

Caffeinated energy drink use and reported effects in young people: a rapid overview of systematic reviews

Final Report

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Caffeinated energy drink use and reported effects in young people: a rapid overview of systematic reviews.

FINAL REPORT

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Abstract

Background

There is concern in the UK about the consumption of caffeinated energy drinks (CEDs) among children and adolescents aged 17 years and under. We aimed to review the existing systematic review research evidence on patterns of CED use in young people and assess the evidence on the effects of CEDs on their physical, mental and social health and wellbeing.

Methods

We conducted an overview of English-language systematic reviews published between 2013 and 2018, identified from database and citation searching. Descriptive data on study characteristics and effects were extracted and synthesised narratively and in tables. Review quality was evaluated using AMSTAR 2 criteria and overall strength of evidence was assessed. We supplemented these data by searching for primary research published from 2016 and briefly describing their study characteristics. The overview protocol was registered in PROSPERO (CRD42018096292).

Findings

We included 13 systematic reviews, covering 74 primary studies relevant to young people, of which just two studies are UK-based. Nearly one-third of young people frequently consume energy drinks, and between 10% and 36% report mixing these with alcohol. Consumption varies by age group and country. Some evidence suggests males consume more energy drinks than females, who may start to consume CEDs at a slightly younger age. There is conflicting evidence of consumption by ethnicity. The two UK studies found that 11% of surveyed young people consume CEDs on a daily basis, and link higher use in males and those with lower socioeconomic status. We found consistent findings across reviews for: physical symptoms (e.g. headaches, sleep-related issues); behavioural effects such as alcohol, smoking and substance use; behaviour disorders; and poorer psychological well-being (e.g. irritation, anger). Contradictory evidence was reported for anxiety and depression; and limited evidence suggested associations with self-harming and suicide-related behaviour. Mixing alcohol with energy drinks was linked to engaging in risky lifestyle behaviours and self-injury. Little evidence described educational and social effects; these reported a negative relationship with school attainment and attendance. Findings were rarely differentiated by age, ethnicity or socio-economic status. The reviews were rated as low or critically low quality, due to methodological limitations in the design and execution of reviews.

Conclusion

We found that a wide range of worldwide CED prevalence rates are reported. Limited UK evidence suggests daily use by one in ten young people. While there is some association of energy drink use with physical symptoms and lifestyle effects, and unclear mental and behavioural effects, the study designs of the research and the quality of the systematic reviews limits the strength of the conclusions. More robust observational evidence is warranted.

Executive Summary

Background

Caffeinated energy drinks (CEDs) are increasingly prevalent in everyday life, accounting for billions in global sales revenue. Energy drinks containing caffeine are typically marketed with claims that they can boost energy, reduce fatigue, improve concentrations and enhance mental alertness. However, widespread concern is growing about the use and effects of consumption of CEDs, particularly amongst children and adolescents ('young people') under age 18.

This population is thought to be at more risk of ill effects than adults; and a range of physical, psychological and behavioural factors have been associated with high or chronic consumption of CEDs. Young males and minority ethnic and lower socio-economic groups may be at higher risk. Research on the consumption of CEDs in this population has been synthesised, but findings remain unclear. Reviews appear to vary in their methods and report a wide range of findings on prevalence and effects; and the influence of social situations, peers and parents is not well understood.

The UK government has announced recently a commitment to introduce legislation to end the retail sales of energy drinks to children aged under 18 years. Questions remain about their patterns of CED use, the effects on their physical, mental and social health and wellbeing, and subsequent effects of use on their behaviour and life-course outcomes. A range of prevalence estimates and effects have been reported in evidence syntheses, and the quality of these evidence syntheses thus far has not been assessed. It is also unclear whether newer primary research is available to add to the synthesised evidence.

Aims and Research Questions

To explore the use of CEDs and their effects amongst young people, we considered the following research questions:

- (1) *What is the nature and extent of CED consumption amongst young people aged 17 years or under in the UK?*
- (2) *What impact does the use of CEDs have on young people's physical and mental health and behaviour?*

Methods

The research questions posed suggested that an overview of reviews design was most appropriate. Background scoping identified several systematic reviews focused on caffeine and/or energy drinks in a range of age groups including children and young people. Allowing systematic and transparent methods, an overview of reviews identifies and appraises existing evidence syntheses. This is a useful approach where several systematic reviews exist on a topic and when a rapid assessment of the evidence is required.

Systematic reviews were identified by searching databases that contain research literature in health, mental health, general science and social science, for reviews that were published

between January 2013 and 15 May 2018. To supplement the data arising from reviews and ensure all current research was located, a second search was undertaken to identify primary studies of research published since the date of the last systematic review search.

All located citations were screened initially on title and abstract, and (in the case of systematic reviews) again on the basis of the full report, using criteria addressing: language; date; systematic review or primary study design; population; and prevalence, patterns or effects of CED consumption.

To characterise included reviews, bespoke data extraction frameworks were developed and applied to describe a range of review characteristics (e.g. publication year, review aims, target population). Quality assessment was conducted using AMSTAR 2 criteria. Descriptive data on characteristics and effects were extracted and summarised narratively and in tabular format. The strength of evidence was discussed by the research team, considering the findings across reviews, overall risk of bias, the 'fit' between review questions and our overview questions, and the consistency, precision and publication bias of combined findings.

After establishing coding and quality rating agreement, data on review characteristics were extracted by one researcher and checked by a second. Two researchers independently undertook quality assessment of all included reviews and met to agree ratings, with disagreements resolved by a third researcher where needed. To assure quality of data extraction and risk of bias assessments, a random sample of reviews was assessed by a third reviewer. Review characteristics and findings were extracted into EPPI-Reviewer software and tabulated using Word and Excel.

Results

After locating and screening 654 unique references on the basis of title and abstract, 76 reports were retrieved. Of these, a total of 13 were identified as systematic reviews and included in this overview. Most included systematic reviews reported findings on a wider range than is the focus of this overview (11/13, 85%), but reported findings for young people aged 17 years or younger separately. Only two reviews included research focused solely on young people (Dawodu and Cleaver 2017, Visram et al. 2016). Most reviews included findings from participants aged 10 to 19 years of age, and all focused on mixed gender. Socio-economic status of participants was not reported in any reviews.

Findings from studies of UK young people were limited to only two primary studies (Richards et al. 2015, Richards and Smith 2015, Richards and Smith 2016b; EFSA NDA Panel 2015), reported across four reviews (Bleich and Vercammen 2018; Richards and Smith 2016a; Verster and Koenig 2018; Visram et al. 2016). The three papers by Richards and colleagues reported findings from a single study conducted with young people (11 to 17 years old) who attended three secondary schools in the South West of England. This was a large longitudinal study collecting cross-sectional data at two time points, with data on self-assessed mental health collected at the second data collection point only (n=2,307). The EFSA NDA Panel (2015) surveyed 31,070 children and young people (3 to 18 years old) from sixteen European countries, presenting findings specific to an unknown number of UK participants as a subgroup.

Prevalence

Across six reviews, prevalence rates of CED consumption in young people vary widely and a variety of measures are reported. Overall, between half and two thirds of all young people surveyed had tried CEDs at some point; and nearly one third report either frequent or heavy use. Use of alcohol mixed with energy drinks (AmEDs) ranged from 10% to 36% of young people. These rates appear to vary by age group and by country. Some evidence suggests gender differences, in that females may start to consume CEDs at a younger age, and males may consume more frequently and more heavily. Conflicting findings were reported for higher CED use amongst Black, Hispanic and Aboriginal ethnic groups. The context of CED use included exams, parties, friends' houses and family gatherings. In general, reviews reported that young people have limited knowledge of CED ingredients and reported conflicting findings regarding their critical awareness of the safety of CEDs. A wide range of motivations for CED use were described, including taste, energy, curiosity, peer/family influences, parental (dis)approval, wanting to socialise/party, to suppress appetite, and to enhance sports performance. Review authors reported that AmED use was linked to wanting to socialise/party, to drink more alcohol and to reduce alcohol side effects. No reviews reported findings for parental knowledge or behaviours related to young people's CED use.

Effects

Evidence (largely cross-sectional) reported in twelve reviews demonstrated the existence of a relationship between CED use and various physical symptoms and behaviours. Consistent findings indicate that consumption is associated with a number of physical symptoms including headaches, stomach aches and low appetite. Evidence also commonly indicates a link to sleep-related issues. Reviews of case reports have documented the occurrence of adverse physical effects, (most notably cardiovascular events), following consumption of energy drinks in different quantities and over varying time periods. Review authors reported a relationship between CEDs and a range of lifestyle behaviours. Findings from a considerable number of identified studies across reviews suggest a consistent association between CED consumption and substance use (alcohol, smoking and illicit drug use). Furthermore, mixing alcohol with CEDs has also been linked to engaging in risky lifestyle behaviours, self-reported injuries, and poorer driving behaviour. Reviews further identified a link between CED use and hyperactivity and behaviour disorders. Retrospective analyses of poison centre data have provided additional evidence of a relationship between CED use and hyperactivity and physical health symptoms. Evidence has suggested a link between CEDs and poorer psychological well-being in terms of greater irritation and anger. Conflicting evidence is reported on the relationships between energy drink consumption and common mental health conditions such as anxiety and depression. Additionally, a small number of studies reported in reviews identified an association between self-harming and suicide related behaviour. Studies examining the educational or social effects of CED consumption are lacking, but there is some evidence which points to a negative relationship with school attainment and attendance. Few findings were reported in the included reviews on the effects of CEDs disaggregated by gender, ethnicity or socio-economic status.

UK perspective

Findings from studies of UK young people were limited to only two primary studies. These suggest that around 11% of surveyed young people consume CEDs on a daily basis; and that higher use is associated with being male and with lower socio-economic status. Effects in

UK samples are less clear, suggesting that CED use may be associated with sleep disturbances, poor school attendance/achievement and poor nutritional choices. However reported relationships between CED use and mental health effects such as stress, anxiety or depression may be influenced by other factors, such as frequency of caffeinated energy drink use or skipping breakfast.

Discussion

This systematic overview of reviews sought to answer two specific research questions:

(1) What is the nature and extent of CED consumption amongst young people aged 17 years or under in the UK?

Six reviews report varying rates of prevalence of CED consumption in young people using a variety of different measures. Overall, reviews report that between half and two thirds of all young people surveyed have tried CEDs at some point; and up to nearly one third report either frequent or heavy use. The prevalence of alcohol mixed with energy drink (AmED) use ranges from 10% to 36% of young people. These findings suggest that a potentially large proportion of young people are exceeding recommended daily caffeine intake (EFSA NDA Panel 2015; NHS Digital 2017).

Reviews reported differing prevalence findings by age group, with an increasing pattern of use emerging in older age groups. Several reviews reported a gender difference, suggesting that males may have more frequent or heavier use of CEDs. However, one review reported that females may start consuming CEDs slightly earlier than males. Reviews reported both higher and lower CED use amongst Black youth in comparison to Hispanic and Aboriginal ethnic groups, or in comparison to White participants.

In general, the findings from across these systematic reviews are consistent with those reported in other (non-systematic) reviews (Ruxton 2014; Reid et al. 2017; Thomson et al. 2014; Zucconi et al. 2013). However, reviews reported differences in prevalence (within and between each other). Further, differences in effects according to gender, age, ethnicity and socio-economic status are unclear, particularly for UK populations. This is due to limited information from UK-based surveys. There is also limited information from studies that included younger age groups, i.e. those aged 12 years and under. Findings from studies of UK young people were limited. Only two primary studies were reported in included reviews. These suggest that around 11% of surveyed young people consume CEDs on a daily basis; and that higher use is associated with being male and with a lower socio-economic status.

(2) What impact does the use of CEDs have on young people's physical and mental health and behaviour?

Evidence from largely cross-sectional studies reported in twelve reviews suggested an existence of a relationship between CED use and various physical and behavioural effects. Consistent findings from multiple cross-sectional and one longitudinal study indicate that consumption is associated with a number of physical symptoms. Reviews of case reports have most frequently documented adverse cardiovascular events, following consumption of

energy drinks in different quantities and over varying time periods. However, no evidence was found that suggested any potential mechanisms of effect linked to CED use. The range of effects reported across these 12 systematic reviews are consistent with those reported in other (non-systematic) reviews (Heckman et al. 2010; Seifert et al. 2011; Wolk et al. 2012). However, it has also been suggested that differences in effects may be influenced by genetics (Clark and Landolt Hans 2017).

Nineteen studies identified in reviews suggest a consistent association between CED consumption and lifestyle behaviours. Mixing alcohol with CEDs has also been linked to engaging in risky lifestyle behaviours, self-reported injuries, and poorer driving behaviour. A link was also suggested between CED use and hyperactivity and behaviour disorders. Evidence has suggested a link between CEDs and poorer psychological well-being in terms of greater irritation and anger. Contradictory evidence was presented on the relationship between CED consumption and anxiety and depression. Two studies identified an association between CED use and self-harm and suicide-related behaviour. Studies examining the educational or social effects of CED consumption are lacking, but there is some evidence which points to a negative relationship with school attainment and attendance. Few reviews reported the effects of CEDs disaggregated by gender, ethnicity or socio-economic status.

Studies of UK participants report mixed evidence that CED use may be associated with sleep disturbances, poor school attendance/achievement, poor nutritional choices. However, these effects may also be influenced by other factors (such as frequency or skipping breakfast) in relation to mental health effects such as stress, anxiety or depression.

Recommended limits of CED use in young people suggest between 2.5 and 3 mg per kg of body weight per day (EFSA NDA Panel 2015; Ruxton 2014; Wikoff et al. 2017). This overview provides very limited evidence of weak quality, particularly with respect to UK populations, that this is being exceeded by the majority of young people who report CED use. However, there are findings to suggest that a small proportion of young people may exceed this amount. Findings from a larger number of studies of effect suggest weak evidence of an association between CED use and physical symptoms. Similarly, we noted weak evidence of an association between CED use and lifestyle behaviours. Evidence is unclear of an association between CED use and mental health or educational/social effects; and limited UK evidence to suggest a weak association between CED use and poorer health effects in males and young people of lower socio-economic status. More recent CED primary research published since 2016 is largely non-UK and of cross-sectional design.

Strengths and limitations

Based on multiple systematic reviews, this robust overview provides comprehensive findings. These allow us to take stock of what is currently known on this important public health issue, while identifying gaps in comparable and reliable evidence. There are a number of limitations to the reviews, including selective reporting in reviews, wider age ranges than those required by our overview, and limited sub-group analyses. Methodological limitations in these reviews merit caution in considering the validity of the findings reported, which suggest a wide range of rates of consumption and associated effects. All included reviews were rated to be of 'low' or 'critically low' methodological quality using AMSTAR 2 criteria. This was, in part, due to the reliance on cross-sectional or case-report

designs which lack a comparison group. In addition, the use of a wide range of measures that conflated frequency and dosage limited efforts to find consistent evidence of a common consumption pattern. A slight overlap between primary studies included across reviews was noted.

Conclusions

We set out to review the evidence on the prevalence and likely effects of CED use in young people under age 18 years. We located 13 systematic reviews which reported findings from 74 relevant studies, which suggested a wide variation in worldwide CED prevalence, scant evidence of low daily use in UK young people, a consistent association with physical symptoms and lifestyle effects, and unclear mental health and behavioural effects. However, the strength of our conclusions is limited by the challenges of ascertaining causal relationships on epidemiological evidence and by the methodological quality of included reviews. More robust UK-based evidence based on cohort observational data is warranted.

1 Background

1.1 Rationale

Caffeinated energy drinks (CEDs) are increasingly prevalent in everyday life, with global sales estimated to top USD 60 billion in the next five years (Curran and Marczyński 2017). Energy drinks containing caffeine include Red Bull®, Monster Energy®, and Rockstar®. These are typically marketed with claims that they can boost energy, decrease fatigue, improve concentration and enhance mental alertness. However, concerns about marketing and consumption have led some countries to regulate a name change from ‘energy’ to ‘stimulant’ drinks (Barker 2018). Some professional organisations suggest banning sales of CEDs to children and young people (Schneider and Benjamin 2011). CEDs are sold in most EU member states. Cautionary labelling, aimed at children and pregnant women, is required for those CEDs that contain more than 150 mg/l of caffeine (NHS England 2014). Consumption of CEDs in the UK are amongst the highest worldwide for all age groups, and UK adolescents consume more than in other European countries (Hargreaves et al. 2018; Zucconi et al. 2018). Recently, several large UK grocery stores have voluntarily stopped selling energy drinks to those under 16 years of age (Smithers 2018; Cox 2018), and the British Soft Drinks Association has introduced a voluntary code of practice relating to the labelling and marketing of high caffeine drinks (Hargreaves et al. 2018). However, sales are likely to continue in smaller convenience stores nationwide, and online gaming sites are reported to advertise CED use widely (Fleming 2018). The UK government has announced recently a commitment to introduce legislation to end the retail sales of energy drinks to children under age 18 years (Department of Health and Social Care 2018).

Many energy drinks contain large amounts of sugar and stimulants, such as caffeine and guarana, as well as varying amounts of carbohydrate, protein, amino acids, vitamins, sodium, and other minerals. While the sugar content is associated with obesity and dental caries (Heckman et al. 2010), less is known about the effects of caffeine in energy drinks, with evidence mostly coming from animal studies (EFSA NDA Panel 2015). Caffeine may potentiate the action of the sugar content, causing insulin to be released (Gonzalez-Dominguez et al. 2017). While sugar content in some brands has been reduced, caffeine levels remain high (Hashem et al. 2017).

Primary studies about prevalence and consumption of CEDs in children and young people are widely available and these studies have been synthesised, but the findings remain unclear. Reviews and surveys conducted in Canada, New Zealand and the USA suggest that between 30% and 74% of adolescents consume CEDs (Reid et al. 2017; Seifert et al. 2011; Thomson et al. 2014), with a significant number of young people exceeding the recommendations for maximum daily consumption (Reid et al. 2017). An EU survey noted that of all respondents who consume energy drinks, 68% were adolescents aged 10 to 18 years and 18% were children aged 3 to 10 years (Zucconi et al. 2013). Energy drinks accounted for 13% of young people’s and 43% of children’s total daily caffeine exposure. In the UK, children and adolescents’ consumption was the seventh highest of 16 EU countries surveyed. However, this survey is now over five years old and it is not clear whether these data are based on self-reported

use or whether more robust measures (e.g. diaries, sales and receipts, saliva or urine analysis) were obtained.

Young people are thought to be at more risk of ill effects from chronic CED consumption, compared with older people, who may experience beneficial effects (Curran and Marczynski 2017). Almost half of all caffeine overdoses reported in the USA in 2007 were amongst people under 19 years of age (Seifert et al. 2011), increasing to over three-quarters of all US CED overdoses reported in 2016 (Gummin et al. 2017). These figures indicate that young people are a high-risk group.

Caffeine is contained in other food and drink; and caffeine intake from energy drinks must be considered in the context of this background intake of caffeine (EFSA NDA Panel 2015). However, it is unclear how much caffeine is too much for children and young people. For example, some authors suggest that no adverse effects of caffeine are noted in children who consume less than 3 mg per kg of body weight per day (Heckman et al. 2010). Others claim that an intake of 2.5 mg per kg of body weight per day, equating to one or two cups of tea or one small cup of coffee, should be the maximum allowed (Ruxton 2014). Further, it is unknown whether caffeine exerts an independent action on the effects or symptoms seen, or whether other energy drink additives may also contribute (Ali et al. 2015; Curran and Marczynski 2017; Shearer 2014; Wolk et al. 2012).

A range of physical, psychological and behavioural factors have been reported to be associated with high or chronic consumption of CEDs (Heckman et al. 2010; Seifert et al. 2011; Thomson et al. 2014; Ruxton 2014; Wolk et al. 2012; Dawodu and Cleaver 2017; Owens et al. 2014; Peacock et al. 2014; Rath 2012; Visram et al. 2016). Consumption rates have been found to be higher in young males than females, and independent associations are noted amongst minority ethnic and lower socio-economic groups (Reid et al. 2017; Thomson et al. 2014; Zucconi et al. 2013; Ali et al. 2015; Visram et al. 2016; Grandner et al. 2014).

Questions remain about children and young people's patterns of use of CEDs in the UK, the effects on their physical, mental and social health and wellbeing, and subsequent effects on their behaviour and life-course outcomes. A range of effects has been reported in evidence syntheses, and the quality of this evidence has not been assessed. It is also unclear what recently published primary research could add to the synthesised evidence.

2 Aims and methods

2.1 Aims

To explore caffeinated energy drink (CED) use and effects amongst children and adolescents ('young people'), we considered the following research questions:

- (1) What is the nature and extent of CED consumption amongst young people under the age of 18 years in the UK?*
- (2) What impact does the use of CEDs have on young people's physical and mental health and behaviour?*

The age range specified reflects policy interest relating to consumption and effects in those aged under 18 years, for the purpose of informing policy decisions on regulation of CED sales to this age group.

2.2 Methods

The context in which this project was commissioned, and the research questions posed, suggested that an 'overview of reviews' design was most appropriate. Background scoping identified several systematic reviews focused on caffeine and/or energy drinks in a range of age groups including children and young people. Allowing systematic and transparent methods, an overview of reviews identifies and appraises existing systematic reviews. This is a useful approach where several systematic reviews exist on a topic and when a rapid assessment of the evidence is required (Caird et al. 2015; Lunny et al. 2016).

To identify any more recently published primary research, we supplemented the reviews data with selected information from recent primary research, published since the last review search dates (2016 onwards). Due to the timelines of this review, the information from this more recent primary research (not included in the systematic reviews) was coded and descriptively summarised. This was intended to supplement the systematic reviews by identifying the extent and broad content of newer primary research that had not yet been reviewed. The methods and results of this search are reported in **Appendix 1**.

For the purpose of clarity, the following definitions are used: 'overview' refers to the design of our project; 'reviews' refer to the systematic reviews included in this overview; 'studies' refer to the primary research studies included in the systematic reviews; and 'primary research' refers to the newer research studies identified since the most current reviews were published.

2.2.1 Information sources

A preliminary scoping search revealed a number of reviews in the past five years, suggesting that full searching within the past five years would identify a useful dataset of reviews. This timeframe was chosen to ensure that the most up-to-date reviews were considered. Health, mental health, general science and social science databases were searched for within the

timeframe from 2013 to the date of search (15 May 2018). These include MEDLINE (OVID SP), PsycINFO (OVID SP), Web of Science (Social Science Citation Index, Science Citation Index, Emerging Sources Citation Index), BIOSIS, and Scopus. Focussed searches were undertaken using Google Scholar and the Bielefeld Academic Search Engine (BASE). The searches were supplemented by searching PROSPERO, forward citation searching of thirteen systematic reviews using Google Scholar, and research citations identified from an earlier scoping search. The searches were developed by an information specialist (CS) and structured around three concepts of 'energy drinks', 'caffeine' and 'systematic reviews'. Search terms for each concept comprised database-controlled vocabulary and synonyms and related terms in the titles and abstracts. The full search strategy that was applied in MEDLINE is shown in **Appendix 2**. This search was adapted for use in the other databases.

Following a pilot screening stage, all citations were screened initially on the basis of title and abstract. Potentially relevant reviews were retrieved, and full-text reports rescreened.

2.2.2 Inclusion/exclusion criteria

Systematic review citations were assessed for inclusion/exclusion using the criteria below. To be included, the citation must:

- Be published in English (since the team does not have capacity to search for and examine evidence in all languages we will include only those available in English language);
- Be published since 2013;
- Be a systematic review (as a minimum: searched two sources and stated inclusion criteria);
- Be about CED consumption. CEDs contain caffeine, sugar or sweeteners and other ingredients with a nutritional or physiological function, and do not include soft drinks that only contain caffeine for flavouring purposes, such as cola-type beverages. As energy drinks are generally expected to contain caffeine, where caffeine was not mentioned in the abstract, the full-text was checked. Additionally, where abstracts focused on soft drinks in a way that may imply a focus on CED, the full-text was checked.
- Present data collected separately from children or adolescents up to/including age 17 (i.e. review is either focused on young people or presents sub-group data for this age group) (where these criteria is unclear at title and abstract, the full-text was checked);
- Examine patterns of CED use OR examine the relationship between CED consumption and effects on physical, mental, social or behavioural outcomes; and
- Contain extractable outcome data.

2.2.3 Data items

Bespoke data extraction frameworks were developed to code the reviews according to key characteristics, which built on existing research in the area. These codes described the type of evidence available, including:

- Year of publication;

- Country of primary author conducting the review (with UK separated into England, Scotland, Wales and Northern Ireland where data were provided);
- Number of studies included in the review;
- Study design(s) (e.g., cross-sectional or longitudinal survey);
- Aims of review and main topic focus;
- Target population (e.g., health condition, and at-risk group);
- Participant characteristics (e.g., age, and gender);
- Consumption characteristics (e.g., caffeine concentration, number/frequency and context of intake, location of purchase, time of day consumed, and parental awareness of consumption);
- Physical, mental, social and behavioural effects (e.g., palpitations, anxiety, sleep disturbance, attainment, employment, and risk-taking behaviour);
- Quality assessment characteristics and rating.

Other characteristics were added as they emerged from the data, including funding and participant setting. This was a change from the review protocol. The coding tool is provided in **Appendix 3**.

2.2.4 Review ‘outcomes’: prevalence and reported effects data extraction

Descriptive data on patterns of consumption and reported effects of CED use were extracted from review findings, or where these were not reported separately for young people, from relevant studies included in the reviews. Prevalence rates and sub-group analyses were reported, including any review-level effects sizes for statistical associations. All reported effects were extracted, including cardiovascular, neurocognitive, risk taking, performance, and attainment measures. To understand the range of effects, these were categorised into physical, mental, behavioural and educational/social domains. Additional effects were extracted and categorised as they emerged from the reviews.

2.2.5 Risk of bias in reviews

All relevant full-text reviews were retrieved and assessed for methodological quality according to AMSTAR 2 criteria (Shea et al. 2017):

- PICO components
- Protocol
- Study design explanation
- Comprehensive search strategy
- Duplicate study selection
- Duplicate data extraction
- Details of excluded studies
- Description of included studies
- Risk of bias assessment of included studies (RCTs/non-RCTs)
- Funding sources
- Meta-analysis methods
- Meta-analysis test of influence of risk of bias assessment from individual studies

- Risk of bias from individual studies discussed
- Heterogeneity
- Publication bias
- Review authors report conflicts of interest
- Relevance to overview questions

Although AMSTAR 2 was developed primarily to assess effectiveness reviews, it was considered appropriate for this overview because it covers observational as well as experimental studies. Further details on the AMSTAR 2 tool are provided in **Appendix 4**. Criteria ratings were assessed to determine whether more than one critical item was failed or not; and categories of quality utilised (i.e. critically low, low, medium and high), if and where appropriate. Two researchers independently quality-assessed each review and agreed ratings. Disagreements were resolved by a third researcher.

2.2.6 Data synthesis

The synthesis examined the characteristics of reviews, in order to understand their different aims, populations, types of energy drinks, consumption, reported effects on young people categorised into physical, mental, behavioural and educational/social domains, and review quality. Patterns of acquisition and use in children and young people, parental involvement and awareness, differences in intake between socio-economic groups and links with risk-taking behaviour are reported, where reviews examined these issues. Any findings supporting mechanisms of action, such as CED use resulting in interrupted sleep, are reported, where data from reviews of longitudinal studies permit. Findings are presented in tabular format and narratively synthesised.

2.2.7 Exploring bias

In order to consider the influence of ‘double-counting’ of studies across reviews, the overlap of included studies was determined and the corrected covered area (CCA) was calculated (Pieper et al. 2014). Publication bias by format (i.e. published versus unpublished) and by year was considered using assessment of the review characteristics table.

2.2.8 Strength of evidence

While applying GRADE criteria to overviews of reviews is not routine, it is recognised that this is in development and is good practice (Brennan et al. 2017). The strength of the evidence was considered in the synthesis stage of the overview. Reviewers met to consider and discuss the findings across reviews, overall risk of bias, indirectness or fit between review questions and our overview questions, and inconsistency, imprecision, and potential for publication bias.

2.2.9 Quality assurance

Ethics approval by UCL Institute of Education was sought and obtained. The review protocol was registered on PROSPERO (ID CRD42018096292). Review stages were managed using

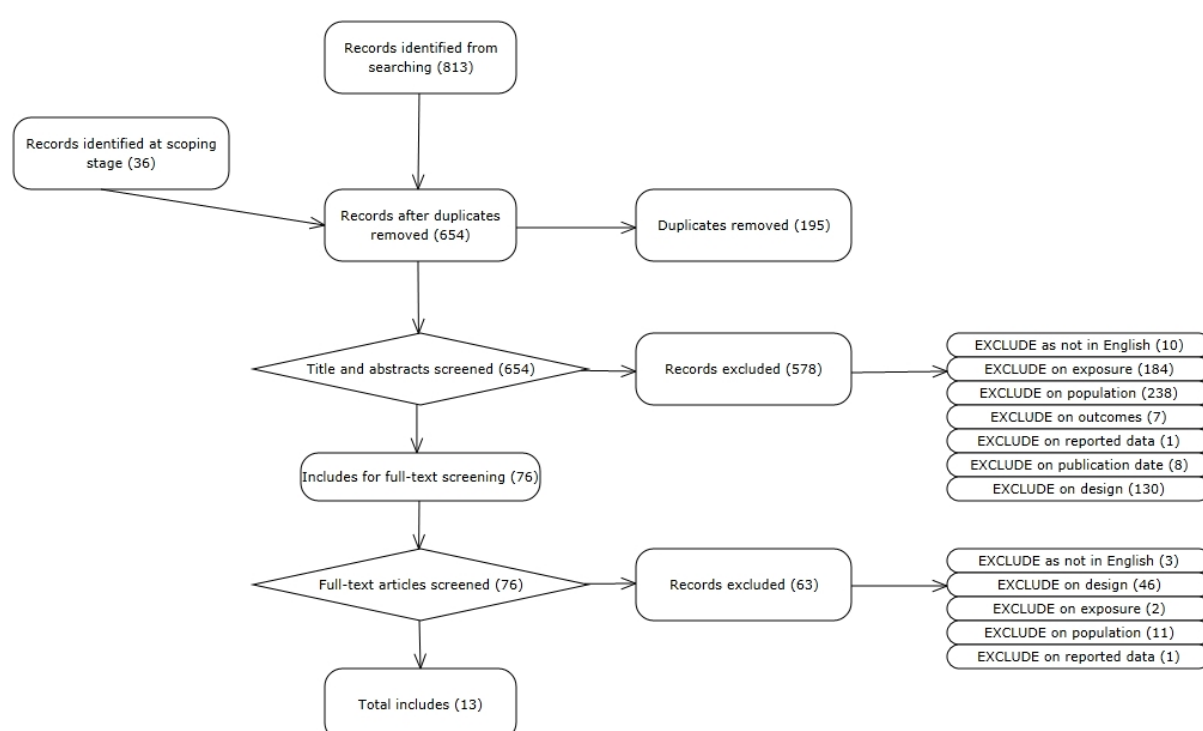
specialist software: located citations (titles and abstracts) were uploaded into EPPI-Reviewer (specialist systematic review software), for the management of publication retrieval, coding and synthesis (Thomas et al. 2010). Title and abstract screening was undertaken independently by four researchers following double screening of 20 citations to ensure consistency of each researcher in applying the eligibility criteria. Two members of the research team screened a subset of full-text papers using the inclusion/exclusion criteria until an inter-rater agreement of at least 90% was attained. This was followed by single-researcher screening. Disagreements or queries on inclusion were referred to a third researcher, as needed. A similar process was applied during data extraction, with a second researcher checking extracted data. Two members of the research team quality-assessed a common set of reviews and met to discuss them, to establish consistency. Once consistency was achieved, quality assessment of each review was undertaken by one researcher and checked by a second, with remaining disagreements in ratings resolved by a third researcher, where needed. Quality-assurance checks of data extraction and risk of bias assessment were conducted, using a random sample of included reviews.

3 Results

3.1 Flow of reviews through the overview process

The searches and preliminary scoping search for systematic reviews located 849 citations. After duplicates were removed, 654 citations were screened against our eligibility criteria. The screening identified 76 potentially relevant citations where full text was retrieved, and of these, 13 systematic reviews met inclusion criteria. The reference list of these reviews is provided in **Appendix 5**. The flow of literature is shown in Figure 3.1.

Figure 3.1 PRISMA diagram



Most citations were excluded because they did not report findings specific to children and young people (n=249), were not about CED intake (n=186) or were not systematic reviews (n=176). A list of studies excluded at full text is provided in **Appendix 6**.

3.2 Description of included reviews

The 13 included reviews were published between 2013 and 2018. Their populations and focus and area of interest are reported in Table 3.1 below.

Table 3.1 Reviews: population, focus and area of interest

Review	Focused on CED use	Focused on young people only	Reports prevalence	Reports effects
Dawodu and Cleaver (2017)	✓	✓	✓	✓
Visram et al. (2016)	✓	✓	✓	✓
Bleich and Vercammen (2018)	x	✓	x	✓
Verster et al. (2018a)	✓ (AmED)	x	✓	✓
Verster and Koenig (2018b)	x	x	✓	x
Roemer and Stockwell (2017)	✓ (AmED)	x	✓	✓
Alhyas et al. (2016)	✓	x	✓	✓
Lippi et al. (2016)	✓	x	x	✓
Richards and Smith (2016a)	✓	x	x	✓
Ali et al. (2015)	✓	x	x	✓
Bull et al. (2015)	✓	x	x	✓
Goldfarb et al. (2014)	✓	x	x	✓
Buck et al. (2013)	✓	x	x	✓

AmED - alcohol mixed with energy drinks

Their complete characteristics are shown in tabular format in **Appendix 7**. Structured summaries of each included review are found in **Appendix 8**.

Very few reviews were focused specifically on young people's use of CEDs; most either focused on a broader population range or a broader range of drinks. Only two reviews aimed to assess CEDs in particular, and specifically in young people (Dawodu and Cleaver 2017; Visram et al. 2016). Three reviews assessed young people only (Bleich and Vercammen 2018; Dawodu and Cleaver 2017; Visram et al. 2016), while all the other reviews included either young adults (n=2) or the whole population (n=8). Nine reviews focused on CEDs; two focused on alcohol mixed with energy drinks (Roemer and Stockwell 2017; Verster et al. 2018); one focused on sugar-sweetened beverages, of which CEDs were one type (Bleich and Vercammen 2018), and one focused on caffeine intake, which included CEDs (Verster and Koenig 2018).

Most reviews reported no funding conflicts or other conflicts of interest. Two reviews reported charity funding (Bleich and Vercammen 2018; Visram et al. 2016), two reported institutional funding (Bull et al. 2015; Roemer and Stockwell 2017), and two reported commercial funding (Verster et al. 2018, Verster and Koenig 2018; from Red Bull). The most recent search date was May 2017 (Bleich and Vercammen 2018), with the most comprehensive and relevant review (Visram et al. 2016) searching to April, 2016¹. These findings guided our decision to search for new primary research from 2016 onward (see Appendix 1 for more details). Five of the 13 reviews were published within the last two years. Three reviews were published in the current year (Bleich and Vercammen 2018;

¹ For this reason, the search to locate further primary studies included only studies from 2016 onwards.

Verster and Koenig 2018; Verster et al. 2018), and two were published in 2017 (Dawodu and Cleaver 2017; Roemer and Stockwell 2017). Reviews by Bleich and Vercammen (2018) and Verster et al. (2018) searched up until approximately early 2017. Visram et al. (2016) conducted the most comprehensive search for relevant studies. They searched nine academic databases and used Google and the OpenGrey repository. Of the other 12 included reviews, only Dawodu and Cleaver (2017) searched more than three databases.

These reviews included a total of 74 studies but most reviews (11 of 13) were not focused specifically on our questions of interest and contributed few relevant studies. The two more directly focused reviews contributed 11 studies (Dawodu and Cleaver 2017) and 46 studies (Visram et al. 2016)². Five reviews contributed case studies (Ali et al. 2015; Buck et al. 2013; Bull et al. 2015; Goldfarb et al. 2014; Lippi et al. 2016), while the remaining reviews contributed findings from mostly cross-sectional surveys. Two reviews also found intervention studies (Richards and Smith 2016a; Visram et al. 2016), and Visram et al. (2016) further reported the results of qualitative and mixed-method studies.

The age of the participants ranged from 2 to 24 years, with most reviews including people from 10 to 19 years. Gender was generally mixed or not reported in reviews. Single-gender research was rare: one all-female study (Aluqmany et al. 2013) was reported in Alhyas et al. (2016), and three all-male studies (Abian-Vicen et al. 2014; Faris et al. 2015; Peters et al. 2010) were reported across two reviews (Richards and Smith 2016a; Visram et al. 2016). Socio-economic status was not reported in any review, although it was used as a covariate in some studies reported in the review by Roemer and Stockwell (2017).

3.2.1 Relevant UK-based research

Out of the thirteen included reviews, four were UK-based (Bull et al. 2015; Dawodu et al. 2017; Richards and Smith 2016a; Visram et al. 2016). Four reviews included UK-based research (Bleich and Vercammen 2018; Richards and Smith 2016a; Visram et al. 2016; Verster and Koenig 2018). No reviews were focused solely on UK studies.

Bleich and Vercammen (2018) synthesised evidence about the impact of sugar-sweetened beverages on children's health, including caffeine-related effects. The review by Richards and Smith (2016a) examined the relationship between chronic energy drink use and mental health outcomes. Visram et al. (2016) examined energy drink consumption by young people, attitudes towards energy drinks, and associations with health, social, behavioural and educational outcomes. Verster and Koenig (2018) reviewed global evidence on the caffeine intake of children, adolescents and adults.

In total, only four reports of two UK studies were identified from reviews that focused on young people (Richards and Smith 2016b; EFSA NDA Panel 2015; Richards et al. 2015; Richards and Smith 2015). The three papers by Richards and colleagues reported findings from a single study conducted with young people (11 to 17 years old) who attended three secondary schools in the South West of England. This was a large longitudinal study

² One of the studies in Visram (Bunting) included a subgroup of people aged 16 to 21 years, which is mainly outside our age range.

collecting cross-sectional data at two time points, with data on self-assessed mental health collected at the second data collection point only (n=2,307). The EFSA (2015) study surveyed children and adolescents (3 to 18 years old) from 22 European countries, presenting findings specific to UK participants as a sub-group (i.e. 2.6% of the total sample). The findings for prevalence and effects from these UK studies will be reported separately under subsequent sections.

3.3 Quality assessment of included reviews

3.3.1 Risk of bias

Overall, the reviews included in this overview were rated as being of low or critically low quality, based on AMSTAR 2 criteria. Risk of bias ratings for each review are provided in **Appendix 9**. Eleven of the 13 systematic reviews were assessed as critically low in quality, which means that they had flaws in two or more critical domains. Reviews most often failed these domains because they: did not report protocol registration; did not report adequate searches; did not justify exclusions; did not assess risk of bias across included studies; failed to report analytic methods did not consider the risk of bias in their results; or did not report publication bias. Of those reviews rated as critically low, only one was fully relevant to our overview question (Dawodu and Cleaver 2017). The other two reviews were assessed as low quality (Bull et al. 2015; Visram et al. 2016). One of these was fully relevant to the overview questions (Visram et al. 2016). Both reviews had only one flaw in a critical domain, although they also had flaws in non-critical domains. Only one of these two (Visram et al. 2016) was also assessed as fully relevant to our review question.

None of the reviews reported their included studies' sources of funding. All reviews partly met the criteria for a comprehensive search strategy. Only two reviews conducted any meta-analysis, and only three reviews included RCTs. This meant that five of the AMSTAR 2 criteria did not apply to most reviews included in this overview. Three reviews referred to a protocol, but only one of these reported any deviations from the registered protocol (Bull et al. 2015). Visram et al. (2016) met the most quality criteria (10, plus two partly met), Bull et al. (2015) fully met only five of the criteria (four partly met) but was still rated as low quality. Ali et al. (2015) and Verster et al. (2018) met the fewest criteria (two), with two partly met.

Overall, the Visram et al. (2016) review was most relevant and highest in quality, although this was still low. This review identified 46 articles, including most of those in the other reviews (see overlap table). The review by Dawodu and Cleaver (2017) was relevant, but lower in quality, and the Bull et al. (2015) review was better in quality, but less relevant to our overview question. The remaining reviews contributed very little information from few included studies.

3.3.2 Overlap of included studies across reviews

Together, the thirteen reviews included seventy-six papers reporting seventy-four studies that contained participants under 18 years old. These are detailed in **Appendix 10**. A study was only included from a specific review if sufficient detail was provided in the paper for

the reader to determine that the sample comprised individuals of the relevant age. Two studies were excluded owing to a lack of age-disaggregated results. These were i) Jackson et al. (2013) (included in Dawodu and Cleaver 2017), ii) Walther et al. (2014) (included in Richards and Smith 2016a). A further paper by Franckle et al. (2015) (included in the review by Bleich and Vercammen 2018) was also excluded owing to a lack of detail about the findings related to CED consumption. Out of the 76 included papers, 26 (36%) were cited in multiple reviews. The extent of overlap was calculated using the Corrected Covered Area (CCA) formula (Pieper et al. 2014). This gave an overall value of 3.5%, which represents a ‘slight’ overlap between reviews³.

3.4 Prevalence

Summary

- Prevalence rates vary widely across studies conducted in several countries.
- A wide range of measures of CED use are reported.
- Between half and two thirds of all young people surveyed had tried CEDs at some point.
- Reviews reported between 10% and 36% of young people had never used alcohol mixed with energy drinks (AmEDs).
- Four reviews reported that males consume more frequently and more heavily.
- One review noted that females may start to consume CEDs slightly earlier than males.
- Conflicting findings were reported for higher use in Black, Hispanic and Aboriginal ethnic groups.
- Only two UK-based studies of CED prevalence were located.
- UK studies suggest that around 11% of surveyed young people consume CEDs on a daily basis; and that higher use is associated with being male and with lower socio-economic status.
- CED use was reported during exams, at parties, friends’ houses and family gatherings.
- Conflicting findings were reported for young people’s knowledge and critical awareness of CEDs.
- A wide range of motivations for CED use were reported, including taste, energy, curiosity, peer/family influences, parental (dis)approval.
- Young people’s reported motivations to use AmEDs included wanting to socialise/party, to suppress appetite, and to enhance sports performance.
- No reviews reported findings for parental knowledge or behaviours related to young people’s CED use.

³ CCA interpretation: 0-5% = slight; 6-10%= moderate; 11-15%= high; >15%= very high (Pieper et al. 2014)

Prevalence information relating to young people was provided in six included reviews (Alhyas et al. 2016; Dawodu and Cleaver 2017; Roemer and Stockwell 2017; Verster et al. 2018; Verster and Koenig 2018; Visram et al. 2016), each of which utilised cross-sectional surveys. Other designs were also included in some reviews, including secondary data analyses (Dawodu and Cleaver 2017; Verster and Koenig 2018; Visram et al. 2016), and longitudinal surveys, qualitative/mixed-methods studies, and intervention evaluations (Visram et al. 2016).

3.4.1 Reported frequency of use

Frequency of use was reported using a range of metrics across three of the six reviews (Alhyas et al. 2016; Dawodu and Cleaver 2017; Verster et al. 2018). Only one review combined findings statistically: a random-effects meta-analysis determined the overall prevalence of the consumption of CED amongst children and young people to be 65.3% (95% CI 41.6 to 102.3, four studies) (Alhyas et al. 2016).

One review (Dawodu and Cleaver 2017) reported the proportion of participants who consumed CEDs alone within the past year. This ranged from 13.3% to 62% in two studies (Azagba et al. 2014; Emond et al. 2014). Those who consumed once per month or more was reported at 20% from one study (Azagba et al. 2014).

More frequent use of CEDs also varied widely. Thirteen percent of participants from one study (Azagba et al. 2014) reported ‘recently’ consuming CEDs. One study reported 15% of participants consuming CEDs once per week (Larson et al. 2014). However, two studies from the Alhyas et al. (2016) review reported more frequent weekly use of CEDs: 56.3% of participants in one study (Musaiger and Zagzoog 2014) reporting drinking one or two CEDs per week. Al-Hazzaa et al. (2011) reported that 24.8% of participants drank CEDs three days per week; and Musaiger and Zagzoog (2014) noted that 26% drank more than five CEDs per week.

The reported percentage of respondents who had consumed alcohol mixed with energy drinks (AmED) in the past year or ever, ranged from 10% (Nowak and Jasionowski 2015) to 36% (Bonar et al. 2015). In another review (Verster et al. 2018), participants reporting AmED use in the past year ranged from 13% to 46.1% across three studies (Azagba et al. 2013; Azagba and Sharaf 2014; Flotta et al. 2014).

Overall, these values suggest a wide variation in how often and how much CED use is reported by young people.

3.4.2 Reported CED dosage or type

Only two reviews reported the type of CED and its caffeine content (Verster et al. 2018; Verster and Koenig 2018); both were funded by the manufacturer (Red Bull). The caffeine dosages of CEDs were reported in diverse ways. For example, one review (Verster and Koenig 2018) reported the percentage of daily caffeine intake arising from energy drinks. This ranged from 0.6% in Germany in 2010/2011 (Lachenmeier et al. 2013), through 2% for 5 to 12 years, and 3% for 13 to 15 years, in New Zealand (Ministry of Health 2003), 5% in the USA (13 to 17 years, Mitchell et al. 2014), 5.3% in Belgium (EFSA NDA Panel 2015), 6% in the USA (2 to 22 years, Branum et al. 2014) and Australia (Galaxy Poll 2013), 8.1% in the Netherlands

(EFSA NDA Panel 2015), up to 11% in the UK (EFSA NDA Panel 2015; Zucconi et al. 2013). One survey reported that 69% of caffeine was from drinks, but only 3% of these drinks were energy drinks (Beckford et al. 2015), while another reported that 13% of caffeine was from energy drinks, in CED drinkers aged 10 to 18 years, and 42% in ED drinkers aged 3 to 10 years (Zucconi et al. 2013). The amount consumed ranged from 0.18mg/kg of body weight/day (3 to 10 years; Zucconi et al. 2013), through 0.26mg/kg body weight/day (10 to 18 years; Zucconi et al. 2013) to 18mg/day (2 to 16 years; Beckford et al. 2015).

3.4.3 CED use by age, gender and ethnicity

Two reviews (Verster et al. 2018; Visram et al. 2016) reported mixed results for prevalence by age. In Verster et al. (2018), the authors reported on one study which found that CED consumers were more likely to be younger (Azagba et al. 2013), but another found no such association (Flotta et al. 2014). The authors of another review reported that age was a predictor of use, but the direction of the effect varied by study (Visram et al. 2016). One review (Alhyas et al. 2016) reported that males started drinking CED at 17.1 (SD 1.2) years, while females started slightly younger at 16.7 (SD 1.3) years. Eight studies included in this review found that older children drank more CEDs (Azagba et al. 2013; Emond et al. 2014; Faris et al. 2015; Gallimberti et al. 2013; Gallimberti et al. 2015; Kumar et al. 2014; Magnezi et al. 2015; Richards and Smith 2016b), while four studies reported that younger children drank more (Arria et al. 2014; Azagba et al. 2014; Nowak and Jasionowski 2015; Terry-McElrath et al. 2014). One study found that consumption peaked at age 14 to 15 years (Gambon et al. 2011), and another study found that more females were younger, but more males were older (Reid et al. 2015). Nowak and Jasionowski (2015) also reported that although drinkers of EDs were younger, those who mixed it with alcohol were more likely to be older. Two of the studies that found that more drinkers were older focussed specifically on AmED (Azagba et al. 2013; Magnezi et al. 2015), with age ranges of 12 to 18 and 14 to 18 years. The four studies that found that more drinkers were younger had age ranges of 12 to 18, 12 to 20, and 13 to 18 (two studies) years. Those studies that did not assess AmED, and found that more drinkers were older, had more varied ranges; 10 to 16, 11 to 13, 11 to 16, 12 to 17, 12 to 18, and 15 to 23 years. The measures of prevalence (ever drank, drank in last year, regularly drink, etc.) also varied, where reported.

Prevalence differences by gender were more consistent. Five reviews (one low quality) found that males drank more than females (Alhyas et al. 2016; Dawodu and Cleaver 2017; Roemer and Stockwell 2017; Verster et al. 2018; Visram et al. 2016). The remaining review (Verster and Koenig 2018) did not report gender differences.

Findings from some reviews suggested a relationship between CED use and ethnicity, but these contradicted each other. One review (Verster et al. 2018) reported that in two studies (Azagba et al. 2013; Martz et al. 2015) AmED consumers were more likely to be Black or Hispanic/Other ethnicity. Another review, which was rated low-quality (Visram et al. 2016), included these two studies plus three more (Park et al. 2012; Reid et al. 2015⁴; Schwartz et

⁴ The study by Reid is included in Verster 2018a, but they did not report the age range

al. 2015). Visram et al. (2016) reported that Martz et al. (2015) found that Black students were less likely to consume EDs than White or Hispanic students, while the other studies all found that Black or Aboriginal students were more likely to drink EDs⁵. The remaining reviews did not report ethnic differences.

3.4.4 UK-based research on CED prevalence

The findings from one study, of UK participants, suggest frequent but low prevalence of CED use. An analysis conducted by EFSA NDA Panel (2015) of survey data from 22 European countries found that energy drinks contributed 11% of the daily caffeine intake of UK adolescents (10-17 years old). This was reported to be the highest proportion amongst all of the surveyed European countries (EFSA NDA Panel 2015).

Findings from one UK-based study suggest variations in CED use. The paper by Richards and Smith (2016a) identified significant associations between consuming energy drinks once a week or more and students being male, older, eligible for free school meals and having special educational needs (Visram et al. 2016). No other findings were located specific to ethnicity or age for UK populations.

3.4.5 Context of CED use

One review mentioned exams as a context for CED use (Alhyas et al. 2016). Findings from one study in this review reported that 38.9% of school students consumed CEDs during exams (Almalak et al. 2014).

Other reviews reported a range of contexts in which mixing CEDs with alcoholic beverages took place. Two studies from one review (Verster et al. 2018) noted that 36.9% rated it as important/very important to consume AmEDs ‘to celebrate/party’, 27.3% ‘to socialise’ (Flotta et al. 2014); and 10.4% reported consuming AmEDs for ‘social reasons’ (Magnezi et al. 2015). These findings are supported by the one systematic review that reported specific findings about the circumstances in which young people consumed CEDs. Visram et al. (2016) noted that consumption of AmEDs in 15 to 17 year-olds takes place at parties, friends’ houses, and at family gatherings (Jones 2011). No evidence was located which reported parental purchasing of CEDs for child consumption, nor their awareness of the purpose, composition or effects of CEDs.

Two reviews suggested a link between CED use and alcohol or other substance use, although little evidence asking participants directly was provided. For example, Dawodu and Cleaver (2017) examined the relationship between substance use (i.e. alcohol, drugs, or cigarettes) and CEDs, reporting a statistically significant positive association from eight included studies (Azagba et al. 2014; Emond et al. 2014; Evren and Evren 2015; Gallimberti et al. 2013; Hamilton et al. 2013; Larson et al. 2014; Miyake and Marmorstein 2015; Terry-McElrath et al. 2014).

⁵ Martz reported that Black students were less likely to consume AmEDs.

3.4.6 Motivations

Young people's motivations for consuming energy drinks were explored across three reviews (Alhyas et al. 2016; Verster et al. 2018; Visram et al. 2016). These identified a variety of reasons.

Taste was noted as a major motivation for consuming CEDs, arising from five studies (Bunting et al. 2013; Flotta et al. 2014; Magnezi et al. 2015; Musaiger and Zagzoog 2014; O'Dea 2003) across all three reviews. However, the proportion of participants who rated this highly ranged from 21.0% to 58.4%, where values were reported. Over three-quarters of participants (80.6%) reported using AmEDs to improve the taste of alcohol (Magnezi et al. 2015).

This was followed by an identified desire for **energy**, reported in five included studies (Aluqmany et al. 2013; Bunting et al. 2013; Magnezi et al. 2015; Musaiger and Zagzoog 2014; O'Dea 2003) across all three reviews. Reported values ranged from 11.0% (Magnezi et al. 2015) to 43% (Musaiger and Zagzoog 2014) of participants across studies.

Curiosity was also identified in two reviews (Alhyas et al. 2016; Verster et al. 2018), but to differing degrees. One included study reported 51.8% of respondents citing curiosity as a reason (Musaiger and Zagzoog 2014). In another industry-funded review examining AmED, one included study reported only 14.6% using AmED because of curiosity (Magnezi et al. 2015).

Some reviews reported contradictory findings concerning participant motivations. For example, one study in Alhyas et al. (2016) noted **peer/family influence** as a reason (71.8 - 90.9% of family members or friends consumed CEDs) (Al-Hazaa et al. 2011). However, participants in one study identified in Verster et al. (2018) noted that 48.1% of participants rated as 'not important' that 'everyone else is doing it' when using alcohol mixed with energy drinks (Flotta et al. 2014). This difference may be attributable to industry funding in the Verster et al. (2018) study and its focus on AmEDs. Another study reported in Visram et al. (2016) noted that **parental approval/disapproval** influenced their intake of CEDs (Costa et al. 2014) but did not provide data.

Verster et al. (2018) identified that in one study (Flotta et al. 2014), just over one third of participants (36.9%) rated using AmEDs '**to celebrate or party**' as 'important' or 'very important'; while about one quarter of participants similarly rated using AmEDs '**to socialise**' (27.3%). Another study from this review noted that 10.4% of Israelis aged 14 to 18 years reported AmED consumption for social reasons (Magnezi et al. 2015). The authors of this review also reported that just over half of participants in one study did not consider 'to get work done' (53.5%) an important reason for drinking AmED, and just under half rated as 'not important' that it was 'cheap' (48.7%) or to 'be comfortable with the opposite sex' (48.5%) (Flotta et al. 2014). One quarter of participants in another included study reported using AmEDs to 'feel drunk' (24.6%) (Magnezi et al. 2015). In this study, fewer participants cited other reasons, including to drink more alcohol (11.7%), and to reduce alcohol side-effects (8.4%) (Magnezi et al. 2015).

Two reviews noted differences in motivation by gender. One study (Bryant Ludden and Wolfson 2010) identified in Visram et al. (2016) noted that more girls than boys chose energy

drinks because they expected them to **suppress their appetite**. In another study, the authors noted that males were more likely than females to take EDs to **help with their sports performance** (O'Dea 2003). One study in Alhyas et al. (2016) (Musaiger and Zagzoog 2014) noted 'significant differences' in motivation by gender ($p < 0.001$) for taste, curiosity, and energy, but did not provide further data.

3.4.7 Knowledge and beliefs

Conflicting findings were noted across three reviews related to young people's knowledge and beliefs concerning CEDs (Alhyas et al. 2016; Dawodu and Cleaver 2017; Visram et al. 2016). Alhyas et al. (2016) and Visram et al. (2016) reported that young people had limited knowledge of the active ingredients of energy drinks, based on findings from three studies. One of these reported that 69.9% did not know the active ingredients of CED (Aluqmany et al. 2013); another noted that around half of male and female respondents did not know CED ingredients (47% male v. 52.3% female); and similar proportions knew that CEDs contained caffeine (53.2% of males, and 48.3% of females) (Musaiger and Zagzoog 2014). Visram et al. (2016) reported findings from one qualitative study which suggested that young people had limited knowledge of CED ingredients or limited ability to differentiate CEDs from other types of beverages (Costa et al. 2014). However, participants in a study by Gallimberti et al. (2013) reported in Dawodu and Cleaver (2017) noted that young people who were aware of the potential damage that could result from CEDs consumed them less. These findings suggest limited knowledge about CED content and conflicting information about the level of young people's critical awareness regarding their safety.

3.5 Reported CED effects

Summary

- Physical and behavioural effects of CED consumption were most commonly reported across 12 included reviews.
- The consumption of CEDs has been associated with a number of physical symptoms including headaches, stomach aches and low appetite.
- Research has also identified an association between CED consumption and various sleep-related issues.
- Reviews of case reports have described individuals experiencing adverse physical effects, (most notably cardiovascular events), following CED consumption.
- Multiple studies have reported a relationship between CED consumption and a range of lifestyle behaviours, particularly alcohol use, smoking and illicit drug use.
- Mixing alcohol with CEDs has also been linked to risky health-related behaviours and self-reported injuries.
- Heightened sensation seeking has been linked to CED consumption in several studies.
- Included reviews also reported some evidence of a relationship between CED use and impulsivity, hyperactivity and behavioural disorders.

- Conflicting evidence was identified on the relationship between CED consumption and mental health issues such as anxiety and depression. Two studies reported an association between CED consumption and self-harm or suicide related behaviour.
- There is some evidence that suggests a negative relationship between CED consumption and academic attendance and achievement. However overall, there is a lack of studies which have examined the relationship between CED use and educational or other social outcomes.
- Included reviews reported only very limited results on the effects of CEDs disaggregated by gender, ethnicity or socio-economic status.

In total, 12 out of the 13 reviews reported findings on the effects of CED in children and young people (Alhyas et al. 2016; Ali et al. 2015; Bleich and Vercammen 2018; Bull et al. 2015; Buck et al. 2013; Dawodu and Cleaver 2017; Goldfarb et al. 2014; Lippi et al. 2016; Richards and Smith 2016a; Roemer and Stockwell 2017; Verster et al. 2018; Visram et al. 2016). These were categorised into four domains: physical, behavioural, mental health and educational/social effects.

Physical effects of CED consumption, such as headaches, tiredness and problems sleeping, were reported in 11 reviews (Alhyas et al. 2016; Ali et al. 2015; Bleich and Vercammen 2018; Bull et al. 2015; Buck et al. 2013; Dawodu and Cleaver 2017; Goldfarb et al. 2014; Lippi et al. 2016; Roemer and Stockwell 2017; Verster et al. 2018; Visram et al. 2016). **Behavioural effects**, including risky lifestyle behaviours, behavioural disorders and accidental injuries were reported in five reviews (Bleich and Vercammen 2018; Dawodu and Cleaver 2017; Roemer and Stockwell 2017; Verster et al. 2018; Visram et al. 2016). Six reviews reported effects related to **mental health and mental functioning**, for example common mental health conditions (anxiety and depression), self-harm, along with other aspects of psychological well-being and executive function (Alhyas et al. 2016; Bleich and Vercammen 2018; Dawodu and Cleaver 2017; Richards and Smith 2016a; Verster et al. 2018; Visram et al. 2016). Finally, only two reviews reported **educational/social effects**, including academic attainment and school attendance (Verster et al. 2018; Visram et al. 2016).

The included studies in the twelve reviews reporting effects were predominantly cross-sectional surveys (n=7) and secondary data analyses (Alhyas et al. 2016; Bleich and Vercammen 2018; Dawodu and Cleaver 2017; Richards and Smith 2016a; Roemer and Stockwell 2017; Verster et al. 2018; Visram et al. 2016). Six of the included studies were longitudinal surveys (Choi et al. 2016; Martz et al. 2015; Miyake and Marmorstein 2015; Marmorstein 2016; Richards and Smith 2016b; Tucker et al. 2016). Four were experimental studies (Abian-Vicen et al. 2014; Gallo-Salazar et al. 2015; Temple et al. 2010; Wing et al. 2015), which were included across three reviews (Bleich and Vercammen 2018; Verster et al. 2018; Visram et al. 2016). Five of the reviews also reported findings from case reports (Ali et al. 2015; Buck et al. 2013; Bull et al. 2015; Goldfarb et al. 2014; Lippi et al. 2016). Specific findings from each of the four categories of effects follow.

3.5.1 *Physical effects*

Two reviews (Bleich and Vercammen 2018; Visram et al. 2016) identified consistent evidence, from four cross-sectional surveys, of a relationship between CED consumption and

physical symptoms, including headaches, stomach aches and low appetite (Bashir et al. 2016; Huhtinen et al. 2013; Koivusilta et al. 2016; Kristjansson et al. 2014). Visram et al. (2016) further reported findings from an experimental study which found dose dependent increases in diastolic blood pressure and decreases in heart rate following consumption of drinks containing varying amounts of caffeine (Temple et al. 2010).

The relationship between sleep-related issues and CED consumption was examined in three included reviews (Bleich and Vercammen 2018; Dawodu and Cleaver 2017; Visram et al. 2016). Multiple cross-sectional surveys reported an association between CED consumption and problems sleeping, tiredness/fatigue, and sleep dissatisfaction (Faris et al. 2015; Huhtinen et al. 2013; Koivusilta et al. 2016; Kristjansson et al. 2014; Park et al. 2016; Richards and Smith 2016b; Van Batenburg-Eddes et al. 2014). One US study of young people in Grades 6 to 12, reported by Dawodu and Cleaver (2017), found no significant association between CED consumption and sleep duration (Larson et al. 2014).

Evidence from one study, reported by Visram et al. (2016), indicated that the relationship between CED use and some physical health symptoms, such as headaches, stomach aches and sleeping difficulties, was partly mediated through young people going to bed late (Koivusilta et al. 2016).

Gender, ethnicity, socio-economic status and physical effects

One review reported physical effects of CEDs by gender, ethnicity or socio-economic status. Visram et al. (2016) outlined findings from a gender-based analysis of the relationship between physical symptoms and CED consumption. For both boys and girls, symptom prevalence generally increased with greater consumption of CEDs. However, there was also evidence suggesting that some physical symptoms (such as headaches, stomach aches and sleeping problems) may be more common in girls than boys (Kristjansson et al. 2014).

Two studies, comprising single-sex samples of school students, reported differing physical effects. For example, Alhyas et al. (2016) reported findings from one cross-sectional survey, conducted in Saudi Arabia, with 600 female secondary-school students. Analysis revealed that 60% of the students who consumed CEDs felt they became more energetic. Twenty-nine percent of the students also reported that they had experienced menstrual changes or an alteration in voice tone. Just over one quarter (28%) of the young women who consumed CEDs had tried to stop, and over a third of them (35%) reported experiencing withdrawal symptoms (Aluqmany et al. 2013). Visram et al. (2016) included another study from Saudi Arabia that was conducted with approximately 1,000 boys aged 12 to 18 years old (Faris et al. 2015). Results showed that 24% of CED users experienced a reduction in sleeping hours, 19% changes in cardiac activity, and 17% reported becoming 'energised'.

Quantity of CEDs and physical effects

Evidence from reviews of case reports indicated that CED consumption can have negative effects on cardiovascular function, in particular. In total, five reviews (Ali et al. 2015; Buck et al. 2013; Bull et al. 2015; Goldfarb et al. 2014; Lippi et al. 2016) included nine case reports detailing the physical health consequences associated with the consumption of CEDs in individuals under 18 years old (Di Rocco et al. 2011, two cases; Dufendach et al. 2012; Izquierdo Fos et al. 2012; Polat et al. 2013; Schöffl et al. 2011; Terlizzi et al. 2008; Usman

and Jawaid 2012; Wilson et al. 2012). Seven of the nine cases involved young males between the ages of 13 and 17 years old.

In eight of the nine case reports, a range of adverse cardiovascular events was reported, which followed consumption of CEDs in different quantities and over varying time periods. Goldfarb et al. (2014) reviewed one report of the cases of two males aged 14 and 16 years old, who experienced atrial fibrillation shortly after consuming an unknown quantity of energy drink, and one individual had also co-ingested vodka. One of the cases (14 years old) experienced similar symptoms five days previously, following the consumption of a Red Bull energy drink (this report was also included in the reviews by Ali et al. 2015 and Buck et al. 2013). Lippi et al. (2016) included a report of the case of a 13-year old male who suffered an ST-elevation myocardial infarction (STEMI) associated with spontaneous coronary artery dissection, after consuming an energy drink for the first time during the previous night.

In several cases, adverse health effects followed excessive consumption of CEDs. Lippi et al. (2016) along with two other reviews (Ali et al. 2015; Goldfarb et al. 2014) detailed the experience of another male (17 years old) who experienced myocardial ischemia/coronary artery vasospasm shortly after consuming many CEDs (5 to 7 cans). No associated acute triggers for myocardial ischemia other than energy drinks could be identified in either of the case studies reported by Lippi et al. (2016).

Another case involved a young male who experienced renal effects after mixing CEDs and alcohol. Bull et al. (2015) reported the case of a 17-year-old who suffered renal failure after consuming a very large quantity of energy drink in combination with vodka, equating to 780mg caffeine, 4,600mg taurine, and 380g alcohol. It was reported that the combined effect of the caffeine and taurine reduced the impact of the alcohol.

Longer-term consumption of CEDs has also been linked to individuals experiencing adverse cardiovascular events. Ali et al. (2015) described the case of a South Asian boy, aged 16 years, who experienced intermittent palpitations after consuming three cans of energy drink per day for two weeks. Another case, reported by both Ali et al. (2015) and Goldfarb et al. (2014), involved a 13-year-old boy who experienced atrial fibrillation. He was described as having a history of 'chronic' energy drink consumption and had experienced two previous episodes of similar symptoms. Furthermore, two reviews (Buck et al. 2013; Goldfarb et al. 2014) described the experience of a 13-year-old female, who suffered palpitations, chest pain, tremors and dizziness after consumption of a large amount of an energy drink every other day for two weeks. She was subsequently diagnosed with long QT syndrome, after testing identified a genetic mutation. Finally, the case of a 16-year-old female who had experienced orthostatic intolerance for three months was included in the Buck et al. (2013) review. She consumed four to five cans of energy drink (Red Bull) prior to developing symptoms. After one week of not consuming energy drinks, her symptoms resolved.

3.5.2 Behavioural effects

Three reviews presented findings on the relationship between the consumption of CEDs by young people and a range of health-related behaviours (Bleich and Vercammen 2018; Dawodu and Cleaver 2017; Visram et al. 2016). Most studies suggested that CED consumption was related to substance use. In particular, multiple cross-sectional surveys found consistent

evidence of a positive relationship between CED consumption and alcohol use, smoking, and use of other substances (Azagba and Sharaf 2014; Cotter et al. 2013; Emond et al. 2014; Evren and Evren 2015; Gallimberti et al. 2013; Gambon et al. 2011; Hamilton et al. 2013; Ilie et al. 2015; Larson et al. 2014; Locatelli et al. 2012; Nowak and Jasionowski 2015; Terry-McElrath et al. 2014). Visram et al. (2016) further reported findings from two longitudinal surveys showing that CED use at baseline predicted either the number of drinking days or the frequency of alcohol consumption at follow-up (Choi et al. 2016; Miyake and Marmorstein 2015).

The reviews by Dawodu and Cleaver (2017) and Visram et al. (2016) included research by Terry-McElrath et al. (2014), which was conducted with secondary-school students in the USA. Dawodu and Cleaver (2017) reported that the associations, identified in the study, between CED consumption and past 30-day alcohol, smoking and use of illicit drugs, were found to be significantly stronger than the associations between substance use and regular or diet soft drinks.

Three reviews identified significant relationships between CED use and behaviour disorders. Bleich and Vercammen (2018) included a North American longitudinal study that found evidence of a relationship between caffeinated CED use and attention deficit/hyperactivity disorder, inattention and hyperactivity (Marmorstein 2016). Both Dawodu and Cleaver (2017) and Visram et al. (2016) also identified cross-sectional evidence of an independent association between CED usage and risk of hyperactivity/inattention, which remained after the analysis was adjusted for several potential confounders (Schwartz et al. 2015). Impulsivity was also found to be associated with an increased likelihood of CED consumption in one study (Evren and Evren 2015) included in the review by Dawodu and Cleaver (2017). The links between hyperactivity, other adverse health outcomes (including the physical symptoms detailed in the previous section) and CED consumption are also supported by several retrospective analyses of poison-centre data, included in the review by Visram et al. (2016) (Gunja and Brown 2012; Hernandez et al. 2009; Seifert et al. 2011; Seifert et al. 2013).

Sensation seeking is another aspect of behaviour linked to CED use in several included reviews. The relationship between sensation seeking and CED consumption was examined in studies reported in reviews by Bleich and Vercammen (2018), Dawodu and Cleaver (2017) and Visram et al. (2016). Evidence from several cross-sectional studies, across the three reviews, demonstrated a relationship between heightened sensation seeking and CED use (Azagba et al. 2014; Emond et al. 2014; Evren and Evren 2015; Hamilton et al. 2013). One longitudinal study, included by Visram et al. (2016), found a significant association between baseline levels of sensation seeking and frequency of CED use (Miyake and Marmorstein 2015).

Mixing alcohol and CED use and behavioural effects

Mixing alcohol with CEDs (AmEDs) has been associated with some risky lifestyle behaviours in young people. Two reviews (Verster et al. 2018; Visram et al. 2016), that included studies examining AmED consumption amongst individuals under 18 years old, reported significant associations with binge drinking, smoking, use of other illicit substances, delinquent behaviour, and an increased number of sexual partners (Azagba et al. 2013; Azagba and

Sharaf 2014; Flotta et al. 2014; Martz et al. 2015; Tucker et al. 2016). However, Verster et al. (2018) reported that Flotta et al. (2014) found no significant association with binge drinking.

Cross-sectional evidence has demonstrated a link between AmED use and various types of injury. One study, identified by two reviews (Roemer and Stockwell 2017; Visram et al. 2016), reported an association between the consumption of AmEDs and recent traumatic brain injury (Ilie et al. 2015). Roemer and Stockwell (2017) further reported results from another study, which identified relationships between AmED use and alcohol-related injury, and injuries requiring a doctor (Kponee et al. 2014). Both Dawodu and Cleaver (2017) and Visram et al. (2016) also reported evidence of a link between using CEDs without alcohol and self-reported medical treatment for an injury (Hamilton et al. 2013).

There is some evidence that AmED use can have a negative impact on individuals' driving behaviour. One study included in reviews by Roemer and Stockwell (2017), Verster et al. (2018) and Visram et al. (2016) demonstrated an association between AmED consumption and alcohol-related unsafe driving, and an increased risk of motor vehicle accidents, following alcohol use, after controlling for other variables (Martz et al. 2015).

Some positive aspects of CEDs and behaviour were reported. Visram et al. (2016) identified two RCTs that found positive effects of CEDs on some aspects of sports performance (Abian-Vicen et al. 2014; Gallo-Salazar et al. 2015).

Gender, ethnicity, socio-economic status and behavioural effects

Findings on the behavioural effects of CEDs, disaggregated by gender, ethnicity or socio-economic status, were rarely reported, and no evidence of differences was found. In terms of gender and ethnicity, associations between CED consumption and several health-related behaviours, including smoking, alcohol use, low physical activity and unsafe driving behaviour, were identified in a sample of boys aged 12 to 18 years, from Saudi Arabia (Faris et al. 2015). Furthermore, both Dawodu and Cleaver (2017) and Visram et al. (2016) reported findings from a retrospective review of data from the Ontario Student Drug Use and Health Survey (Hamilton et al. 2013). This found a strong association between CED consumption and lifestyle behaviours, including alcohol use, smoking and illicit drug use. Notably, the gender of participants was found to not be a significant moderator of the associations identified.

3.5.3 Mental and psychological health

Six reviews included 11 papers from 10 studies on the mental health effects of CED use (Aluqmany et al. 2013; Azagba et al. 2014; Evren and Evren 2015; Marmorstein 2016; Park et al. 2016; Peters et al. 2010; Richards and Smith 2015; Richards and Smith 2016b; Tucker et al. 2016; Vilija and Romualdas 2014; Wing et al. 2015).

Overall, mixed evidence on the relationships between CED consumption and stress, anxiety, and depression was identified. For example, associations between CED use and stress, anxiety or depression were reported in four reviews (Bleich and Vercammen 2018; Dawodu and Cleaver 2017; Richards and Smith 2016a; Visram et al. 2016). These findings came from three cross-sectional surveys (Azagba and Sharaf 2014; Evren and Evren 2015; Park et al.

2016). However, Richards and Smith (2016a) also reported that the association between anxiety, depression and CED consumption identified by Evren and Evren (2015) became non-significant when a multivariate analysis of the data was conducted. Furthermore, other cross-sectional/longitudinal surveys have found no association between caffeine from CED consumption alone and depression, panic, stress or anxiety (Marmorstein 2016; Richards and Smith 2015; Richards and Smith 2016b).

Limited evidence from two reviews suggested a relationship between self-harm or suicide-related behaviour and CED consumption. Both Richards and Smith (2016a) and Visram et al. (2016) identified findings from a multivariate analysis of positive associations between CED use and self-harm and suicidal thoughts in a sample of 15- to 16-year-olds from Turkey (Evren and Evren 2015). Another study, included by Bleich and Vercammen (2018), found associations between the consumption of CEDs and suicidal ideation, planning and attempt, in a nationally representative sample of Korean adolescents (12- to 18-year-olds) (Park et al. 2016).

In addition to findings related to common mental health conditions and self-harm/suicide, a small amount of evidence was identified suggesting the existence of a relationship between post-traumatic stress disorder (PTSD) and CED consumption. Both Richards and Smith (2016a) and Visram et al. (2016) reported findings from one study, which identified a positive correlation between frequency of CED consumption and PTSD symptoms, even after controlling for several variables (gender, index trauma, physical activity, smoking, and sense of coherence). However, positive associations were also found between PTSD symptoms and other food products, including flavoured milk, coffee, and fast food. The analysis may also have been confounded by grouping CEDs with sports drinks (Vilija and Romualdas 2014).

The findings from one randomised controlled trial (Wing et al. 2015) were seen to suggest a link between CED use and mental health and behavioural issues. This sleep-focused RCT from Hong Kong, reported by Richards and Smith (2016a), found improvements in the intervention group relative to the controls, around mental health status, total difficulty, conduct problems, and hyperactivity. Notably, the intervention group was significantly less likely to consume CEDs three times per week or more, compared with the control group. Richards and Smith stated that it was not possible to tell from the data reported whether this difference in CED consumption was associated with the improvements in mental health identified, but they considered it plausible.

CED use has also been linked to other psychological states and poorer mental functioning. Across four reviews (Bleich and Vercammen 2018; Dawodu and Cleaver 2017; Richards and Smith 2016a; Visram et al. (2016), evidence from cross-sectional research demonstrated an association between CED consumption and greater irritation, and anger (Evren and Evren 2015; Huhtinen et al. 2013; Koivusilta et al. 2016). Furthermore, another cross-sectional study identified by Dawodu and Cleaver (2017) and Visram et al. (2016) found greater problems with executive functioning, including metacognition and behaviour regulation, in 11- to 16-year-olds who consumed an average of one or more CEDs per day (Van Batenburg-Eddes et al. 2014).

Gender, ethnicity, socio-economic status and mental health

Two reviews reported results from studies comprising single-sex samples. The study by Aluqmany et al. (2013), included in the review by Alhyas et al. (2016), found that 22% of the female students who consumed CEDs felt that they had experienced mood changes. Richards and Smith (2016a) included a study by Peters et al. (2010) who found no significant association between 30-day prior use of CEDs and PTSD symptoms in a sample of 170 low-income African American/Latino males. No evidence was identified on the relationships between CED use, mental health and socio-economic status.

Mixing alcohol with CED use and mental health

The review by Verster et al. (2018) cited evidence from one US study, which found no significant differences in the mental health of high-school students who consumed CEDs mixed with alcohol (AmED) when compared with non AmED-drinking students (Tucker et al. 2016).

3.5.4 Educational/social effects

Across the 12 reviews, few studies were identified that examined the relationship between CED use and educational or social effects. However, there was some evidence to suggest that consumption of CEDs may be associated with negative impacts. Visram et al. (2016) detailed one longitudinal UK study that found an association between consuming CEDs once a week or more, and poorer school attendance, amongst secondary-school students (Richards and Smith 2016b). It was also reported that students with higher academic averages (70% or more) were less likely to consume CEDs (Azagba et al. 2013). Verster et al. (2018) reported evidence from three studies of an association between AmED consumption and lower grades, and school absence (Azagba et al. 2013; Tucker et al. 2016; Martz et al. 2015).

3.5.5 Effects in UK samples

Associations between CED use and effects in UK samples are less clear. Richards and Smith (2015) found no significant association between caffeine intake from energy drinks and stress, anxiety, or depression (Richards and Smith 2016a). A subsequent analysis reported by Visram et al. (2016) found that high stress levels were associated with being a member of a frequent energy drink/infrequent breakfast grouping. However, a regression analysis also revealed that energy drink consumption alone did not predict stress, anxiety or depression at six-month follow-up (Richards and Smith 2016b). Analyses further revealed that those secondary-school students who drank energy drinks once a week or more were found to sleep fewer hours per night, have poorer school attendance and have a higher 'junk food' score (Richards and Smith 2016b). Richards et al. (2015) found a positive association between energy drink use and low general health in students (n=2,030). However, this analysis was based on the combined consumption of energy drinks, cola and chewing gum; the effects of energy drinks were not reported separately (Richards and Smith 2016a).

4 Discussion and conclusions

This overview of systematic reviews sought to answer two specific research questions (RQ):

(RQ1) What is the nature and extent of CED consumption amongst young people aged 17 years or under in the UK?

Across six reviews, prevalence rates of CED consumption in young people varied widely. Different consumption measures were used in the studies, which impacts on the ability to interpret the findings, including consistency. Overall, reviews report that between half and two thirds of all young people surveyed have tried CEDs at some point; and up to nearly one third report either frequent or heavy use. Findings reporting the prevalence of alcohol mixed with energy drink (AmED) use ranges more widely, from 10% to 69% of young people. These findings suggest that a potentially large proportion of young people are exceeding recommended daily caffeine intake (EFSA NDA Panel 2015; NHS Digital 2017).

There is limited evidence to suggest that different groups have different levels of CED consumption. Across reviews, differing prevalence rates by age group were reported, with an increasing pattern of use emerging in older age groups most often reported. Consistent findings for a gender difference were found across several reviews, suggesting that males may have more frequent or heavier use of CEDs. However, some reviews reported that females may start consuming CEDs at a younger age than males. Conflicting findings were reported for ethnic variations in use, as reviews reported both higher and lower CED use amongst Black youth in comparison to Hispanic and Aboriginal ethnic groups, or in comparison to White participants.

In considering the prevalence of CED use, it is important to understand the ‘context’ or situations in which young people consume CEDs, their reasons for doing so, and their knowledge of the drink and its effects. However, very limited data were available, with one review reporting exams as one context of CED use in young people, citing one study. More data were available about the context of AmED use were reported, which included parties, friends’ houses and family gatherings. A wide range of motivations for CED use were also described, including taste, energy, curiosity, peer/family influence, parental (dis)approval, to socialise/party, to suppress appetite, and to enhance sports performance. Young people’s reported motivations for AmED use were similar to those for CED use. AmED use was linked to wanting to socialise/party, to drink more alcohol and to reduce alcohol side effects. Findings also suggest that young people have limited knowledge of CED ingredients and report conflicting findings regarding their critical awareness of the safety of CEDs. However, no evidence was located which reported parental purchasing of CEDs for child consumption, nor their awareness of the purpose, composition or effects of CEDs. This limits the extent to which parental influences are understood.

The low number of studies reporting these mixed findings made it difficult to attribute discrepancies across reviews to differences in gender, age, ethnicity or socio-economic status. Context was reported for CEDs by one study of high school and university students

in Saudi Arabia. The studies reporting context for AmED use were predominantly in young people aged 14 years or older, suggesting its use in those under 14 years has not been studied or does not take place. This is a research gap. Findings for differences in context and motivations of AmED use by gender were mixed, with some studies reporting differences in rates between males and females and others suggesting similar rates. No reported differences were noted in context, motivations or knowledge by differences in studies' ethnic group or socio-economic status.

In general, the findings from across these systematic reviews are consistent with those reported elsewhere (Ruxton 2014; Reid et al. 2017; Thomson et al. 2014; Zucconi et al. 2013). However, differences in prevalence and effects by gender, age, ethnicity and socio-economic status are not clear, particularly for UK populations. This is due to limited information from UK-based surveys. There is also limited information from studies that included younger age groups, i.e. those aged 12 years and under. Only two UK studies were included in reviews. These suggest that around 11% of surveyed young people consume CEDs on a daily basis; and that higher rates of consumption are associated with being male and with lower socio-economic status. However, these findings were generated from a sample of unknown number of UK young people within a larger EU-based study. Eight new (since 2016) UK-based studies were located, of which two were reported in the reviews included in this overview. Another 67 non-UK CED primary research studies were also identified (see Appendix 1), predominantly of cross-sectional design. These may provide more consistently measured data on prevalence and reported effects, although little of it appears to be longitudinal or to utilise comparison groups.

(RQ2) What impact does the use of CEDs have on young people's physical and mental health and behaviour?

Evidence of largely cross-sectional studies reported in twelve included reviews demonstrated the existence of a relationship between CED use and various physical and behavioural effects. Consistent findings indicate that consumption is associated with a number of physical symptoms, including headaches, stomach aches and low appetite. Evidence also commonly indicates a link to sleep-related issues. Reviews of case reports have documented adverse physical effects, most notably cardiovascular events, following consumption of energy drinks in different quantities and over varying time periods. However, no evidence was located that suggested any potential mechanisms of effect linked to CED use. In general, the range of effects reported across these systematic reviews are consistent with those reported elsewhere (Heckman et al. 2010; Seifert et al. 2011; Wolk et al. 2012). However, it has also been suggested that differences in effects may be influenced by genetics (Clark and Landolt Hans 2017).

A considerable number of identified studies have examined the relationship between CEDs and a range of lifestyle behaviours. Findings demonstrate a consistent association between CED consumption and substance use (alcohol, smoking and illicit drug use). Furthermore, mixing alcohol with CEDs has also been linked to engaging in risky lifestyle behaviours, self-reported injuries, and poorer driving behaviour. Reviews further identified a link between CED use and hyperactivity and behaviour disorders. Retrospective analyses of poison centre

data have provided additional evidence of a relationship between CED use and hyperactivity and physical health symptoms.

Evidence has suggested a link between CEDs and poorer psychological well-being in terms of greater irritation and anger. Evidence is mixed on the relationships between CED consumption and common mental health conditions, such as anxiety and depression. Additionally, a small number of studies identified an association between self-harm and suicide-related behaviour.

Studies examining the educational or social effects of CED consumption are lacking, but there is some evidence which points to a negative relationship with school attainment and attendance. Few findings were reported in the included reviews on the effects of CEDs disaggregated by gender, ethnicity or socio-economic status.

Most of the reported associations between CED and adverse effects are derived from non-UK research. Effects in UK samples are less clear, providing mixed evidence that CED use may be associated with sleep disturbances, poor school attendance/achievement and poor nutritional choices. However, these effects may covary with other factors (such as frequency or skipping breakfast) in relation to mental health effects such as stress, anxiety or depression.

Recommended limits of caffeine use in young people suggest between 2.5 and 3 mg per kg of body weight per day (EFSA NDA Panel 2015; Ruxton 2014; Wikoff et al. 2017), although there is lack of agreement about these figures (Harris and Munsell 2015; Hodge et al. 2010; Mitchell et al. 2014). In considering the weight of these findings, this overview provides very limited evidence of weak quality, particularly with respect to UK populations, that this is being exceeded by the majority of young people who report CED use. However, there are findings to suggest that a modest proportion of young people may exceed this amount. Findings from a larger number of studies of effect suggest weak evidence of an association between CED use and physical symptoms. Similarly, weak evidence of an association between CED use and lifestyle behaviours is noted. However, there is very weak evidence of an association between CED use and mental health or educational/social effects; and limited UK evidence to suggest a weak association between CED use and poorer health effects in males and young people of lower socio-economic status.

Strengths and limitations

Based on multiple systematic reviews, this robust overview provides comprehensive findings. These allow us to take stock of what is currently known on this important public health issue, while identifying gaps in comparable and reliable evidence. While a wide range of rates of consumption patterns and associated effects were reported, some limitations of the dataset may reduce confidence in the generalisability of these overview findings to the UK. The possibility of selective reporting of findings by review authors could have potentially limited the reporting of findings in our overview. Consumption rates for CEDs and AmEDs were often reported together, which may lead to spurious conclusions about the reasons for or context of use. Very little UK-based research was included across these reviews, but more recent UK-based primary research has been located which may provide further insights into

prevalence and use. Findings were reported across reviews for populations with a wider age range than that of our overview; and disaggregation was not always possible. Little information was reported from sub-group analyses that examined differences by gender, age, ethnicity or socio-economic status. Newer primary research has been identified which may examine these gaps.

Methodological considerations of the included reviews may also merit caution in considering the validity of the findings. All included reviews were rated to be of 'low' or 'critically low' methodological quality using AMSTAR 2 criteria, which may be, in part, a reflection of its reliance on reporting of methods. The overview also noted that a large number of studies included in those reviews were of cross-sectional or case report design. Because most studies of effects did not have a comparison group of participants with lower or no CED use, it is possible that findings are biased, potentially overestimating reported effects and not representative of the whole population (Karlsson and Bergmark 2015). In addition, the use of a wide range of measures that conflated frequency and dosage limited efforts to find consistent evidence of a common consumption pattern.

While a slight overlap between studies included across reviews was noted, this did not appear to adversely affect the conclusions drawn by authors. For example, findings from Visram et al. (2016) and Dawodu and Cleaver (2017) had 11 studies which were reported in both reviews. Authors in both reviews came to similar conclusions regarding energy drink use and behaviour.

Future research recommendations

There are several implications for future research arising from this overview of reviews. More robust design conduct and reporting of primary research studies and systematic reviews will add to the confidence that can be placed in researchers' conclusions. The lack of common measures suggests a need for CED core outcome set development similar to those currently being developed for trials (Williamson et al. 2012). This would facilitate the comparison and pooling of existing research evidence, building a global evidence base.

While background scoping of older age groups suggested that young people over 18 are consuming CEDs in a different context related to higher education or working life (ADD Benson et al. 2014; Peacock et al. 2014; Verster et al. 2016), evidence of use and effects in children aged 12 years and under is lacking. An evidence synthesis of primary research published within the past three years could usefully update the existing located reviews.

Research examining young people's experiences of CED use would provide another useful perspective. Evidence syntheses of qualitative studies addressing young people's experiences of CED consumption and effects between the ages of 18 and 25 years could also could provide insights into potential modifiers of consumption.

A need is warranted for a robust UK national-level longitudinal survey of young people's consumption of CEDs, in order to determine prevalence and likely effects of the entire age range of young people over time. This type of study will take time to set up, so in the meantime cohort observational data examining prevalence and effects could be

interrogated. National- and international-level population data sets across the UK Data Service could be assembled. Surveys relevant to CED use in young people are likely to include the General Lifestyle Survey, Health Survey for England/Wales, the Millennium Cohort Study and the Families and Children Study (UK Data Service 2018). The next stage of this project will explore the feasibility of accessing these data (Brunton et al. 2018).

5 References

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Appendix 1. Identifying recent CED primary research

Rationale

To ensure that this overview was as current as possible, we supplemented the reviews data with findings from primary research published since the search of the most recent systematic review was undertaken.

Methods

We search for primary research published between January 2016 and 21 May 2018. Any citations of primary research that were identified from systematic review screening were also considered. The same databases were searched as for the systematic review search, except PROSPERO. The same search strategy was used in each source, combining two concepts of 'energy drinks' and 'caffeine' and omitting the concept of 'systematic reviews'.

We screened primary research references that examined CED use, and/or the effects of CED use. We included references based on retrieved titles and abstracts, if they:

- Were published in English;
- Were published since 2016;
- Were a primary study;
- Were about CED consumption;
- Reported a focus on children and/or young people up to/including age 17 years;
- Examined patterns of CED use OR examined the relationship between CED consumption and the effects on physical, mental, social or behavioural outcomes;
- Contained extractable outcome data.

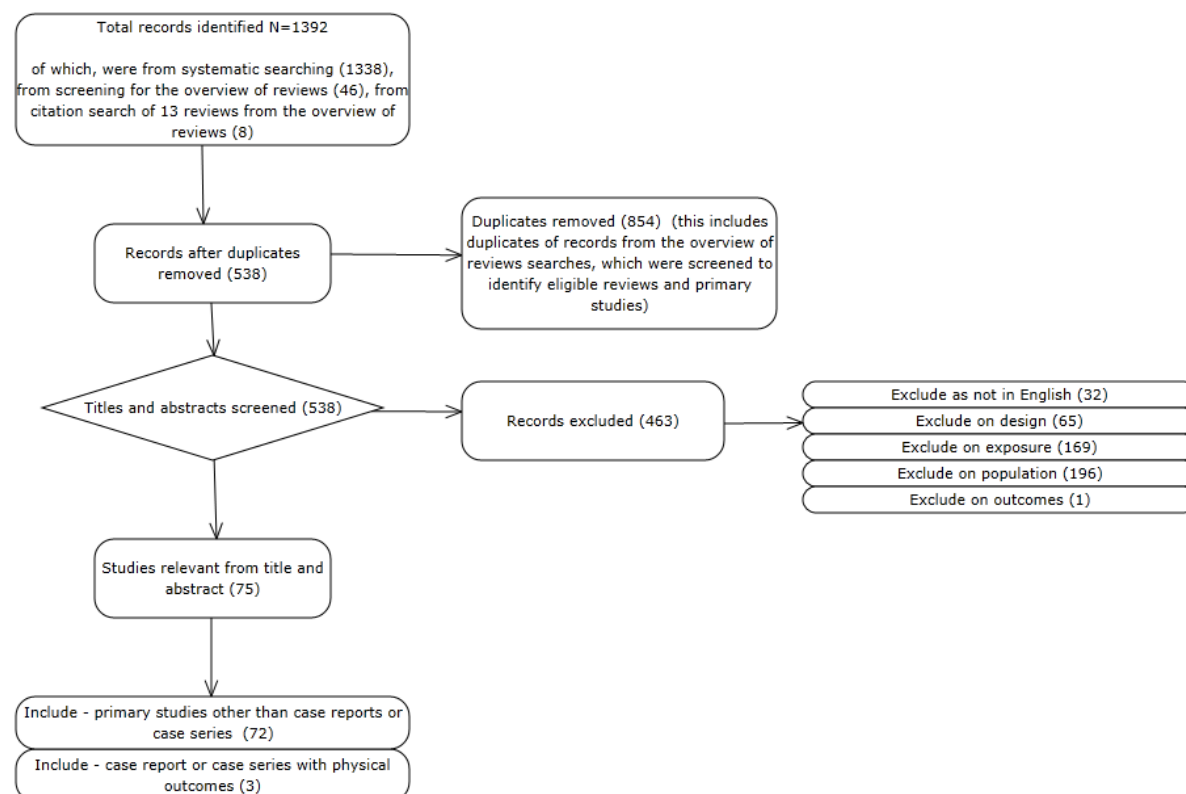
Primary research was coded on the basis of title and abstract for country of origin and study design, where described. Primary research was not quality assessed as only titles and abstracts were available. Findings were descriptively analysed and narrative findings presented below. One researcher screened and coded all located references. All references were managed and analysed using EPPI-Reviewer© software.

Findings

Flow of primary research through the overview process

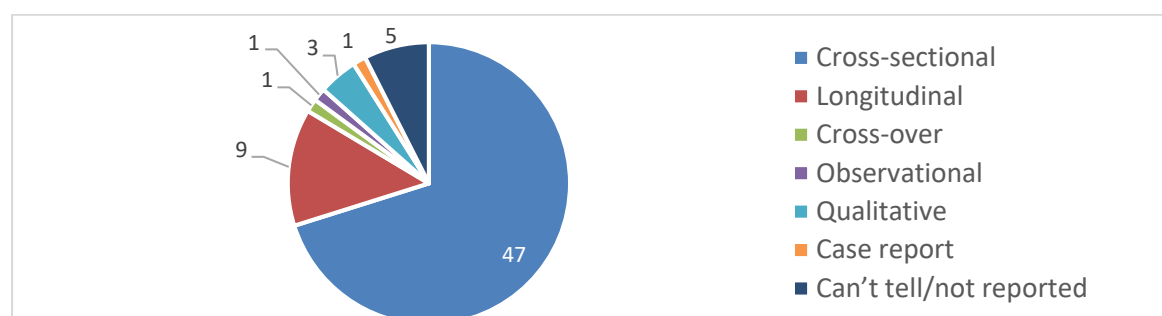
The search and screening of primary research published between January 2016 and 21 May 2018 identified 538 citations following duplicate removal. These were screened on title and abstract against our inclusion criteria. This identified 75 relevant pieces of primary research, as shown in Figure 3.2.

Figure 3.2 Flow of primary research



Of those 75 references published since 2016 and included on the basis of title and abstract, only eight are UK-based. One of these was a case series (Eagling et al. 2016) and one was a case report (Robin et al. 2018). Two more are cross-sectional surveys (Fairchild et al. 2017, Richards 2016), one of which reports on a study within our overview (Richards and Smith 2016b); and the other is a qualitative study of young people's beliefs about CED use (Visram et al. 2017). One longitudinal and one mixed methods UK-based primary study each were located (Richards and Smith 2016c, Richards and Smith 2016d). The remaining 67 non-UK references report a range of designs, as shown in Figure 3.3 below.

Figure 3.3 Non-UK Primary research references, 2016-2018: Study design (N=67)



A large majority of the 67 non-UK primary research references appear to report cross-sectional studies (n=47 references), followed by longitudinal studies (n=9), qualitative designs (n=3), and one each of a placebo-controlled crossover design, observational study and case report. Five references did not report clearly a study design. The reference list of all 75 primary research references is provided below.

References

* = UK population

+ = considered in overview analysis

Longitudinal studies (n=11)

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Marmorstein Naomi R (2016) Energy drink and coffee consumption and psychopathology symptoms among early adolescents: Cross-sectional and longitudinal associations. *Journal of Caffeine Research* 6: 64-72.

Martyn D, Lau A, Richardson P, Roberts A (2018) Temporal patterns of caffeine intake in the United States. *Food and Chemical Toxicology* 111: 71-83.

* Richards G, Smith Andrew P (2016b) Breakfast and energy drink consumption in secondary school children: Breakfast omission, in isolation or in combination with frequent energy drink use, is associated with stress, anxiety, and depression cross-sectionally, but not at 6-month follow-up. *Frontiers in Psychology* 7: 105.

* Richards G, Smith AP (2016c) Caffeine Consumption and General Health in Secondary School Children: A Cross-sectional and Longitudinal Analysis. *Frontiers in Nutrition* 3: 52

Sather TE, Woolsey CL, Williams Jr RD, Evans Jr MW, Cromartie F (2016) Age of first use of energy beverages predicts future maximal consumption among naval pilot and flight officer candidates. *Addictive Behaviors Reports* 3: 9-13.

Tran NL, Barraj LM, Bi X, Jack MM (2016) Trends and patterns of caffeine consumption among US teenagers and young adults, NHANES 2003-2012. *Food & Chemical Toxicology* 94: 227-242.

Tucker Joan S, Troxel Wendy M, Ewing Brett A, D'Amico Elizabeth J (2016) Alcohol mixed with energy drinks: Associations with risky drinking and functioning in high school. *Drug and Alcohol Dependence* 167: 36-41.

Observational/experimental studies (n=2)

Temple JL, Ziegler AM, Epstein LH (2016) Influence of Price and Labeling on Energy Drink Purchasing in an Experimental Convenience Store. *Journal of Nutrition Education and Behavior* 48: 54-59.e51.

Temple JL, Ziegler AM, Graczyk AM, Crandall AK (2017) Reinforcing Value of Caffeinated and Noncaffeinated Beverages After Acute Exposure in Children and Adolescents. *Journal of Caffeine Research* 7: 133-141.

Cross-sectional studies (n=49)

Bashir D, Reed-Schrader E, Olympia RP, Brady J, Rivera R, Serra T, Weber C (2016) Clinical Symptoms and Adverse Effects Associated With Energy Drink Consumption in Adolescents. *Pediatric Emergency Care* 32: 751-755.

Bašková M, Baška T, Holubčíková J (2016) Consumption of sweetened soft drinks and energy drinks in adolescents in Slovakia: implications for paediatric nursing. *Central European Journal of Nursing and Midwifery* 7: 390-395.

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Costa BM, Hayley A, Miller P (2016) Adolescent energy drink consumption: An Australian perspective. *Appetite* 105: 638-642.

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Fairchild RM, Broughton D, Morgan MZ (2017) Knowledge of and attitudes to sports drinks of adolescents living in South Wales, UK. *British Dental Journal* 222: 931-935.

Galland BC, Gray AR, Penno J, Smith C, Lobb C, Taylor RW (2017) Gender differences in sleep hygiene practices and sleep quality in New Zealand adolescents aged 15 to 17 years. *Sleep Health* 3: 77-83.

Gera M, Kalra S, Gupta P (2016) Caffeine intake among adolescents in Delhi. *Indian Journal of Community Medicine* 41: 151-153.

Giovanini de Oliveira Sartori A, Vieira da Silva, M (2016) Caffeine in Brazil: intake, socioeconomic and demographic determinants, and major dietary sources. *Nutrire* 41:11.

Ha D, Song I, Jang G, Lee EK, Shin JY (2017) Use pattern and predictors of use of highly caffeinated energy drinks among South Korean adolescents: a study using the Health Belief Model. *BMJ open* 7: e017224.

Holubcikova J, Kolarcik P, Madarasova Geckova A, Joppova E, van Dijk JP, Reijneveld S, A. (2017) Young adolescents who combine alcohol and energy drinks have a higher risk of reporting negative behavioural outcomes. *International Journal of Public Health* 62: 379-386.

Holubcikova J, Kolarcik P, Madarasova Geckova A, Reijneveld S, van Dijk J (2017) Regular energy drink consumption is associated with the risk of health and behavioural problems in adolescents. *European Journal of Pediatrics* 176: 599-605.

Jackson DB, Leal WE, Posick C, Vaughn MG, Olivan M (2018) The Role of Adolescent Victimization in Energy Drink Consumption: Monitoring the Future, 2010-2016. *Journal of community health*: 1-8.

Katz DL (2016) Energy drink consumption in Israeli youth: Public health & the perils of energetic marketing. *Israel Journal of Health Policy Research* 5: 9.

Khan SR, Cottler LB, Striley CW (2016) Correlates of use of alcohol mixed with energy drinks among youth across 10 US metropolitan areas. *Drug and Alcohol Dependence* 163: 236-241.

Kim J-S, Kim K, Seo Y (2017) Associations between korean adolescents' energy drink consumption and suicidal ideation and attempts. *Archives of Psychiatric Nursing* 32: 331-336.

Kim SY, Sim S, Choi HG (2017) High stress, lack of sleep, low school performance, and suicide attempts are associated with high energy drink intake in adolescents. *PLoS ONE* 12: e0187759.

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Leal WE, Jackson DB (2018) Energy drinks and escalation in drug use severity: An emergent hazard to adolescent health. *Preventive Medicine* 111: 391-396.

Mann MJ, Smith ML, Kristjansson AL (2016) Energy drink consumption and substance use risk in middle school students. *Preventive Medicine Reports* 3: 279-282.

Marmorstein Naomi R (2017) Interactions between energy drink consumption and sleep problems: Associations with alcohol use among young adolescents. *Journal of Caffeine Research* 7: 111-116.

Martins A, Ferreira C, Sousa D, Costa S (2018) Consumption patterns of energy drinks in Portuguese adolescents from a city in northern Portugal. *Acta Medica Portuguesa* 31: 207-212.

Miller KE, Dermen KH, Lucke JF (2017) Intoxication-Related Alcohol Mixed with Energy Drink Expectancies Scale: Initial Development and Validation. *Alcoholism: Clinical and Experimental Research* 41: 1228-1238.

Nienhuis K, Van Hoof JJ, Van der Lely N (2018) Direct Clinical Health Effects of the Consumption of Alcohol Mixed With Energy Drink in Dutch Adolescents. *Journal of Child and Adolescent Substance Abuse* 27: 125-132.

Nordt SP, Claudius I, Rangan C, Armijo E, Milano P, Yanger S, Tomaszewski C (2017) Reasons for energy drink use and reported adverse effects among adolescent emergency department patients. *Pediatric Emergency Care* 33: 770-773.

Nowak D, Jasionowski A (2016) Analysis of consumption of energy drinks by a group of adolescent athletes. *International Journal of Environmental Research and Public Health* 13.

⁺Park S, Lee Y, Lee JH (2016) Association between energy drink intake, sleep, stress, and suicidality in Korean adolescents: Energy drink use in isolation or in combination with junk food consumption. *Nutrition Journal* 15(1): 87.

Park SH, Lee SH, Chang KJ (2017) Intake-related factors and educational needs regarding energy drinks in female high school students in the Incheon area. *Journal of Nutrition and Health* 50: 460-471.

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⁺*Richards G (2016) *Caffeinated energy drink use in adolescents and young adults: associations with mental health, academic performance, and problem behaviour [PhD Thesis]*. Cardiff University.

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Santangelo B, Lapolla R, Rutigliano I, Pettoello M, Campanozzi A (2018) Nearly half of the adolescents in an Italian school-based study exceeded the recommended upper limits for daily caffeine consumption. *Acta Paediatrica* 107: 1055-1059.

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Wilson MN, Cumming T, Burkhalter R, B. Langille DB, Ogilvie R, Asbridge M (2018) Driving under the influence behaviours among high school students who mix alcohol with energy drinks. *Preventive Medicine* 111: 402-409.

Zytnick D, Park S, Onufrak SJ (2016) Child and Caregiver Attitudes About Sports Drinks and Weekly Sports Drink Intake Among U.S. Youth. *American Journal of Health Promotion* 30: e110-119.

Mixed methods studies (n=1)

*Richards GV, Smith AP (2016d) Associations between energy drink consumption and school attendance, academic attainment, and problem behaviour: a cross-sectional and longitudinal analysis. *The Lancet* 388 (Supplement 2): S101-S101.

Qualitative studies (n=4)

Ludden AB, O'Brien EM, Pasch KE (2017) Beliefs, Behaviors, and Contexts of Adolescent Caffeine Use: A Focus Group Study. *Substance Use and Misuse* 52: 1207-1218.

McCrary C, White CM, Bowman C, Fenton N, Reid JL, Hammond D (2017) Perceptions and Knowledge of CEDs: Results of Focus Groups With Canadian Youth. *Journal of Nutrition Education and Behavior* 49: 304-311.e306.

Turton P, Piche L, Battram DS (2016) Adolescent Attitudes and Beliefs Regarding Caffeine and the Consumption of Caffeinated Beverages. *Journal of Nutrition Education and Behavior* 48: 181-189.

*Visram S, Crossley SJ, Cheetham M, Lake A (2017) Children and young people's perceptions of energy drinks: A qualitative study. *PLoS ONE* 12.

Case reports or case series (n=3)

Butragueño LL, Del Castillo TB, Herrero MM (2016) Energy drinks as a trigger factor for seizures in paediatric patients: A case report. *Neurologia*: epub 21 Oct.

*Eagling VA, Lupton DJ, McGrory CE, Thomas SHL, Thompson JP, Vale JA, Eddleston M (2016) Caffeine-containing energy drinks and caffeine poisoning in school-age children (5-16 years): TOXBASE (R) access and enquiry data. *Clinical Toxicology* 54: 463-463.

*Robin S, Buchanan R, Poole R (2018) Energy drinks and adolescents - A hepatic health hazard? *Journal of Hepatology* 68: 856-857.

Design Unclear/Not reported (n=5)

Cofini V, Cecilia Maria R, Giacomo DD, Binkin N, Orio DF (2016) Energy drinks consumption in Italian adolescents: preliminary data of social, psychological and behavioral features. *Minerva pediatrica*.

Housman JM, Williams RD, Woolsey CL (2016) Impact of alcohol and alcohol mixed with energy drinks on non-medical prescription stimulant use in a nationally representative sample of 12th-grade students. *The American journal on addictions* 25: 378-384.

Ryu SH (2016) Energy drink consumption status and associated factors among male and female high school students in Deajon area. *Korean Journal of Food and Nutrition* 29: 899-910.

Sampasa-Kanyinga H, Chaput J-P (2016) Consumption of sugar-sweetened beverages and energy drinks and adherence to physical activity and screen time recommendations among adolescents. *International journal of adolescent medicine and health* 29.

Santangelo B, Lapolla R, Rutigliano I, Pettoello M, Massimo, Campanozzi A (2016) Caffeine consumption in adolescents: from coffee to energy drinks and back again. *Journal of Pediatric Gastroenterology and Nutrition* <http://hdlhandle.net/11369/339689>.

Appendix 2: MEDLINE Search strategy

Databases: Ovid MEDLINE(R) Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) <1946 to Present>

Date searched: 15 May 2018

No. of results: 99

- 1 ((energy adj3 drink?) or (energy adj3 beverage?) or (soft adj3 drink?) or (soft adj3 beverage?) or (carbonated adj3 drink?) or (carbonated adj3 beverage?) or (sport? adj3 drink?) or (sport? adj3 beverage?) or (sugar? adj3 drink?) or (sugar? adj3 beverage?) or (soda? adj3 drink?) or (soda? adj3 beverage?) or (flavor* adj3 drink?) or (flavor* adj3 beverage?) or (flavour* adj3 drink?) or (flavour* adj3 beverage?) or (sweet* adj3 drink?) or (sweet* adj3 beverage?)).ti,ab,kw. (9509)
- 2 (caffeine* or guarana).ti,ab,kw. or Caffeine/ (32008)
- 3 1 and 2 (852)
- 4 exp Energy drinks/ (551)
- 5 3 or 4 (1150)
- 6 (((("synthesis" or "systematic") and ("evidence" or "research" or "review")) or ("review" and (integrat* or critical* or "mapping" or "comprehensive" or "evidence" or "research" or "literature")))).ti. or ((systematic adj2 review*) or ("meta-analysis" or "Review articles" or "systematic review*" or "Overview of reviews" or "Review of Reviews") or ("data synthesis" or "evidence synthesis" or "metasynthesis" or "meta-synthesis" or "narrative synthesis" or "qualitative synthesis" or "quantitative synthesis" or "realist synthesis" or "research synthesis" or "synthesis of evidence" or "thematic synthesis" or "systematic map*" or "metaanaly*" or "meta-analy*" or "systematic overview*" or "systematic review*" or "systematically review*" or "bibliographic search" or "database search" or "electronic search" or "handsearch*" or "hand search*" or "keyword search" or "literature search" or "search term*" or "literature review" or "overview of reviews" or "review literature" or "reviewed the literature" or "reviews studies" or "scoping stud*" or "overview study" or "meta-ethnograph*" or "meta-epidemiological" or "data extraction" or "meta-regression" or "narrative review" or "art review" or "scoping review" or "iterative review" or "meta-summary")).ti,ab,kw. (421553)
- 7 limit 5 to (meta analysis or "review" or systematic reviews) (148)
- 8 5 and 6 (49)
- 9 7 or 8 (158)
- 10 limit 9 to yr="2013 -Current" (99)

Appendix 3: Coding tool

For each included review, use the exact authors' words where possible and reference the page number.

Year of publication

- 2013
- 2014
- 2015
- 2016
- 2017
- 2018

Primary studies

- Number of Primary Studies
State the number of primary studies in Info and give the first author and year - in alphabetical order!

Country of included studies

Country of included studies

Just tick the boxes - no need to list all countries - could indicate the number of studies in each group - if clear

- UK
Add in the info whether it is England, Scotland, Wales etc.
- North America
Includes USA and Canada
- Europe (non-UK)
Can name the countries in info, but don't need to
- Asia
- Australia
- Other
Name the country

Searches

- Sources searched
List the databases and other sources searched.
- Search range of dates
Add the latest search date in Info

Primary study designs

Tick all that apply - identify the types of study that were sought or included, depending on which is reported.

- Secondary data analyses
E.g., retrospective analyses of database information or national statistics
- Surveys
- Qualitative studies
- Intervention
Randomised trials or non-randomised trials - state in Info if any restrictions
- Case reports
- Other
State the type in Info
- Not reported

Aims of the review

In Info copy and paste in the aims as stated in the abstract or introduction

Focus

No details just tick the boxes

- Health effects
Physical, mental, behavioural, social
- Prevalence
Patterns of acquisition, and parental involvement and awareness, as well as patterns of consumption
- Other
Anything that is not health or prevalence, such as motives.

Target population

Who were the authors aiming to include

- Children in general
- Children with health conditions
- Children at risk of
Name the risk in Info
- Children with other characteristics
Name the characteristics in Info
- General - adults and children

Participant characteristics

Characteristics of those we are interested in and the included population as a whole

- Age - whole review
State mean and SD, or median and range, or state not reported, in Info
- Age of children or relevant group

- Male - whole review
- Male - relevant group
- Female - whole review
- Female - relevant group
- SocioEconomic Status - whole review
State in Info, mean and range in each group, if reported - or state NR
- SES - relevant group

Dosage

Do review authors report any information about how many, how often or how strong?

- Number/frequency of drinks
Add details in Info
- Caffeine content
Add in Info - any specific statements or definitions on the caffeine content of drinks consumed
- Social context of intake
e.g., at school, while studying, at home, for sports, etc.
- Named drink/s
List drinks if named

Effects

Report those summarised in the discussion as relevant - principal findings

- Physical
List measures used in Info
- Mental
List measures reported in Info
- Social
List measures in Info
for example, school attainment, school attendance, social cohesiveness
- Behaviour
List measures in Info
- Not applicable
No health outcomes

Funding

- Funding source
Report if relevant

Appendix 4: AMSTAR 2 tool

(Shea et al. 2017)

1. PICO components

Did the research questions and inclusion criteria for the review include the components of PICO (Participants, Intervention, Comparator, Outcomes)?

- Yes

For Yes:

Population

Intervention

Comparator

Outcome

Optional (recommended):

Timeframe for follow-up

Needs a clear statement of population (even if it is any person), exposure (intervention), and outcome.

Comparator is usually not relevant here.

- No

2. Protocol

Did the report of the review contain an explicit statement that the review methods were established prior to the conduct of the review and did the report justify any significant deviations from the protocol?

- Yes

For Yes: The authors state that they had a written protocol or guide that included ALL the following: review question(s),

a search strategy,

inclusion/exclusion criteria,

a risk of bias assessment, plus the protocol should be registered and should also have specified:

a meta-analysis/synthesis plan, if appropriate,

a plan for investigating causes of heterogeneity,

justification for any deviations from the protocol

- No

- Partial Yes

The authors state that they had a written protocol or guide that included ALL the following:

review question(s)

a search strategy

inclusion/exclusion criteria

a risk of bias assessment

3. Study design explanation

Did the review authors explain their selection of the study designs for inclusion in the review? Any attempt at explanation is valid.

- Yes
*For Yes, the review should satisfy ONE of the following:
Explanation for including only RCTs
OR explanation for including only NRSI
OR explanation for including both RCTs and NRSI*
- No

4. Comprehensive search strategy

Did the review authors use a comprehensive literature search strategy?

- Yes
*For yes all the following:
searched at least 2 databases (relevant to research question),
provided key word and/or search strategy,
justified publication restrictions (e.g. language),
searched the reference lists / bibliographies of included studies,
searched trial/study registries,
included/consulted content experts in the field,
where relevant, searched for grey literature,
conducted search within 24 months of completion of the review.*
- No
- Partial Yes
*For Partial Yes (all the following):
searched at least 2 databases (relevant to research question),
provided key word and/or search strategy,
justified publication restrictions (e.g. language)
Note: We changed this to "reported publication restrictions" not "justified"*

5. Duplicate study selection

Did the review authors perform study selection in duplicate?

- Yes
*For Yes, either ONE of the following:
at least two reviewers independently agreed on selection of eligible studies and achieved consensus on which studies to include OR Two reviewers selected a sample of eligible studies and achieved good agreement (at least 80 percent), with the remainder selected by one reviewer.*
- No

6. Duplicate data extraction

Did the review authors perform data extraction in duplicate?

- Yes
*For Yes, either ONE of the following:
at least two reviewers achieved consensus on which data to extract from included studies OR two reviewers extracted data from a sample of eligible studies and achieved good agreement (at least 80 percent), with the remainder extracted by one reviewer.*
- No

7. Details of excluded studies

Did the review authors provide a list of excluded studies and justify the exclusions?

- Yes
*For Yes:
Provided a list of all potentially relevant studies that were read in full-text form but excluded from the review, and
Justified the exclusion from the review of each potentially relevant study*
- No
- Partial Yes
*For Partial Yes:
Provided a list of all potentially relevant studies that were read in full-text form but excluded from the review*

8. Description of included studies

Did the review authors describe the included studies in adequate detail?

- Yes
*For Yes (all of the following):
described research designs,
described population in detail,
described intervention in detail (including doses where relevant),
described comparator in detail (including doses where relevant),
described outcomes
described study's setting,
timeframe for follow-up*
- No
- Partial Yes
*For Partial Yes (all the following):
described populations,
described interventions,
described comparators,
described outcomes,
described research designs*

9a. Risk of Bias (RoB) assessment (RCTs)

Did the review authors use a satisfactory technique for assessing the risk of bias (RoB) in individual studies (RCTs) that were included in the review?

- RCTs Yes
*For RCTs Yes, must have assessed RoB from:
unconcealed allocation,
lack of blinding of patients and assessors when assessing outcomes (unnecessary for objective outcomes such as all cause mortality),
allocation sequence that was not truly random,
selection of the reported result from among multiple measurements or analyses of a specified outcome*
- RCTs No
- RCTs Partial Yes
*For Partial Yes, must have assessed RoB from:
unconcealed allocation,
lack of blinding of patients and assessors when assessing outcomes (unnecessary for objective outcomes such as all cause mortality)*
- Includes only NRSIs
This (NRSI) includes all other study designs - including surveys, qualitative studies, and case reports.

9b. RoB assessment (NRSIs)

Did the review authors use a satisfactory technique for assessing the risk of bias (RoB) in individual studies (NRSIs) that were included in the review?

- NRSIs Yes
*For NRSIs Yes, must have assessed RoB from:
confounding,
selection bias,
methods used to ascertain exposures and outcomes,
selection of the reported result from among multiple measurements or analyses of a specified outcome*
- NRSIs No
- NRSIs Partial Yes
*For NRSIs Partial Yes, must have assessed RoB from:
confounding,
selection bias*
- Includes only RCTs

10. Funding sources

Did the review authors report on the sources of funding for the studies included in the review?

- Yes
For Yes: must have reported on the sources of funding for individual studies

included in the review. Note: Reporting that the reviewers looked for this information but it was not reported by study authors also qualifies

- No

11a. RCTs Meta-analysis

If meta-analysis was performed did the review authors use appropriate methods for statistical combination of results (RCTs)?

- RCTs Yes
*For Yes:
The authors justified combining the data in a meta-analysis,
AND they used an appropriate weighted technique to combine study results and
adjusted for heterogeneity if present,
AND investigated the causes of any heterogeneity*
- RCTs No
- RCTs No meta-analysis conducted
IE - Not relevant - no RCTs included or no meta-analysis conducted

11b. NRSIs Meta-analysis (MA)

If meta-analysis was performed did the review authors use appropriate methods for statistical combination of results (NRSIs)?

- NRSIs Yes
*For Yes:
The authors justified combining the data in a meta-analysis,
AND they used an appropriate weighted technique to combine study results,
adjusting for heterogeneity if present,
AND they statistically combined effect estimates from NRSI that were adjusted for
confounding, rather than combining raw data, or justified combining raw data
when adjusted effect estimates
were not available,
AND they reported separate summary estimates for RCTs and NRSI separately when
both were included in the review.*
- NRSIs No
- NRSIs No meta-analysis conducted
*NRSIs are any other study, use this if no meta-analysis conducted, or only RCTs
included*

12. MA: RoB in individual studies

If meta-analysis was performed, did the review authors assess the potential impact of RoB in individual studies on the results of the meta-analysis or other evidence synthesis?

- Yes
*For Yes:
included only low risk of bias RCTs
OR
if the pooled estimate was based on RCTs and/or NRSI at variable RoB, the authors
performed analyses to investigate possible impact of RoB on summary estimates of*

effect.

- No
- No meta-analysis conducted

13. RoB: discussion of results

Did the review authors account for RoB in individual studies when interpreting/discussing the results of the review?

- Yes
For Yes:
Included only low risk of bias RCTs
OR, if RCTs with moderate or high RoB, or NRSI were included, the review provided a discussion of the likely impact of RoB on the results.
- No

14. Heterogeneity

Did the review authors provide a satisfactory explanation for, and discussion of, any heterogeneity observed in the results of the review? I.e. did they discuss any conflicting results?

- Yes
For Yes:
There was no significant heterogeneity in the results,
OR if heterogeneity was present, the authors performed an investigation of sources of any heterogeneity in the results and discussed the impact of this on the results of the review
- No

15. Publication bias

If they performed quantitative synthesis did the review authors carry out an adequate investigation of publication bias (small study bias) and discuss its likely impact on the results of the review?

- Yes
For Yes:
performed graphical or statistical tests for publication bias and discussed the likelihood and magnitude of impact of publication bias
- No
- No meta-analysis conducted

16. Reports conflicts of interest

Did the review authors report any potential sources of conflict of interest, including any funding they received for conducting the review?

- Yes
For Yes:

The authors reported no competing interests

OR

The authors described their funding sources and how they managed potential conflicts of interest

- No

17. Relevance

"Considers the relevance of the review question and the basis of evidence claims by the review, including the quality and suitability of review methods, the studies included and/or the sufficiency of the evidence produced". (from page 283 of EPPI book (Gough, Oliver, and Thomas 2017))

- Yes
 - Focussed on Children - majority of cases*
 - Focussed on CEDs*
 - Focussed on Outcomes of Interest*
 - Good design - not just case reports*
- No
 - Not focussed on Children*
 - Not focussed on CEDs*
 - Not focussed on Outcomes of interest*
- Partial Yes
 - Meets some - not all*
 - Case reports - three or fewer cases*
 - Can give reasons for partial in info..*

18. Overall rating

- High
- Moderate
- Low
- Critically low

Appendix 5: List of reviews included in the overview

Alhyas L, El K, AlGhaferi H (2016) Energy drinks in the Gulf Cooperation Council states: A review. *JRSM Open* 7: 2054270415593717.

Ali F, Rehman H, Babayan Z, Stapleton D, Joshi DD (2015) Energy drinks and their adverse health effects: A systematic review of the current evidence. *Postgraduate medicine* 127: 308-322.

Bleich SN, Vercammen KA (2018) The negative impact of sugar-sweetened beverages on children's health: an update of the literature. *BMC Obesity* 5: 6.

Buck R, Dixon J, Matjasich L, Petersen R (2013) *Energy Drink Consumption Among Adolescents and Young Adults: Health Effects and Implications for Practice*. Westminster College <https://collections.lib.utah.edu/ark:/87278/s6b88h9n>.

Bull S, Brown T, Burnett K, Ashdown L, Rushton L (2015) *Extensive literature search as preparatory work for the safety assessment for caffeine*. EFSA External Scientific Report. <https://efsa.onlinelibrary.wiley.com/doi/abs/10.2903/sp.efsa.2015.EN-561>

Dawodu A, Cleaver K (2017) Behavioural correlates of energy drink consumption among adolescents: A review of the literature. *Journal of Child Health Care* 21: 446-462.

Goldfarb M, Tellier C, Thanassoulis G (2014) Review of published cases of adverse cardiovascular events after ingestion of energy drinks. *American Journal of Cardiology* 113: 168-172.

Lippi G, Cervellin G, Sanchis-Gomar F (2016) Energy Drinks and Myocardial Ischemia: A Review of Case Reports. *Cardiovascular Toxicology* 16: 207-212.

Richards G, Smith AP (2016) A Review of Energy Drinks and Mental Health, with a Focus on Stress, Anxiety, and Depression. *Journal of Caffeine Research* 6: 49-63.

Roemer A, Stockwell T (2017) Alcohol Mixed With Energy Drinks and Risk of Injury: A Systematic Review. *Journal of Studies on Alcohol and Drugs* 78: 175-183.

Verster JC, Benson S, Johnson SJ, Alford C, Godefroy SB, Scholey A (2018) Alcohol mixed with energy drink (AMED): A critical review. *Human Psychopharmacology: Clinical and Experimental* 33: e2650.

Verster JC, Koenig J (2018) Caffeine intake and its sources: A review of national representative studies. *Critical Reviews in Food Science and Nutrition* 58: 1250-1259.

Visram S, Cheetham M, Riby DM, Crossley SJ, Lake AA (2016) Consumption of energy drinks by children and young people: a rapid review examining evidence of physical effects and consumer attitudes. *BMJ open* 6: e010380.

Appendix 6. Excluded studies by reason for exclusion

Excluded as Not in English

Manrique CI, Arroyave-Hoyos CL, Galvis-Pareja D (2018) CEDs: Neurological and cardiovascular effects. *Iatreia* 31: 65-75.

Petit A, Karila L, Lejoyeux M (2015) [Abuse of energy drinks: does it pose a risk?]. *Presse Medicale* 44: 261-270.

Shalygin LD, Eganyan RA (2016) Energy drinks are a real danger to the health of children, adolescents, young people, and the adult population. Part 2. Risks associated with consumption of alcohol-containing energy drinks. World Health Organization guidelines. Legislative regulation in different countries. *Profilakticheskaya Meditsina* 19: 51-57.

Excluded on Design - not a systematic review

Ahluwalia N, Herrick K (2015) Caffeine intake from food and beverage sources and trends among children and adolescents in the United States: review of national quantitative studies from 1999 to 2011. *Advances in Nutrition* 6: 102-111.

Al-Shaar L, Vercammen K, Lu C, Richardson S, Tamez M, Mattei J (2017) Health Effects and Public Health Concerns of Energy Drink Consumption in the United States: A Mini-Review. *Frontiers in Public Health* 5: 225.

Arria AM, Bugbee BA, Caldeira KM, Vincent KB (2014) Evidence and knowledge gaps for the association between energy drink use and high-risk behaviors among adolescents and young adults. *Nutrition Reviews* 72 Suppl 1: 87-97.

Beauchamp G, Amaducci A, Cook M (2017) Caffeine Toxicity: A Brief Review and Update. *Clinical Pediatric Emergency Medicine* 18: 197-202.

Bedi N, Dewan P, Gupta P (2014) Energy drinks: potions of illusion. *Indian Pediatrics* 51: 529-533.

Blankson KL, Thompson AM, Ahrendt DM, Patrick V (2013) Energy drinks: what teenagers (and their doctors) should know. *Pediatrics in Review* 34: 55-62.

Breda JJ, Whiting SH, Encarnacao R, Norberg S, Jones R, Reinap M, Jewell J (2014) Energy drink consumption in europe: a review of the risks, adverse health effects, and policy options to respond. *Frontiers in Public Health* 2: 134.

Campbell B, Wilborn C, La B, Taylor L, Nelson MT, Greenwood M, Ziegenfuss TN, Lopez HL, Hoffman JR, Stout JR, Schmitz S, Collins R, Kalman DS, Antonio J, Kreider RB (2013) International Society of Sports Nutrition position stand: Energy drinks. *Journal of the International Society of Sports Nutrition* 10.

Cappelletti S, Piacentino D, Sani G, Aromatario M (2015) Caffeine: Cognitive and physical performance enhancer or psychoactive drug? *Current Neuropharmacology* 13: 71-88.

Carskadon MA, Tarokh L (2014) Developmental changes in sleep biology and potential effects on adolescent behavior and caffeine use. *Nutrition Reviews* 72 Suppl 1: 60-64.

Curran CP, Marczyński CA (2017) Taurine, caffeine, and energy drinks: Reviewing the risks to the adolescent brain. *Birth Defects Research* 109: 1640-1648.

EFSA NDA Panel (2015) Scientific Opinion on the safety of caffeine. *EFSA Journal* 13: 4102.

Franke AG, Bagusat C, Rust S, Engel A, Lieb K (2014) Substances used and prevalence rates of pharmacological cognitive enhancement among healthy subjects. *European Archives of Psychiatry & Clinical Neuroscience* 264 Suppl 1: S83-90.

Gonzalez W, Altieri PI, Alvarado E, Banchs HL, Colon E, Escobales N, Crespo M (2015) Celiac trunk and branches dissection due to energy drink consumption and heavy resistance exercise: case report and review of literature. *Boletín - Asociación Médica de Puerto Rico* 107: 38-40.

Grandner MA, Knutson KL, Troxel W, Hale L, Jean-Louis G, Miller KE (2014) Implications of sleep and energy drink use for health disparities. *Nutrition Reviews* 72 Supplement 1: 14-22.

Harris JL, Munsell CR (2015) Energy drinks and adolescents: what's the harm? *Nutrition Reviews* 73: 247-257.

Ibrahim NK, Iftikhar R (2014) Energy drinks: Getting wings but at what health cost? *Pakistan Journal of Medical Sciences* 30: 1415-1419.

Linden AN, Lau-Barraco C (2014) A qualitative review of psychosocial risk factors associated with caffeinated alcohol use. *Experimental and Clinical Psychopharmacology* 22: 144-153.

Mangi MA, Rehman H, Rafique M, Illovsy M (2017) Energy Drinks and the Risk of Cardiovascular Disease: A Review of Current Literature. *Cureus* 9: e1322.

Marczyński CA, Fillmore MT (2014) Energy drinks mixed with alcohol: what are the risks? *Nutrition Reviews* 72 Suppl 1: 98-107.

Marczyński CA (2015) Can energy drinks increase the desire for more alcohol? *Advances in Nutrition* 6: 96-101.

Mattioli Anna V (2015) Caffeine and atrial fibrillation. In: Preedy V (ed.) *Coffee in Health and Disease Prevention*. Elsevier, pages 691-698.

Mattioli AV (2014) Beverages of daily life: Impact of caffeine on atrial fibrillation. *Journal of Atrial Fibrillation* 7.

Meyer F, Timmons BW, Wilk B (2013) Water, Hydration and Sports Drink. In: *Nutrition and Enhanced Sports Performance: Muscle Building, Endurance, and Strength*. Elsevier Inc., pages 377-384.

Miller P (2013) Energy drinks and alcohol: Research supported by industry may be downplaying harms. *BMJ (Online)* 347.

Mosca A, Della C, Sartorelli MR, Ferretti F, Nicita F, Vania A, Nobili V (2016) Beverage consumption and paediatric NAFLD. *Eating & Weight Disorders: EWD* 21: 581-588.

Nelson ME, Bryant SM, Aks SE (2014) Emerging drugs of abuse. *Disease-a-Month* 60: 110-132.

Owens J, Au R, Carskadon M, Millman R, Wolfson A, Braverman PK, Adelman WP, Breuner CC, Levine DA, Marcell AV, Murray PJ, O'Brien RF (2014a) Insufficient sleep in adolescents and young adults: An update on causes and consequences. *Pediatrics* 134: e921-e932.

Owens JA, Mindell J, Baylor A (2014b) Effect of energy drink and caffeinated beverage consumption on sleep, mood, and performance in children and adolescents. *Nutrition Reviews* 72: 65-71.

Pennella S, Farinetti A, Mattioli AV (2015) Caffeine, Energy Drinks and Atrial Fibrillation: A Mini-Review. *BAOJ Nutrition* 1: 1-4.

Pomeranz JL, Munsell CR, Harris JL (2013) Energy drinks: An emerging public health hazard for youth. *Journal of Public Health Policy* 34: 254-271.

Rotstein J, Barber J, Strowbridge C, Hayward S, Huang R, Godefroy Samuel B (2013) Energy Drinks: An Assessment of the Potential Health Risks in the Canadian Context. InTech.

Safefood (2016) *Energy drinks in Ireland - a review*. Safefood.
<https://doi.org/10.14655/105129-975722>

Sanchis-Gomar F, Pareja-Galeano H, Cervellin G, Lippi G, Earnest CP (2015) Energy drink overconsumption in adolescents: implications for arrhythmias and other cardiovascular events. *Canadian Journal of Cardiology* 31: 572-575.

Schaffer SW, Shimada K, Jong CJ, Ito T, Azuma J, Takahashi K (2014) Effect of taurine and potential interactions with caffeine on cardiovascular function. *Amino Acids* 46: 1147-1157.

Smith AP (2013) Caffeine and CEDs. In: *Principles of Addiction*. Elsevier Inc., pages 777-785.

Smolinske Susan C (2017) Dietary Supplements in Children. *Pediatric Clinics of North America* 64: 1243.

Striley CW, Khan SR (2014) Review of the energy drink literature from 2013: findings continue to support most risk from mixing with alcohol. *Current Opinion in Psychiatry* 27: 263-268.

Turagam MK, Velagapudi P, Kocheril AG, Alpert MA (2015) Commonly consumed beverages in daily life: do they cause atrial fibrillation? *Clinical Cardiology* 38: 317-322.

Visram S, Hashem K (2016) *Energy drinks : what's the evidence?* The Food Research Collaboration.

Waheed A, Sadhna D, Gupta A, Patel P, Jabin F, Rajput SK (2015) Beverages: Alternative medicine and health benefits. *International Journal of Pharmacy and Technology* 6: 7568-7586.

Wassef B, Kohansieh M, Makaryus AN (2017) Effects of energy drinks on the cardiovascular system. *World Journal of Cardiology* 9: 796-806.

Wesensten NJ (2014) Legitimacy of concerns about caffeine and energy drink consumption. *Nutrition Reviews* 72 Suppl 1: 78-86.

Zacher J, May E, Horlitz M, Pingel S (2018) Binge drinking alcohol with caffeinated "energy drinks", prolonged emesis and spontaneous coronary artery dissection: a case report, review of the literature and postulation of a pathomechanism. *Clinical Research in Cardiology* 04: 04.

Zucconi S, Volpato C, Adinolfi F, Gandini E, Gentile E, Loi A, Fioriti L (2013) Gathering consumption data on specific consumer groups of energy drinks. *EFSA Supporting Publications* 10: 394E.

Zulli A, Smith RM, Kubatka P, Novak J, Uehara Y, Loftus H, Qaradakhi T, Pohanka M, Kobylak N, Zagatina A, Klimas J, Hayes A, La R, Soucek M, Kruzliak P (2016) Caffeine and cardiovascular diseases: critical review of current research. *European Journal of Nutrition* 55: 1331-1343.

Excluded on Exposure - not about CEDs (or no section on ED)

Clark I, Landolt Hans P (2017) Coffee, caffeine, and sleep: A systematic review of epidemiological studies and randomized controlled trials. *Sleep medicine reviews* 31: 70-78.

Ruxton CH (2014) The suitability of caffeinated drinks for children: a systematic review of randomised controlled trials, observational studies and expert panel guidelines. *Journal of human nutrition and dietetics: the official journal of the British Dietetic Association* 27: 342-357.

Excluded on Population - not about Children (or no separate data for children)

Benson S, Verster JC, Alford C, Scholey A (2014) Effects of mixing alcohol with caffeinated beverages on subjective intoxication: a systematic review and meta-analysis. *Neuroscience and biobehavioral reviews* 47: 16-21.

Burrows T, Pursey K, Neve M, Stanwell P (2013) What are the health implications associated with the consumption of energy drinks? A systematic review. *Nutrition Reviews* 71: 135-148.

Correa M, San M, López-Cruz L, Bayarri P, Monferrer L, Salamone JD (2014) Caffeine modulation of alcohol intake: Impact on its psychomotor effects and withdrawal. In: *Caffeine: Consumption, Side Effects and Impact on Performance and Mood*. Nova Science Publishers, Inc., pages 89-112.

Grasser EK, Miles-Chan JL, Charriere N, Loonam CR, Dulloo AG, Montani JP (2016) Energy Drinks and Their Impact on the Cardiovascular System: Potential Mechanisms. *Advances in Nutrition* 7: 950-960.

Lalanne L, Lutz PE, Paille F (2017) Acute impact of caffeinated alcoholic beverages on cognition: A systematic review. *Progress in Neuro-Psychopharmacology & Biological Psychiatry* 76: 188-194.

Ok G, Lee Nan H, Jung Hyun C, Jeon S, Kim K, Kang M, Lee S (2017) Effects Of Energy Drink On Power Performance: Meta-analysis. *Medicine & Science in Sports & Exercise* 49: 294.

Peacock A, Pennay A, Droste N, Bruno R, Lubman DI (2014) 'High' risk? A systematic review of the acute outcomes of mixing alcohol with energy drinks. *Addiction (Abingdon, England)* 109: 1612-1633.

Souza DB, Del C, Casonatto J, Polito MD (2017) Acute effects of caffeine-containing energy drinks on physical performance: a systematic review and meta-analysis. *European Journal of Nutrition* 56: 13-27.

Verster JC, Benson S, Johnson SJ, Scholey A, Alford C (2016) Mixing alcohol with energy drink (AMED) and total alcohol consumption: a systematic review and meta-analysis. *Human Psychopharmacology* 31: 2-10.

Voskoboinik A, Kalman JM, Kistler PM (2018) Caffeine and Arrhythmias: Time to Grind the Data. *JACC: Clinical Electrophysiology* 4: 425-432.

Whitehead N, White H (2013) Systematic review of randomised controlled trials of the effects of caffeine or caffeinated drinks on blood glucose concentrations and insulin sensitivity in people with diabetes mellitus. *Journal of Human Nutrition and Dietetics* 26: 111-125.

Excluded on Data - no extractable relevant data

Shah SA, Chu BW, Lacey CS, Riddock IC, Lee M, Dargush AE (2016) Impact of Acute Energy Drink Consumption on Blood Pressure Parameters: A Meta-analysis. *Annals of Pharmacotherapy* 50: 808-815.

Appendix 7: Characteristics of included reviews

First Author (Year) and Review aims	Methods	Population	Exposure and Outcomes
<p>Alhyas (2016) - <i>United Arab Emirates</i></p> <p>Aims of the review - <i>To assess the starting age, prevalence and patterns of consumption, awareness of energy drink contents and side-effects, differences between genders, motives for consumption, and associations with substance abuse, for adolescents and young adults (up to 34 years), in the Gulf Co-operation Council states</i></p> <p>Focus Health effects Prevalence Other - <i>Awareness of energy drink contents and associated side-effects, and motives for energy drink consumption</i></p> <p>Funding - <i>None declared</i></p>	<p>Sources searched - <i>MEDLINE and Embase</i></p> <p>Search range of dates - <i>1950 to 15th July 2014 (MEDLINE), and 1947 to 15th July 2014 (Embase)</i></p> <p>Number of primary studies - <i>5 out of 9 included studies collected data from participants of an age relevant to the current review</i></p> <p>Country of relevant studies <i>Asia - n=5</i></p> <p>Design of relevant studies <i>Surveys - five cross-sectional (one multi-stage)</i></p>	<p>Target population General - adults and children - <i>Students at University or School</i></p> <p>Participant age Whole review - <i>12 to 25 years (where reported)</i> Relevant studies - <i>12 to 19 years (five studies)</i></p> <p>Participant gender Whole review - <i>all mixed (% not reported), except one - all female</i> Relevant studies - <i>four of the five studies were mixed, one was all female</i></p> <p>Participant SES Whole review - <i>not reported</i> Relevant studies - <i>not reported</i></p>	<p>Number/frequency of drinks - <i>consumption/prevalence reported as an outcome in all five relevant studies</i></p> <p>Caffeine content - <i>not reported</i></p> <p>Social context of intake - <i>one study focused on energy drink consumption during exams</i></p> <p>Named drink/s - <i>no brands reported</i></p> <p>Physical effects - <i>one study reported energy levels and body changes (voice tone and menstrual changes)</i></p> <p>Mental effects - <i>mood changes</i></p>

First Author (Year) and Review aims	Methods	Population	Exposure and Outcomes
<p>Ali (2015)</p> <p>- USA and Pakistan</p> <p>Aims of the review</p> <p>- To review significant adverse health events after the ingestion of energy drinks</p> <p>Focus</p> <p>Health effects</p> <p>Funding</p> <p>- declared no conflicts of interest</p>	<p>Sources searched</p> <p>- PubMed and Google-Scholar. Reference lists were also searched</p> <p>Search range of dates</p> <p>- January 1980 to May 2014</p> <p>Number of primary studies</p> <p>- 26 case reports were included in the whole review. Four related to an individual under 18 years old. Case reports were not matched to a reference in the review</p> <p>Country of relevant studies</p> <p>North America - n=2 Europe (non-UK) - n=1 Asia - n=1</p> <p>Design of relevant studies</p> <p>Case reports</p>	<p>Target population</p> <p>General - adults and children</p> <p>Participant age</p> <p>Whole review - 13 to 85 years Relevant studies - 13 to 17 years</p> <p>Participant gender</p> <p>Whole review - 19 of 26 cases were male Relevant studies - all cases were male</p> <p>Participant SES</p> <p>Whole review - not reported Relevant studies - not reported</p>	<p>Number/frequency of drinks</p> <p>- Case 1: 3 cans of energy drinks/day for two weeks - Case 2: 250 mL of an ED before the adverse health event - Case 3: one energy drink/day - Case 4: 3-4 Red Bull, 2-3 Monster</p> <p>Caffeine content</p> <p>- not reported</p> <p>Social context of intake</p> <p>- not reported</p> <p>Named drink/s</p> <p>- Case 3: Red Bull and Monster</p> <p>Physical effects</p> <p>- palpitations, angina</p>

First Author (Year) and Review aims	Methods	Population	Exposure and Outcomes
<p>Bleich (2018) - USA</p> <p>Aims of the review - To synthesise the existing evidence regarding the impact of sugar-sweetened beverages consumption on children's health (overweight/obesity, insulin resistance, dental caries, and caffeine-related effects)</p> <p>Focus Health effects</p> <p>Funding - Robert Wood Johnson Foundation Healthy Eating Research Program</p>	<p>Sources searched - PubMed, Web of Science and PAIS International. Reference lists of relevant articles were also searched</p> <p>Search range of dates - 2007 to 2017 (received by publisher May 2017)</p> <p>Number of primary studies - 7 or 8 relevant studies on caffeine-related effects of energy drinks (Franckle is referenced in the text, but not in the table)</p> <p>Country of relevant studies UK - SW England (Richards) North America - n=3 Europe (non-UK) - n=2 Asia - n=1</p> <p>Design of relevant studies Surveys - six cross-sectional surveys, one longitudinal survey</p>	<p>Target population Children in general</p> <p>Participant age Whole review - 2 to 19 years Relevant studies - 10 to 18 years</p> <p>Participant gender Whole review - not reported Relevant studies - not reported, assumed to be mixed</p> <p>Participant SES Whole review - not reported Relevant studies - not reported</p>	<p>Number/frequency of drinks - identified as a unit of analysis</p> <p>Caffeine content - not reported "a 250 mL energy drink has an average of 80 mg of caffeine (range: 27-87 mg)"</p> <p>Social context of intake - not reported</p> <p>Named drink/s - not reported</p> <p>Physical effects - sleep-related issues (including quality & quantity of sleep), headaches, stomach ache</p> <p>Mental effects - depressive symptoms, anxiety, sleep, suicide</p> <p>Behavioural effects - risk-taking behaviour (such as cigarette, marijuana and drug use), ADHD, conduct, appetite</p>

First Author (Year) and Review aims	Methods	Population	Exposure and Outcomes
<p>Buck (2013)</p> <p>- USA</p> <p>Aims of the review</p> <p>- To identify physical and mental health effects of energy drink consumption</p> <p>Focus</p> <p>Health effects</p> <p>Funding</p> <p>- No external funding</p>	<p>Sources searched</p> <p>- CINAHL and MEDLINE</p> <p>Search range of dates</p> <p>- 2008 to 2013</p> <p>Number of primary studies</p> <p>- 23 papers in the whole review. Six appear to have involved individuals under 18 years old and energy drinks. Only three reported extractable data.</p> <p>Country of relevant studies</p> <p>North America - n=1 Europe (non-UK) - n=1 Australia - n=1</p> <p>Design of relevant studies</p> <p>Case reports - n=3</p>	<p>Target population</p> <p>General - adults and children</p> <p>Participant age</p> <p>Whole review - adolescents and young adults Relevant studies - 13 to 16 years</p> <p>Participant gender</p> <p>Whole review - not reported Relevant studies - one case report male, and two female</p> <p>Participant SES</p> <p>Whole review - not reported Relevant studies - not reported</p>	<p>Number/frequency of drinks</p> <p>- one Red Bull five days prior to symptoms; after drinking an energy drink; and four to five cans of Red Bull</p> <p>Caffeine content</p> <p>- not reported - Red Bull n=2</p> <p>Social context of intake</p> <p>- one case report professional volleyball player; another individual who had participated in a race</p> <p>Named drink/s</p> <p>- Red Bull n=2</p> <p>Physical effects</p> <p>- arrhythmia/palpitations/tachycardia and systolic murmur, chest pain</p>

First Author (Year) and Review aims	Methods	Population	Exposure and Outcomes
<p>Bull (2015) - <i>United Kingdom (Europe)</i></p> <p>Aims of the review - <i>One aim was to investigate adverse health effects following energy drink consumption (containing caffeine, taurine and/or glucuronolactone) in children</i></p> <p>Focus Health effects</p> <p>Funding - <i>European Food Safety Authority</i></p>	<p>Sources searched - <i>Scopus, Web of Science and PubMed</i></p> <p>Search range of dates - 1997 to May 2013</p> <p>Number of primary studies - <i>six studies in the section on the effects of caffeine and other substances in energy drinks, of which two cited in the narrative as relating to adolescents</i></p> <p>Country of relevant studies Other - <i>not reported</i></p> <p>Design of relevant studies Case reports Other - <i>one review (Seifert)</i></p>	<p>Target population General - adults and children</p> <p>Participant age Whole review - <i>Infants up to 11mths, Children 3 to 9 years, Adolescents 10 to 17 years, and Adults 18 years or older</i> Relevant studies - <i>10 to 17 years (no data under 10 years)</i></p> <p>Participant gender Whole review - <i>Mixed, not fully reported</i> Relevant studies - <i>One case study male</i></p> <p>Participant SES Whole review - <i>not reported</i> Relevant studies - <i>not reported</i></p>	<p>Number/frequency of drinks - <i>one case study 3L energy drink in combination with 1L vodka</i></p> <p>Caffeine content - <i>minimum caffeine level to cause symptoms was 200mg (4mg/kg), which caused jitteriness in a 13-year-old, and the maximum level was 1,622mg (35.5mg/kg) in a 14-year-old</i></p> <p>Social context of intake - <i>not reported</i></p> <p>Physical effects - <i>renal failure, jitteriness</i></p>

First Author (Year) and Review aims	Methods	Population	Exposure and Outcomes
<p>Dawodu (2017) - <i>United Kingdom</i></p> <p>Aims of the review - <i>To explore behavioural correlates of energy drink consumption among adolescents</i></p> <p>Focus Health effects Prevalence Other - <i>knowledge/awareness</i></p> <p>Funding - <i>No funding</i></p>	<p>Sources searched - <i>CINAHL, MEDLINE, PsycINFO, Psychology and Behavioural Sciences Collection, Academic Search Premier and SPORTDiscus, plus Google Scholar. Handsearched reference lists</i></p> <p>Search range of dates - <i>From 2010 to July 2015. Search updated October 2016, nothing added or not reported</i></p> <p>Number of primary studies - <i>12 studies</i></p> <p>Country of relevant studies North America - <i>n=8</i> Europe (non-UK) - <i>n=4</i></p> <p>Design of relevant studies Secondary data analyses - <i>one</i> Surveys - <i>11 cross-sectional (one computer-assisted telephone interview)</i></p>	<p>Target population Children in general</p> <p>Participant age Whole review - <i>10 to 25 years</i> Relevant studies - <i>10 to 18 years</i></p> <p>Participant gender Whole review - <i>Mixed</i> Relevant studies - <i>All mixed</i></p> <p>Participant SES Whole review - <i>not reported</i> Relevant studies - <i>not reported</i></p>	<p>Number/frequency of drinks - <i>half of the included studies reported consumption or consumption patterns</i></p> <p>Caffeine content - <i>not reported</i></p> <p>Social context of intake - <i>not reported</i></p> <p>Named drink/s - <i>not reported</i></p> <p>Physical effects - <i>sleep-related outcomes, executive functioning, hyperactivity, inattention</i></p> <p>Mental effects - <i>psychological well-being, including sensation seeking, anxiety, depression, anger, impulsivity, self-harm and suicidal thoughts</i></p> <p>Behavioural effects - <i>risk-taking, including alcohol and substance use, and smoking</i></p>

First Author (Year) and Review aims	Methods	Population	Exposure and Outcomes
<p>Goldfarb (2014)</p> <p>- Canada</p> <p>Aims of the review</p> <p>- To review the available literature for cases of cardiovascular events temporally related to energy drink consumption, and include two cases of cardiac arrest after energy drink consumption</p> <p>Focus</p> <p>Health effects</p> <p>Funding</p> <p>- Declared no conflicts of interest</p>	<p>Sources searched</p> <p>- MEDLINE, Embase, a manual search, plus studies from own institution</p> <p>Search range of dates</p> <p>- 1/1/1980 to 1/2/2013</p> <p>Number of primary studies</p> <p>- 17 cases, five of children (in four studies)</p> <p>Country of relevant studies</p> <p>- not reported</p> <p>Design of relevant studies</p> <p>Case reports</p>	<p>Target population</p> <p>General - adults and children</p> <p>Participant age</p> <p>Whole review</p> <p>- 13 to 58 years, median: 23 years</p> <p>Relevant studies</p> <p>- 13 to 17 years (five cases)</p> <p>Participant gender</p> <p>Whole review</p> <p>- 13 of 17 cases were male</p> <p>Relevant studies</p> <p>- 4 of 5 cases were male</p> <p>Participant SES</p> <p>Whole review</p> <p>- not reported</p> <p>Relevant studies</p> <p>- not reported</p>	<p>Number/frequency of drinks</p> <p>- partly reported as 5-7 energy drinks; one energy drink every other day for two weeks; and chronic energy drink consumption (more than 200mg caffeine per day from energy drinks for a week or more).</p> <p>Caffeine content</p> <p>- in 3 of 5 studies caffeine consumed was 85 mg, 160mg and 560-800mg</p> <p>Social context of intake</p> <p>- not reported</p> <p>Named drink/s</p> <p>- in 3 of 5 studies Red Bull, Red bull and vodka, Red Bull and Monster</p> <p>Physical effects</p> <p>- cardiovascular events: atrial fibrillation, presented as palpitations (3), prolonged QT [presenting as palpitations, chest pain, tremors and dizziness] (1), ST elevation, presenting as severe chest pain (1)</p>

First Author (Year) and Review aims	Methods	Population	Exposure and Outcomes
<p>Lippi (2016) - <i>Italy and Spain</i></p> <p>Aims of the review - <i>To identify evidence about the potential link between energy drinks and myocardial ischaemia</i></p> <p>Focus Health effects</p> <p>Funding - <i>No conflicts of interest</i></p>	<p>Sources searched - <i>MEDLINE, Scopus and ISI Web of Science. Reference lists were also hand searched</i></p> <p>Search range of dates - <i>No date restriction; included studies were 2009 to 2015</i></p> <p>Number of primary studies - <i>eight case reports were included, two were under 18 years old</i></p> <p>Country of relevant studies - <i>not reported</i></p> <p>Design of relevant studies Case reports</p>	<p>Target population General - adults and children</p> <p>Participant age Whole review - <i>13 to 32 years</i> Relevant studies - <i>13 years and 17 years</i></p> <p>Participant gender Whole review - <i>All male</i> Relevant studies - <i>Both cases were male</i></p> <p>Participant SES Whole review - <i>not reported</i> Relevant studies - <i>not reported</i></p>	<p>Number/frequency of drinks - <i>5 to 7 cans, and consumption of first energy drink</i></p> <p>Caffeine content - <i>not reported</i></p> <p>Social context of intake - <i>not reported, and first time consumption of an energy drink, during the previous night</i></p> <p>Named drink/s - <i>not reported</i></p> <p>Physical effects - <i>angina; diagnosed STEMI (ST elevation myocardial infarction), and STEMI; tests revealed coronary artery dissection</i></p>

First Author (Year) and Review aims	Methods	Population	Exposure and Outcomes
<p>Richards (2016) - <i>United Kingdom</i></p> <p>Aims of the review - <i>To review the literature relating to chronic energy drink use and its associations with mental health outcomes</i></p> <p>Focus Health effects</p> <p>Funding - <i>No competing financial interests</i></p>	<p>Sources searched - <i>PubMed and PsycINFO plus reference lists</i></p> <p>Search range of dates - <i>1990 to 2015</i></p> <p>Number of primary studies - <i>12 case reports from eight papers, none involved individuals less than 18 years old. Review also included 20 other studies, eight involved individuals less than 18 years old</i></p> <p>Country of relevant studies UK - <i>n=2</i> North America - <i>n=2</i> Europe (non-UK) - <i>n=3</i> Asia - <i>n=1</i></p> <p>Design of relevant studies Surveys - <i>seven cross-sectional</i> Intervention - <i>one cluster RCT</i></p>	<p>Target population General - adults and children</p> <p>Participant age Whole review - <i>25 to 43 years old (12 cases), and 20 other studies not reported</i> Relevant studies - <i>9 to 24 years (8 studies)</i></p> <p>Participant gender Whole review - <i>9 out of the 12 cases were male. Two other studies were male only, others not reported</i> Relevant studies - <i>one study male only, others not reported</i></p> <p>Participant SES Whole review - <i>not reported</i> Relevant studies - <i>not reported</i></p>	<p>Number/frequency of drinks - <i>not reported</i></p> <p>Caffeine content - <i>not reported</i></p> <p>Social context of intake - <i>not reported</i></p> <p>Named drink/s - <i>not reported</i></p> <p>Mental effects - <i>PTSD, stress, anxiety depression, self-harm, suicidal thoughts, and well-being</i></p>

First Author (Year) and Review aims	Methods	Population	Exposure and Outcomes
<p>Roemer (2017) - Canada</p> <p>Aims of the review - To examine the relationship between alcohol mixed with energy drinks (AmED) and injury, relative to alcohol alone</p> <p>Focus Health effects Prevalence</p> <p>Funding - Canadian Institute of Health Research</p>	<p>Sources searched - EBSCO and PubMed</p> <p>Search range of dates - Jan 1981 to Jan 2016</p> <p>Number of primary studies - 13 studies; three collected data from high-school students</p> <p>Country of relevant studies North America - n=3</p> <p>Design of relevant studies Surveys - three cross-sectional</p>	<p>Target population General - adults and children</p> <p>Participant age Whole review - 11 to 65 years Relevant studies - 11 to 20 years</p> <p>Participant gender Whole review - Most were mixed Relevant studies - All were mixed</p> <p>Participant SES Whole review - not reported Relevant studies - not reported - but was a confounder/covariate in two studies</p>	<p>Number/frequency of drinks - gender differences in AmED use were reported in two studies</p> <p>Caffeine content - not reported</p> <p>Social context of intake - consumed with alcohol</p> <p>Named drink/s - not reported</p> <p>Physical effects - traumatic brain injuries, alcohol-related injuries, and car crashes</p> <p>Behavioural effects - unsafe driving, motor vehicle accidents, and binge drinking</p>

First Author (Year) and Review aims	Methods	Population	Exposure and Outcomes
<p>Verster (2018) - Netherlands, Australia, Canada and United Kingdom</p> <p>Aims of the review - To critically review the evidence on the prevalence of, motives for, and correlates of alcohol mixed with energy drink (AmED) consumption, and whether this affects alcohol consumption, subjective intoxication, and risk taking</p> <p>Focus Health effects Prevalence Other - Motives for AmED consumption</p> <p>Funding - Red Bull</p>	<p>Sources searched - PubMed, Embase, and PsycLit</p> <p>Search range of dates - Inception to 2nd March 2017</p> <p>Primary studies Number - 80 papers were included; the number with relevant samples is unclear. At least 15 appear to have had age-relevant samples, only five had relevant information to extract</p> <p>Country of relevant studies North America - n=3 Europe (non-UK) - Italy Asia - Israel</p> <p>Design of relevant studies Surveys</p>	<p>Target population General - adults and children</p> <p>Participant age Whole review - not reported - children and adults Relevant studies - 14 to 19 years (five studies)</p> <p>Participant gender Whole review - not reported Relevant studies - not reported</p> <p>Participant SES Whole review - not reported Relevant studies - not reported</p>	<p>Number/frequency of drinks - reported in several studies in including differences by gender and ethnicity, but not for children/young people</p> <p>Caffeine content - not reported</p> <p>Social context of intake - motives for AmED consumption were reported in several studies</p> <p>Named drink/s - not specified for children/young people</p> <p>Physical effects - traumatic brain injury</p> <p>Mental effects - mental health outcomes</p> <p>Social effects - school absence and academic achievement</p> <p>Behavioural effects - risky behaviour, including alcohol and drug use, binge drinking, smoking, violence, sexual behaviour</p>

First Author (Year) and Review aims	Methods	Population	Exposure and Outcomes
<p>Verster (2018b) - <i>Netherlands, Australia, and Austria</i></p> <p>Aims of the review - <i>To summarise current daily caffeine intake of children, adolescents, and adults, and trends in caffeine intake over the past decade</i></p> <p>Focus Prevalence</p> <p>Funding - <i>Funded by Red Bull</i></p>	<p>Sources searched - <i>PubMed/MEDLINE and Embase</i></p> <p>Search range of dates - <i>1997 to 2nd October 2015</i></p> <p>Number of primary studies - <i>18 overall; eight related to energy drinks and people under 18 years old</i></p> <p>Country of relevant studies UK - <i>small part of a European study</i> North America - <i>n=2</i> Europe (non-UK) - <i>n=3</i> Australia - <i>n=2</i> Other - <i>New Zealand n=1</i></p> <p>Design of relevant studies Secondary data analyses - <i>at least two were of the of US National Health and Nutrition Examination Survey (NHANES) Surveys</i></p>	<p>Target population General - <i>adults and children</i></p> <p>Participant age Whole review - <i>children and adults</i> Relevant studies - <i>two years old and over</i></p> <p>Participant gender Whole review - <i>not reported</i> Relevant studies - <i>not reported</i></p> <p>Participant SES Whole review - <i>not reported</i> Relevant studies - <i>not reported</i></p>	<p>Number/frequency of drinks - <i>all studies reported on prevalence of energy drinks consumption</i></p> <p>Caffeine content - <i>percentage of caffeine from CED use was reported</i></p> <p>Social context of intake - <i>not reported</i></p> <p>Named drink/s - <i>not reported</i></p> <p>Effects - <i>no effects reported</i></p>

First Author (Year) and Review aims	Methods	Population	Exposure and Outcomes
<p>Visram (2016) - <i>United Kingdom</i></p> <p>Aims of the review - <i>To examine the evidence for any associations between children and young people's consumption of energy drinks and their health and well-being, social, behavioural or educational outcomes; determine whether the size and direction of any associations vary with the quantity or frequency of drinks consumed; and explore their attitudes towards the drinks and, in particular, which factors motivate them to consume or not consume them</i></p> <p>Focus Health effects Prevalence Other - <i>knowledge/awareness and motives</i></p> <p>Funding - <i>The Children's Foundation (registered charity no. 1000013)</i></p>	<p>Sources searched - <i>ASSIA, CINAHL, the Cochrane Library, DARE, EMBASE, ERIC, MEDLINE, PsycINFO, Web of Science, OpenGrey and the Internet (using Google)</i></p> <p>Search range of dates - <i>January 2000 to April 2016</i></p> <p>Primary studies Number - <i>46 studies</i></p> <p>Country of relevant studies UK - <i>n=1</i> North America - <i>n=22</i> Europe (non-UK) - <i>n=12</i> Asia - <i>Saudi n=3, Israel n=1</i> Australia - <i>n=5</i> Other - <i>Brazil n=1, New Zealand n=1</i></p> <p>Design of relevant studies Secondary data analyses - <i>four retrospective analyses</i> Surveys - <i>31 cross-sectional and four longitudinal</i> Qualitative studies - <i>four qualitative and mixed methods</i> Intervention - <i>three experimental</i></p>	<p>Target population Children in general</p> <p>Participant age Whole review - <i>10 to 20 years</i> Relevant studies - <i>10 to 20 years</i></p> <p>Participant gender Whole review - <i>two male only, the rest were mixed</i> Relevant studies - <i>two male, others mixed</i></p> <p>Participant SES Whole review - <i>not reported</i> Relevant studies - <i>not reported</i></p>	<p>Number/frequency of drinks - <i>consumption reported in some studies as an outcome</i></p> <p>Caffeine content - <i>three experimental studies; two used commercially available energy drinks (dose: 3mg caffeine/kg body weight) and third used drinks containing 0mg, 50mg, 100mg or 200mg of caffeine</i></p> <p>Social context of intake - <i>some studies focused on sports setting; Some studies focused on energy drinks consumption with alcohol</i></p> <p>Named drink/s - <i>not reported</i></p> <p>Physical effects - <i>headache, sleeping problems, tiredness/fatigue, stomach aches, hyperactivity, physical activity and sports performance</i></p> <p>Mental effects - <i>depression, and lifetime traumatic experiences</i></p> <p>Social effects</p>

First Author (Year) and Review aims	Methods	Population	Exposure and Outcomes
			<p>- <i>educational outcomes related to academic performance</i></p> <p>Behavioural effects</p> <p>- <i>sensation seeking, use of alcohol and/or binge drinking, smoking or susceptibility to smoking and other substance use</i></p>

Appendix 8: Structured summaries

Ali F, Rehman H, Babayan Z, Stapleton D, Joshi DD. (2015) Energy drinks and their adverse health effects: A systematic review of the current evidence. *Postgraduate Medicine*, 127(3), pp.308-22. doi: 10.1080/00325481.2015.1001712

This systematic review (Ali 2015) aimed to examine the adverse health effects associated with CED (ED) consumption in any quantity. Although 43 case reports were included, involving people of different ages (13 to 85 years), gender, race and countries, only 26 case reports were listed in this review. Four cases, from the USA (n=2), Spain and Pakistan were under 18 years; all were male, aged 13, 14, 16 and 17 years); adverse events included palpitations and angina after consuming various quantities of ED. Symptoms resolved after stopping ED or treatment. The review authors referred to a study (Seifert 2013) which suggested that almost half the cases of ED-related toxicity were due to unintentional exposure in children aged < 6 years.

Overall, this systematic review was rated as ‘critically low’, using the AMSTAR 2 critical appraisal tool, due to methodological limitations and no quality assessment of the case studies from which findings from different individuals were reported. There was a lack of important details and the references, for the case reports, were not given in the paper.

Alhyas L, El Kashef A, AlGhaferi H. (2016) Energy drinks in the Gulf Cooperation Council states: A review. *JRSM Open*, 7, doi: 10.1177/2054270415593717.

This systematic review (Alhyas 2016) aimed to examine the prevalence, pattern of use, and motivation for consuming CEDs (ED), awareness of the contents and potential side-effects of ED, gender differences in ED consumption and relationship between ED consumption and substance use (smoking, alcohol and drugs). Of the nine cross-sectional studies included, five (published between 2011 and 2014) involved 6,138 adolescents and school children aged 12 to 19 years, residing in the Gulf States.

Meta-analysis, using random effects, showed that the prevalence of ED consumption was 65.3% (95% CI 41.6 to 102.3; four studies) among school children. Males consumed energy drinks more than females (Musaiger) and ED consumption started at the average age of 16.7 years for females compared with 17.1 years for males (Kilani, $p < 0.001$).

Among those who consumed EDs, 31.9% of males aged 12 to 19 years and 24.7% of females drank one to two cans a week, and 22.2% of males and 4% of females drank over five cans a week (Musaiger). In another study (Al Hazza), 16.3% of males and 8.5% of females drank EDs more than three days per week. Over half of the respondents did not know the active ingredients of EDs, and that EDs contained caffeine. Reported side-effects included mood changes, becoming more energetic, and developing body changes, such as change in the voice tone and menstrual changes. Taste, increasing vitality, curiosity, being alert, peer pressure, and family consumers were the frequently quoted reasons for ED use.

Overall, this systematic review was rated as ‘critically low’ using the AMSTAR 2 critical appraisal tool due to methodological limitations and poor reporting. Quality assessment of included studies and subgroup analysis were not reported and there was a lack of sufficient detail. The population addressed in this review related to adults, as well as children, in the Gulf States, so not all of the findings were relevant, and they may not apply to children who consume EDs in other countries.

Bleich SN and Vercammen KA. (2018) The negative impact of sugar-sweetened beverages on children's health: an update of the literature. BMC Obesity, 5, pp.6.

This recently conducted systematic review aimed to synthesise the existing evidence about the impact of sugar-sweetened beverage consumption on child and adolescent health. Comprised of cross-sectional, longitudinal and intervention studies conducted in high-income countries, authors sought to examine relationships between any type of sugar-sweetened beverage and health outcomes, reporting findings separately for children and adolescents. Arising from six cross-sectional studies, authors reported relationships between CED use and sleep-related issues, increased headaches, risk taking behaviour, stress, depressive symptoms, and suicidal ideation, plan or attempt, irritation, stomach ache, and low appetite. Findings from one longitudinal study suggested a relationship between CED use and attention deficit/hyperactivity disorder, inattention and hyperactivity; but no longitudinal evidence of association between CED use and depression, panic or anxiety.

Authors did not report or discuss the methodological quality of included primary studies, and the review team rated this systematic review as critically low. While this systematic review was focused directly on children and adolescents, it provided limited information on CED use within a wider remit of research examining sugar-sweetened beverages.

Buck R, Dixon J, Matjasich L, Petersen R. (2013) Energy Drink Consumption Among Adolescents and Young Adults: Health Effects and Implications for Practice. Westminster College.

This systematic review (Buck 2013) aimed to evaluate the potential physiological and psychological health benefits and risks of CED (ED) consumption among adolescents and young adults. Of the 23 included studies, three were relevant case studies, which were from North America, Australia and Europe, and reported heart problems after ED consumption by teenagers. One was a 13-year-old girl, who was diagnosed with long QT syndrome. The second was a 14-year-old boy, who had tachycardia (fast heart rate), and recovered fully. The third was a 16-year-old girl who had orthostatic intolerances when drinking Red Bull, and she recovered when she stopped drinking it.

Overall, this systematic review was rated as 'critically low' using the AMSTAR 2 critical appraisal tool due to methodological limitations and poor reporting. There was a lack of important details about the included studies to be certain of the strength of the evidence, which was of limited relevance to our review (only three case studies). There was no assessment of the quality of the included studies.

Bull S, Brown T, Burnett K, Ashdown L, Rushton L. (2015) Extensive literature search as preparatory work for the safety assessment for caffeine. EFSA supporting publication. EN-561 EFSA-Q-2013-00419.

This systematic review aimed to investigate adverse health effects following caffeine consumption. This included the adverse health effects of caffeine intake in combination with other substances in energy drinks. The section of the report examining the effects of caffeine and other substances in energy drinks included six included studies. The review included mixed study types, including reviews that reported a new analysis of data. Two of the six studies (one case study & one review) reported findings from individuals under 18

years old. The case study reported the experience of a 17 year old boy who suffered renal failure after consuming 3L of energy drink in combination with 1L vodka, equating to 4600mg taurine, 780mg caffeine and 380g alcohol. The minimum caffeine level needed to cause symptoms was reported to be 200mg (4 mg/kg) in a 13 year old who had jitteriness.

Authors assessed the methodological quality of non-randomised epidemiology studies using the Newcastle Ottawa Scale, and intervention studies were evaluated using the Cochrane 'Risk of Bias' tool. It is not however clear if case studies and reviews were assessed. In terms of funding, the report was commissioned by the European Food Safety Authority. There is no statement acknowledging the presence or absence of a conflict of interest by the authors of the report. This review was assessed as 'partially relevant' as it was, in part, focused on CEDs and reported outcomes of interest, but the majority of studies related to energy drinks were not focused on individuals under 18 years old. The review team rated overall confidence in this systematic review as 'low'. The review only focused on adverse health effects and did not include studies that either reported no effect or an inverse effect. The authors only incorporated primary studies that were not already considered for the two broader questions, which related to adverse effects of caffeine and caffeine with alcohol in general, and not solely focussed on energy drinks. The evidence tables are not available with the published narrative review.

Dawodu A and Cleaver K. (2017) Behavioural correlates of energy drink consumption among adolescents: A review of the literature. *Journal of Child Health Care*, 21(4): 446-462.

This systematic review aimed to determine whether an association existed between adverse behaviour and consumption of energy drinks. The review included 12 primary studies, all but one of which were focused on individuals under 18 years old or reported age disaggregated findings for that age group. The remaining study (Jackson et al., 2013) reported on adolescents and young adults as a whole (13-25 yrs). All of the eleven studies were conducted in Western countries (North America, n=7; Europe, non UK, n=4). A lack of UK studies was noted. Ten studies were a cross-sectional design and one involved a secondary data analysis. Included studies reported an association between consumption of energy drinks and alcohol, and other risky behaviours including illicit drug and tobacco use.

Four studies reported data on the prevalence of ED consumption in young people. One Canadian study found that nearly two-thirds (62%) of students in years 7-12 had consumed energy drinks at least once in the previous year and 20% reported having them once or more per month. A US study found that amongst respondents aged 15-17 years, 13% had recently consumed an energy drink, and approximately 10% had ever consumed an energy drink mixed with alcohol. Another study conducted in the USA found that nearly 15% of students in years 6-12 consumed an energy at least once a week. The review incorrectly reports the findings of Nowak and Jasionowski (2015) in Table 1. This study of junior and senior high school students in Poland found that energy drinks were consumed by 67% of respondents. Twenty percent consumed energy drinks once a month, and 16% reported consumption daily, several times a week or once a week. Several studies reported that energy drink consumption was higher in boys than girls.

Energy drink consumption was reported to impact negatively on executive functions and increase hyperactivity/inattention symptoms. An inverse association between energy drink consumption and sleep duration was reported to exist. Findings from the review also suggested an association between ED consumption and psychological states (including

sensation seeking, depression, anxiety symptoms, anger and impulsivity scores) as well as self-harming behaviour and suicidal thoughts.

Authors did not report the methodological quality of included primary studies though they reported conducting a quality assessment. The authors declared no funding and no conflict of interest. This review was assessed as 'relevant' as it was focused on CEDs, reported outcomes of interest and a majority of primary studies were focused on children and adolescents under 18 years old. Our research team rated overall confidence in this systematic review as 'critically low'. There was a lack of detail provided on the quality assessment to be certain of the strength of the evidence, and the data was mainly based upon self-reported consumption and outcomes. However, there were large sample sizes for most studies. There was varying detail on the magnitude of the results, and the significance of the results is not clear.

Goldfarb M, Tellier C, Thanassoulis G. (2014) Review of published cases of adverse cardiovascular events after ingestion of energy drinks. *American Journal of Cardiology*, 113: 168-172

This systematic review aimed to review the literature for cases of cardiovascular events temporally related to energy drink consumption. The review was comprised of 17 case studies in 14 reports and included two other unpublished cases. Five of these cases involved individuals under the age of 18 years old (4 males and 1 females, ages ranged from 13 to 17 years old). No other personal information about individuals or geographical details were reported. Three reports involved atrial fibrillation associated with energy drinks; in two of these cases, symptoms occurred shortly after consumption of energy drinks, and one individual had also co-ingested vodka. The third case had a history of chronic energy drink consumption, corresponding to over 200mg caffeine per day for at least one week. He had experienced two previous episodes of similar symptoms. A fourth case was associated with electrophysiological changes without arrhythmia. This related to a 13 year-old female, who presented to the emergency department with palpitations, chest pain, tremors and dizziness after consumption of a large amount of an energy drink every other day for two weeks. She was diagnosed with long QT syndrome after testing identified a genetic mutation. The fifth case involved ST elevation, presenting as severe chest pain and occurred shortly after consuming five to seven energy drinks. The authors concluded that vulnerable individuals such as young people should be advised that caution is warranted with heavy energy drink consumption and/or with concomitant alcohol or drug ingestion. The authors declared no conflicts of interest with their review. The review authors did not report or discuss the methodological quality of included primary studies. This review was assessed as 'partially relevant' as it was focused on CEDs and reported outcomes of interest, though it comprised of case reports, and the majority were focused on adults. The review team rated overall confidence in this systematic review as 'critically low'.

Lippi G, Cervellin G, Sanchis-Gomar F. (2016) Energy drinks and myocardial ischemia: a review of case reports. *Cardiovascular Toxicology*, 16:207-212.

This systematic review aimed to identify evidence about the potential link between energy drinks and myocardial ischaemia. The review was comprised of eight case reports, but only two out of the eight involved individuals under the age of 18 years old. Both of the cases involved males, one aged 13 years old and the other aged 17 years. No other personal information about individuals or geographical details were reported. Both individuals were diagnosed with ST elevation myocardial infarction (STEMI). In one case, a STEMI occurred following a large consumption of energy drink (5 to 7 cans). In the second case, the

individual suffered a STEMI associated with spontaneous coronary artery dissection after consuming an energy drink for the first time during the previous night. No associated acute triggers for myocardial ischemia other than energy drinks could be identified in either of the case reports. Authors did not report or discuss the methodological quality of included primary studies. The authors reported that they had no conflict of interest. This review was assessed as 'partially relevant' as it was focused on CEDs and reported outcomes of interest, but the majority of case reports were focused on adults. The review team rated overall confidence in this systematic review as 'critically low'.

Richards G and Smith A. (2016) A review of energy drinks and mental health, with a focus on stress, anxiety, and depression. *Journal of Caffeine Research*, 6(2):49-63.

This systematic review aimed to examine chronic energy drink use and its association with mental health outcomes. Authors did not define what was meant by 'chronic' energy drink use. Included studies focused largely on stress, anxiety and depression, but other mental health outcomes were reported. Studies examining short term beneficial effects on mood or performance were not included. The whole review included nineteen primary studies of varying designs and twelve case reports from eight papers. Only six of the primary studies (reported in seven papers) and none of the case reports contained extractable data from young people under 18 years old. Four of the age-relevant studies were conducted in Western countries (UK, n=1; Europe, n=1; North America, n=2). Two were conducted in Asia (Turkey and Hong Kong).

The review reported mixed evidence from six cross-sectional studies on the association between energy drink consumption and stress, anxiety, depression and posttraumatic stress disorder (PTSD). Two studies reported a positive association between energy drink use and depression. However, the positive association between depression and energy drink consumption disappeared in one of the studies when a multivariate data analysis was conducted. Another study found no association between caffeine from energy drink consumption and depression, stress or anxiety. A multivariate analysis found evidence of positive associations between energy drink use and self-harming behaviour and suicidal thoughts. One study also found a positive correlation between frequency of energy drink consumption and PTSD symptoms, even after controlling for a number of variables (sex, index trauma, physical activity, smoking, and sense of coherence). However, positive associations were also found between PTSD symptoms and other food products including flavoured milk, coffee, and fast food. The analysis may also have been confounded by grouping energy drinks with sports drinks. One UK study suggested a positive association between energy drink use and low general health. However, the analysis was based on the combined consumption of energy drinks, caffeinated soft drinks and chewing gum. The effects of energy drinks separately were not reported.

One sleep-focused randomised controlled trial (RCT) from Hong Kong reported improvements in the intervention group relative to the controls regarding mental health status, total difficulty, conduct problems, and hyperactivity. Notably, the intervention group was significantly less likely to consume energy drinks three times per a week or more compared to the control group. The review authors stated that it was not possible to tell from the data reported whether this difference in energy drink consumption was associated with improvements in mental health, but they considered it plausible. A number of other 'marginally significant' effects were reported in relation to stress and PTSD, but as this is not an appropriate statistical term, these results should be considered non-significant.

A formal assessment of the methodological quality of included primary studies was not reported, but the authors did highlight some methodological issues with individual studies.

The authors stated that they had no competing financial interests in relation to their study. This review was assessed as ‘partially relevant’ as it was focused on CEDs and reported outcomes of interest, but the majority of primary studies and all the case reports were focused on adults. The review team rated overall confidence in this systematic review as ‘critically low’.

Roemer A and Stockwell T. (2017) Alcohol mixed with energy drinks and risk of injury: a systematic review. *Journal of Studies on Alcohol and Drugs*, 78, 175-183

This systematic review aimed to examine the relationship between alcohol mixed with caffeinated energy drinks (AmED) and injury. The association between AmED use and a number of behavioural and physical outcomes were reported. The review included 13 cross-sectional studies, three of which involved individuals under 18 years old. All three age-relevant studies collected data from mixed gender US high school students in years 7-12. Studies reported an association between AmED use and alcohol-related unsafe driving, and increased risk of motor vehicle accidents after drinking. An association was also reported between AmED use and traumatic brain injury, binge drinking, alcohol-related injury and injuries requiring a doctor. Findings related to sex differences in AMED consumption were reported in two studies. One study found no sex difference in AmED use. In contrast, the other study reported that males consumed the highest amount of AmED. Authors indicated that some quality assessment was performed and study quality was also considered in the synthesis. However, it does not appear that the methodological quality of included primary studies was formally assessed using a specific RoB tool. The review was funded by the Canadian Institute for Health Research. This review was assessed as ‘partially relevant’ as it was focused on CEDs and reported outcomes of interest, but the majority of primary studies were focused on adults. The review team rated overall confidence in this systematic review as ‘critically low’.

Verster JC, Benson S, Johnson SJ, Alford C, Godefroy SB, Scholey A. (2018) Alcohol mixed with energy drink (AMED): A critical review. *Human Psychopharmacology: Clinical and Experimental*, 33, e2650. <https://doi.org/10.1002/hup.2650>

This systematic review searched to March, 2017. It aimed to critically review the evidence on the prevalence of, motives for, and correlates of alcohol mixed with energy drink (AmED) consumption, and whether this affects alcohol consumption, subjective intoxication, and risk taking, in the general population. Eighty studies were included, but only five were relevant to this review. These five studies were all surveys, and were conducted in the USA, Canada (n=2), Italy and Israel. One survey found that AmED increased alcohol intake. The prevalence in Canadian students was 17.3 to 20%. Consumers were more likely to be young, of Black/other ethnicity, play team sport, be absent from school, have more spending money, smoke, and use marijuana; but consumption was not associated with a lower grade point average (Azagba 2013). A second survey (Azagba 2014), found that 13% of Canadian high-school children had drunk at least one ED in the past year. A third survey found that 13% of US 14- or 17-year-olds reported AmED consumption in the past month, and it was associated with more alcohol consumed, poorer grades, delinquent behaviour, substance-use-related unsafe driving, drug use, and being intoxicated in public, with no significant differences in mental health, social functioning, and academic aspirations (Tucker). Two surveys assessed motives. In one (Flotta), Italian children rated the following as important or highly important: to celebrate/party (36.9%), to socialise (27.3%), and liking the taste (21.0%); and the following as not important: to get work done (53.5%), it’s cheap (48.7%), to be comfortable with the opposite gender (48.5%), and everyone else is doing it (48.1%).

The prevalence of consumption was 46.1%. AmED consumers, aged 15 to 19 years, were more likely to be male, smoke, use marijuana, have more sex partners, and be in a car with a driver who has drunk alcohol, but not binge drink, not be younger, not drink drive, and not wear a seatbelt. In the other (Magnezi), the reasons, reported by Israelis aged 14 to 18 years, were to improve the taste of alcohol (80.6%), feel drunk (24.6%), curiosity (14.6%), to be awake (13.9%), to drink more alcohol (11.7%), to be social (10.4%), and to reduce the side-effects of alcohol (8.4%). The authors did not assess the methodological quality of these studies, and the systematic review was rated as critically low in quality (AMSTAR 2 rating). This commercially funded (by Red Bull) review included surveys only, and was not specifically focussed on children, nor on energy drinks alone, meaning it has little relevance to this review.

Verster JC, Koenig J. (2018). Caffeine intake and its sources: A review of national representative studies. *Critical Reviews in Food Science & Nutrition*, 58, pp.1250-9.

This systematic review, which searched up to October 2015, aimed to summarise the current daily caffeine intake of children, adolescents, and adults, and trends in caffeine intake over the past decade. It included secondary analyses of large national datasets, and surveys, with relevant studies set in the UK (n=1), Europe, USA, Australia and New Zealand. The authors assessed the prevalence of caffeine consumption, reporting some findings separately for energy drinks in children and adolescents (n=8 studies). The percentage of caffeine that was from energy drinks ranged from 0.6% in Germany in 2010/2011 (Lachenmeier), through 2% for 5 to 12 years, and 3% for 13 to 15 years, in New Zealand (NZ National Child Nutrition Survey), 5% in the USA (13 to 17 years, Mitchell), 5.3% in Belgium (European Food Safety Authority), 6% in the USA (2 to 22 years, Branum) and Australia (Australian Beverage Council), 8.1% in the Netherlands (European Food Safety Authority) to 11% in the UK (only 2.6% of participants in this European study were from the UK; European Food Safety Authority). One survey reported that 69% of caffeine was from drinks, but only 3% of these drinks were energy drinks (Beckford), while another reported that 13% of caffeine was from energy drinks, in ED drinkers aged 10 to 18, and 42% in ED drinkers aged 3 to 10 years (Zucconi). The amount consumed ranged from 0.18mg/kg of body weight/day (3 to 10 years; Zucconi), through 0.26mg/kg bw/d (10 to 18 years; Zucconi) to 18mg/day (2 to 16 years; Beckford). The authors concluded that energy drinks did not significantly contribute to daily caffeine intake in children. They did not report or discuss the methodological quality of most of the included primary studies, and the review team rated this systematic review as of critically low quality. This commercially funded (Red Bull) systematic review was focused neither on children and adolescents, nor on energy drinks, and it provided very little relevant information.

Visram S, Cheetham M, Riby DM, Crossley SJ, Lake AA. (2016) Consumption of energy drinks by children and young people: a rapid review examining evidence of physical effects and consumer attitudes. *BMJ Open*, e010380.

This systematic review searched up to April 2016 and assessed associations between children and young people's consumption of energy drinks and their health and well-being, social, behavioural or educational outcomes, and their attitudes towards the drinks. Forty-six studies were included; three were RCTs, 31 were cross-sectional, four were longitudinal, four were secondary data analyses, and four were qualitative focus groups (4). They were conducted in the UK (1), Europe (12), North America (22), Australia (5), Asia (2), Brazil (1), or New Zealand (1). The authors examined the relationships between energy drinks and health outcomes, prevalence and motives for consumption, in children and adolescents,

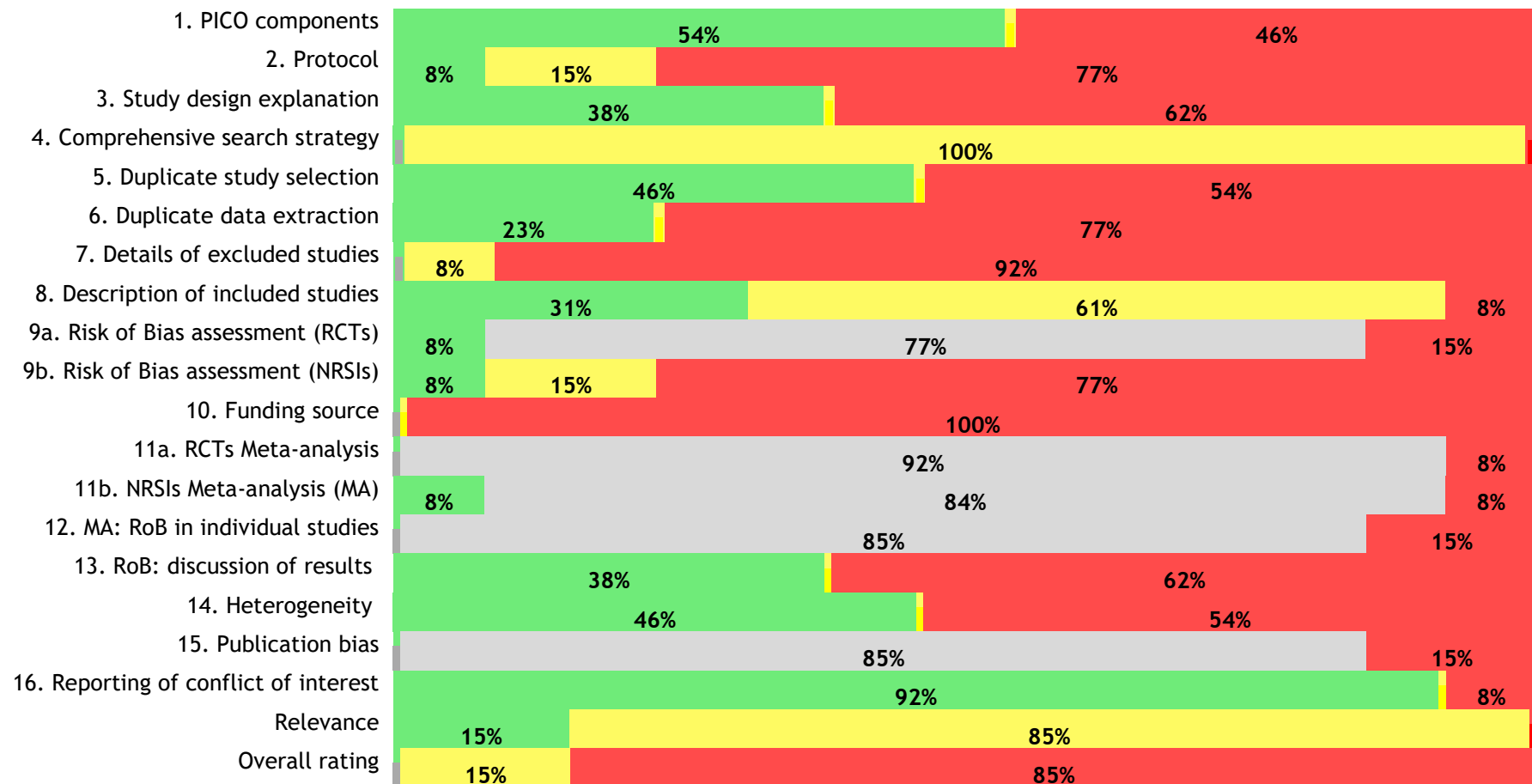
aged 10 to 21 years⁶. Two RCTs found positive effects of an energy drink on some aspects of sports performance. Several cross-sectional studies suggested that energy drink use was strongly linked with higher rates of smoking, alcohol and other substance use, as well as physical symptoms, such as headaches, stomach aches, hyperactivity and insomnia. Boys consumed more energy drinks than girls, and age was a predictor of use, but the direction of this effect varied across studies. Sedentary and physically active children both consumed large amounts, suggesting links with sport and screen-based recreation. The qualitative focus groups reported beneficial effects on young people's bodies and sports performance, with few negative effects reported and little knowledge of energy drink ingredients. Taste and energy-seeking were selected as the main motives for consumption. Advertising and brand loyalty were major influences on attitudes to energy drinks, and family and friends were important. Twenty-three studies were rated as strong quality, and 23 were rated as moderate quality. The systematic review was rated low quality (the critical flaw being a lack of details on the excluded studies) by this review team. The review was focused directly on children and adolescents, and on energy drinks, providing a reasonable summary of the evidence.

⁶ Two studies were outside the target age range, one assessed 16 to 35 years, with a subgroup of ages 16 to 21 years (Bunting), and the other assessed 15 to 23 years, with 15 to 17 years as a subgroup (Emond).

Appendix 9: Risk of bias ratings

First Author (Year)	1. PICO components	2. Protocol	3. Study design explanation	4. Comprehensive search strategy	5. Duplicate study selection	6. Duplicate data extraction	7. Details of excluded studies	8. Description of included studies	9a. Risk of Bias assessment (RCTs)	9b. Risk of Bias assessment (NRSIs)	10. Funding source	11a. RCTs Meta-analysis	11b. NRSIs Meta-analysis (MA)	12. MA: Rob in individual studies	13. Rob: discussion of results	14. Heterogeneity	15. Publication bias	16. Reporting of conflict of interest	Relevance	Overall rating
Alhyas (2016)	+	-	-	P	-	-	-	P	NA	-	-	NA	+	-	-	-	-	+	P	CL
Ali (2015)	-	-	-	P	+	-	-	P	NA	-	-	NA	NA	NA	-	-	NA	+	P	CL
Bleich (2018)	+	-	-	P	-	-	-	+	NA	-	-	NA	NA	NA	-	-	NA	+	P	CL
Buck (2013)	+	-	-	P	-	+	-	-	NA	-	-	NA	NA	NA	-	-	NA	+	P	CL
Bull (2015)	+	+	-	P	+	+	P	P	NA	P	-	NA	NA	NA	-	+	NA	-	P	Low
Dawodu (2017)	+	-	-	P	+	-	-	P	NA	-	-	NA	NA	NA	-	-	NA	+	+	CL
Goldfarb (2014)	-	-	+	P	+	-	-	P	NA	-	-	NA	NA	NA	-	+	NA	+	P	CL
Lippi (2016)	-	-	+	P	+	-	-	P	NA	-	-	NA	NA	NA	+	+	NA	+	P	CL
Richards (2016)	-	-	-	P	-	-	-	+	-	-	-	NA	NA	NA	+	-	NA	+	P	CL
Roemer (2017)	-	P	-	P	-	+	-	+	NA	P	-	NA	NA	NA	+	+	NA	+	P	CL
Verster (2018a)	-	-	+	P	-	-	-	P	-	-	-	-	-	-	-	-	-	+	P	CL
Verster (2018b)	+	-	+	P	-	-	-	P	NA	-	-	NA	NA	NA	+	+	NA	+	P	CL
Visram (2016)	+	P	+	P	+	-	-	+	+	+	-	NA	NA	NA	+	+	NA	+	+	Low

Key: + = criterion met; - = criterion not met; P=criterion partially met; CL=critically low; NA=not applicable



Appendix 10: Overlap of primary studies included across reviews

	Review		Bleich 2018	Verster Koenig 2018	Verster 2018	Dawodu 2017	Roemer 2017	Alhyas 2016	Lippi 2016	Richards 2016	Visram 2016	Ali 2015	Bull 2015	Goldfarb 2014	Buck 2013	Overlap
	Included Studies	Country														
1	Abian-Vicen (2014)	Spain									✓					
2	Al-Hazzaa (2011)	Saudi Arabia						✓								
3	Al-Hazzaa (2014)	Saudi Arabia									✓					
4	Almalak (2014)	Saudi Arabia						✓								
5	Aluqmany (2013)	Saudi Arabia						✓								
6	Arria (2014)	USA									✓					
7	*Azagba (2013)	Canada			✓						✓					2
8	*Azagba (2014)	Canada	✓			✓				✓	✓					4
9	Azagba & Sharaf (2014)	Canada			✓						✓					2
10	Bashir (2016)	USA	✓													
11	Beckford (2015)	Australia		✓												
12	Branum (2014)	USA		✓												
13	Bryant Ludden (2010)	USA									✓					
14	Bunting (2013) ¹	N Zealand									✓					
15	Choi (2016)	USA									✓					
16	Cotter (2013)	USA									✓					
17	Costa (2014)	Australia									✓					
18	*Di Rocco (2011)	USA										✓		✓	✓	3
19	*Dufendach (2012) / Gray ²	NR												✓	✓	2

	Review		Bleich 2018	Verster Koenig 2018	Verster 2018	Dawodu 2017	Roemer 2017	Alhyas 2016	Lippi 2016	Richards 2016	Visram 2016	Ali 2015	Bull 2015	Goldfarb 2014	Buck 2013	Overlap
	Included Studies	Country														
20	EFSA (2015)	Europe		✓												
21	*Emond (2014)	USA				✓					✓					2
22	*Evren (2015)	Turkey				✓				✓	✓					3
23	Faris (2015)	Saudi Arabia									✓					
24	Flotta (2014)	Italy			✓											
25	Galaxy poll (ABC) (2013)	Australia		✓												
26	*Gallimberti (2013)	Italy				✓					✓					2
27	Gallimberti (2015)	Italy									✓					
28	Gallo-Salazar (2015)	Spain									✓					
29	Gambon (2011)	Netherlands									✓					
30	Gunja (2012)	Australia									✓					
31	*Hamilton (2013)	Canada				✓					✓					2
32	Hernandez (2009)	USA									✓					
33	Huhtinen (2013)	Finland									✓					
34	*Ilie (2015)	Canada					✓				✓					2
35	*Izquierdo 2012	Spain										✓		✓		2
36	Jones (2011)	Australia									✓					
37	Kilani (2013)	Oman						✓								
38	*Koivusilta (2016)	Finland	✓								✓					2
39	Kponee (2014)	USA					✓									
40	*Kristjansson (2014)	Iceland	✓								✓					2
41	Kumar (2014)	USA									✓					

	Review		Bleich 2018	Verster Koenig 2018	Verster 2018	Dawodu 2017	Roemer 2017	Alhyas 2016	Lippi 2016	Richards 2016	Visram 2016	Ali 2015	Bull 2015	Goldfarb 2014	Buck 2013	Overlap
	Included Studies	Country														
42	Lachenmeier (2013)	Germany		✓												
43	*Larson (2014)	USA				✓					✓					2
44	Locatelli (2012)	Brazil									✓					
45	Lubman (2014)	Australia									✓					
46	*Magnezi (2015)	Israel			✓						✓					2
47	Marmorstein (2016)	USA	✓													
48	*Martz (2015)	USA			✓		✓				✓					3
49	Mitchell (2014)	USA		✓												
50	*Miyake (2015)	USA				✓					✓					2
51	*Musaiger (2014)	Saudi Arabia						✓			✓					2
52	NZCNS (2002)	N Zealand		✓												
53	*Nowak (2015)	Poland				✓					✓					2
54	O'Dea (2003)	Australia									✓					
55	Park (2012)	USA									✓					
56	Park (2016)	Korea	✓													
57	Peters (2010)	USA								✓						
58	Polat (2013)	NR							✓							
59	Reid (2015)	Canada									✓					
60	*Richards & Smith (2015)	UK	✓							✓						2
61	Richards (2015)	UK								✓						
62	Richards (2016)	UK									✓					
63	Schoffl (2011)	NR											✓			

	Review		Bleich 2018	Verster Koenig 2018	Verster 2018	Dawodu 2017	Roemer 2017	Alhyas 2016	Lippi 2016	Richards 2016	Visram 2016	Ali 2015	Bull 2015	Goldfarb 2014	Buck 2013	Overlap
	Included Studies	Country														
64	*Schwartz (2015)	USA				✓					✓					2
65	*Seifert (2011) ⁴	USA									✓		✓			2
66	Seifert (2013)	USA									✓					
67	Temple (2010)	USA									✓					
68	Terlizzi (2008)	NR													✓	
69	*Terry-McElrath (2014)	USA				✓					✓					2
70	Tucker (2016)	USA			✓											
71	Usman (2012)	Pakistan										✓				
72	*Van Batenburg-Eddes (2014)	Netherlands				✓					✓					2
73	*Vilija (2014)	Lithuania								✓	✓					2
74	*Wilson (2012)	USA							✓			✓		✓		3
75	Wing (2015)	Hong Kong								✓						
76	Zucconi (2013)	Europe		✓												
	Totals		7	8	6	11	3	5	2	7	46	4	2	4	3	

*cited in more than one included review.

1 The study by Bunting et al (2013) collected data from focus groups participants aged (16-21). The proportion of the sample that was under 18 years old is not reported.

2 Buck et al. (2013) detailed a case cited by Gray et al (2012). However, in the paper by Gray et al., the same case is attributed to Dufendach et al. (2012).

3 The three papers by Richards et al. report outcomes from one research study

4 Seifert et al. (2011) is a review not a primary study

The study by Di Rocco et al. (2011) was not cited in the review by Ali et al (2015). However, one of the age relevant cases included in the Ali et al. (2015) review was consistent with the details reported by Di Rocco and so was attributed to that paper.