed alone, as indicated by rigorous cross-sectional descriptive research. These findings typically have not been reflected in experimental research, possibly due to the low doses administered relative to typical self-reported 'real-life' intake. AmED consumers generally report more hazardous alcohol consumption patterns and greater engagement in risk-taking behaviour than alcohol consumers. While most studies had equivocal findings, two studies showed lower odds of risk-taking behaviour for AmED relative to alcohol drinking sessions but limitations with respect to the outcome measures used restrict conclusions in regards to the behavioural outcomes of AmED use.

Conclusions: Mixing alcohol with energy drinks may exert a dual effect, increasing stimulation-based effects and reducing sedation-based outcomes; the clinical severity and dose threshold has not been established. At this stage it is unclear whether these changes in the nature of intoxication translate into greater alcohol intake and risk-taking behaviour.

The consumption of alcohol mixed with energy drinks (AmED) is a recent phenomenon, and queries have been raised regarding whether this practice may be associated with increasing alcohol-related harms (1). Studies targeting adolescents and young adults, key risk groups for hazardous drinking, indicate widespread use (23%-48% reporting recent AmED use) (2, 3). Among these subgroups, some consumers report combining alcohol with energy drinks (EDs) to facilitate a more positive intoxication experience and reduce alcohol's sedating effects (4). This assumption of oppositional behavioural effects is logical based on constituent pharmacodynamics (5). Energy drinks (EDs) alone typically facilitate performance and increase self-reported alertness and stimulation. In contrast, alcohol typically impairs performance, with self-reported increases in sedation. It has been theorised that the stimulant effects of EDs mask the depressant effects of alcohol, reducing physiological and psychological sedation-based effects (e.g., fatigue), while increasing stimulation (e.g., alertness, energy) (5, 6). This state of intoxication, which has been referred to as 'wide-awake drunkenness' (7), may impair consumers' ability to estimate intoxication. While the evidence-base supporting this premise has been challenged (8), AmED-induced underestimation of intoxication has been proposed to result in behavioural changes, specifically: (i) more hazardous drinking practices and (ii) poorer risk assessment and increased risk-taking behaviour (9). These theorised behavioural changes may increase the possibility of additional alcohol-related harms.

AmED research has expanded rapidly following increasing recognition of these theorised harms and a number of reviews have been published in this area. However, these reviews (8, 10-15) have either focused only on the use of ED alone (without alcohol), failed to adopt a systematic literature search, or have not provided comparable quantitative outcomes across the reviewed studies. To date, there has been no formal objective systematic synthesis of the

literature to determine whether AmED poses additional harms relative to alcohol. An integration of the literature is timely from a political and health standpoint (16, 17), with several countries currently developing policy responses to AmED (18, 19). As such, the primary objective of this article is to systematically review AmED research to determine whether co-consumption of energy drinks and alcohol poses additional harms relative to alcohol alone on: (i) physiological, psychological, cognitive, and psychomotor outcomes, (ii) hazardous drinking practices, and (iii) risk-taking behaviour.

Methods

Search Strategy

The study selection and data extraction process were outlined in a protocol (S1). Studies were identified by author AP¹ via Pubmed, PsycInfo, and Embase (last search May 8, 2013). Each ED-related search term (“*energy drink**”, “*Red Bull*”) was combined with the term *alcohol**, entered in conjunction with: *risk**, *behavio**, *adverse**, *effect**, *harm**, *health**, *excess**, *consum**, *intake** (Figure S2). AP¹ removed duplicates and completed initial eligibility screening based on publication criteria. Content assessment (based on title/abstract) was performed by AP¹ and ND using a standardised template; assessment was not blind, with full-text revision where necessary. Disagreement between reviewers regarding exclusion occurred for 15.1% of articles ($n=8$); disagreements were resolved by consensus.

Inclusion/Exclusion Criteria

Publication criteria. Studies adopting descriptive, observational analytic, and human experimental designs were included; animal studies, case studies, qualitative papers, reviews, methodology papers, and commentaries were excluded. Peer-reviewed journal articles

published in English between January 1990 and April 2013 with the search terms in title/abstract were included.

Content criteria. Due to the discrepancy in definitions of ED and AmED beverages across studies, we defined AmED use as consumption of: (i) pre-mixed beverages, (ii) hand-mixed beverages, or (iii) separate beverages in the same drinking session. EDs were defined as functional beverages which contain caffeine, sugars, and taurine; other ingredients may include glucuronolactone, B vitamins, herbal extracts (1).

As the objective was to examine relative likelihood of harms after AmED and alcohol, articles were included if they reported comparison of AmED versus alcohol consumers (between-subjects), or AmED versus alcohol consumption (within-subjects) in regards to: (i) physiological, psychological, cognitive and psychomotor outcomes, (ii) alcohol consumption and alcohol priming, or (iii) risk-taking behaviour.

Data Extraction and Analysis

A data extraction sheet, piloted on five random studies, was used by AP¹ and AP² to extract the following information: study aim, design, sample characteristics, sampling method, primary measures, method of administration, outcomes, conclusions, limitations, funding, and conflicts of interest. The Joanna Briggs Institute Critical Appraisal Checklist for Descriptive Studies (20), Joanna Briggs Critical Appraisal Criteria for Cohort/Case-Control Studies (20), and the Cochrane Collaboration tool were used for quality assessment (21). Reviewers were not blind to publication details. Data was requested from authors for seven articles (4-6, 22-25). Disagreement on any of the key information was resolved by discussion

and a final decision by ND where no consensus was reached. While no studies were removed based on quality assessment, these outcomes were qualitatively considered in the synthesis.

Odds ratios (OR) were calculated based on reported descriptive and inferential statistics.

Correlation between paired comparisons was estimated as .050 unless otherwise specified.

Outcomes were grouped within each theme area as: (i) self-reported drinking outcomes in natural scenarios (retrospective or prospective) for (a) AmED versus alcohol consumers, and (b) AmED versus alcohol sessions, (ii) self-reported outcomes of AmED versus alcohol administration in laboratory-based settings, and (iii) objective outcomes of AmED versus alcohol administration in laboratory-based settings.

Results

Sample for Synthesis

Eighty-seven articles were retrieved after duplicate removal (Figure 1). Nineteen studies were included in the final sample following exclusion (Table 1).

Figure 1 and Table 1 approximately here

Physiological Outcomes

Self-reported physiological outcomes of AmED versus alcohol consumption were assessed in three studies of consumers' real-life drinking experiences (26-28) and one study of consumers' expectations for drinking sessions (29) (Table 2). Varying assessment methodologies and tools were administered across these studies, including a 10-point severity scale (28), dichotomous (yes/no) response options (27) or categories (outcome present/absent) (26), and a 4-point agreement rating expectancy scale (29). Of these studies,

only one defined AmED as simultaneous use within the one beverage (26); de Haan, et al. (27) and Woolsey and colleagues (29, 30) defined AmED use as simultaneous use within the one beverage or consumed separately within two or four hours of each other, and Penning, et al. (28) did not specify how AmED was defined for participants. Only two experimental laboratory studies were identified; one assessed self-reported physiological state via 100-point visual analogue scale intensity ratings (5), while the other objectively assessed a limited range of physiological outcomes (22) (Table 2). There were no case-control or case crossover studies identified comparing alcohol- and AmED-related adverse exposures reported to emergency departments or poison information call centres.

Studies assessing self-reported drinking experiences typically indicated significantly greater odds of musculoskeletal and cardiovascular elevations, and significantly lower odds of gastrointestinal upset, after AmED. For example, Peacock, et al. (26) found that consumers reporting simultaneous AmED use had higher odds of tremors and irregular heartbeat in AmED versus alcohol sessions. These consumers reported typical AmED intake of 2.4 standard 250mL EDs (~160mg caffeine). In contrast, Penning, et al. (28) reported equivalent odds for 'rapid heartbeat' and 'gastrointestinal upset' for AmED and alcohol consumers' ratings of their last hangover experience following consumption of the respective beverages; AmED consumers typically ingested 196.7mg of caffeine. However, de Haan, et al. (27) and Peacock, et al. (26) reported significantly lower odds of nausea after AmED relative to alcohol consumption.

In addition, participants in Peacock et al.'s study showed significantly lower odds of self-reported general functioning impairment, namely vision and walking, during AmED versus alcohol sessions despite similar levels of alcohol consumption (26). However, in other

aspects of functioning (e.g., sleep), participants reported increased odds of impairment (26, 29), or a shift in the type of impairment. For example, Peacock, et al. (26) found lower odds of slurred speech, and higher odds of increased speech speed, during AmED versus alcohol sessions.

Table 2 approximately here

Similar disturbances are evident when examining other central nervous system (CNS) outcomes, with higher odds of agitation and ‘jolt and crash episodes’ in AmED sessions (26). In contrast, retrospective studies of other physiological outcomes (e.g., dizziness, headache) had equivalent odds across session type or were inconsistent across studies. However, these studies may underestimate AmED outcomes: Penning, et al. (28) only asked consumers to reflect on experience in one drinking session, and did not clearly define AmED use. Peacock, et al. (26) only identified the outcome as present in the last six months if participants responded ‘half the time’ or more often, excluding lower frequency occurrences. However, this study is methodologically robust, in that a clear definition of AmED use was provided to participants, and within-subject comparisons were adopted to rule out between-subject variability.

In contrast with this research, the placebo-controlled double-blind experimental study assessing self-reported outcomes showed equivalent odds for musculoskeletal, cardiovascular, gastrointestinal, general functioning, and CNS disturbance ratings when consumers ingested alcohol (0.6g/kg or 1.0g/kg) with and without ED (3.57mL/kg), with the exception of increased salivation 120 minutes after AmED administration (5). The latter double-blind, placebo-controlled, within-subjects study by Ferreira, et al. (22) showed that

blood pressure was significantly decreased after administration of alcohol (1.0g/kg) with ED (3.57mL/kg) compared to alcohol without ED; consistent with caffeine's peak absorption time (30-60 minutes) (31), this effect was only evident at the later time point (30 minutes) (22). These studies are methodologically strong, in that comparison of AmED and alcohol outcomes was within-subject, and blinding procedures were adopted to minimise the impact of confounding variables. However, it is important to note that the ED dose administered is equivalent to approximately one standard 250mL ED (80mg caffeine) per 70kg person. In contrast, AmED consumers in the aforementioned cross-sectional descriptive studies report typically ingesting a higher volume of ED with alcohol, with 61% of those surveyed by Woolsey and colleagues (29, 30) typically consuming three or more EDs (approximately 240mg caffeine) with alcohol.

Psychological Outcomes

Self-reported psychological outcomes of AmED versus alcohol were assessed in three studies of consumers' real-life drinking experiences (26-28) and one study of consumers' expectations for drinking sessions (29) (Table 3). Again, the number and type of outcomes assessed were not standardised across studies. Despite the fact that these studies adopted different definitions of AmED use, they generally showed significantly higher odds of stimulation (26), alertness (26, 29), and energy (26), and significantly lower odds of fatigue (26, 27), clumsiness (29), confusion (26), and sadness (26), during AmED sessions. Penning, et al. (28) reported equivalent odds for 'tiredness' however, ratings were specific to the hangover experience and only reflected one drinking experience. The coherence in outcomes across these studies, and the strengths of the methodology adopted (i.e., within-subject comparison) lends weight to the results of the cross-sectional descriptive research by Peacock, et al. (26) and de Haan, et al (27).

*** Table 3 approximately here***

This pattern of increased stimulation and decreased sedation has implications for the experience of other mood states. Peacock, et al. (26) reported higher odds of feeling irritable and ‘on edge’, and lower odds of feeling calm, carefree, friendly, outgoing, and sociable, during AmED relative to alcohol sessions. This psychological profile did not translate into more antisocial mood states, with equivalent odds of feeling annoyed or aggressive across session type (26). Peacock, et al. (26) reported lower odds of feeling disinhibited during AmED sessions; however, other impulsive mood states (e.g., daring, adventuresome) showed equivalent odds across session type (26, 29).

In contrast to the physiological research, there was a greater body of experimental research available assessing psychological outcomes. Five double-blind placebo-controlled experimental studies were identified (Table 4); four of these studies (6, 23, 24, 32) focused on assessing stimulation and sedation via a validated measure, the Biphase Alcohol Effects Scale (33), whilst the other (34) adopted a more general measure of psychological state, the Profile of Mood States (35). The former four studies partially reflect real-life drinking experiences, in that participants generally reported significantly higher stimulation scores after ingesting alcohol (peak mean breath alcohol concentration (BrAC) .043% to 0.89%) with ED (1.82mL/kg to 3.57mL/kg) relative to alcohol alone (6, 23, 24, 32). However, these studies did not typically identify AmED-induced reduced sedation, with equivalent odds for BAES sedation scores (6, 23, 24, 32). Mental fatigue ratings were generally equivalent (5, 32), with the exception of one study showing decreased ratings after AmED (23).

These experimental studies are well designed, in that the majority involved within-subject comparison of outcomes, ruling out between-subject variability. Furthermore, double-blind procedures were adopted in most cases, minimising the impact of confounding variables. However, these studies involved administration of a low ED dose, equivalent to one standard 250mL ED (80mg caffeine) per 70kg person. There has been one study using higher doses: Alford, et al. (36) administered participants two alcohol doses (peak BrAC .046% and .087%) across the session; following a between-subjects design, placebo or active ED (250mL; 80mg caffeine) was co-administered with each alcohol dose. In contrast with previous findings, this study revealed significantly *lower* ratings of 'clearheaded' and 'energetic' after the first dose, and significantly *higher* subscale scores for 'mentally slow', 'clumsy', and 'drowsy' after both doses, when ED was co-ingested. It should be noted that systematic between-subject variability in ratings for those in the active ED condition versus those in the placebo ED condition could contribute to these differences.

*** Table 4 approximately here***

Cognitive and Motor Outcomes

To date, there has been little consistency in outcomes across cognitive studies; this may be due to the small number of measurements for each area of interest, the various tasks adopted, and the different point during the blood alcohol concentration curve at which each are assessed. For example, Alford, et al. (36) reported that AmED significantly decreased interference on the Stroop task, reflecting increased inhibitory control, whereas Marczynski, et al. (6) found equivalent rates of inhibition failures after valid and invalid cues on the Cued Go/No-Go task after AmED relative to alcohol. These discrepant methodological approaches make definitive conclusions regarding the relative cognitive effects of AmED challenging. In

contrast, equivalence between AmED and alcohol administration has been consistently demonstrated across studies for motor outcomes, with similar performance on fine and gross motor performance regardless of whether ED was co-ingested with alcohol or not. A strength of this research area is that the majority of studies investigated the effects of a similar alcohol (0.65g/kg) and ED (3.57mL/kg) dose, enabling comparison based on intake. However, as aforementioned, the doses administered in this context typically fell below that reported by consumers in cross-sectional descriptive research.

*** Table 5 approximately here***

Alcohol Intake and Priming

Seven studies were included that compared retrospective self-reported consumption patterns of AmED versus alcohol consumers (between-subject comparison) and four studies that compared AmED versus alcohol consumption patterns among AmED consumers (within-subject comparison: Table 6). While these studies typically adopted similar indices of alcohol consumption with quantitative responses, a clear strength of this research area, the retrospective assessment period varied from 'tonight' to 'in the last year'. The authors of one paper declined the request for data (25). Only one experimental study was identified in this area assessing motivation to drink following a priming dose; no studies were identified assessing ad libitum alcohol consumption following priming.

Studies undertaking between-subjects comparisons consistently indicate that AmED consumers report: (i) greater typical and maximum alcohol intake, (ii) more frequent alcohol use, and (ii) more frequent drunk/binge sessions. These results suggest that AmED consumers are riskier drinkers relative to alcohol consumers. Between-subjects field research assessing event level consumption and intoxication by AmED and alcohol consumers have revealed

divergent outcomes: one study has shown a trend towards higher mean BrAC for AmED consumers (37), whilst the other showed equivalent mean BrAC for the two consumer groups (38).

*** Table 6 approximately here***

Within-subject comparison of alcohol consumption patterns are more mixed. Three studies (2, 26, 39) have shown significantly increased alcohol intake during AmED sessions relative to alcohol sessions, while two studies (27, 29) have shown the reverse. The former three studies defined AmED use as simultaneous use in one beverage (26), simultaneous or premixed use (2) or ED use within one hour of alcohol consumption (39), whereas the latter studies defined AmED use as ED consumption within two hours (27) (29) of alcohol consumption. The latter studies have also shown significantly lower maximum alcohol intake, frequency of use, and binge/drunken session frequency during AmED sessions (27, 29).

The placebo-controlled between-subjects double-blind experimental study (24) assessing motivation for alcohol intake following AmED and alcohol priming showed no significant difference in priming ratings at 10 (OR=1.27, 95% CI[0.41,3.91], $p=.679$), 20 (OR=1.68, 95% CI[0.54,5.21], $p=.366$), 40 (OR=2.32, 95% CI[0.74,7.25], $p=.147$), 60 (OR=1.49, 95% CI[0.48,4.61], $p=.485$), or 80 (OR=1.57, 95% CI[0.51,4.84], $p=.435$) minutes. Baseline change scores were not calculated as ratings were compared across time within treatment condition. While no group differences were evident for baseline ratings ($ps>.070$), OR analyses may not account for differences between treatment groups which existed prior to administration.

Risk-Taking

Two studies were identified comparing retrospective self-reported behaviour by AmED versus alcohol consumers (Table 7), one study was identified comparing AmED versus alcohol consumers' engagement in alcohol-specific risk-taking (4), and one study was identified comparing engagement in risk-taking by AmED and alcohol consumers after ingesting the respective beverage (25); the request for data was declined for the latter study. These studies typically assessed select risk-taking behaviours relating to driving and sexual risk-taking, licit and illicit drug use, and physical harm, although items, and the retrospective reference period, were not standardised across studies. Only two within-subject studies were identified, both adopting subjective self-report measures (26, 27), as well as one study examining risk-taking expectations (29) (Table 7). Only one experimental study was identified assessing the acute effects of AmED and alcohol on objective risk-taking. This dearth of within-subjects studies, particularly those circumventing self-report issues by adopting objective measures or utilising case-control/case crossover assessments of alcohol-related injuries reported to emergency departments, limits inferences regarding the pharmacological impact of ED and alcohol co-ingestion on risk-taking. It should be noted that several of the studies undertaking between-subject comparison did control for some potential systematic individual differences (e.g., level of alcohol consumption, general risk-taking behaviour) between consumer groups in their original analyses (2, 4). While this approach does not fully address issues of between-subject variability, it does strengthen inferences regarding risk-taking behaviour by AmED consumers.

Those studies undertaking between-subject comparison of general risk-taking showed increased odds of general risk-taking (2) and tobacco and illicit drug use (2, 27) among AmED users. Similarly, the study comparing engagement in alcohol-specific risk-taking,

showed that AmED consumers reported significantly increased odds of taking and having been taken advantage of sexually, being physically hurt or injured, requiring medical treatment, being a passenger in a car with a driver over the legal alcohol limit and driving whilst under the influence (4).

The results of the within-consumer retrospective comparison studies directly contrast with these outcomes (26, 27). In these studies, participants reported consistently lower odds of risk-taking in AmED sessions across a range of behaviours, including driving, sexual risk-taking, financial risk-taking, aggressive and anti-social behaviour, licit and illicit drug use, and physical harm/injury and psychological distress. Only two outcomes were discrepant: de Haan, et al. (27) reported equivalent odds of 'being in a physical fight' and 'passing out' whilst Peacock, et al. (26) reported lower odds of aggressive and antisocial behaviour in AmED sessions. While these studies are methodologically stronger in regards to design, the analyses did not take into account frequency of AmED versus alcohol sessions and typical intake, a factor which should be considered in future research.

*** Table 7 approximately here***

In contrast, the experimental within-subject objective comparison of risk-taking has revealed divergent results compared to retrospective self-report. The experimental study adopted the Balloon Analogue Risk Task (40), where participants are reimbursed for each pump of a simulated balloon if they discontinue prior to the predetermined explosion point; if the balloon explodes the money is forfeited. This study revealed equivalent odds of risk-taking, as indexed by the adjusted number of pumps (OR=1.43, 95%CI[0.73, 2.82], $p=.301$), total earnings (OR=0.79, 95%CI[0.40, 1.55], $p=.494$), and total number of explosions (OR=1.65,

95%CI[0.83, 3.28], $p=.149$), after administration of alcohol (mean peak BrAC .068%) with and without EDs (3.57mL/kg). However, it should be noted that there was no effect of alcohol on task performance, which impaired the potential ability to identify interactive effects.

Discussion

Available Evidence

Overall, the body of literature on AmED is typically dominated by retrospective self-report studies. With the exception of the alcohol intake research, the types of items assessed, item wording, and response type generally differ across studies. Furthermore, in some areas there is a predominance of between-subject research, meaning that individual differences between consumer groups confound conclusions regarding the effect of AmED, although several of these studies controlled for some potential between-subject variability in their analyses. Few experimental studies were identified, particularly in regards to studies adopting objective outcome measures. Cross-sectional descriptive research provides valuable information to researchers, health professionals, and policy-makers, as it reflects the ‘real-world’ drinking experiences of consumers. However, it should be noted that the reliance on self-reported drinking experience data, particularly retrospective data, introduces other potential contributing psychological (e.g., expectancy), individual (e.g., trait personality), and environmental (e.g., drinking environment) factors which could influence outcomes, as well as methodological concerns (e.g., recall bias). In regards to assessing the direct pharmacological effects of AmED versus alcohol, experimental laboratory-based research provides the strongest evidence for direct attribution to the effects of the drinks, although case-control and case crossover studies comparing alcohol- and AmED-related emergency department and poison information call centre data could also provide valuable insight into

adverse exposures and harms post-consumption (providing the co-consumption of energy drinks is accurately recorded by clinical staff). Despite the increase in AmED research over the past few years (68% of the reviewed articles were published between 2011 and 2013), the general dearth of research in this area is surprising considering the public attention dedicated to this consumption trend (41, 42) and current endeavours to determine an appropriate policy response.

General Overview

Physiological Outcomes

The preliminary evidence from research assessing self-reported outcomes of AmED consumption indicates potential changes to the nature of intoxication; the cross-sectional descriptive within-subject studies consistently indicate that consumers are more likely to self-report experiencing musculoskeletal (e.g., tremors), cardiovascular (e.g., increased heart rate), and CNS (e.g., agitation) disturbance after AmED. It is theorised that these outcomes may be a consequence of the stimulatory effects of EDs, consistent with the common side-effects of caffeine overconsumption (43). Consumers also report reduced sedation-based outcomes, specifically: nausea, walking difficulty, and vision difficulties. The dual effect of ED co-ingestion is illustrated most clearly when examining transient speech impairment, with consumers reporting increased odds of faster speech, and lower odds of slurred speech, in AmED sessions. Several primary intoxication outcomes (e.g., dizziness, headache) showed equivalent odds in AmED and alcohol sessions. The experimental research undertaken by Ferreira and colleagues (5, 22) is particularly enlightening, in that it directly assessed the pharmacological effects of AmED versus alcohol on objective and subjective physiological outcomes in a controlled environment. Whilst this research showed little evidence of AmED-induced changes in physiological state relative to alcohol, the low dosing protocols adopted

restrict inferences regarding the consequences of AmED use at the higher quantities typically reported by consumers.

Psychological Outcomes

The profile of increased stimulation and decreased sedation during AmED consumption is generally mirrored in self-reported real-life psychological outcomes evident in the cross-sectional descriptive studies. The experimental literature is more contrary. Participants typically report enhanced stimulation after laboratory-based AmED administration. In contrast, ratings of sedation typically do not differ between AmED and alcohol treatment conditions. These effects are typically recorded at low ED doses (one standard 250mL ED per 70kg person). However, potential dose-dependent effects of AmED were identified, in that the only study which administered a moderate ED dose (two standard 250mL EDs administered approximately one hour apart) revealed decreased stimulation-related psychological outcomes and increased sedation-related psychological outcomes after AmED administration (36). However, as acknowledged by the authors, the outcomes may be a function of the methodology. No studies were identified which systematically assessed the dose-dependent effects of ED with a set alcohol dose.

Cognitive and Psychomotor Outcomes

Those experimental laboratory-based studies adopting within-subjects comparison of objective behavioural impairment post-AmED and alcohol administration offer the best indication as to the direct pharmacological effects of combined use (e.g., 6, 23). However, the lack of standardisation in the aspects of cognitive and motor performance assessed across the few studies conducted undermines definitive conclusions regarding the relative cognitive effect of AmED and alcohol. While the literature consistently indicates that ED co-ingestion

does not alter motor outcomes, these studies have only involved administration of a single low ED dose. Consequently, there is no solid evidence-base assessing the dose-dependent effects of AmED, making conclusions regarding the interactive effect of AmED on cognitive and motor outcomes difficult.

Hazardous Drinking

AmED physiological and psychological outcomes are theorised to increase the likelihood of excess alcohol intake and risk-taking behaviour by decreasing sedation-based cues of intoxication (5, 6), creating a ‘wide-awake drunkenness’ state (7). This review consistently indicated that AmED consumers report more risky drinking practices than alcohol consumers. However, the few studies comparing alcohol intake in AmED versus alcohol sessions have provided mixed support for this hypothesis, with several revealing *increased* intake (2, 26, 39) whilst others indicate *decreased* intake (27, 29) in AmED sessions. Attempts to reconcile these results point predominantly to the lack of standardisation in defining AmED, however it is important to note that all but one (26) of these studies focused only on college student consumers, a subgroup who typically display high-risk drinking practices (44). Comparison of alcohol intake following an acute AmED and alcohol priming dose in a controlled setting would control for external influences. However, no experimental studies examining ad-libitum alcohol consumption following an AmED or alcohol priming dose were identified. The only experimental study to indirectly assess the effects of AmED on alcohol consumption, via ratings of motivation to drink, showed equivalent outcomes. Consequently, the hypothesis that AmED consumption increases subsequent alcohol intake cannot be discounted due to the equivocal nature of the literature.

Risk-Taking

The reviewed research consistently indicated that AmED consumers report greater risk-taking behaviour relative to alcohol consumers. However, the only two cross-sectional descriptive within-subject research involving self-report of risk-taking behaviour showed that AmED consumers self-report less risk-taking in AmED versus alcohol sessions (26, 27) and one study showed lower odds of disinhibition in AmED sessions (26). These results contradict common assumptions regarding the behavioural effects of AmED (9). One explanation may be that AmED-induced increases in alertness may improve consumers' attentional capacity for decision-making (26). These studies were methodologically robust, in that they adopted within-subject comparison of AmED versus alcohol outcomes, ruling out between-subject variability, and reflected consumers' 'real-world' drinking experiences. However, these preliminary outcomes may underestimate risk-taking in AmED sessions, in that analyses did not account for the relative frequency of AmED and alcohol sessions (45, 46). Only one experimental study exploring risk-taking propensity was identified, contradicting common assumptions regarding the behavioural effects of AmED and revealing equivalent odds of risk-taking after AmED and alcohol (32), potentially a consequence of poor task sensitivity to the low doses administered. No studies were identified assessing the dose-dependent effects of AmED on risk-taking to determine whether interactive AmED effects on risk-taking become apparent at doses similar to those ingested in real-life drinking contexts.

Limitations

The current evidence-base is strong in regards to the reporting of physiological and psychological real-world drinking experiences following AmED versus alcohol consumption for the same individuals. However, there is no data currently available as to the relative clinical severity and dose threshold at which physiological and psychological changes of AmED occur. While there are guidelines outlining the recommended maximum daily caffeine

intake (e.g., Food Standards Australia and New Zealand (47)) to minimise adverse outcomes, laboratory-based research controlling for external confounds has generally shown no difference in physiological, psychological, cognitive, psychomotor, and behavioural outcomes following AmED and alcohol administration. However, these studies have generally investigated the effect of ED co-ingestion at a dose lower than that typically ingested in real-life settings, restricting ecological validity and generalizability. In this instance, case-control or case crossover studies comparing AmED- and alcohol-related adverse events identified in emergency department and poison information call centre data could be beneficial for the development of public health policy.

It should also be considered that these conclusions are primarily based on consumers' retrospective reflection on a number of drinking sessions over an extended time period, with potentially variable intake in each session and concomitant use of other licit and illicit substances. It is premature to attribute these outcomes solely to the pharmacological effects of co-ingestion. Discrepancies between retrospective and prospective reports suggest that AmED consumers may have specific expectations regarding AmED intoxication which may not be evidence-based. It has been well-established that consumer expectancies regarding the interactive caffeine and alcohol effects can alter performance independent of actual administration (48); whether these results translate to AmED consumers' intoxication experience remains unexplored. Following from this point, it may be that the individual's attitudes to, and expectancies and motivations for, AmED consumption influence retrospective reporting of the consequences of AmED versus alcohol use; such issues can be circumvented by objective measurement of outcomes, typically in a laboratory-based setting. While laboratory-based assessment can reduce ecological validity, the controlled environment and beverage blinding can reduce the impact of these confounding variables.

Outcomes can be objectively assessed to eliminate potential self-report biases and within-subject designs control systematic individual differences. Acute dosing protocols can link specific doses with changed outcomes. As aforementioned, this review revealed no experimental research assessing high ED doses or the dose-dependency of ED effects when co-ingested with a set alcohol dose. As such, we cannot determine whether the self-reported outcomes are an accurate reflection of the pharmacological effects of AmED or a product of intertwined environmental (e.g., drinking environment), psychological (e.g., expectancy effects), and methodological (e.g., recall bias) factors. Whilst it will be necessary to assess the effects of consumer' expectancies on AmED physiological, psychological, and behavioural consequences in future research, it is important to note that the potential confounding role of expectancies in past research does not render the results of these studies invalid; the potential harms of AmED use may be due to a combination of pharmacological, individual, and situational factors.

Another consideration when interpreting these outcomes is that omission of operationalized descriptions of AmED use in some studies could leave the definition of use open to participant interpretation. Lack of standardisation in defining AmED use across studies may also undermine comparison of outcomes, particularly as AmED use can be differentially categorised as consumption of pre-mixed beverages, hand-mixed beverages, or a combination of both practices, as well as alcohol and EDs consumed in the same container or in the same session (sometimes up to four hours apart). This is an important consideration as it would seem plausible that consumption of both beverages in the same session but hours apart would be related to different motivations of use than simultaneous consumption. In addition, a limitation of survey studies is that many do not ask participants to specify the quantity of energy drink units they refer to in their self-reported consumption (i.e., whether one ED unit

is equivalent to 125mL, 250mL or even 500mL). While our review was restricted to studies which specifically looked at EDs (as opposed to other caffeinated products), in several studies no information about the composition and quantity of primary ingredients was detailed in manuscripts (although it is important to note that this information may have been provided to participants). As a consequence, the diverging results may be reflective of differing patterns of use and beverage types across studies.

These issues also pertain to characterising the causal link between AmED consumption and likelihood of excess alcohol intake and risk-taking behaviour. The general dearth of research coupled with heterogeneous outcome measures used across studies has impeded the construction of a strong evidence-base assessing whether AmED offers additional behavioural harms relative to alcohol. This is particularly true of the few risk-taking studies conducted, which have utilised measures which are difficult to compare, such as self-reported sexual risk-taking and balloon popping using the BART. Furthermore, average alcohol intake in AmED versus alcohol drinking sessions was not statistically controlled in the present analyses when comparing retrospective self-reported behavioural outcomes of use (although it should be noted that several studies controlled for alcohol consumption practices in original between-subject comparisons). Given the various definitions of AmED use, and discrepant outcomes in regards to alcohol intake when mixing versus consuming alcohol alone, it is crucial to take into consideration level of intoxication when comparing rates of risk-taking. This review consistently indicated that AmED consumers comprise a subgroup with a higher predisposition towards risky behaviour. Potential state-dependent changes in behavioural outcomes, coupled with a trait tendency towards risky behaviour, could place this consumer group at higher risk of experiencing or causing harm. Harm reduction policies should be

targeted at this group to ensure that consumers are educated regarding the potential side-effects of AmED.

As a consequence of ethical constraints for laboratory-based administration of the amount of alcohol and EDs consumed in naturalistic sessions, experimental studies have generally investigated the effect of ED co-ingestion at a dose lower than that typically ingested in real-life settings, restricting ecological validity and generalizability. As such, it is imperative that further experimental research is undertaken to determine the clinical severity and dose threshold at which AmED-induced changes in the physiological, psychological, and behavioural nature of intoxication occur, in conjunction with further within-subject epidemiological studies adopting clear operationalized descriptions of AmED (in relation to serving size, simultaneous consumption and beverage type), consistent time frames (i.e. past month) and with alcohol consumption controlled for in analyses. Whilst taking into account the ethical constraints surrounding dosing in a laboratory context, it is important that future experimental research is directed at characterising the profile associated with co-administration of alcohol with ED doses which fall below, match, and exceed maximum recommended intake guidelines for policy relevance, and which reflect typical self-reported intake by consumers to maximise ecological validity.

Finally, it is important to note that of the 19 studies that qualified for inclusion in the review, three studies (27, 28, 36) were either funded by industry or undertaken by researchers who have been sponsored or supported by industry. For the most part, these studies indicated no difference or less hazardous outcomes following AmED use relative to alcohol use. A recent editorial by Miller (49) raised concerns about industry funding in AmED research, arguing that it raises questions of propriety and confidence in the research findings. However,

devising matched placebo samples for double-blind experimental studies is also an acknowledged difficulty in this field of research (one experimental study included in this review administered placebo samples provided by industry (32)). The balance between scientific rigour and integrity in AmED research requires attention, in that confidence in the research design, as well as in the conduct and interpretation of outcomes, must be maximised to ensure a solid, objective evidence-base.

Conclusions

In sum, the cross-sectional descriptive research involving within-subject comparison of AmED versus alcohol outcomes consistently indicated that AmED may exert a dual effect, increasing stimulation-based outcomes and reducing specific sedation-based physiological outcomes relative to when alcohol is consumed without ED. While the experimental research comparing the effects of AmED versus alcohol administration offered the best indication of the pharmacological effects of the beverages, showing little change in physiological, psychological, and behavioural intoxication state, the low doses administered relative to self-reported consumer intake restricted inferences regarding 'real-life' intoxication experience. The cross-sectional descriptive and experimental literature is mixed as to whether these changes in the nature of intoxication translate into an increased likelihood of greater alcohol intake and risk-taking behaviour. Despite the growth in AmED popularity, there is a dearth of research assessing the relative effects of alcohol ingested with and without ED at naturalistic consumption levels. As such, it is imperative that further research is undertaken to determine the clinical severity and dose threshold at which AmED-induced changes in the physiological, psychological, and behavioural nature of intoxication occur. At present, the existing literature provides valuable insight into changes to the nature of

intoxication post-AmED consumption, with significant implications for public health,
particularly in regards to the risk of increased stimulation-based side-effects.

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Figure 1. Flow diagram of number of records included at the identification, screening, eligibility, and synthesis stages.

Table 1

Characteristics of Included Studies (N=19)

Study ^a	Study Design ^b	Method	Sample N ^c	Definition of AmED Use for Self-Report of Consumption ^d	Sample Characteristics
Brache and Stockwell (2)	Cross-sectional descriptive ^{# ^}	Online self-administered survey	465 ALC=305 AmED=105	Simultaneous use	Canadian university student convenience sample (n=205* males; M=20.0, SD=6.7, range 17-51 years)
de Haan, et al. (27) ^{1,2}	Cross-sectional descriptive ^{# ^}	Online self-administered survey	4424 ALC=3185 AmED=1239	Simultaneous use and subsequent use (within two hours)	Dutch university student convenience sample (Alcohol consumers: n=1438* male; M=22.1, SD=2.6 years; AmED consumers: n=1730*; M=21.5, SD=2.3 years)
O'Brien, et al. (4)	Cross-sectional observational [#]	Online self-administered survey	4237 ALC=2189 AmED=697	'Mixed'; definition not specified	United States university student stratified random sample (n=1638 males; M=20.4, SD=2.8 years)
Peacock, et al. (26)	Cross-sectional descriptive [^]	Online self-administered survey	408	Simultaneous use	Australian community convenience sample who reported AmED use (n=159*; M=23.1, SD=3.8, range=18-35 years)
Peacock, et al. (50)	Cross-sectional descriptive [^]	Online self-administered survey	408	Simultaneous use	Australian community convenience sample who reported AmED use (n=159*; M=23.1, SD=3.8, range=18-35 years)
Penning, et al. (28) ²	Cross-sectional descriptive [#]	Online or paper self-administered survey	549 ALC=480 AmED=24	'Consumed together'; definition not specified	Dutch university student convenience sample (n=177 male; M=20.4, SD=3.5 years)
Price, et al. (39)	Cross-sectional descriptive [^]	Semi-structured standardised face-to-face interviews	72 AmED=10	Simultaneous use and subsequent use (within one hour)	Canadian university student sample who reported ED use (n=31 male; range 17-29 years)

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Rossheim and Thombs (37)	Cross-sectional observational [#]	Re-analysis of data from Thombs, et al. (25), Thombs, et al. (38)	413 <i>ALC=326</i> <i>AmED=25</i>	Simultaneous use	Random sample of exiting bar patrons in a United States college bar district who had consumed alcohol that night (<i>n</i> =253* male; whole sample age n.s)
Thombs, et al. (38)	Cross-sectional observational [#]	Structured face-to-face interview; self-administered pen and paper questionnaire	256 <i>ALC=180</i> <i>AmED=10</i>	Simultaneous use	Random sample of exiting bar patrons in a United States college bar district who had consumed alcohol that night (<i>n</i> =157* male; whole sample age n.s)
Thombs, et al. (25)	Cross-sectional descriptive [#]	Structured face-to-face interview; self-administered pen and paper questionnaire	697 <i>ALC=602</i> <i>AmED=45</i>	Simultaneous and subsequent use (within 12 hours)	Random- and self-selected sample of exiting bar patrons in a United States college bar district who had consumed alcohol that night (whole sample sex/age n.s)
Woolsey, et al. (29)	Cross-sectional descriptive ^{# ^}	Survey (administration method n.s)	401 <i>ALC=165</i> <i>AmED=150[#]</i> <i>AmED=132[^]</i>	Simultaneous and subsequent use (within four hours)	United States university student athlete convenience sample (<i>n</i> =257 male; <i>M</i> =19.8, range 18-23 years)
Woolsey (30)	Cross-sectional descriptive ^{# ^}	Re-analysis of data from Woolsey, et al. (29)	401 <i>ALC=165</i> <i>AmED=150</i>	Simultaneous and subsequent use (within four hours)	United States university student athlete convenience sample (<i>n</i> =257 male; <i>M</i> =19.8, range 18-23 years)
Alford, et al. (36)²	Human experimental mixed [#]	Double-blind placebo-controlled multi-dose administration of a standard 250mL ED or 0mL ED with alcohol (intended peak BAC .046% and 0.1%), and placebo alcohol (peak mean BrAC drink 1=.047%; drink 2=.094%)	20	NA	Healthy regular alcohol consumers who had tried an ED before (<i>n</i> =10 male; <i>M</i> =24.5, range 19-33 years)
Ferreira, et al. (22)	Human experimental crossover [^]	Double-blind placebo-controlled administration of: (i) placebo, (ii) 1.0/kg alcohol, (iii) 3.57mL/kg ED (equivalent to a standard 250mL ED per 70kg person), and (iv) AmED (peak mean BrAC n.s)	14	NA	Healthy moderate male alcohol and ED consumers recruited from the general community (<i>M</i> =24, <i>SD</i> =3 years)
Ferreira, et al. (5)	Human experimental mixed [^]	Double-blind placebo-controlled administration of: (i) alcohol (0.6g/kg or 1.0g/kg), (ii) 3.57mL/kg ED (equivalent to a standard 250mL ED per 70kg person) and (iii) alcohol and ED (peak mean BrAC 0.6g/kg=.050%; 1.0g/kg=.099%)	26	NA	Healthy male moderate alcohol and ED consumers recruited from the general community (<i>M</i> =23.0, <i>SD</i> =3.0 years)
Marczinski, et al. (6)	Human experimental parallel [#]	Double-blind placebo-controlled administration of: (i) placebo, (ii) 0.65g/kg alcohol, (iii) 3.57mL/kg ED (equivalent to a standard 250mL ED per 70kg person) or (iv) AmED (peak mean BrAC .089%)	56	NA	Healthy regular caffeine, alcohol, and ED consumers recruited from the university community (<i>n</i> =9 male; <i>M</i> =23.8, <i>SD</i> =3.4, range 21-33 years)

Marczinski, et al. (23)	Human experimental crossover [^]	Double-blind placebo-controlled administration of (i) placebo, (ii) 0.65g/kg alcohol, (iii) 3.57mL/kg ED (equivalent to a standard 250mL ED per 70kg person) or (iv) AmED (peak mean BrAC .071%)	18	NA	Healthy regular caffeine, alcohol, and ED consumers recruited from the university community (<i>n</i> =9 male; <i>M</i> =22.9, <i>SD</i> =2.5, range 21-28 years)
Marczinski, et al. (24)	Human experimental parallel [#]	Double-blind placebo-controlled administration of: (i) placebo, (ii) 0.91mL/kg alcohol, (iii) 1.82mL/kg ED (equivalent to half a standard 250mL ED per 70kg person), or (iv) AmED (peak mean BrAC .043%)	80	NA	Healthy regular male caffeine, alcohol, and ED consumers recruited from the university community (<i>n</i> =40 male; <i>M</i> =23.5, <i>SD</i> =3.1, range 21-33 years)
Peacock, et al. (51) ²	Human experimental crossover [^]	Single-blind placebo-controlled administration of (i) placebo, (ii) 0.5g/kg alcohol, (iii) 1.82mL/kg ED, or (iv) AmED (peak mean BrAC .068%)	28	NA	Healthy regular caffeine, alcohol, and ED consumers recruited from the general community (<i>n</i> =13 male; <i>M</i> =19.5, <i>SD</i> =1.8, range 18-25 years)

Note. ^a Note that ¹ indicates that the study was funded by industry, ² indicates that scientific advisors to industry were involved in the study design and manuscript preparation, and ³ indicates that placebo samples were provided by industry. ^b Note that [^] indicates within-subject comparisons for AmED-related analyses, whereas [#] indicates a between-subject design. ^c This number reflects the number of participants included in analyses; ALC=alcohol consumer sample size, AmED=AmED consumer sample size. ^d This column outlines the definition of AmED use provided to participants taking part in self-report cross-sectional descriptive research; 'simultaneous use' refers to mixing alcohol and ED in the one beverage and 'subsequent use' refers to consuming the alcohol and EDs within the specified time frame (not necessarily in the same beverage). ED: energy drink; AmED: alcohol mixed with energy drink; n.s: not specified; NA: not applicable * indicates that values were calculated from data supplied in the original manuscript.

Table 2

Odds Ratio (OR) for Subjective Physiological Outcomes After AmED Relative to Alcohol Based on (i) Retrospective Self-Report of Drinking Experiences in Naturalistic Settings, and (ii) Current Report of Acute Dosing Effects in Laboratory Settings

	Between-Subject Self-Report of Drinking Experiences			Within-Subject Self-Report of Drinking Experiences					Self-Report of Acute Dosing Experience (Laboratory Setting)				Objective Measurement of Acute Dosing Experience (Laboratory Setting)				
Outcome	Penning, et al. (28) ^{#a}			de Haan, et al. (27) ^{^a}		Peacock, et al. (26) ^{^a}		Woolsey, et al. (29) ^{^a}		Ferreira, et al. (5) ^{^b}				Ferreira, et al. (22) ^{^c}			
	Last hangover ^d			Last year ^d		Last six months ^d		Future AmED sessions ^d		30 minutes ^d		120 minutes ^d		15 minutes ^d		30 minutes ^d	
	OR (95% CI) ^e	<i>p</i>		OR (95% CI) ^e	<i>p</i>	OR (95% CI) ^e	<i>p</i>	OR (95% CI) ^e	OR (95% CI) ^e	<i>p</i>	<i>p</i>	OR (95% CI) ^e	<i>p</i>	OR (95% CI) ^e	<i>p</i>	OR (95% CI) ^e	<i>p</i>
<u>Musculoskeletal:</u>																	
Tension	-	-		-	-	-	-	-	-	1.50 (0.74, 3.05)	.257	0.75 (0.37, 1.50)	.412	-	-	-	-
Weakness	-	-		-	-	-	-	-	-	0.90 (0.50, 1.81)	.771	0.65 (0.32, 1.31)	.229	-	-	-	-
Tremors	-	-		-	-	2.48 (1.88, 3.27)	<.001	-	-	0.72 (0.35, 1.44)	.350	0.77 (0.38, 1.56)	.472	-	-	-	-
<u>Cardiovascular:</u>																	
Irregular heartbeat				-	-	5.79 (3.84, 8.73)	<.001	-	-	-	-	-	-	-	-	-	-
Rapid heartbeat	0.58 (0.27, 1.21)	.148		-	-	-	-	7.09 (4.80, 10.48)	<.001	0.87 (0.43, 1.75)	.698	1.19 (0.59, 2.39)	.629	-	-	-	-
<u>Gastrointestinal:</u>																	
Stomach ache	0.77 (0.37, 1.62)	.495		-	-	-	-	-	-	-	-	-	-	-	-	-	-
Nausea~	0.85 (0.40, 1.78)	.663		0.03 (0.02, 0.05)	<.001	0.82 (0.68, 0.97)	.023	-	-	1.00 (0.50, 2.01)	1.00	0.87 (0.43, 1.74)	.685	-	-	-	-
Vomiting~	-	-		-	-	0.93 (0.74, 1.17)	.548	-	-	-	-	-	-	-	-	-	-
<u>Disruption of Functioning:</u>																	

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Alterations in hearing	-	-	-	-	1.17 (0.97, 1.41)	.108	-	-	1.00 (0.50, 2.01)	1.00	0.69 (0.34, 1.39)	.295	-	-	-	-
Alterations in vision	-	-	-	-	0.85 (0.73, 0.99)	.038	-	-	0.63 (0.31, 1.28)	.202	1.00 (0.50, 2.01)	1.00	-	-	-	-
Alterations in breathing	-	-	-	-	1.32 (0.90, 1.95)	.158	-	-	1.00 (0.50, 2.01)	1.00	1.00 (0.50, 2.01)	1.00	-	-	-	-
Alteration in walking	-	-	-	-	0.78 (0.68, 0.90)	.001	-	-	1.34 (0.66, 2.70)	.417	1.00 (0.50, 2.01)	1.00	-	-	-	-
Alteration in motor coordination	-	-	-	-	-	-	-	-	0.67 (0.33, 1.35)	.263	0.59 (0.29, 1.20)	.146	-	-	-	-
Alteration in speech	-	-	-	-	-	-	-	-	1.00 (0.50, 2.0)	1.00	1.00 (0.50, 2.01)	1.00	-	-	-	-
Increased speech	-	-	-	-	1.33 (1.11, 1.59)	.002	-	-	-	-	-	-	-	-	-	-
Speech slurred	-	-	-	-	0.68 (0.58, 0.80)	<.001	-	-	-	-	-	-	-	-	-	-
Inability to sleep or disrupted sleep	-	-	-	-	4.13 (3.08, 5.54)	<.001	4.13 (2.89, 5.88)	<.001	-	-	-	-	-	-	-	-
Reduced appetite	0.77 (0.37, 1.62)	.496	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Other CNS Disturbance:																
Dizziness	1.21 (0.58, 2.55)	.611	-	-	0.93 (0.81, 1.07)	.330	0.53 (0.38, 0.72)	<.001	0.90 (0.45, 1.80)	.756	0.69 (0.34, 1.40)	.305	-	-	-	-
Perspiration	-	-	-	-	1.15 (0.97, 1.37)	.107	-	-	0.61 (0.30, 1.25)	.176	1.12 (0.56, 2.24)	.758	-	-	-	-
Thirst	0.89 (0.42, 1.86)	.750	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Salivation	-	-	-	-	1.13 (0.93, 1.39)	.225	-	-	1.19 (0.59, 2.39)	.631	2.68 (1.27, 5.65)	.010	-	-	-	-
Headache	0.94 (0.45, 1.98)	.873	-	-	0.94 (0.80, 1.10)	.414	-	-	0.74 (0.37, 1.50)	.403	0.81 (0.40, 1.63)	.551	-	-	-	-
Agitation	-	-	-	-	2.06 (1.54, 2.76)	<.001	-	-	1.78 (0.87, 3.65)	.112	1.10 (0.55, 2.21)	.789	-	-	-	-
'Jolt and crash episode'	-	-	-	-	1.64 (1.29, 2.08)	<.001	-	-	-	-	-	-	-	-	-	-
Overall wellbeing	-	-	-	-	-	-	-	-	1.29 (0.64, 2.59)	.482	-	-	-	-	-	-

Objective Outcomes:											
Blood pressure	-	-	-	-	-	-	-	-	-	-	-
										0.60 (0.23, 1.58)	.298
										0.16 (0.05, 0.52)	.002

Note. ^a Note that ^ indicates within-subject comparisons for AmED-related analyses, whereas # indicates between-subject design. The outcomes reported by Penning, et al. (28) reflect between-consumer ratings of AmED versus alcohol hangover experiences when they last consumed the respective beverages, whereas outcomes reported by de Haan, et al. (27) and Peacock, et al. (26) reflect within-consumer comparison of outcomes in the last year and last six months respectively in AmED versus alcohol drinking sessions; the former study involved dichotomous responses (yes/no) while in the latter study response options were grouped as outcome present ('half the time', 'most of the time', 'all of the time') or outcome absent ('none of the time', 'less than half the time'). Outcomes reported by Woolsey, et al. (29) also comprise within-consumer comparison, except AmED consumers were asked to report their expected behaviour in future AmED and alcohol drinking sessions, endorsing the likelihood of the outcome on a 4-point scale from 1 'disagree' to 4 'agree'. ^b The outcomes reported by Ferreira, et al. (5) reflect within-subject comparison of 100-mm visual-analogue change from baseline ratings after consuming 0.6g/kg or 1.0g/kg alcohol with or without 3.57mL/kg ED. ^c The outcomes reported by Ferreira, et al. (22) represent blood pressure (medium beats per minute) recorded using a semiautomatic sphygmomanometer after administration of 1.0g/kg alcohol with 3.57mL/kg ED. ^d Note that these times represent the time reference period for reporting (self-report of drinking experiences) or the minutes between beverage administration and subjective outcome administration (experimental research); note that those in italics only provided the time for commencing the test battery as a whole. ^e Odds ratios were calculated using the means and standard deviations or percentages/counts provided in-text, with the exception of those indicated by a ^, which were calculated using the means and *t*-statistic. An odds ratio of 1 indicates the event is equiprobable (or that the means are similar) for each consumer/in each session, > 1 indicates the event is more likely to occur (or that a higher mean was recorded) for AmED versus alcohol consumers/in AmED sessions relative to alcohol sessions, and <1 indicates the event is less likely to occur (or that a lower mean was recorded) for AmED versus alcohol consumers/in AmED sessions relative to alcohol sessions. ~Note that for the items 'nausea' and 'vomiting', de Haan, et al. (27) grouped the two outcomes as one item ('I have felt very sick to my stomach or thrown up after drinking'), whilst Peacock, et al. (26) limited assessed these two outcomes separately. OR: odds ratio; 95% CI: 95% confidence interval. A 'jolt and crash episode' refers to a sudden increase in energy followed by a sudden drop in energy. OR: odds ratio; 95% CI: 95% confidence interval; AmED: alcohol mixed with energy drink.

Table 3

Odds Ratio (OR) for Subjective Psychological Outcomes After AmED Relative to Alcohol Based on Retrospective Self-Report of Drinking Experiences in Naturalistic Settings

Outcome	Between-Subject Self-Report of Drinking Experiences		Within-Subject Self-Report of Drinking Experiences					
	Penning, et al. (28) ^{#a}		de Haan, et al. (27) ^{^a}		Peacock, et al. (26) ^{^a}		Woolsey, et al. (29) ^{^a}	
	Last hangover ^b		Last year ^b		Last six months ^b		Future drinking sessions ^b	
	OR (95% CI) ^c	<i>p</i>	OR (95% CI) ^c	<i>p</i>	OR (95% CI) ^c	<i>p</i>	OR (95% CI) ^c	<i>p</i>
<u>Stimulatory Mood:</u>								
Stimulation	-	-	-	-	1.42 (1.22-1.66)	<.001	-	-
Alert/Clearheaded	-	-	-	-	2.34 (1.94-2.84)	<.001	5.98 (4.10, 8.73)	<.001
Energetic	-	-	-	-	1.79 (1.42-2.26)	<.001	-	-
Active	-	-	-	-	1.16 (0.99-1.35)	.071	-	-
<u>Sedation Mood:</u>								
Fatigued/Tired/Drowsy	0.81 (0.38, 1.70)	.569	0.25 (0.22, 0.28)	<.001	0.42 (0.34-0.54)	<.001	-	-
Clumsy	-	-	-	-	-	-	0.39 (0.28, 0.54)	<.001
Confused/ Mentally slow	-	-	-	-	0.68 (0.57, 0.80)	<.001	-	-
Sad	-	-	-	-	0.53 (0.38, 0.74)	<.001	-	-
<u>Antisocial Mood:</u>								
Feeling nervous/jittery/on edge	-	-	-	-	1.73 (1.33-2.24)	<.001	6.55 (4.46, 9.63)	<.001
Feeling annoyed	-	-	-	-	0.90 (0.73-1.12)	.336	-	-
Feeling aggressive	-	-	-	-	1.22 (0.95-1.57)	.126	-	-
Feeling moody	-	-	-	-	-	-	1.10 (0.81, 1.50)	.556
Feeling irritable	-	-	-	-	1.30 (1.03-1.64)	.028	-	-

<u>Novelty-Seeking Mood:</u>							
Daring	-	-	-	-	1.01 (0.93, 1.01)	.796	0.79 (0.58, 1.08) .145
Impulsive	-	-	-	-	0.92 (0.83, 1.01)	.087	- -
Disinhibited/Boisterous	-	-	-	-	0.83 (0.75, 0.92)	.001	1.02 (0.75, 1.39) .906
Adventuresome/Courageous	-	-	-	-	0.92 (0.81, 1.04)	.179	1.04 (0.77, 1.42) .786
<u>Positive Mood:</u>							
Calm	-	-	-	-	0.50 (0.42, 0.59)	<.001	- -
Carefree	-	-	-	-	0.73 (0.63, 0.84)	<.001	- -
Friendly	-	-	-	-	0.58 (0.44, 0.78)	<.001	- -
Outgoing	-	-	-	-	0.77 (0.63, 0.95)	.016	- -
Sociable	-	-	-	-	0.67 (0.51, 0.88)	.004	- -

Note. ^a Note that ^ indicates within-subject comparisons for AmED-related analyses, whereas # indicates between-subject design. The outcomes reported by Penning et al. reflect between-consumer ratings of AmED versus alcohol hangover experiences when they last consumed the respective beverages, whereas outcomes reported by de Haan, et al. (27) and Peacock, et al. (26) reflect within-consumer comparison of outcomes in the last year and last six months respectively in AmED versus alcohol drinking sessions; the former study involved dichotomous responses (yes/no) while in the latter study response options were grouped as outcome present ('half the time', 'most of the time', 'all of the time') or outcome absent ('none of the time', 'less than half the time'). Outcomes reported by Woolsey, et al. (29) also comprise within-consumer comparison, except AmED consumers were asked to report their expected behaviour in future AmED and alcohol drinking sessions, endorsing the likelihood of the outcome on a 4-point scale from 1 'disagree' to 4 'agree'. ^b Note that these times represent the time reference period for reporting. ^c Odds ratios were calculated using the means and standard deviations or percentages/counts provided in-text, with the exception of those indicated by a ^, which were calculated using the means and *t*-statistic. An odds ratio of 1 indicates the event is equiprobable (or that the means are similar) for each consumer/in each session, > 1 indicates the event is more likely to occur (or that a higher mean was recorded) for AmED versus alcohol consumers/in AmED sessions relative to alcohol sessions, and <1 indicates the event is less likely to occur (or that a lower mean was recorded) for AmED versus alcohol consumers/in AmED sessions relative to alcohol sessions. OR: odds ratio; 95% CI: 95% confidence interval; AmED: alcohol mixed with energy drink.

Table 4

Odds Ratio (OR) for Subjective Psychological Outcomes After AmED Relative to Alcohol Based on Acute Dosing in Experimental Settings

	Alford, et al. (36) ^{#a}				Ferreira, et al. (5) ^{^a}				Marczinski, et al. (6) ^{#a}		Marczinski, et al. (23) ^{^a}		Marczinski, et al. (24) ^{#a}				Peacock, et al. (32) ^{^a}			
	Drink 1: 45 minutes		Drink 2: 45 minutes		30 minutes		120 minutes		70 minutes		60 minutes		33 minutes		55 minutes		30 minutes		125 minutes	
	OR (95% CI) ^c	p	OR (95% CI) ^c	p	OR (95% CI) ^c	p	OR (95% CI) ^c	p	OR (95% CI) ^c	p	OR (95% CI) ^c	p	OR (95% CI) ^c	p	OR (95% CI) ^c	p	OR (95% CI) ^c	p	OR (95% CI) ^c	p
<u>Stimulatory Mood:</u>																				
Stimulation	-	-	-	-	-	-	-	-	2.60 (0.66, 10.18)	.171	2.53 (1.04, 6.16)*	.041	2.60 (0.83, 8.17)	.101	4.17 (1.30, 13.41)	.016	2.47 (1.18, 5.18)	.016	1.56 (0.77, 3.16)	.221
Alert/Clearheaded	0.16 (0.03, 0.85)	.032	0.04 (0.01, 0.24)	.001	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Energetic	0.63 (0.13, 3.10)	.567	0.01 (0.00, 0.11)	<.001	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
<u>Sedation Mood:</u>																				
Sedation	-	-	-	-	-	-	-	-	#	#	0.61 (0.26, 1.43)	.256	0.81 (0.26, 2.48)	.707	0.91 (0.30, 2.81)	.874	1.50 (0.74, 3.04)	.261	0.82 (0.41, 1.65)	.575
Mental Fatigue/Drowsy	37.27 (5.33, 260.76)	<.001	269.16 (25.61, 2829.35)	<.001	0.82 (0.41, 1.64)	.567	0.91 (0.45, 1.83)	.794	#	#	0.31 (0.12, 0.78)*	.013	-	-	-	-	0.98 (0.49, 1.97)	.954	0.90 (0.45, 1.81)	.768
Clumsy	68.72 (8.75, 539.50)	<.001	9.09 (1.61, 51.33)	.012	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Confused/Mentally slow	0.23 (0.04, 1.22)	.085	0.01 (0.00, 0.06)	<.001	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

Note.^a Note that ^ indicates within-subject comparisons for AmED-related analyses, whereas # indicates between-subject design. The outcomes reported by: (i) Alford, et al. (36) reflect between-subject comparison of change from baseline ratings after drink 1 (.046% BrAC) and drink 2 (.087% BrAC) of alcohol with or without 250mL ED, (ii) Ferreira, et al. (5) reflect within-subject comparison of ratings at 30 minutes after consuming 0.6g/kg or 1.0g/kg alcohol with or without 3.57mL/kg ED, (iii) Marczinski, et al. (6) reflect between-subject comparison of change from baseline ratings after 0.65g/kg alcohol with or without 3.57mL/kg ED, (iv) Marczinski, et al. (23) reflect within-subject comparison of ratings after 0.65g/kg alcohol with or without 3.57mL/kg ED, (v) Marczinski, et al. (24) reflect between-subject comparison of ratings after 0.65g/kg alcohol with or without 3.57mL/kg ED, , and (vi) Peacock, et al. (32) reflect within-subject

comparison of change from baseline ratings after consuming 0.50g/kg alcohol with or without 3.57mL/kg ED. All items were rated on 100-mm visual analogue scale (anchors: 0 'not at all' to 100 'very much') with the exception of: (i) stimulation and sedation, assessed using the Biphasic Alcohol Effects Scale (BAES), where subscale scores are derived following 11-point Likert ratings of 7 stimulant and 7 sedation adjectives, and (ii) outcomes reported by Alford, et al. (36), who used 100-mm visual analogue scales from the Profile of Mood States (35) representing bipolar adjective pairs of clearheaded-muzzy, clumsy-well-coordinated, energetic-lethargic, drowsy-alert, and mentally slow-quick witted. ^b Note that these times represent the minutes between beverage administration and subjective outcome administration; those in italics only provided the time for commencing the test battery as a whole. ^c Odds ratios were calculated using the means and standard deviations or percentages/counts provided in-text, with the exception of those indicated by a ^, which were calculated using the means and *t*-statistic. An odds ratio of 1 indicates the event is equiprobable (or that the means are similar) for each consumer/in each session, > 1 indicates the event is more likely to occur (or that a higher mean was recorded) for AmED versus alcohol consumers/in AmED sessions relative to alcohol sessions, and <1 indicates the event is less likely to occur (or that a lower mean was recorded) for AmED versus alcohol consumers/in AmED sessions relative to alcohol sessions. # indicates that the data was not requested from the author. OR: odds ratio; 95% CI: 95% confidence interval; AmED: alcohol mixed with energy drink.

Table 5

Odds Ratio (OR) for Objective Cognitive and Motor Outcomes after AmED Relative to Alcohol Following Acute Dosing in Laboratory-Based Settings

	Alford, et al. (36) ^{a#}				Ferreira, et al. (5) ^{a^}						Marczinski, et al. (6) ^{a#}		Marczinski, et al. (23) ^{a^}			
Cognitive and Motor Outcomes	<i>Drink 1: 45 minutes^b</i>		<i>Drink 2: 45 minutes^b</i>		<i>30 minutes (0.6g/kg)^b</i>		<i>30 minutes (1.0g/kg)^b</i>		<i>120 minutes (0.6g/kg)^b</i>		<i>120 minutes (1.0g/kg)^b</i>		<i>45 minutes^b</i>		<i>45 minutes^b</i>	
	OR (95% CI) ^c	<i>p</i>	OR (95% CI) ^c	<i>p</i>	OR (95% CI) ^c	<i>p</i>	OR (95% CI) ^c	<i>p</i>	OR (95% CI) ^c	<i>p</i>	OR (95% CI) ^c	<i>p</i>	OR (95% CI) ^c	<i>p</i>	OR (95% CI) ^c	<i>p</i>
Reaction time																
<i>Visual Reaction Time (CogReHab 95s), Cued Go/No-Go task (reaction time)</i>	-	-	-	-	2.33 (0.79, 6.85)	.126	1.00 (0.39, 2.59)	0.99	0.32 (0.10, 0.99)	.047	0.76 (0.29, 1.97)	.567			-	-
Flicker discrimination																
<i>Critical Flicker Fusion Threshold</i>	0.18 (0.03, 0.96)	.045	8.54 (1.53, 47.87)	.015	-		-		-		-		-	-	-	-
Divided attention:																
- Choice Reaction Time	1.67 (0.34, 8.25)	.529	0.12 (0.02, 0.66)	.015	-		-		-		-		-	-	-	-
													<i>Valid cue:</i> 0.16 (0.0, 0.67)	.012	-	-
- Recognition Reaction Time	0.23 (0.04, 1.22)	.085	0.05 (0.01, 0.30)	.001	-		-		-		-		<i>Invalid cue:</i> 0.35 (0.09, 1.39)	.137	-	-
Immediate memory																
<i>Immediate Memory Task</i>	828.11 (60.30, 11372.44)	<.001	0.39 (0.08, 1.97)	.255	-		-		-		-		-	-	-	-
Delayed memory																
<i>Delayed Memory Task</i>	0.48 (0.10, 2.41)	.376	4.30 (0.82, 22.45)	.084	-		-		-		-		-	-	-	-
Inhibition																
<i>Stroop Cognitive Interference task (errors), Cued Go/No-Go task (inhibition failures)</i>	0.01 (0.00, 0.06)	<.001	0.00 (0.00, 0.05)	<.001	-		-		-		-		<i>Valid cue:</i> 0.32 (0.08, 1.26) <i>Invalid cue:</i> 1.00 (0.26, 3.83)	.102 0.99	-	-
Information processing																
<i>Psychological Refractory Period Task</i>	-	-	-	-	-		-		-		-		-	-	0.49 (0.20, 1.17)	.106
Visuo-motor control:																
- Fine motor control	-	-	-	-	0.72 (0.26, 2.03)	.537	1.12 (0.43, 2.81)	.815	1.25 (0.45, 3.51)	.667	0.94 (0.36, 2.43)	.902	-	-	1.72 (0.73, 4.04)	.217

Grooved Pegboard Task,
Purdue Pegboard Task:
Assembly

2.90)

3.51)

2.44)

- Gross motor control
Purdue Pegboard Task:
Right Hand

1.24 (0.54,
2.89) .610

Note. ^a Note that ^ indicates within-subject comparisons for AmED-related analyses, whereas # indicates between-subject design. The outcomes reported by: (i) Alford, et al. (36) reflect between-subject comparison of the change from baseline in performance outcomes on the a critical flicker fusion threshold task, choice reaction time task, word memory task, and Stroop cognitive interference task after drink 1 (.046% BrAC) and drink 2 (.087% BrAC) of alcohol with or without 250mL ED, (ii) Ferreira, et al. (5) reflect within-subject comparison of outcomes on the PSS CogReHab 95® and Grooved Pegboard test after consuming 0.6g/kg or 1.0g/kg alcohol with or without 3.57mL/kg ED, (iii) Marczyński, et al. (6) reflect between-subject comparison of the change from baseline in performance outcomes after 0.65g/kg alcohol with or without 3.57mL/kg ED after valid and invalid cued performance on a Cued Go/No-Go Task, and (iv) Marczyński, et al. (23) reflect within-subject comparison of outcomes on a Psychological Refractory Period task and Purdue Pegboard task after 0.65g/kg alcohol with or without 3.57mL/kg ED. ^b Note that these times represent the minutes between beverage administration and test administration; note that those in italics only provided the time for commencing the test battery as a whole. ^c Odds ratios were calculated using the means and standard deviations or percentages/counts provided in-text, with the exception of those indicated by a ^, which were calculated using the means and *t*-statistic. An odds ratio of 1 indicates the event is equiprobable (or that the means are similar) for each consumer/in each session, > 1 indicates the event is more likely to occur (or that a higher mean was recorded) for AmED versus alcohol consumers/in AmED sessions relative to alcohol sessions, and <1 indicates the event is less likely to occur (or that a lower mean was recorded) for AmED versus alcohol consumers/in AmED sessions relative to alcohol sessions. OR: odds ratio; 95% CI: 95% confidence interval; AmED: alcohol mixed with energy drink.

Table 6

Odds Ratio (OR) For Self-Reported Intake and Frequency of Alcohol Use in Naturalistic Settings (i) by AmED versus Alcohol Consumers and (ii) in AmED versus Alcohol Drinking Sessions

Study ^a	Reporting Time Period	Typical Intake		Maximum Intake		Use Frequency		Binge Use Frequency ^a		Drunk/Intoxicated Day Frequency ^b		Mean BrAC	
		OR (95% CI) ^c	<i>p</i>	OR (95% CI) ^c	<i>p</i>	OR (95% CI) ^c	<i>p</i>	OR (95% CI) ^c	<i>p</i>	OR (95% CI) ^c	<i>p</i>	OR (95% CI) ^c	<i>p</i>
<u>Between-Subject Comparison: Alcohol Quantity/Frequency for AmED versus Alcohol Consumer</u>													
Brache and Stockwell (2)	Last month	5.30 (3.49, 8.05)	<.001	5.58 (3.67, 8.49)	<.001	1.38 (0.92, 2.06)	.119	5.25 (3.46, 7.98)	<.001	3.61 (2.39, 5.46)^	<.001	-	-
de Haan, et al. (27)	Last month	2.80 (2.48, 3.16)	<.001	2.40 (2.13, 2.71)	<.001	1.45 (1.29, 1.64)	<.001	2.28 (2.03, 2.58)	<.001	2.13 (1.89, 2.41)	<.001	-	-
O'Brien, et al. (4)	Last month	1.44 (1.23, 1.68)	<.001	1.83 (1.57, 2.14)	<.001	-	-	2.06 (1.76, 2.40)	<.001	2.00 (1.71, 2.34) ^	<.001	-	-
Penning, et al. (28)	Last week	1.72 (0.82, 3.62)	.154	-	-	-	-	-	-	-	-	-	-
Rossheim and Thombs (37)	Tonight	-	-	-	-	-	-	-	-	-	-	2.23 (0.93, 5.32)	.072
Thombs, et al. (38)	Tonight	-	-	-	-	-	-	-	-	-	-	1.85 (0.58, 5.88)	.297
Woolsey, et al. (29), Woolsey (30)	Last year	3.56 (2.35, 5.38)*	<.001	6.14 (4.01, 9.40)*	<.001	3.45 (2.28, 5.21)*	<.001	4.33 (2.85, 6.57)	<.001	-	-	-	-

Within-Subject Comparison: Alcohol Quantity/Frequency for AmED versus Alcohol Drinking Sessions

Brache and Stockwell (2)	Last month	1.72 (1.21, 2.46)*	.003	-	-	-	-	-	-	-	-	-	-
de Haan, et al. (27)	Last month	0.75 (0.69, 0.82)	<.001	0.17 (0.14, 0.20)	<.001	0.08 (0.07, .010)	<.001	0.19 (0.17, 0.21)	<.001	0.34 (0.31, 0.38)	<.001	-	-
Peacock, et al. (26), Peacock, et al. (50)	Last month (alcohol)/Last 6 months (AmED)	1.26 (1.05, 1.51)*	.012	-	-	-	-	-	-	-	-	-	-
Price, et al. (39)	Last week	5.43 (1.41, 20.88)*	.014	-	-	-	-	-	-	-	-	-	-
Woolsey, et al. (29), Woolsey (30)	Last year	0.42 (0.30, 0.58)	<.001	0.24 (0.17, 0.35)	<.001	0.16 (0.11, 0.24)	<.001	0.20 (0.14, 0.29)	<.001	-	-	-	-

Note. ^a Note that Brache and Stockwell (2) and O'Brien, et al. (4) defined 'binge drinking' as four or more standard drinks for females and five or more standard drinks for males, de Haan, et al. (27) defined 'binge-drinking' as more than four/five standard drinks for females and males respectively, and Woolsey (30) and Woolsey, et al. (29) defined 'binge-drinking' as consuming five or more standard drinks for males and females. ^b Those studies indicated with a ^ asked participants reported the number of drunk days in a typical week. Note also that Brache and Stockwell (2) asked participants to report the number of days 'intoxicated' while de Haan, et al. (27) and O'Brien, et al. (4) asked participants to report the number of 'drunk' days. ^c Odds ratios were calculated using the means and standard deviations or percentages/counts provided in-text, with the exception of those indicated by a *, which were calculated using the means and *t*-statistic. An odds ratio of 1 indicates the event is equiprobable (or that the means are similar) for each consumer/in each session, > 1 indicates the event is more likely to occur (or that a higher mean was recorded) for AmED versus alcohol consumers/in AmED sessions relative to alcohol sessions, and <1 indicates the event is less likely to occur (or that a lower mean was recorded) for AmED versus alcohol consumers/in AmED sessions relative to alcohol sessions. OR: odds ratio; 95% CI: 95% confidence interval; AmED: alcohol mixed with energy drink.

Table 7

Odds Ratio (OR) for (i) Self-Reported Retrospective General Risk-Taking Behaviour by AmED versus Alcohol Consumers, (ii) Self-Reported Alcohol-Related Risk-Taking Behaviour by AmED versus Alcohol Consumers, and (iii) Self-Reported Retrospective Risk-Taking Behaviour by AmED Consumers during AmED versus Alcohol Drinking Sessions

Outcome	Self-Reported General Risk-Taking Behaviour (Between-Subjects) ^a				Self-Reported Alcohol-Related Risk-Taking Behaviour (Between-Subjects) ^b		Self-Reported Risk-Taking Behaviour After AmED and Alcohol (Within-Subjects) ^c					
	Brache and Stockwell (2)#		de Haan, et al. (27)#		O'Brien, et al. (4)#		de Haan, et al. (27)^		Peacock, et al. (26)^		Woolsey, et al. (29)^	
	Last 12 months		n.s		Past 30 days		Last year		Last six months		Future drinking sessions	
	OR (95% CI) ^d	p	OR (95% CI) ^d	p	OR (95% CI) ^d	p	OR (95% CI) ^d	p	OR (95% CI) ^d	p	OR (95% CI) ^d	p
General Risk-Taking:												
Took risks while drinking	2.48 (1.65, 3.72)	<.001	-	-	-	-	0.48 (0.42, 0.56)	<.001	-	-	1.07 (0.79, 1.46)	.655
Driving Risk-Taking:												
Drove a motor vehicle after drinking	-	-	-	-	2.29 (1.88, 2.77)	<.001	0.55 (0.40, 0.76)	<.001	0.21 (0.13, 0.34)	<.001	1.38 (1.01, 1.89)	.043
Passenger while driver over the legal alcohol limit	-	-	-	-	2.19 (1.83, 2.63)	<.001	-	-	0.24 (0.16, 0.36)	<.001	-	-
Seatbelt omission	-	-	-	-	-	-	-	-	0.38 (0.25, 0.57)	<.001	-	-
In a vehicle with an illegal passenger number	-	-	-	-	-	-	-	-	0.34 (0.26, 0.46)	<.001	-	-

In a vehicle exceeding speed limit by at least 10%	-	-	-	-	-	-	-	-	-	0.58 (0.42, 0.81)	.001	-	-
<u>Sexual Risk-Taking:</u>													
Had sex with someone recently met	-	-	-	-	-	-	-	-	-	0.47 (0.38, 0.58)	<.001	-	-
Did not use contraception	-	-	-	-	-	-	-	-	-	0.51 (0.41, 0.62)	<.001	-	-
Was touched in an unwanted sexual way	-	-	-	-	1.78 (1.22, 2.59)	.003	-	-	-	0.41 (0.29, 0.57)	<.001	-	-
Touched someone in an unwanted sexual way	-	-	-	-	2.22 (1.34, 3.70)	.002	-	-	-	0.56 (0.36, 0.85)	.007	-	-
Got in sexual situations later regretted	-	-	-	-	-	-	0.41 (0.33, 0.51)	<.001	-	-	-	-	-
<u>Financial Risk-Taking:</u>													
Spent more money than planned	-	-	-	-	-	-	-	-	-	0.47 (0.37, 0.60)	<.001	-	-
Gambled	-	-	-	-	-	-	-	-	-	0.34 (0.25, 0.46)	<.001	-	-
<u>Aggressive and Antisocial Behaviour:</u>													
Verbally fought~	-	-	-	-	-	-	0.62 (0.47, 0.83)	<.001	-	0.41 (0.33, 0.51)	<.001	-	-
Physically fought~	-	-	-	-	-	-	0.98 (0.73, 1.31)	.880	-	0.50 (0.38, 0.67)	<.001	1.06 (0.78, 1.44)	0.724
Act aggressively	-	-	-	-	-	-	-	-	-	-	-	1.68 (1.23, 2.31)	<.001
Asked to leave and/or kicked out of a drinking establishment	-	-	-	-	-	-	-	-	-	0.45 (0.34, 0.60)	<.001	-	-

Alcohol and Energy Drink Systematic Review

Vandalised	-	-	-	-	-	-	-	-	0.29 (0.13, 0.65)	.003	-	-
Cautioned, restrained, charged, and/or fined by the police	-	-	-	-	-	-	-	-	0.36 (0.17, 0.78)	.010	-	-
Acted on a dare which could cause harm to myself and/or others	-	-	-	-	-	-	-	-	0.53 (0.40, 0.71)	<.001	-	-

Licit and Illicit Drug Use:

Smoked cigarettes	-	-	2.37 (2.06, 2.72)	<.001	-	-	-	-	0.59 (0.51, 0.69)	<.001	-	-
Drank more alcohol than planned	-	-	-	-	-	-	-	-	0.54 (0.43, 0.68)	<.001	-	-
Used legal drugs ~	-	-	0.99 (0.85, 1.16)	.887	-	-	-	-	0.56 (0.44, 0.71)	<.001	-	-
Used illegal drugs ~	3.27 (1.76, 6.09)	<.001	2.20 (1.91, 2.54)	<.001	-	-	-	-	0.42 (0.33, 0.53)	<.001	-	-

Physical Harm:

Passed out	-	-	-	-	-	-	1.24 (0.82, 1.88)	0.299	0.47 (0.38, 0.59)	<.001	-	-
Physically hurt or injured~	-	-	-	-	2.24 (1.68, 2.98)	<.001	0.52 (0.41, 0.65)	<.001	0.46 (0.36, 0.58)	<.001	1.17 (0.86, 1.60)	.325
Required medical treatment	-	-	-	-	2.20 (1.20, 4.02)	.011	-	-	0.24 (0.08, 0.73)	.012	-	-

Psychological Distress:

Behaved in a way which resulted in me later experiencing guilt or regret~	-	-	-	-	-	-	0.47 (0.39, 0.56)	<.001	0.36 (0.30, 0.44)	<.001	-	-
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Behaved in a way
which resulted in me
later experiencing
humiliation or
embarrassment

0.03 (0.02,
0.05) <.001 0.50
(0.42,
0.60) <.001 - -

Note. ^a Note that ^ indicates within-subject comparisons for AmED-related analyses, whereas # indicates between-subject comparisons. The outcomes reported by Brache and Stockwell (2) and de Haan, et al. (27) reflect between-subject comparison of general behaviour in the last 12 months for AmED versus alcohol consumers. ^b The outcomes reported by: (i) O'Brien, et al. (4) reflect between-subject comparison of alcohol-related consequences in the last 30 days for AmED versus alcohol consumers, and (ii) Thombs, et al. (25) reflect between-subject comparison of prospective behaviour for AmED and alcohol consumers whilst under the influence of the respective beverages. ^c The outcomes reported by: (i) de Haan, et al. (27) and Peacock, et al. (26) reflect within-subject comparison of outcomes in the last year and last six months respectively in AmED versus alcohol drinking sessions, with both studies comprising dichotomous responses (yes/no), and (ii) Woolsey, et al. (29) reflect within-subject comparison of prospective expectations of outcomes in AmED and alcohol drinking sessions, endorsing the likelihood of the outcome on a 4-point Likert scale from 1 'disagree' to 4 'agree'. ^e Odds ratios were calculated using the means and standard deviations or percentages/counts provided in-text, with the exception of those indicated by a *, which were calculated using the means and *t*-statistic. An odds ratio of 1 indicates the event is equiprobable (or that the means are similar) for each consumer/in each session, > 1 indicates the event is more likely to occur (or that a higher mean was recorded) for AmED versus alcohol consumers/in AmED sessions relative to alcohol sessions, and <1 indicates the event is less likely to occur (or that a lower mean was recorded) for AmED versus alcohol consumers/in AmED sessions relative to alcohol sessions. ~ For the item 'verbally fought' de Haan, et al. (27) specified that this comprised being 'very rude, obnoxious or insulting'. For the item 'more likely to fight' Peacock, et al. (26) specified that this referred only to physical fighting while Woolsey, et al. (29) and de Haan, et al. (27) did not specify whether 'fighting' referred to physical or verbal interaction. For the item 'used legal drugs' Peacock, et al. (26) specified that this referred only to recreational use whereas de Haan, et al. (27) referred to medication use in general. For the item 'used illegal drugs' Brache and Stockwell (2) specified that this referred only to stimulant drugs, while de Haan, et al. (27) referred to drug use in general. For the item 'physically hurt or injured' Peacock, et al. (26) limited this to harm specific to the consumer while de Haan, et al. (27) specified that the physical hurt or harm could be to the consumer or others around them. For the item "behaved in a way which resulted in me later experiencing guilt or regret" de Haan, et al. (27) worded this item as "While drinking, I have said or done embarrassing things". OR: odds ratio; 95% CI: 95% confidence interval; AmED: alcohol mixed with energy drink; n.s: not specified.

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