A rapid scoping review of harm reduction strategies for ecstasy (MDMA) users in recreational settings

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Systematic Review

Keywords: MDMA, Ecstasy, Harm Reduction, Scoping Review

Posted Date: January 3rd, 2024

DOI: https://doi.org/10.21203/rs.3.rs-2178425/v3

Additional Declarations: The authors declare no competing interests.

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ABSTRACT

Background: Adverse drug reactions (ADRs) can occur due to ecstasy use, and the number of people dying due to drug-related deaths has increased in the past 10 years. Harm reduction strategies could help prevent ADRs or decrease the incidence of life-threatening health consequences due to ecstasy use. However, no reviews have explored the breadth of evidence available on ecstasy harm reduction strategies.

Methods: A rapid scoping review was conducted using adapted JBI methodology to identify the prevalence and nature of harm reduction strategies that ecstasy users employ in recreational settings, with both peer-reviewed research and user-oriented drug information websites explored. Five databases (CINAHL, EMBASE, Medline, PsycINFO, CENTRAL) were searched for English language records from database inception to August 2022. User-oriented websites were identified via the project's stakeholder group and Google searches.

Results: Twenty reports representing 19 studies (one randomised control trial, nine quantitative descriptive studies and nine qualitative studies) were included. A wide variety of harm reduction strategies were reported, including drug-specific strategies (for example, limiting the amount of ecstasy consumed, buying from trusted sources, drug checking (pill testing)); behavioural strategies (for example, monitoring fluid (water) consumption, taking a rest break to regulate temperature, avoiding alcohol and mixing with other drugs; preloading and post-loading); and peer-related strategies (for example not using alone, looking out for friends). Ecstasy users obtain information on ecstasy's effects and/or harm reduction practices from a variety of sources including friends, nightclubs, TV news, drug leaflets, music magazines and user-oriented information websites. Fourteen user-oriented websites providing ecstasy-specific harm reduction information were identified, and strategies focused on dosage and frequency of use, interaction with other substances and prevention of health consequences, such as heatstroke, or dehydration among others. However, only two webpages provided citations to the evidence used for the content.

Conclusions: While numerous harm reduction strategies exist, employing them can depend on the users' overall goal/s which might also encompass avoiding comedown or increasing their high. Moreover, users' previous experience can influence how and when they adhere to harm reduction. More efficient ways of communicating harms and harm reduction strategies might be needed.

KEYWORDS

MDMA, Ecstasy, Harm Reduction, Scoping Review,

Introduction

Ecstasy (3,4-methylenedioxymethamphetamine – MDMA) is a common recreational drug and sought effects include euphoria and feelings of happiness [1] along with increased energy, musical appreciation and emotional closeness with others [2]. Illicitly acquired MDMA can vary in appearance, with crystalline and tablet forms available [2]. The consistency of crystalline MDMA can range from crystals to crushed powder, and can be prepared into capsules or "bombs" (cigarette paper wraps) for oral consumption with colours presenting from shades of beige to brown or off-white [2]. Modern ecstasy tablets typically feature logos, fictional characters or other cultural references and are available in a range of shapes and colours [2].

Ecstasy is often taken in settings such as night clubs and raves where an individual engages in prolonged and vigorous dancing often coupled with high temperatures while drinking very little water [3]. As a consequence, hyperpyrexia (hyperthermia; heatstroke) are frequently reported adverse drug reactions (ADRs) [4, 5]. Another ADR that is frequently reported is water intoxication with secondary low sodium levels, referred to as hyponatremia [4, 5]. The concurrent use of MDMA and alcohol may increase the risk of hyperthermia and hyponatremia [4]. Other ADRs as described in published case reports range from milder problems, such as restlessness, insomnia, bruxism/muscular clenching, nausea and dry mouth, to serious health issues including psychiatric problems, hepatotoxicity secondary to hyperthermia, cardiac and/or respiratory disorders, acute renal failure, aplastic anaemia, allergic reactions and anaphylaxis, eye and skin conditions [5]. Although rare, the use of MDMA can also lead to seizure, coma and death, largely due to hyperthermia or hyponatraemia associated to water intoxication [6].

Since 1995 when Leah Betts' ecstasy-related death was reported, the media continues to report on the stories of other young people who have tragically died as a result of taking this drug [7]. Lorna Spinks died at a nightclub in 2001 after consuming ecstasy [8], while Callum

Gill lost his life on his way to a music festival in 2017 [9]. Leah Heyes and Corey Kendall had serious adverse reactions to ecstasy in 2019 [10, 11], and James Diss unfortunately died in 2021 when he ingested drugs at a warehouse event [12]. Joelle Welsh became ill in a nightclub after taking ecstasy and died in hospital due to “acute toxic effects of MDMA” in 2021 [13]. One of the most recent deaths was of a 16-year-old, who is believed to have taken a specific type of ecstasy during the Leeds Festival in 2022 [14].

Whilst relatively rare [5], MDMA/ecstasy-related deaths have increased in England and Wales in the past decade, with the most recent figures reporting 67 deaths in 2021 compared to just 13 in 2011[15]. Harm reduction refers to the use of strategies that could help prevent ADRs or decrease the incidence of damaging health consequences relating to drug use [16]. Examples include drinking water or juice to supplement the fluid lost through profuse sweating and limiting intake of caffeinated energy drinks and alcohol, which have a diuretic effect [4]. Harm reduction interventions that have been suggested to limit MDMA-related ADRs include providing free water to event attendees and providing “chill out” spaces at venues to improve temperature control. Educational interventions seek to improve knowledge of ecstasy users and night time economy stakeholders regarding the importance of controlling body temperature and fluid intake, recognising the early signs of an ADR and the importance of promptly seeking medical assistance [3, 4, 17].

Unlike prescription medicines produced under highly regulated and reproducible conditions, the illicit drug MDMA is most often synthesised and distributed via criminal gangs without due regard for quality control. This means that ADRs may occur due to drug mislabelling/misidentification, the presence of contaminants, or inaccurate tablet dosing [18]. A public health intervention that has become increasingly available over recent years at festivals [19] through organisations such as DanceSafe (US) and the Loop (UK) is drug checking (pill testing) services [20, 21]. Such services invite users to submit substances for

chemical analysis and may provide individualised advice as part of a health consultation or intervention [21, 22].

Previous literature reviews have explored an overview of ecstasy use [23]; the harmful health effects of ecstasy [17, 24]; and mechanisms leading to hyperpyrexia and hyponatremia [4]. One further review [22] sought to identify what is known about drug checking services and people who use drugs, with just a brief mention of ecstasy. To date, however, no reviews have explored harm reduction strategies specific to ecstasy (MDMA).

The aim of this rapid scoping review was to map the harm reduction strategies that ecstasy (MDMA) users employ in recreational settings. Specifically, we identified the prevalence and nature of harm reduction practices and determined where ecstasy users seek harm reduction information. Given that there is a plethora of user-oriented drug information websites for ecstasy, we recognise the importance of the information contained within being credible in that that they contain reliable material relating to risk and harm reduction advice [3]. This rapid scoping review has also determined the ecstasy-specific harm reduction content of user-oriented drug information websites. Knowing the sites and sources of harm reduction information that are used by ecstasy users is important for targeting effective education strategies.

Methods

In order to conduct a scoping review within the required time available a rapid approach was conducted using established methods [25-27] and reported using Preferred Reporting Items for Systematic Reviews and Meta-Analyses Scoping Review extension (PRISMA-ScR) [28]. Using a streamlined process (e.g. searching fewer databases and omitting critical appraisal) a rapid review can provide high-quality evidence and knowledge [29]. Rapid scoping reviews have been conducted across a wide range of health-related topics for the purposes of

identifying key concepts or knowledge gap within a short timeframe [30-33]. Our registered study protocol on Open Science Framework can be found at: https://osf.io/tf427/.

Eligibility criteria

The eligibility criteria are presented using PCC framework [27], Participants (P), Concept (C) and Context (C) and can be found in Table 1 below

Table 1: Eligibility criteria

	Inclusion criteria	**Exclusion criteria**
Participants	Ecstasy users	Other recreational drugs
Concept	Harm reduction strategies used to avoid ecstasy-related side effects, 'comedown' and neurotoxicity	Policy approaches Mass media campaigns Schools-based harm reduction education programs University and college interventions Workplace interventions Strategies used to enhance positive ecstasy experience
Context	Any location where Ecstasy may be consumed	
Study design	All quantitative and qualitative study designs	

Searching for research evidence

Four databases (on the EBSCO platform – CINAHL; on the OVID platform - EMBASE, Medline, APA PsycINFO and CENTRAL) were searched for English language records from database inception to August 2022 using the keywords methylenedioxy-N-methylamphetamine OR MDMA OR ecstasy AND harm reduction OR modify) (see Additional file 1). Forward and backward citation tracking was undertaken using the web-based system Citation Chaser™[34]. All records were imported into reference software package EndNote X20™, duplicates removed and then all the records that remained were imported into the web-based systematic review software Rayyan™.

Searching for websites

We consulted with the project stakeholder group [35] to identify UK based websites that provided harm reduction information on ecstasy and also conducted a Google search [36]. For the Google search the following terms were used: harm reduction and ecstasy; harm reduction and MDMA; safe and MDMA; safe and ecstasy. One reviewer (DE) conducted the search and subsequently screened the first page of each Google output for relevant UK websites.

Study selection process

Two reviewers (DE, EG) screened the titles and abstracts of records using Rayyan™ and any disagreements were resolved through discussion. Full texts were retrieved for records that met the inclusion criteria and for those where a decision could not be made based on the title and/or abstract alone. Full-text screening (with the aid of a screening tool) was then conducted by one reviewer (DE, JCs), and all decisions were checked by another (JC, CB, BH) with any disagreements resolved through discussion.

Data extraction

For the research studies all demographic data (country, focus, participants, age, gender, recruitment, study design and methods) were extracted directly into tables by one reviewer (DE, JCs) and checked by another (JCs, DE). Findings relevant to the review objectives were extracted by one reviewer (DE, JCs) and 50% checked for accuracy by another (JCs, DE). The software package NVIVO 12 Plus™ was used to facilitate this process. Quality appraisal was not conducted.

For the websites all relevant details (title of the webpage, country of publication, date of publication, url of the organisation, source and url of any specific MDMA harm reduction information) were extracted directly into tables by one reviewer (DE, JCs) and checked by another (JCs, DE). The software package NVIVO 12 Plus™ was used to facilitate this process.

Presentation of results

The review findings are presented in tables and as narrative summary following the approach described by Arksey and O'Malley [25] and updated by Levac [26] and describe how the results relate to the review objectives and research question.

Study inclusions

Figure 1 shows the PRISMA-ScR flow diagram for study selection process [28]. Of the 877 records identified, 37 full-text reports were assessed for eligibility. Seventeen full-text reports did not meet the inclusion criteria (see Additional file 2). A total of 20 reports (representing 19 studies) were included. In addition, after duplicates had been removed 30 websites were assessed for eligibility and a total of 15 were included. Fifteen websites were excluded (see Additional file 3).

Insert Figure 1 around here

Characteristics of included studies

Publication type

Twenty reports representing 19 studies (see Tables 2 to 4) were selected for inclusion. There was one randomised control trial [37], nine quantitative descriptive studies [16, 38-44] and nine qualitative studies (across 10 reports) [18, 45-53].

Insert Tables 2 to 4 around here

Country of publication

The included studies were conducted in Australia (n=6) [16, 42, 44, 45, 49, 54], the USA (n=5 studies across six reports) [18, 40, 41, 46, 47, 52], the UK (n=2) [50, 51] and the

Netherlands [37]. Additionally, four studies were conducted across multiple countries, which often included USA, UK, Canada, among others, such as European countries, Mexico, and New Zealand [38, 39, 43, 48]).

Participant details

Across the included studies the participants were all ecstasy users (n=14 studies across 15 reports) [16, 18, 37-41, 43, 45, 47, 49-53] or ecstasy sellers [46], adult key informants which included drug checkers, drug sellers, or having extensive experience using or testing for new psychoactive substances [48] or music festival attendees of which a proportion had at some point used MDMA at a music festival [42, 44, 54].

Most of the studies focused on young adults with nine studies (represented across 10 reports) [16, 18, 37, 40, 42, 47-49, 51, 53] with participants reporting a mean age of under 30 years (mean age ranged from 21 to 28 years) and one further study reporting a median age of 25 years [52]. In 11 of the studies [16, 18, 37-39, 42, 45, 46, 49, 50, 52] some of the participants were 30-year-olds. Overall, the youngest participant across the included studies was 16 [37], while the oldest was in the 51-60 age range [50].

Characteristics of included websites

Fourteen webpages were included, and further details are provided within Table 5.

Insert Table 5 around here

Review findings

Prevalence and nature of harm reduction practices

A wide variety of harm reduction strategies for ecstasy (MDMA) users in recreational settings were reported including drug-related strategies, peer-related strategies and behavioural

strategies (see Table 6). These were used to either avoid ecstasy-related side-effects, 'comedown' (hangover experiences) and/or neurotoxicity effects.

Regarding prevalence, Davis and Rosenberg [39] reported that three quarters of those surveyed, regardless of whether a person was an occasional or regular ecstasy user or lived in the UK or USA, had employed 11 strategies at least once in the two-month assessment period out of 19 harm reduction practices proposed by the authors. The proposed harm reduction practices included ones presented in Table 6, as well as strategies aiming to enhance the effect of ecstasy, such as getting into a good mood prior to drug use [39]. All participants in the study by Allott and Redman [16] had used at least one strategy from a predetermined list.

Findings from the qualitative studies however reported that young people are not always concerned about the potential health risks of taking ecstasy as they have no personal experience of ADRs and there is often a disparity between the harm reduction strategies that young people report they engage in and their actual behaviour [45]. Although many young people are aware of the risks, Singer and Schesnul [52] reported that for some young people the benefits of ecstasy are more important to them than the potential harms and this justifies its use.

Drug-related strategies

Ten studies focused on or mentioned drug checking (pill testing) as a potential harm reduction strategy which can be conducted either by using ecstasy self-testing kits, through using drug checking (pill testing) operations provided by harm reduction organisations at venues / events, and through laboratories which are set up for drug testing [16, 38, 39, 42, 44, 49, 50, 52-54].

Some participants across the studies reported visually inspecting the shape, size and colour of an ecstasy pill for signs of adulteration [49, 52].

Two studies reported on the psychological determinants of behaviour that influence drug checking (pill testing) intentions [38, 44]. One study found that attitudes, subjective norms and behavioural control (psychological determinants of behaviour) were found to have a significant positive association ($p<0.001$) with drug checking (pill testing) intentions [38]. Greater baseline intentions to use drug checking (pill testing) services were a statistically significant predictor of engaging in this harm-reduction behaviour ($p=0.018$) during a 2–3-month follow-up period [38]. Murphy et al's. [44] findings support this as attitudes ($p<0.001$), subjective norms ($p<0.001$), and perceived behavioural control ($p<0.05$) were all found to significantly predict intention to use fixed offsite drug checking (pill testing) services. However, the authors differentiated between fixed offsite and onsite drug checking (pill testing), and further findings indicated that in contrast to fixed offsite drug checking (pill testing), subjective norms were the only significant predictors ($p<0.001$) of onsite drug checking (pill testing) services [44]. Additionally, Murphy et al. [44] explored intention to use ecstasy if drug checking (pill testing) was available and found that the availability of drug checking (pill testing) did not increase non-users' or experienced users' intention to consume the drug (p values not reported).

Risk reduction/pill consumption practices following drug checking (pill testing) results were explored across three studies. Southey et al. [54] reported that regular (daily, weekly or fortnightly) ecstasy users in Australia were more likely to take the drug regardless of the presence of possible adulterants, than rare (to six monthly, yearly or one time) users. The hypothetical drug checking (pill testing) scenarios in the study by Hollett and Gately [42] described either an inconclusive test (unknown substance), the detection of a high MDMA dose, or a harmful adulterant (such as paramethoxyamphetamine (PMA) or paramethoxymethamphetamine (PMMA). It was shown that ecstasy users only reported a

significantly greater likelihood of following harm reduction strategies compared to maintaining harm reduction intentions if known harmful adulterants were identified. Additionally, harm-reducing behaviours were significantly less likely for those who scored highly in 'sensation seeking' and particularly if a test result indicated a high MDMA dose ($p<0.01$) [42]. Qualitative findings show that some ecstasy users chose not to use the drug even though they had paid for it because on drug checking (pill testing) it was found to contain adulterants [53].

Limiting the frequency and intensity of use was mentioned by participants across nine studies [16, 39, 43, 45, 46, 49, 50, 52, 53]. This involved starting small, thereby minimising the quantity used in one go such as taking half a tablet, licking the tablet or dissolving the tablet under the tongue instead of swallowing. Other strategies included measuring the exact dose, limiting the total amount used within one session and spacing out the time between sessions (using it just monthly or just at weekends or on special occasions). Murphy et al. [43] reported that ecstasy users who exhibited a tangible level of concern were significantly more likely to limit their consumption as a precaution against the negative effects of ecstasy compared to those who were not concerned ($p=0.033$). It was also demonstrated that females were significantly more likely to limit their consumption than males ($p=0.003$) and that males were significantly more likely to take rest breaks than females ($\chi2=5.70$, $p=0.017$). Associations across specific age groups were not reported.

Other drug-related strategies which were identified included acquiring ecstasy pills from a trusted source to reduce the chance of having a pill that contains adulterants [39, 45, 46, 48-53], only using in familiar /comfortable surroundings or safe places where accessible assistance is available if needed [39, 46, 52, 53], and using a new batch of ecstasy tablets only after seeing how others reacted to it [39, 46].

Table 6: Strategies used to avoid ecstasy-related side effects, 'comedown' and neurotoxicity

	Quantitative Studies								Qualitative studies								
	Allott and Redman 2006 [16]	Davis and Rosenberg 2016 [38]	Davis and Rosenberg 2017 [39]w	Murphy et al 2021 [44]	Murphy et al. 2006 [43]	Hollett and Gately 2019 [42]	Southey et al 2020 [54]	Hansen et al. 2001 [45]	Jacinto et al 2008 [46]	Kelly 2007 [53]	Kelly 2009 [47]	Palamar and Sonmez 2022 [48]	Panagopoulos and Ricciardeli 2005 [49]	Rigg and Lawental 2018 [55]	Sharifmonfared and Hammersley 2020 [50]	Shewan et al. 2000 [51]	Singer and Scensul 2011 [52]
Drug specific strategies																	
Limiting frequency/Intensity of use	Y		Y		Y			Y	Y	Y			Y		Y		Y
Buying from a trusted source			Y					Y	Y	Y		Y	Y		Y	Y	Y
See how others react to new batch			Y						Y								
Drug checking (Pill testing services)	Y	Y	Y	Y		Y	Y			Y			Y		Y		Y
Only using in certain locations			Y						Y	Y							Y
Peer related strategies																	
Looking out for others / new users		Y						Y	Y	Y			Y		Y	Y	Y
Not using alone			Y					Y	Y	Y			Y		Y	Y	Y
Behavioural strategies																	
Avoid mixing with other drugs								Y							Y		
Preloading/post-loading	Y	Y	Y		Y			Y	Y	Y	Y						Y
Avoid mixing with alcohol					Y				Y	Y					Y		Y
Chilling out	Y		Y	Y	Y					Y			Y				
Staying hydrated	Y		Y		Y			Y	Y	Y		Y	Y	Y	Y		Y

Key: Y: Yes – strategy mentioned in published report

[a] The importance of staying hydrated was mentioned, although participants "hydrated" with alcohol. Reasons for this included: being singled out for not drinking alcohol and being unaware that alcohol can accelerate dehydration.

Peer strategies

The peer-related strategies which were identified included not using alone and only using in the presence of trusted friends [39, 45, 46, 49-53]. Additionally, it was felt to be important that friends looked out for each other, especially first-time users [38, 45, 46, 49-53]. The participants in the study by Jacinto et al. [46]. were sellers of ecstasy and they described their role as sometimes acting as “guides” or “trip sitters”

Behavioural strategies

A behavioural strategy that was mentioned across six of the included studies was ‘chilling out’ [16, 38, 43, 44, 49, 53]. In the context of harm reduction, chilling out involved taking regular breaks from a hot dance floor somewhere with a lower ambient temperature, often in designated rooms. This was used as a potential harm reduction strategy in order to minimise the risk of hyperthermia.

Drinking water to minimise the risk of dehydration and overheating was a frequently reported strategy across the included studies [16, 39, 43, 45, 46, 48-50, 52, 53, 55]. However, there were often issues with the supply of free water and cost of bottled water across some venues; in some outdoor festivals, long queues hindered some attendees from rehydrating [48, 53]. There was limited reference about not drinking too much water, to avoid the risk of hyponatraemia/water toxicity, with participants in just one study referring to this practice [49].

Participants across five of the included studies reported that they chose not to mix ecstasy with alcohol [43, 46, 50, 52, 53]. The reasons given included: to maximise the pleasurable effects [46, 50, 52], to minimize hangover (‘*comedown’*) effects [46, 53] and to manage the risk of dehydration [53]. However, participants within two further studies [48, 55] reported that they would mix alcohol and ecstasy as they were unaware of its dehydration effects [55] and

because it is often cheaper to obtain alcohol than water [48]. Controlling the number of other drugs consumed at the same time as ecstasy, especially class 1 drugs such as cocaine or heroin, was a behaviour reported by participants across two studies [45, 50] although in three studies participants reported polydrug use as a perceived means to minimise harm especially for the “comedown” period particularly with class 2 drugs such as cannabis [49, 51, 52].

Preloading and post-loading as potential harm reduction strategies were reported by participants across 10 studies [16, 38, 39, 43, 45-47, 49, 52, 53]. This involves consuming prescription or over the counter medications to reduce serotonin depletion either before the consumption of ecstasy (preloading) or afterwards to deal with the coming down effects of ecstasy (post-loading) [45, 49]. Substances consumed as part of preloading/post-loading ranged from pharmaceuticals to natural supplements and foods (see Table 7). Reasons reported for engaging in preloading/post-loading were: harm reduction which included wanting to reduce comedown, hangover or crash [16], to facilitate sleep [45, 49], to mitigate post-ecstasy depression [46, 47, 53], to lessen physical side effects such as body aches and to replenish the body [16, 46, 52], to decrease the chance of neurotoxicity [16, 47, 53] and in some instances to increase the enjoyable highs of ecstasy [16, 47, 53]. Three studies investigated the factors associated with preloading/post-loading behaviour [16, 38, 43]. Allott and Redman [16] found that being younger ($p=0.011$) and the number of times ecstasy had been used (more than 50 times) ($p=0.007$) were significantly associated with engaging in preloading behaviour, while post-loading was significantly associated with the number of times ecstasy had been used (more than 50) ($p=0.001$) and frequency (monthly or more) ($p=0.036$). However, this contradicted the findings of Davis and Rosenberg [38], who found that people who used ecstasy less frequently were significantly more likely to engage in preloading/ post-loading strategies ($p=0.012$). There was also a significant association ($p=0.046$) between the strength of a person’s habit to preloading/post-loading and how likely were to engage in this behaviour [38]. Murphy et al.[43] reported that ecstasy users who exhibited a tangible level of

concern about harm were significantly more likely to take vitamin tablets as a precaution against the negative effects of ecstasy compared to those who were not concerned (p=0.026).

Sources of harm reduction information

Five quantitative descriptive studies looked at where ecstasy users obtained information on ecstasy's effects and/or harm reduction practices from [16, 40, 41, 43, 55]. Two studies reported that the most popular source of harm reduction information was friends [40, 43]. Additionally, Murphy et al. [43] reported that females were significantly more likely to use friends as a source of harm reduction information than males (p=0.005). Across four of the studies [16, 40, 41, 43] around a third of respondents indicated other popular sources for harm reduction information were nightclubs, TV news, drug leaflets, music magazines and user-oriented drug information websites. Where nightclubs were chosen as a source of harm reduction information about ecstasy, the authors noted that it was not clear whether this related to having contact with others or whether printed information was available at such venues [43]. Although user-oriented drug information websites (such as DanceSafe and Erowid) were not amongst the top choice of sources of harm-reduction information [40] they were, however, deemed by some to be dependable [41] and accurate sources [40]. Falck et al. [40] reported that educated users (p=0.004) and younger users (p=0.005) were significantly more likely to obtain harm-reduction information about ecstasy from the internet. Allott and Redman [16] also reported on where ecstasy users found out about preloading and post-loading and the most popular source was from their partner or friends, followed by the internet. Similar to Allot and Redman [16], participants in the work of Rigg and Lawental [55] mentioned that they learnt about the dehydrating effect of ecstasy from friends and the internet, highlighting the importance of these two information sources.

One randomised controlled trial [37] was identified and this comprised two experiments. The first compared a harm reduction leaflet to a neutral information leaflet and the second

compared a harm reduction leaflet or harm reduction info-card. The leaflet was just above 1,200 words and was folded to credit card format on eight double-sided pages and the info-card was around 400 words with a weblink to further information. The leaflet contained information about the effects and risks related to ecstasy use and specific tips about how to use the drug in a safer way with specific recommendations to drink enough water while using ecstasy. The outcomes were concerned with whether ecstasy users had a more negative attitude and intention toward ecstasy use as a result of reading harm reduction information. The study was unable to demonstrate a change in outcome measures following the intervention and differences in responses between ecstasy users and non-users were not statistically significant ($p>0.05$).

Harm reduction content of user-oriented drug information webpages

A visual summary of the type of ecstasy (MDMA) specific harm reduction information that is covered across the content of the 14 user-oriented drug information webpages (referred to as webpages through the rest of the text) is presented in Table 8. All webpages provided information about dehydration risks and almost all provided information about hyperthermia/heatstroke (13/14), interactions with alcohol (13/14), initiating use with a low test dose (13/14), interactions with other illicit drugs (12/14), identifying when to seek help (12/14), waiting for a defined period between use (11/14) and hyponatraemia/overhydration (11/14). Relatively fewer webpages provided information on interactions with prescribed medications (7/14), not using alone (7/14), recommendations on dosage or dosing strategies (6/14), information on drug checking (pill testing) (6/14) and looking out for friends (6/14). Information or recommendations were rarely provided regarding frequency of use (2/14), the safe use of supplements (2/14) or pre-existing conditions which may contraindicate use (5/14). None of the webpages were able to provide a ‘one-stop shop’ of all relevant information.

Discussion

Young people and adults who consume ecstasy (MDMA) in recreational settings use a wide range of harm reduction strategies as a precaution against ADR, although others having balanced the risk still intend to consume ecstasy. Palamar and Sonmez [48] suggested that this is particularly problematic at festivals, as such annual events are often likened to 'mini vacations', with regular users frequently dosing and re-dosing, mixing drugs and not adhering to harm reduction recommendations like drinking fluid and taking rest breaks.

Friends and webpages were amongst the popular sources of ecstasy and harm reduction information [16, 41, 50, 55]. Regarding interventions aiming to provide information to prevent ADRs, we only found one RCT [37] that investigated the effects of harm reduction information via drug leaflets on attitude and intent to use ecstasy. This RCT found that the ecstasy-specific harm reduction leaflets did not have a significant aversive effect against the drug, neither among users nor non-users [39]. In the wider literature about harm reduction information sources and recreational drugs, most research focuses on cannabis. RCTs have investigated the role of motivational interviewing compared to drug information and advice, or a brief interview-based intervention conducted by primary care professionals to reduce cannabis consumption or risks associated with use [56, 57]. One of the RCT findings indicated that motivational interviewing was not significantly more effective in cannabis cessation than information and advice [56], while another RCT showed that primary care interventions could help younger and moderate cannabis users to reduce consumption [57]. However, these studies mainly focused on prevention of cannabis use, and less about harm reduction when someone is likely to keep consuming. This lack of research highlights a gap in information provision interventions for harm reduction both in ecstasy use and other drugs. In addition to RCTs, some qualitative studies highlighted barriers of harm reduction information, mainly in cannabis use. Young people often felt that public health information on cannabis was not credible, as it was too focused on harms [58]. Young people expressed the need for neutral information that was developed by their peers and was presented by individuals they could identify with or famous people [58, 59]. This further supports that there is a need for research

141 **Table 7: Summary of substances used for preloading or postloading across included studies**

Preloading/Post-loading substances		Studies
Pharmaceutical	Antidepressants (SSRIs such as Prozac)	Allot and Redman [16]; Kelly [47, 53]
	Sleeping tablets	Allot and Redman [16]; Panagopoulos and Ricciardelli [49];
	Tranquillisers (e.g. diazepam)	Panagopoulos and Ricciardelli [49]; Hansen et al [45]
	Cold and flu tablets	Panagopoulos and Ricciardelli [49]
	Snorting Adderall	Singer and Schensul [52]
	5-HTP	Allott and Redman [16]; Jacinto et al.[46]; Kelly [47, 53]; Murphy et al. [43]
Natural supplements	Multivitamins / vitamins	Allott and Redman [16]; Kelly 2007, 2009; Singer and Schensul [52]; Murphy et al. [43]
	Vitamin B complex	Allott and Redman [16]; Jacinto et al.[46]
	Vitamin C	Allott and Redman [16]; Jacinto et al.[46]; Kelly [47, 53]
	Ginko biloba	Kelly [47, 53]
	St. John's Wort	Allott and Redman [16]; Kelly [47, 53]
	Magnesium	Allott and Redman [16]
	Potassium	Jacinto et al.[46]
	Antioxidants (e.g., MSM, ALA)	Allott and Redman [16]; Jacinto et al.[46]
Food	Healthy, protein rich foods	Jacinto et al. [46]
	Turkey	Allott and Redman [16]
	Eating power bar	Jacinto et al. [46]; Murphy et al. [43]
	Healthy diet	Allott and Redman [16]; Jacinto et al.[46]; Davis and Rosenberg [39]
Drink	Milk	Allott and Redman [16]
	Guarana or energy drink	Allott and Redman [16]; Jacinto et al.[46]
	Fruit or fruit juice	Allott and Redman [16]; Jacinto et al.[46]; Singer and Schensul [52]

142 Key: ALA: alpha-lipoic acid; MSM: methylsulfonylmethane; SSRI: selective serotonin reuptake inhibitors; 5-HTTP: 5- hydroxy tryptophan

into how harm reduction information could be effectively delivered for people who use ecstasy or other recreational drugs.

Dosage

All except one webpage provided information on initiating ecstasy use with a low 'tester' dose, such as splitting ecstasy tablets into halves or quarters. This was also commonly mentioned as a harm reduction strategy by participants across the included studies. As the strength of ecstasy pills are often unpredictable [60], this an important harm reduction strategy that may present users with an opportunity to avoid ADRs associated with atypically strong tablets or adulterants which produce effects discordant with those of MDMA. Eleven webpages recommended users to wait for a specified period before re-dosing, though recommended times varied from 1 to 3 hours. In some cases, users were recommended to half the amount of MDMA consumed upon each subsequent re-dose; whilst this may be difficult to achieve in the case of ecstasy tablets. Overall, this harm reduction strategy was summarised by several sources in the phrase "start slow, stay low".

Frequency

Generally, the advice that is provided is to only take ecstasy every 2-3 months due to the depletion in serotonin levels [61, 62]. However, only two websites and participants in one of the studies mentioned spacing out the time between sessions [52].

Drug checking (pill testing) services

Ecstasy tablets are recognised to vary in strength (MDMA content) and purity. In some cases, they may contain other substances entirely [2]. Six of the user-oriented drug information websites recommended that users have their ecstasy tested so that they know exactly what is in them and participants across 10 of the studies (53%) reported that they utilised some form of drug checking (pill testing) services as a harm reduction strategy. Drug checking

strategies may vary considerably by the level of sophistication of the analysis. Colorimetric reagent kits lie at the lower end of the spectrum but are highly accessible and may be used at home by individuals. The reagents change colour depending on the substance present and can be used as a presumptive test to qualitatively identify the presence or absence of MDMA in an ecstasy tablet. Whilst useful for identifying tablets in which MDMA is entirely absent (e.g., tablets containing substituted cathinones or amphetamines such as PMMA), they are inaccurate in identifying tablets containing both MDMA and other substances. Moreover, the tests are unable to accurately quantify the MDMA content of tablets and some users may find interpretation difficult [63]. More sophisticated techniques allow for the identification of MDMA content and the presence of adulterants, though require specialist equipment and must be performed in a laboratory. This typically occurs as part of a 'drug testing' or 'drug checking' service. In the UK, service providers include Public Health Wales (WEDINOS Project- https://www.wedinos.org/), TICTAC (https://www.tictac.org.uk/), The Loop https://wearetheloop.org/ and Manchester Drug Analysis and Knowledge Exchange (MANDRAKE - https://www.sutcliffe-research.org/mandrake/). In the context of drug *checking*, results may be communicated to service users as part of a health consultation (e.g., The Loop) [23], or accessed remotely online (e.g., WEDINOS - https://wedinos.org/sample-results). In a systematic review of available evidence, Maghsoudi et al. [22] concluded that drug *checking* services can positively influence the intentions and behaviour of people who use drugs, particularly in cases where analytical results were other than expected. Moreover, Measham and Turnbull [23], found that 59.4% of British festival attendees reportedly moderated their consumption of substances (i.e., took less) when they were identified as being stronger than expected. However, this is in contrast with some of the findings in this rapid scoping review, as Hollett and Gately [42] reported that people would still intend to use ecstasy, even if double dose of MDMA was detected in their tablets. This indicates that further research might be needed regarding how drug checking (pill testing) results influence users' behaviour.

Interactions with alcohol, other drugs and prescription medication

Alcohol is often used concomitantly with ecstasy [particularly at leisure events (e.g., festivals and raves) [17, 48, 55]. However, concurrent alcohol and ecstasy use may contribute to increased risk of adverse drug reactions, such as hyperthermia, dehydration, hyponatraemia, anxiety and hepatotoxicity [4, 64]. In this scoping review we found that 93% of webpages mentioned the risks of mixing ecstasy with alcohol, while out of the included studies, participants in five (26%) mentioned that they avoided mixing the two. Rigg and Lawenthal [55] reported that some of the participants mentioned that they used alcohol to hydrate themselves partially due to a lack of knowledge about the dehydrating effect of alcohol. The antagonistic effects between alcohol and MDMA, which are CNS depressants and stimulants respectively, may dull desired effects. This may conceivably lead to users increasing the amount of MDMA consumed, in order to counteract this effect, as has been observed with other alcohol/stimulant combinations [65].

Eighty six percent of the included webpages in this review cautioned against polydrug use, while only 50% commented on the dangers of mixing ecstasy with prescription medication. Regarding the included peer-reviewed studies, participants in two (11%) declared not taking other drugs while on ecstasy. Due to the lack of human studies, there is a lack of clarity about interactions between ecstasy and other recreational drugs. However, roughly two thirds of MDMA/ecstasy-related deaths in England and Wales involve another drug that isn't alcohol [15]. Combinations such as ecstasy and other amphetamine derivatives can lead to more severe long term cognitive changes and neurotoxicity [66]. Prescription medications, antidepressants and other pharmaceuticals were widely reported to be used in preloading or post-loading strategies to avoid comedown or the neurotoxic effects of ecstasy. However, mixing antidepressants with ecstasy may increase the risk of serotonin syndrome, which may have fatal consequences [67]. Thus, it is important to raise awareness about the drug interactions and highlight what people should not take while using ecstasy.

Some perceived harm reduction strategies, particularly those involving pharmacologically active substances, may increase the risk of ADRs. Participants within three studies in this review [16, 45, 49] reported the use of sedatives (e.g., sleeping tablets/benzodiazepines) as a harm reduction strategy associated with ecstasy use. Ecstasy users may be unaware of the potentially dangerous interactions which occur when using multiple CNS depressants to manage undesired MDMA-related effects such as insomnia or anxiety. For example, in their survey of Australian ecstasy users, Allot and Redman [16] reported that 81.0% of ecstasy users consumed alcohol at the same time as MDMA and 29.3% reported the using sedatives afterwards. Some antidepressants reportedly used in pre/post-loading strategies [16, 47, 53], 53], including SSRIs, may also be associated with increased MDMA-associated mortality [68].

Hydration

All of the webpages provided information on the risk of dehydration and drinking water to mitigate against this and 11 (79%) of the webpages additionally provided information on limiting the amount of water consumed due to the risk of hyponatraemia. It has been reported that women appear to be at a greater risk of hyponatraemia/water intoxication following the use of ecstasy [69]. However, there was limited reference to avoiding overhydration from ecstasy users across the included studies, with participants in just one study referring to this practice [49]. Under Article 3, Section 3 of the Licensing Act 2003 (Mandatory Licensing Conditions) Order 2010, licensed premises in England and Wales must provide free tap water to customers upon request, where this is reasonably available; similar acts are in place in Scotland and Northern Ireland. As evidence suggests that dehydration can lead to hyperthermia, whilst water intoxication can occur when too much is consumed, establishing that an optimal recommended water intake may be helpful. Environmental factors may significantly affect levels of hydration and so it may also be useful to provide ecstasy users with information on recognising the signs of dehydration or water intoxication and when to

seek medical support. Two webpages recommended consuming isotonic sports drinks to reduce the risk of water intoxication. Whilst we were unable to identify any articles examining this in an MDMA-specific context, the consumption of isotonic sports drinks does not appear to reduce the incidence of exercise-induced hyponatraemia [70].

Peer strategies

Seven webpages (50%) recommended that ecstasy is not taken alone but in the company of others and such strategies were reported across eight (42%) of the included studies. Additionally, six webpages (43%) stressed the importance of looking out for others especially friends which was also considered an important strategy by ecstasy users across eight studies (47%). Information provided via leaflets appears to be ineffective at promoting abstinence, though it remains unclear whether they may be useful for disseminating harm reduction information aiming to modify behaviour and risk. As ecstasy users rank partners and friends as the most popular source of information [16], peer-to-peer education may present good opportunities for disseminating drug-related information, including harm reduction advice.

Pre-existing conditions

Only five webpages (36%) highlighted the increased risks associated with taking ecstasy if a person had certain pre-existing conditions or were taking medications for certain conditions which included high blood pressure; heart disease; epilepsy; liver problems; asthma or mental health issues such as depression or anxiety. As for other drugs of the amphetamine class, MDMA is metabolised by cytochrome P450 enzymes, principally the P450 2D6 isoform [71]. This means that any pre-existing medications that are 2D6 inhibitors (such as the anti-depressant fluoxetine (Prozac)) can increase exposure to higher concentrations of MDMA leading to potential overdose. Furthermore, drugs that inhibit multiple P450 isoforms can have even more profound effects. Serious pharmacodynamic drug-drug-interaction concerns can arise through augmentation of MDMA's pro-serotonergic effects (as referenced above in

preloading, post-loading). For example, cases of toxicity or death have been reported when ingesting MDMA with monoamine oxidase inhibitors such as the antidepressant phenelzine [71].

Lack of an evidence base

Evidence supporting the various harm reduction practices identified was found to vary considerably. Given the 'underground' nature of drug use, as well as difficulties in conducting research in this area, some amount of misinformation and urban myth may be expected to exist within the community. This was particularly notable for preloading and postloading strategies, where a range of foods and supplements (e.g., turkey) were reported as used to reduce harms. The use of 5-HTP, a serotonin (5-HT) precursor widely believed by ecstasy users to counteract MDMA-related serotonin depletion and neurotoxicity, is poorly supported by evidence. 5-HTP appears to have mild psychoactive effects when administered orally to human subjects [72], though its impact on MDMA-related risk is unclear. 5-HTP has been found to be beneficial in rodent models when administered parentally, prior to or following MDMA, alongside a peripheral decarboxylase inhibitor [73, 74]. However, the 5-HTP dose administered (50 mg/kg) is markedly higher than what is achievable using oral supplements (50-100 mg/capsule), making it difficult to assess the potential benefits of actual practice.

Only two of the webpages provided any evidence-based citations to support listed harm reduction information. Nine provided links to other websites and six provided links to further information within their own websites. Due to the relative infrequency of occurrence, and difficulties in verifying which practices have been adopted by ecstasy users, building an evidence base for behaviours which reduce the incidence of ADRs is challenging. After all, it is difficult to establish when an ADR has been avoided as a result of a particular behaviour. However, some behaviours known to increase risk, such as concurrent use of SSRIs and other drugs, have been established. It's unclear whether providing citations alongside advice may

improve the adoption of harm reduction practices. Condensed info cards were found to be more effective communication tools than detailed leaflets [37], which may limit the ability to include citations on educational materials. Drug services should seek to involve service users in the design and evaluation of harm reduction educational materials.

Limitations

Conducting a rapid scoping review inherently carries some limitations, as some of the processes, such as screening and data extraction, are modified to produce swift results. It is therefore possible that some studies that could be relevant may not have been included. However, the searches were conducted by an experienced information specialist across several databases, which is a strength of this rapid scoping review and helped identification of a wide range of studies. Although full-text screening and data extraction was conducted by one person, all processes were checked by a second reviewer for accuracy. In addition, user-oriented drug related websites were identified during consultations with topic experts, leading to a wide range of information sources about ecstasy included, which is also a strength of this rapid review. No quality appraisal was conducted, and while this is not a requirement for scoping reviews, this might influence the confidence in the findings.

While initially the focus of this scoping review was young people, the included studies contained a wide age range, including 40-year-olds and over. This might influence the generalisability of the findings. Across the included studies the concept of harm education was interpreted differently, and the same strategies were often used for avoiding ecstasy-related side effects, ‘comedown’, neurotoxicity and for enhancing the positive experience. Additionally, in most quantitative studies participants were asked to choose from a predetermined list as opposed to listing what harm reduction strategies they used. For the qualitative studies participants were often asked about specific harm reduction strategies such

as drug checking (pill testing), preloading/post-loading, monitoring their fluid levels, limiting their consumption or taking rest breaks.

Conclusion

This review was able to identify a wide variety of harm reduction behaviours utilised by people who use MDMA/ecstasy. Harm reduction behaviours can never eliminate the health risks posed by drugs and the safest practice is to avoid use entirely. Nevertheless, several strategies were identified for which there was some evidence of a reduction in risk. Behavioural strategies found to be supported by some evidence including taking breaks to avoid hyperthermia, maintaining adequate (but not excessive) levels of hydration, avoiding particular polydrug combinations, including with alcohol, moderating consumption ("start slow, stay low") and avoiding using alone. Some ADR avoidance strategies, particularly relating to preloading and post-loading, are poorly supported by evidence and, in some cases, may exacerbate potential harm. For example, the use of sedatives and antidepressants to counteract anxiety and insomnia can lead to increase MDMA toxicity through pharmacokinetic drug-drug interactions. Users of ecstasy should be made aware of these potential adverse interactions, though further research is necessary to establish an optimal communication strategy for reaching this group.

Disclaimer

The authors would like to state that they, nor Cardiff University, condone nor justify the use of any illegal substance.

Availability of data and materials

All data generated or analysed during this study are included in this published article and its supplementary files. Additional information may be provided upon reasonable request to the corresponding author.

Abbreviations

ADR: Adverse drug reaction

MDMA: 3,4-methylenedioxymethamphetamine

PMA: Paramethoxyamphetamine

PPMA: Paramethoxymethamphetamine

PRISMA-ScR: PRISMA extension for scoping reviews

References

1. Curran HV, Travill RA: **Mood and cognitive effects of +/-3,4-methylenedioxymethamphetamine (MDMA, 'ecstasy'): week-end 'high' followed by mid-week low.** *Addiction* 1997, **92:**821-831.

2. Pascoe MJ, Radley S, Simmons HTD, Measham F: **The Cathinone Hydra: Increased Cathinone and caffeine adulteration in the English MDMA market after Brexit and COVID-19 lockdowns.** *Drug Science, Policy and Law* 2022, **8:**20503245221099209.

3. Advisory Council on the Misuse of Drugs: **MDMA ('ecstasy'): a review of its harms and classification under the misuse of drugs act 1971.** London Home Office 2008.

4. van Amsterdam J, Brunt TM, Pierce M, van den Brink W: **Hard boiled: alcohol use as a risk factor for MDMA-induced hyperthermia: a systematic review.** *Neurotoxicity Research* 2021, **39:**2120-2133.

5. MAPS: **MDMA Investigator's Brochure.** 13th edition. San Jose: Multidisciplinary Association for Psychedelic Studies (MAPS); 2021.

6. Elkattawy S, Mowafy A, Younes I, Tucktuck M, Agresti J: **Methylenedioxymethamphetamine (MDMA)-induced hyponatremia: case report and literature review.** *Cureus* 2021, **13:**e15223.

7. Gray B: **Leah Betts 25 years on: The tragic photo and story of Essex girl's death that shocked a nation.** In *EssexLive*. Chelmsford: Reach PLC; 2020.

8. Whitney A: **Student on ecstasy 'foamed at the mouth'.** In *Independent*. London: Independent Digital News & Media Limited; 2001.

9. Keate G: **Student Calum Gill died after taking ecstasy for first time.** In *The Times*. London: Times Newspapers Limited; 2017.

10. Jones V, PA reporters: **Mum warns other teens after schoolgirl's ecstasy death.** In *WalesOnline*. London: Reach PLC; 2020.

11. Gantzer O: **Reading Festival death: student nurse died of drug overdose.** In *The Reading Chronicle*. High Wycombe: Newsquest Media Group Ltd.; 2020.

12. Streeting L: **'Caring' Bristol student, 20, died after taking MDMA and ketamine at club night.** In *BristolLive*. Bristol: Reach PLC; 2022.

13. Roig EF: **Student, 19, died after night out with friends, inquest finds.** In *BristolLive*; 2022.

14. Atkinson E: **Boy, 16, dies in suspected ecstasy-related incident at Leeds Festival.** In *Independent*; 2022.

15. Office for National Statistics: **Deaths Related to Drug Poisoning in England and Wales: 2020 Registrations.** Newport: Office for National Statistics; 2021.

16. Allott K, Redman J: **Patterns of use and harm reduction practices of ecstasy users in Australia.** *Drug & Alcohol Dependence* 2006, **82:**168-176.

17. Gowing LR, Henry-Edwards SM, Irvine RJ, Ali RL: **The health effects of ecstasy: a literature review.** *Drug and Alcohol Review* 2002, **21:**53-63.

18. Rigg KK, Sharp A: **Deaths related to MDMA (ecstasy/molly): Prevalence, root causes, and harm reduction interventions.** *Journal of Substance Use* 2018, **23:**345-352.

19. Palamar JJ, Fitzgerald ND, Keyes KM, Cottler LB: **Drug checking at dance festivals: a review with recommendations to increase generalizability of findings.** *Experimental and Clinical Psychopharmacology* 2021, **29:**229-235.

20. Dundes L: **DanceSafe and ecstasy: protection or promotion?** *Journal of Health & Social Policy* 2003, **17:**19-37.

21. Measham F, Turnbull GI: **Intentions, actions and outcomes: a follow up survey on harm reduction practices after using an English festival drug checking service.** *International Journal of Drug Policy* 2021, **Sep:**103270.

22. Maghsoudi N, Tanguay J, Scarfone K, Rammohan I, Ziegler C, Werb D, Scheim AI: **Drug checking services for people who use drugs: a systematic review.** *Addiction* 2022, **117:**532-544.

23. Peters GJ, Kok GA: **A structured review of reasons for ecstasy use and related behaviours: pointers for future research.** *BMC Public Health* 2009, **13:**230.

24. Rodgers J, Buchanan T, Pearson C, Parrott AC, Ling J, Heffernan T, Scholey AB: **Differential experiences of the psychobiological sequelae of ecstasy use: quantitative and qualitative data from an internet study.** *Journal of Psychopharmacology* 2006, **20:**437-446.

25. Arksey H, O'Malley L: **Scoping studies: towards a methodological framework.** *International Journal of Social Research Methodology* 2005, **8:**19-32.

26. Levac D, Colquhoun H, O'Brien KK: **Scoping studies: advancing the methodology.** *Implementation Science* 2010, **5**.

27. Peters MDJ, Marnie C, C. TA, Pollock D, Munn Z, Alexander L, McInerney P, Godfrey CM, Khalil HU: **Updated methodological guidance for the conduct of scoping reviews.** *JBI Evidence Synthesis* 2020, **18:**2119-2123.

28. Tricco AC, Lillie E, Zarin W, O'Brien KKC, H., Levac D, Moher D, Peters MDJH, T., Weeks L, Hempel S, Akl EA, et al: **PRISMA Extension for Scoping Reviews (PRISMA-ScR): checklist and explanation.** *Annals of Internal Medicine* 2018, **169:**467-473.

29. Langlois EV, Straus SE, Antony J, King VJ, Tricco AC: **Using rapid reviews to strengthen health policy and systems and progress towards universal health coverage.** *BMJ Global Health* 2019, **4:**e001178.

30. Barker S, Lynch M, Hopkinson J: **Decision making for people living with dementia by their carers at the end of life: a rapid scoping review.** *International Journal of Palliative Nursing* 2017, **23:**446-456.

31. Côté D, Durant S, MacEachen E, Majowicz, S., Meyer S, Huynh AT, Laberge M, Dubé J: **A rapid scoping review of COVID-19 and vulnerable workers: Intersecting occupational and public health issues.** *American Journal of Industrial Medicine* 2021, **64:**551-566.

32. Threapleton DE, Chung RY, Wong SYS, Wong E, Chau P, Woo J, Chung VCH, Yeoh EK: **Integrated care for older populations and its implementation facilitators and barriers: a rapid scoping review.** *International Journal for Quality in Health Care* 2017, **29:**327-334.

33. Vogt F, Kurup KK, Mussleman P, Habrun C, Crowe M, Woodward A, Jaramillo-Gutierrez G, Kaldor J, Vong S, Del Rio Vilas V: **Contact tracing indicators for COVID-19: Rapid scoping review and conceptual framework.** *PLoS ONE* 2022, **17:**e0264433

34. Haddaway NR, Grainger MJ, Gray CT: **Citationchaser: A tool for transparent and efficient forward and backward citation chasing in systematic searching.** *Research Synthesis Methods* 2022, **13:**533-545.

35. Pollock D, Davies EL, Peters MDJ, Tricco AC, Alexander L, McInerney P, Godfrey CM, Khalil H: **Undertaking a scoping review: A practical guide for nursing and midwifery students, clinicians, researchers, and academics.** *Journal of Advanced Nursing* 2021, **77:**2102-2113.

36. Mahood Q, Van Eerd D, Irvin E: **Searching for grey literature for systematic reviews: challenges and benefits.** *Research Synthesis Methods* 2014, **5:**221-234.

37. Whittingham JRD, Ruiter RAC, Bolier L, Lemmers L, Van Hasselt N, Kok G: **Avoiding counterproductive results: An experimental pretest of a harm reduction intervention on attitude toward party drugs among users and nonusers.** *Substance Use and Misuse* 2009, **44:**532-547.

38. Davis AK, Rosenberg H: **Using the Theory of Planned Behavior to predict implementation of harm reduction strategies among MDMA/ecstasy users.** *Psychology of Addictive Behaviors* 2016, **30:**500-508.

39. Davis AK, Rosenberg H: **Specific harm reduction strategies employed by 3,4-methylenedioxymethamphetmine/ ecstasy users in the United States and the United Kingdom.** *Drug Science, Policy and Law* 2017, **3**.

40. Falck RS, Carlson RG, Wang J, Siegal HA: **Sources of information about MDMA (3,4-methylenedioxymethamphetamine): perceived accuracy, importance, and implications for prevention among young adult users.** *Drug and Alcohol Dependence* 2004, **74:**45-54.

41. Gamma A, Jerome L, Liechti ME, Lumnall HR: **Is ecstasy perceived to be safe? A critical survey.** *Drug and Alcohol Dependence* 2005, **77:**185-193.

42. Hollett RC, Gately N: **Risk intentions following pill test scenarios are predicted by MDMA use history and sensation seeking: A quantitative field study at an Australian music festival.** *Drug & Alcohol Review* 2019, **38:**473-481.

43. Murphy PN, Wareing M, Fisk J: **Users' perceptions of the risks and effects of taking ecstasy (MDMA): a questionnaire study.** *Journal of Psychopharmacology* 2006, **20:**447-455.

44. Murphy S, Bright SJ, Dear G: **Could a drug-checking service increase intention to use ecstasy at a festival? .** 2021, **40:**974-978.

45. Hansen D, Maycock B, Lower T: **'Weddings, parties, and anything...', a qualitiative analysis of ecstasy use in Perth, Western Australia.** *International Journal of Drug Policy* 2001, **12:**181-199.

46. Jacinto C, Duterte M, Sales P, Murphy S: **Maximising the highs and minimising the lows: harm reduction guidance within ecstasy distribution networks.** *International Journal of Drug Policy* 2008, **19:**393-400.

47. Kelly BC: **Mediating MDMA-related harm: Preloading and post-loading among ecstasy-using youth.** *Journal of Psychoactive Drugs* 2009, **41:**19-26.

48. Palamar JJ, Sonmez I: **A qualitative investigation exploring why dance festivals are risky environments for drug use and potential adverse outcomes.** *Harm Reduction Journal* 2022, **19:**12.

49. Panagopoulos I, Ricciardelli LA: **Harm reduction and decision making among recreational ecstasy users.** *International Journal of Drug Policy* 2005, **16:**54-64.

50. Sharifimonfared G, Hammersley R: **Harm reduction and quitting techniques used by heavy MDMA (ecstasy) users.** *Addiction Research & Theory* 2020, **28:**222-230.

51. Shewan D, Dalgarno P, Reith G: **Perceived risk and risk reduction among ecstasy users: the role of drug, set, and setting.** *International Journal of Drug Policy* 2000, **10:**431-453.

52. Singer EO, Schensul JJ: **Negotiating ecstasy risk, reward, and control: a qualitative analysis of drug management patterns among ecstasy-using urban young adults.** *Substance Use & Misuse* 2011, **46:**1675-1689.

53. Kelly BC: **Club drug use and risk management among "Bridge and Tunnel" youth.** *Journal of Drug Issues* 2007, **37:**425-443.

54. Southey M, Kathirgamalingam A, Crawford B, Kaul R, McNamara J, John-Leader F, Heslop J, Pit SW: **Patterns of ecstasy use amongst live music event attendees and their opinions on pill testing: a cross sectional study.** *Substance Abuse Treatment, Prevention & Policy* 2020, **15:**1-13.

55. Rigg KK, Lawental M: **Perceived risk associated with MDMA (ecstasy/molly) use among African Americans: what prevention and treatment providers should know.** *Substance Use & Misuse* 2018, **53:**1076-1083.

56. McCambridge J, Slym RL, Strang J: **Randomized controlled trial of motivational interviewing compared with drug information and advice for early intervention among young cannabis users.** *Addiction* 2008, **103:**1809-1818.

57. Laporte C, Vaillant-Roussel H, Pereira B, Blanc O, Eschalier B, Kinouani S, Brousse G, Llorca P-M, Vorilhon P: **Cannabis and young users—a brief intervention to reduce their consumption (CANABIC): a cluster randomized controlled trial in primary care.** *The Annals of Family Medicine* 2017, **15:**131.

58. Kvillemo P, Strandberg AK, Gripenberg J: **Attitudes to cannabis use and public prevention information among young adults: a qualitative interview study with implications for prevention practice.** *Frontiers in Public Health* 2022, **10**.

59. Moffat BM, Jenkins EK, Johnson JL: **Weeding out the information: an ethnographic approach to exploring how young people make sense of the evidence on cannabis.** *Harm Reduction Journal* 2013, **10:**34.

60. Couchman L, Frinculescu A, Sobreira C, Shine T, Ramsey J, Hecht M, Kipper K, Holt D, Johnston A: **Variability in content and dissolution profiles of MDMA tablets collected in the UK between 2001 and 2018 – A potential risk to users?** *Drug Testing and Analysis* 2019, **11:**1172-1182.

61. **MDMA** [https://www.drugsand.me/drugs/mdma/]

62. Kish SJ, Furukawa Y, Ang L, Vorce SP, Kalasinsky KS: **Striatal serotonin is depleted in brain of a human MDMA (Ecstasy) user.** *Neurology* 2000, **55:**294.

63. Harper L, Powell J, Pijl EM: **An overview of forensic drug testing methods and their suitability for harm reduction point-of-care services.** *Harm Reduction Journal* 2017, **14:**2017.

64. Vercoulen E, Hondebrink L: **Combining ecstasy and ethanol: higher risk for toxicity? A review.** *Critical Reviews in Toxicology* 2021, **51:**1-14.

65. Pennings EJ, Leccese AP, Wolff FA: **Effects of concurrent use of alcohol and cocaine.** *Addiction* 2002, **97:**773-783.

66. Mohamed WM, Ben Hamida S, Cassel JC, de Vasconcelos AP, Jones BC: **MDMA: interactions with other psychoactive drugs.** *Pharmacology, Biochemistry, and Behavior* 2011, **99:**759-774.

67. Dobry Y, Rice T, Sher L: **Ecstasy use and serotonin syndrome: a neglected danger to adolescents and young adults prescribed selective serotonin reuptake inhibitors.** *International Journal of Adolescent Medicine and Health* 2013, **25:**193-199.

68. Cohen IV, Makunts T, Abagyan R, Thomas K: **Concomitant drugs associated with increased mortality for MDMA users reported in a drug safety surveillance database.** *Scientific Reports* 2021, **11:**5997.

69. Rosenson J, Smollin C, Sporer KA, Blanc P, Olson KR: **Patterns of ecstasy-associated hyponatremia in California.** *Annals of Emergency Medicine* 2007, **49:**164-171, 171.e161.

70. Dugas J: **Sodium ingestion and hyponatraemia: sports drinks do not prevent a fall in serum sodium concentration during exercise.** *British Journal of Sports Medicine* 2006, **40:**372.

71. Oesterheld JR, Armstrong SC, Cozza KL: **Ecstasy: pharmacodynamic and pharmacokinetic interactions.** *Psychosomatics* 2004, **45:**84-87.

72. Gendle MH, Golding AC: **Oral administration of 5-hydroxytryptophan (5-HTP) impairs decision making under ambiguity but not under risk: evidence from the Iowa Gambling Task.** *Human Psychopharmacology: Clinical and Experimental* 2010, **25:**491-499.

73. Sprague JE, Huang X, Kanthasamy A, Nichols DE: **Attenuation of 3,4-methylenedioxymethamphetamine (MDMA) induced neurotoxicity with the**

serotonin precursors tryptophan and 5-hydroxytryptophan. *Life Sciences* 1994, **55:**1193-1198.

74. Wang X, Baumann MH, Dersch CM, Rothman RB: **Restoration of 3,4-methylenedioxymethamphetamine-induced 5-HT depletion by the administration of l-5-hydroxytryptophan.** *Neuroscience* 2007, **148:**212-220.

Acknowledgements

We would like to acknowledge Mrs Joan Welsh, Joelle Welsh's grandmother. Joelle, a nursing student at Cardiff University, died due to an adverse drug reaction to ecstasy. Mrs Welsh contacted the University for help in reducing unnecessary deaths related to ecstasy use and requested research into the field of adverse drug reactions. As a response to her request, we have conducted initial literature searches to explore the evidence base, and based on our findings, we have identified gaps in harm reduction.

The following individuals were also involved in shaping the direction of this review

- Dr Sally Anstey, Emeritus reader and personal and public involvement representative
- Dr Mathew Hoskins, Consultant psychiatrist and principal investigator for MDMA-assisted therapy for PTSD trial
- Dr Nicholas Weaver, Lecturer: Mental health, learning disabilities and psychosocial care
- Professor David Whitaker, Head of School, School of Healthcare Sciences
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Funding

There was no funding associated with this work

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Contributions

DE was the principal investigator of this study

EC drafted and executed the search strategy

DE, JCs, JC, EG, BH, CB screened titles and abstracts, conducted full text screening

DE, JCs, JC, JH extracted the data

DE, JCs analysed the data

DE, JCs, MP, AW wrote the first draft of the manuscript

All authors provided comments and revisions on manuscript drafts. All authors read and approved the final manuscript.

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Ethics declarations

Ethics approval and consent to participate

This study did not require ethical approval.

Consent for publication

This study does not contain any individual person's data in any form.

Competing interests

The authors declare the following competing interests:

MP is an unpaid volunteer at The Loop, a drug checking charity. AW chairs the programme board for Public Health Wales' WEDINOS project.

Supplementary information

Additional file 1: Full search strategies

Additional file 2: Excluded studies

Additional file 3: Table of excluded organisational websites

Table 2: Summary of randomised controlled trials

Author/s **Country** **Focus**	**Participants** **Setting / Recruitment**	**Intervention details** **Data collection** **Outcomes / outcome measures**
Whittingham et al. 2009 The Netherlands *Experiment 1* To investigate whether exposure to campaign materials resulted in more personal acceptance of the use of party drugs among young people with and without a history of drug use	Participants *Experiment 1* (n=87) I: Ecstasy users (n=18) / non-users (n=23) C: Ecstasy users (n=19) / non-users (n=27) (Users defined as those who had used ecstasy in the past 2 months) Gender Female (43.7%) Age (years) Mean±SD: 21.49± 2.45 Range: 18-30 Setting Nightlife setting (popular bars and discotheques) Recruitment Researchers working in nightlife settings	Intervention Harm reduction leaflet for ecstasy Participants read a leaflet about ways to reduce health hazards as a result of ecstasy use Control Neutral information leaflet Participants read a neutral text about going out in which drug-related words or themes were avoided Data collection period Not reported Data collection methods Questionnaires Outcome/s of interest Drug use Attitudes and intentions towards ecstasy use Outcome expectancies (beliefs about expected outcomes of ecstasy use Outcome measure/s SQ - Drug use ADQ for attitude, intentions and outcome expectations
Whittingham et al. 2009 The Netherlands *Experiment 2* To evaluate intervention materials aimed at minimizing potential	Participants Experiment 2 (n=161 ecstasy and GHB / / n=92 (ecstasy only)) Ecstasy only I1: (leaflet) (n=27) / I2: (info-card) (n=27) C: (n=38) Gender	Intervention I1: Harm reduction leaflet for ecstasy I2: Harm reduction info-card Participants read a leaflet about ways to reduce health hazards as a result of ecstasy use Control Neutral information leaflet

negative health consequences associated with the use of party drugs	Female (55.3%) Age (years) Mean+SD: 20.61± 3.29 Range: 16-30 Setting Nightlife setting (popular bars and discotheques) Recruitment Researchers working in nightlife settings	Participants read a neutral text about going out in which drug-related words or themes were avoided Data collection period Not reported Data collection methods Questionnaires Outcome/s of interest Attitudes and intentions towards ecstasy use Outcome expectancies (beliefs about expected outcomes of ecstasy use Outcome measure/s ADQ for attitude, intentions and outcome expectations

Key: ADQ: authors developed questionnaire; SQ: single questions

Table 3: Summary of quantitative descriptive studies

Author/s **Country** **Focus**	**Participants** **Setting / Recruitment**	**Data collection** **Outcomes / Outcome measures**
Allott and Redman 2006 Australia To explore the prevalence, nature and factors associated with harm reduction practices employed by ecstasy users in Australia, with a specific focus on the practice of PreL & PostL	Participants Over 18s who have used ecstasy at least once in their lifetime (n=116) Gender Female (51.3%) Age Mean±SD: 26.5± 5.6 Range= 18-41 Setting Any Recruitment (1) convenience sampling and 'snowballing' among individuals known to the researchers (98 questionnaires distributed), and (2) via an advertisement on an ecstasy-related website and e-newsletter	Data collection methods Questionnaires (open & closed responses) Data collection period Between June and Dec 2004 Outcomes of interest Drug checking (Pill testing) Harm reduction strategies PreL and PostL Outcome measure/s Frequency of drug checking (pill testing) Strategies participants endorsed (from a list) in order to avoid negative side effects Knowledge (sources of information) of PreL & PostL Different types of PreL &PostL substances Main sources where PreL & PostL products were obtained Most common reasons for PreL & PostL Frequency of PreL & PostL Factors associated with PreL & PostL
Davis and Rosenberg 2016 UK, USA, Canada, New Zealand To test whether attitudes, subjective norms, and perceived behavioural control were associated with baseline intention to PreL/PostL and baseline	Participants Have had ecstasy at least once during the previous 3 months & planning to consume ecstasy at least once during the 2-month FU period Baseline (n=391) / FU (n=100) Gender *Baseline:* Female (14%) FU: Female (14%) Age (years) *Baseline:* 18-24 (81%); 25-34 (17%); 35-54 (2%) *FU:* 18-24 (78%); 25-34 (21%); 35-54 (1%)	Data collection methods Questionnaires At two time points, baseline & 2MFU Data collection period Baseline: Between May and June 2014 FU: Between July and Aug 2014 Outcomes of interest Attitudes, subjective norms, perceived behavioral control and intentions regarding drug checking (pill testing) & PreL/PostL

intention to drug check (pill test)	Setting Any Recruitment Facebook advertisements	How frequently and automatically an individual had implemented regarding drug checking (pill testing) & PreL/PostL in the past (Habit strength) Ecstasy and substance use Ecstasy harm reduction strategies Outcome measures ADQs - TPB questionnaire - Index of Habit Strength questionnaire - Ecstasy and SU History questionnaire - Ecstasy HRS questionnaire
Davis and Rosenberg 2017 USA, UK To evaluate whether harm reduction interventions varied by country of residence and frequency of ecstasy use	Participants Ecstasy users (n=184) Gender US sample: Female (29%) UK sample: Female (15%) Age (years) US sample: 18-24 (71%); 25-34 (23%); 35-54 (6%) UK sample: 18-24 (71%); 25-34 (26%); 35-54 (3%) Setting Any Recruitment Advertisements on Facebook and postings on other websites, such as reddit.com, pillreports.com, bluelight.ru, and dancesafe.org	Data collection methods Questionnaires (open & closed responses) At two time points, baseline & 2MFU Data collection period Baseline: Between Oct and Nov 2013 FU: Between May and June 2014 Outcomes of interest Ecstasy and substance use Ecstasy harm reduction strategies Outcome measures ADQs - Ecstasy and SU history questionnaire - Ecstasy HRS questionnaire SQ Ecstasy use during 2MFU
Falck et al. 2004 USA To assess the perceived accuracy and the importance of various sources of information	Participants Ecstasy users (n=304) Gender Female (33.%) Age (years) Mean ±SD: 21.2±2.8	Data collection methods Questionnaire Data collection period May to Dec 2002 Outcomes of interest The perceived accuracy of information about ecstasy that participants attributed to various source

about MDMA/ecstasy among young adult users	Setting Any Recruitment Project staff employed ethnographic research methods to identify “ecstasy users” at dance clubs, music festivals, raves, and other venues. Snowballing was also used.	The most important sources of information about ecstasy for participants Whether participants had ever used the Internet to learn about ecstasy Whether participants had ever visited selected Internet sites to learn about ecstasy Outcome measures ADQ - How would you rate the following sources in terms of accuracy of the information they provide about ecstasy? *(list of 16 sources) -“ For you, what is the single most important source of information about ecstasy? - “Have you ever used the Internet to learn about ecstasy?” - “Have you ever visited the DanceSafe.org, Ecstasy.org, or Erowid.org websites to learn about ecstasy?” - “How important has the Internet been to you in learning about ecstasy?”
Gamma et al. 2005 USA To investigate the perceived harmfulness of ecstasy	Participants Ecstasy users (n=883 Non-users (n=40) Gender Not reported Age (years) 18–21 (37.5%); 13–17 (24.9%); 22–25 (22.0%) Setting Any Recruitment Advertisements were posted on e-mail discussion lists, forums, and web pages that provided information about the effects of recreational ecstasy use, or whose target audience was likely to be interested in such matters	Data collection methods Questionnaires (online) Data collection period Nor reported Outcomes of interest Trustworthiness and reliability of sources of information Outcome measures Rank the trustworthiness and reliability of 11 sources of information about illegal drugs, from the least to the most reliable - (USA) government sponsored classroom drugs education and online resources (e.g. Drug Abuse Resistance Education (DARE), freevibe.org), - User-oriented websites (e.g. erowid.org, dancesafe.org), - News outlets (e.g CNN, newspapers) - Friends and family - Professionals (e.g. medical practitioners, educators, and law enforcement officials)
Hollett and Gately 2019 Australia	Participants Music festival attendees (n=276) - Ever used ecstasy (57.2%)	Data collection methods Questionnaire (Ipad) Data collection period

To understand risk behaviour within three drug checking (pill testing) scenarios by determining the individual factors which predict subsequent risky or risk reduction intentions	Gender Female (56.5%) Age (years) Mean±SD: 23.66+6.12 Range 18 to 56 Setting Music festival Recruitment Convenience sample	Not reported Outcomes of interest Predicting risk intentions from MDMA use status and sensation seeking Outcome measures Brief sensation seeking scale ADQ – drug checking (pill testing) scenarios
Murphy et al. 2006 UK, USA, European countries, Australia, Canada To examine ecstasy users' perceptions of the risks associated with their use of ecstasy, their precautions against such risks, and its perceived effects on their lives	Participants Ecstasy users (n=328) Gender Female (42.4%) Age (years) Mean±SD: 22.5± 4.9 Setting Any Recruitment Advertisements in the music magazine 'Club On' and through the website 'www.ecstasy.org.uk'.	Data collection methods Questionnaires (open & closed responses) Data collection period Not reported Outcomes of interest Perceptions of risks and precautions taken Patterns of consumption and behaviour Sources of information about ecstasy and its effects Outcome measures ADQ - Perceived effects of ecstasy use - Ecstasy-using behaviour - Sources of information about the drug by ticking any appropriate options from a list of potential sources (e.g. TV news, friends, music magazines, etc.)
Murphy et al. 2021 Australia Would a drug checking (pill testing) service increase intention to consume ecstasy among	Participants Music festival attendees (n=247) - Ever used ecstasy (212) Gender Female (48%) Age 18-24 (20%); 25-34 (52%); 35+ (13%)	Data collection methods Questionnaires Data collection period 3-day period; but year not reported Outcomes of interest Ecstasy use Substance use

people who have never used ecstasy? Would a drug checking (pill testing) service increase intention to consume ecstasy among people who have previously used ecstasy? What psychological determinants of behaviour predict an individual's intention to use a drug checking (pill testing) service?	Setting Music festival Recruitment Convenience sampling	Intention, attitudes, subjective norms and perceived behavioural control regarding drug checking (pill testing) Outcome measures ADQ- drug checking (pill testing) scenarios and an adapted version of intention, attitudes, subjective norms and perceived behavioural control (Davis and Rosenberg 2016) SUH questionnaire Ecstasy use questionnaire
Southey et al. 2020 Australia To identify patterns of ecstasy use among live music event attendees; explore the opinions and potential usage of illicit drug checking (pill testing) programs and examine factors associated with the likelihood of still taking a pill containing a potential harmful substance	Participants Music festival attendees (n=760) - Used ecstasy (n=558) Gender Female (43.7%) Age (years) 18-19 (28.2%); 20-21 (31.6%); 22-23 (22.3%); 24+ (17.9%) Setting Music festival Recruitment Convenience sampling	Data collection methods Questionnaires Data collection period 2017 Outcomes of interest The proportion of people that have used illicit drugs that would still take a pill after results of drug checking (pill testing) show the presence of unintended drugs or substances Factors are associated with the likelihood of still taking a pill despite a drug checking (pill testing) service detecting a harmful substance in the pill Outcome measures ADQ -adapted from a variety of questionnaires If a harmful substance was detected in your drugs using the drug checking (pill testing) service, how likely would you be to still consume them?

Key: 5 HTTP: 5-hydroxy tryptophan; ADQ: authors developed questionnaire; FU: follow-up: HRS :harm reduction strategy: PostL: Post-loading: PreL: Preloading; SU: substance use: SQ: single question; TBP: Theory of Planned Behaviour

Table 4: Summary of qualitative studies

Author/s **Country** **Focus**	**Participants** **Setting / Recruitment**	**Data collection** **Methodology**
Hansen et al. 2001 Australia To investigate the patterns of use, the meanings associated with use, the perception of risk and the strategies adopted to reduce these risks for a sample of ecstasy users	Participants Ecstasy users (n=31) Gender Female (42%) Age (years) Range; 18-41 The majority were aged from 20–29 years, one-third of the interviewed sample and one-sixth of the total sample were aged over 30 years Setting Any Recruitment Through known associates and advertisements at a University and snowballing techniques	Data collection methods Participant observation, interviews, follow-up interviews, and informal conversations Data collection period Between July 1998 an Feb 2000 Methodology Not reported Data analysis An interpretative framework based upon symbolic interactionism using a constant comparative process
Jacinto et al. 2008 USA To examine the role of pleasure in interviewees' perceived harm reduction practices	Participants Ecstasy sellers (n=120) Gender Females: 23% Age Range: 19-53 Setting Any Recruitment Developing initial relationships with key informants from Ecstasy social scenes and hired these individuals as Community Consultants and then utilized snowball sampling	Data collection methods Key informant interviews and field observations Data collection period Between 2003 and 2006 Methodology Qualitative descriptive Data analysis Grounded theory
Kelly 2007, 2009	Participants	Data collection methods

USA Kelly 2007 This paper explores a range of risk management practices used by youth who utilize club drugs within rave and club subcultures Kelly 2009 To describe the practices of preloading and post-loading as well as the motivations underlying these behaviors among New York City metropolitan area youth	Youth who reported the use of one of four drugs-MDMA, ketamine, methamphetamine, or GHB-within the previous year (n=40) Gender Not reported Age (years) 18 to 25 Mean age of roughly 21 years old Setting Club venues in the Bridge and Tunnel region[a] Recruitment Recruited from club venues using theoretical sampling – no other details provided	Interviews Participant observations Data collection period Spring of 2003 through the Fall of 2004 Methodology Ethnography Data analysis Thematic analysis
Palamar and Sonmez 2022 USA, Canada, Mexico To determine festival-specific risk factors for adverse outcomes related to drug use	Participants Adult key informants (n=35) A drug checker, a drug seller, or report having extensive experience using or testing for new psychoactive substances Gender Female (28.6%) Age (years) Mean±SD: 26.7±5.5 Setting Nightlife and EDM festival scenes, Recruitment Recruited through study flyers on social media and on drug information message board websites commonly frequented by psychonauts Individuals were also via referral from other participants and recruited at harm reduction conferences	Data collection methods Interviews Data collection period 2015 to 2018 Methodology Qualitative descriptive Data analysis Inductive coding and the development of themes
Panagopoulos and Ricciardelli 2005 Australia To ecstasy users identify and manage the harms associated with their drug	Participants Ecstasy users (n=40) Gender Female (30%) Age (years)	Data collection methods Interviews Data collection period Over a 3 month period no further details provided

use, and the underlying decision-making process	Mean±SD: 24.83±4.11 Range: 18-31 Setting Any Recruitment Snowballing	 Methodology Qualitative descriptive Data analysis Development of themes
Rigg and Lawental 2018 USA To identify and characterize the perceived risks that African Americans associate with using MDMA	Participants African American young adults (n=100) Gender Female (31%) Age (years) Mean 28 Range 18-40 18-25 (38%) / 26-35 (42%) / 36-45 (20%) Setting Any Recruitment Posting flyers in high drug activity areas, bus stops, local college campuses, and neighborhoods with large numbers of African Americans Recruitment also included passing out study cards in and around nightclubs Snowballing	Data collection methods Questionnaires (n-100) Interviews (n=15) Data collection period Aug 2014 and Nov 2015 Methodology Mixed methods – descriptive survey and qualitative descriptive as part of a wider study Data analysis Development of themes
Sharifimonfared and Hammersley 2019 UK To examine the strategies that ex-heavy users of MDMA employed to quit, control, or cut down MDMA use	Participants Former heavy MDMA user (n=104/107) Gender Female (17.3%) Age 17-20 (19.2%); 21-30 (63.3%); 31-40 (11.6%); 41-50 (6%); 51-60 (1%) Setting Any	Data collection methods Open ended questions on a survey Data collection period Aug 2015 to April 2016 Methodology Mixed methods – descriptive survey and qualitative descriptive as part of a wider study Data analysis

	Recruitment Promoted in several online portals related to clubbing and MDMA use and various Facebook groups	Thematic analysis
Shewan et al. 2000 UK To provide a qualitative account of the role of social and behavioural factors in both predicting and reducing risk among ecstasy users in Glasgow (Scotland)	Participants Ecstasy users (n=42) Gender Female (43%) Age (years) Mean: 27 Setting Any Recruitment Recruited through networks of ecstasy users and dealers already accessible to the authors from previous research Snowballing	Data collection methods Focus groups Data collection period April to June 1996 Methodology Qualitative descriptive Data analysis Grounded theory
Singer and Schensul 2011 USA To examine: participants' negotiation of perceived risks and benefits of Ecstasy use, behavioural strategies employed to minimize risks, and the relationship of risk–benefit analysis, motivation for use, frequency of use, and polydrug use to participants' sense of control over their Ecstasy use	Participants Ethnically diverse ecstasy users (n=118) Gender Females (49%) Age (years) Range: 18-36 Median: 25 Setting Any Recruitment Flyer advertisements, face-to-face street and event recruitment, and network referral intended to reach hidden networks of users	Data collection methods Interviews Data collection period 2008 to 2009 Methodology Qualitative descriptive Data analysis Development of themes

Key: EDM: electronic dance music

[a] Bridge and Tunnel is local vernacular for youth who hang out or party in Manhattan but who reside in suburban neighbourhoods surrounding New York City. who resided in a suburban county outside New York

Table 5: Summary of included organisational websites

Organisational website **Country of origin / Date** **Url** **Source**	**Type of MDMA specific information**
Bristol Drugs Project UK / undated https://www.bdp.org.uk/ From google search (safe MDMA)	MDMA https://www.bdp.org.uk/get-information/drugs-information/mdma/
Derbyshire Recovery Partnership UK / undated https://www.derbyshirerecoverypartnership.co.uk/ From google search (safe MDMA)	MDMA Stay safe this festival season https://www.derbyshirerecoverypartnership.co.uk/news/stay-safe-this-festive-season/
Drugs and Me UK / 2021 https://www.drugsand.me/ Link from PsyCareUK and The Loop leaflet	MDMA https://www.drugsand.me/drugs/mdma/
EDAS UK / 13/07/2020 https://www.edasuk.org/ From google search (harm reduction ecstasy)	Harm reduction advice for using Ecstasy/MDMA https://www.edasuk.org/news/harm-reduction-advice-for-using-ecstasymdma/
Festival safe UK / 2022 https://www.festivalsafe.com/ From google search (safe MDMA)	Alcohol & other drugs https://www.festivalsafe.com/information/drugs-alcohol
Global Drug Survey UK / 2022 https://www.globaldrugsurvey.com Link from The Psychedelic Society and google search (Safe MDMA)	Thinking of using MDMA for the first time? Here are some things to think about https://www.globaldrugsurvey.com/gds-2018/thinking-of-using-mdma-for-the-first-time-heres-our-checklist-to-help-you-stay-safe/
Oxford Students' Union UK / undated https://www.oxfordsu.org/ From google search (harm reduction ecstasy)	Harm reduction. MDMA. Drug Advice https://www.oxfordsu.org/support/resourcehub/harmreductionmdma/

Pan-Dorset Safeguarding Children Partnership UK / undated https://pdscp.co.uk/ From google search (harm reduction ecstasy)	Harm reduction advice for using Ecstasy/MDMA https://pdscp.co.uk/wp-content/uploads/2020/08/Harm-Reduction-MDMA-words-poster.pdf
Release UK / 2022 https://www.release.org Link via Cardiff Students' Union and google search (harm reduction ecstasy)	Basic harm reduction (section on stimulants eg ecstasy) https://www.release.org.uk/basic-harm-reduction Ecstasy/MDMA https://www.release.org.uk/drugs/ecstasy-mdma/harm-reduction
Scottish Drugs Forum UK / undated https://www.sdf.org.uk/ From google search (harm reduction ecstasy)	Harm reduction information on pills, crystals and powders https://www.sdf.org.uk/harmreductionpillscrystalspowders/
Talk to FRANK UK / undated https://www.talktofrank.com/ Stakeholder recommendation and google search (harm reduction ecstasy)	How do I know what I am taking https://www.talktofrank.com/news/ecstasy-how-do-i-know-what-im-taking Ecstasy https://www.talktofrank.com/drug/ecstasy?a=Ecstasy#how-it-looks-tastes-and-smells
The Loop UK / undated https://wearetheloop.org/ Stakeholder recommendation	Crush Dab Wait https://wearetheloop.org/crush-dab-wait
The Mix UK / 01/09/2021 https://www.themix.org.uk/ From google search (safe MDMA)	MDMA https://www.themix.org.uk/drink-and-drugs/drugs-a-z/mdma-9989.html
The Psychedelic Society UK / undated https://psychedelicsociety.org.uk/ Stakeholder recommendation	Risk and harm reduction: MDMA https://psychedelicsociety.org.uk/risk-harm-reduction/mdma

Key: EDSA: Engage Develop Adapt Succeed

Table 8: Summary of organisational websites and associated MDMA specific information

Organisational website	Evidence Based (Citations provided)	Sources (Links to other websites)	Sources (Further links to own website)	Initial dosage (mg)	Booster doses or redoses	How often (The three-month rule)	Initiate use with low test dose	Wait for defined period between doses	Interactions (Alcohol)	Interactions (Other illicit drugs)	Interactions (Prescription medication)	Drug checking (Pill testing)	Heatstroke (Take breaks, stay cool)	Dehydration (Drink water)	Hyperhydration (Limit water)	Supplements	Pre-existing conditions	When to get help	Look out for your friends / others	Don't use alone
Bristol Drugs Project		Tripsit Drugs and Me	Y[a]	Y	Y	Y	Y	Y	Y	Y		Y*	Y	Y				Y	Y	
Derbyshire Recovery Partnership		Festivalsafe			Y		Y	Y	Y	Y			Y	Y				Y	Y	Y
Drugs and Me	Y	Erowid RollSafe Tripsit		Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y			
EDAS					Y		Y	Y	Y	Y			Y	Y	Y			Y		Y
Festival safe		The Loop SafeSesh Talk to Frank	Y[b]				Y	Y	Y	Y		Y		Y	Y			Y	Y	
Global Drug Survey		The Loop Energy Control Checkit WEDINOS	Y		Y		Y	Y	Y	Y	Y	Y	Y	Y	Y		Y[a]	Y		Y
Oxford Students' Union		Turning point	Y						Y	Y	Y		Y	Y	Y		Y[b]	Y	Y	
PDSCP				Y	Y		Y	Y	Y	Y			Y	Y	Y			Y		Y
Release			Y	Y			Y	Y	Y	Y			Y	Y	Y		Y[c]	Y	Y	Y
Scottish Drugs Forum					Y		Y	Y	Y		Y		Y	Y	Y			Y		
Talk to FRANK					Y		Y	Y		Y			Y	Y	Y		Y[d]			Y
The Loop		Erowid	Y	Y	Y		Y	Y	Y	Y	Y	[e]	Y	Y	Y			Y	Y	
The Mix		Talk to Frank	Y		Y		Y		Y		Y	Y	Y	Y				Y		Y

The Psychedelic Society	Y	Psychonaut Wiki GDS The Loop RollSafe	Y	Y	Y		Y		Y	Y	Y	Y	Y	Y	Y	Y		Y		
Total	2		8	6	11	2	13	11	13	12	7	6	13	14	11	2	5	12	6	7

Key: EDSA: Engage Develop Adapt Succeed; GDS: Global Drugs Survey: PDSCP: Pan-Dorset Safeguarding Children Partnership; Y: Yes (strategy mentioned in webpage)

[a] Medication for epilepsy; psychiatric or heart medication; [b] Heart; [c] High blood pressure; heart disease; epilepsy; liver problems; psych problems like depression or anxiety; [d] Heart; blood pressure problems; epilepsy; asthma; [e] The Loop operate a drug checking service and this information is provided on their main website but not within the specific resources analysed as part of this rapid review

Additional file 1: Full search strategies

CINAHL conducted 09-08-2022

Search number	Description	Results
1	(MH "Methylenedioxymethamphetamine")	1170
2	TI (midomafetamine* or methylenedioxymethamphetamine* or methylenedioxyamphetamine or methylenedioxy-N-methylamphetamine or MDMA or ecstasy) OR AB (midomafetamine* or methylenedioxymethamphetamine* or methylenedioxyamphetamine or methylenedioxy-N-methylamphetamine or MDMA or ecstasy)	1697
3	1 OR 2	1974
4	(MH "Harm Reduction")	4888
5	TI ((harm* or risk*) N3 (reduction or reduce or reducing or minimi?ing or prevention or management)) OR AB ((harm* or risk*) N3 (reduction or reduce or reducing or minimi?ing or prevention or management))	85,939
6	TI (modify* or protect*) N2 factor*) OR AB (modify* or protect*) N2 factor*)	13,152
7	OR 4-6	100,696
8	3 AND 7	150
9	8 limited to English Language	**149**

EMBASE conducted 09-08-2022

Search Number	Description	Results
1	exp midomafetamine/	2,223
2	(midomafetamine* or methylenedioxymethamphetamine* or methylenedioxyamphetamine or methylenedioxy-N-methylamphetamine or MDMA or ecstasy).tw.	8,474
3	1 OR 2	9,288
4	exp harm reduction/	8.031
5	((harm* or risk*) adj3 (reduction or reduce or reducing or minimi?ing or prevention or management)).tw.	253,685
6	((modify* or protect*) adj2 factor*).tw.	48,081
7	OR 4-6	303,006
8	3 AND 7	337
9	8 limited to English Language	**324**

Medline conducted 09-08-2022

Search Number	Description	Results
1	exp N-Methyl-3,4-methylenedioxyamphetamine/	4,149
2	(midomafetamine* or methylenedioxymethamphetamine* or methylenedioxyamphetamine or methylenedioxy-N-methylamphetamine or MDMA or ecstasy).tw.	6,664
3	1 OR 2	6,966

4	exp harm reduction/	3,898
5	((harm* or risk*) adj3 (reduction or reduce or reducing or minimi?ing or prevention or management)).tw.	179,416
6	((modify* or protect*) adj2 factor*).tw.	36,760
7	OR 4-6	216,221
8	3 AND 7	216
9	8 limited to English Language	**209**

APA PsychINFO conducted 09-08-2022

Search Number	Description	Results
1	exp Methylenedioxymethamphetamine/	2,218
2	(midomafetamine* or methylenedioxymethamphetamine* or methylenedioxyamphetamine or methylenedioxy-N-methylamphetamine or MDMA or ecstasy).tw.	3,907
3	1 OR 2	3,953
4	exp harm reduction/	4,336
5	((harm* or risk*) adj3 (reduction or reduce or reducing or minimi?ing or prevention or management)).tw.	38,907
6	((modify* or protect*) adj2 factor*).tw.	19,503
7	OR 4-6	58,535
8	3 AND 7	196
9	8 limited to English Language	**182**

CENTRAL conducted 09-08-2022

Search Number	Description	Results
1	MeSH descriptor: [N-Methyl-3,4-methylenedioxyamphetamine] explode all trees	211
2	midomafetamine* or methylenedioxymethamphetamine* or methylenedioxyamphetamine or methylenedioxy-N-methylamphetamine or MDMA or ecstasy):ti,ab,kw	456
3	1 OR 2	456
4	MeSH descriptor: [Harm Reduction] explode all trees	149
5	((harm* or risk*) NEAR/3 (reduction or reduce or reducing or minimi?ing or prevention or management)):ti,ab,kw	46,397
6	((modify* or protect*) NEAR/2 factor*):ti,ab,kw	1820
7	OR 4-6	47,919
8	3 AND 7	**13**

Additional File 2: Excluded studies

1. Copeland et al 2006: Ecstasy and the concomitant use of pharmaceuticals
   Reason for exclusion: Symptoms after using recreational drugs

2. Chinet et al 2007: Party drug use in techno nights: A field survey among French-speaking Swiss attendees
   Reason for exclusion: Harm reduction in general (all party drugs including alcohol, cannabis, Ecstasy and cocaine)

3. Akram and Galt 1999: A profile of harm-reduction practices and co-use of illicit and licit drugs amongst users of dance drugs
   Reason for exclusion: Harm reduction in general (all illicit drugs including amphetamine, Ecstasy and LSD)

4. Baggott 2002: Preventing problems in Ecstasy users: Reduce use to reduce harm
   Reason for exclusion: Literature review

5. Bellis et al 2002: Healthy nightclubs and recreational substance use. From a harm minimisation to a healthy settings approach
   Reason for exclusion: Discussion article

6. Carlson et al 2004: MDMA/Ecstasy use among young people in Ohio: perceived risk and barriers to intervention
   Reason for exclusion: Ecstasy use

7. Hayner 2002: MDMA misrepresentation: an unresolved problem for Ecstasy users
   Reason for exclusion: Discussion article

8. Henricksen 2022: Harm reduction in the rave community
   Reason for exclusion: Discussion article

9. Lancaster et al 2014: Examining the opinions of people who use drugs towards drug policy in Australia
   Reason for exclusion: Opinions on legalising of certain illicit drugs (including ecstasy)

10. Parrott 2007: Drug-related harm: a complex and difficult concept to scale
    Reason for exclusion: Editorial

11. Sheridan et al 2007: Legal piperazine-containing party pills--a new trend in substance misuse
    Reason for exclusion: Discussion article

12. Carlson et al 2004: MDMA/Ecstasy use among young people in Ohio: Perceived risk and barriers to intervention
    Reason for exclusion: Not about harm reduction

13. Rigg 2017: Motivations for using MDMA (Ecstasy/Molly) among African Americans: Implications for prevention and harm-reduction programs

Reason for exclusion: Not about harm reduction

14. Rodgers et al 2006: Differential experiences of the psychobiological sequelae of ecstasy use: quantitative and qualitative data from an internet study
    Reason for exclusion: Not about harm reduction

15. Sottile 2020: An examination of motives, consequences, and risk behaviors associated with MDMA use
    Reason for exclusion: Unavailable PhD thesis

16. White et al 2006: Risk and benefit perceptions of party drug use
    Reason for exclusion: Not about harm reduction

17. Dundes 2003: DanceSafe and ecstasy: Protection or promotion?
    Reason for exclusion: Effect in users on having DanceSafe (pill checkers) at dance venues

Additional file 3: Table of excluded organisational websites

Organisational website **Country of origin** **Url** **Source**	**Type of information**	**Reason for exclusion**
Alcohol and Drug Foundation Australia https://adf.org.au/ From google search	MDMA specific information: MDMA https://adf.org.au/drug-facts/mdma/	Not produced in the UK
Algonquin College Canada https://www.algonquincollege.com/ From google search	MDMA specific information: Safe MDMA/Molly/Ecstasy use https://www.algonquincollege.com/umbrellaproject/safer-mdma-molly-ecstasy-use/	Not produced in the UK
Cardiff Students' Union https://www.cardiffstudents.com/ UK Stakeholder recommendation	Generic information: Drugs https://www.cardiffstudents.com/advice/health-and-wellbeing/drugs/	NO MDMA specific information
Drug Science UK https://www.cardiffstudents.com/activities/society/drugscience/ Stakeholder recommendation and The Loop	General information about the student society	NO MDMA specific information
Drugs and Alcohol Information and support Ireland https://www.drugs.ie/ From google search	MDMA specific information: MDMA harm reduction information https://www.drugs.ie/mdma_harm_reduction_information/	Not produced in the UK

The Vaults of EROWID USA https://www.erowid.org/ Link from PsyCareUK, TripSit and The Loop	MDMA specific information: MDMA staying healthy https://www.erowid.org/chemicals/mdma/mdma_health2.shtml Tips for Using E Safely https://www.erowid.org/chemicals/mdma/mdma_info2.shtml Water issues with MDMA use https://www.erowid.org/chemicals/mdma/mdma_health_water.shtml	Not produced in the UK
Headpace Australia https://headspace.org.au/ From google search	MDMA specific information: Ecstasy https://headspace.org.au/assets/Uploads/Resource-library/Young-people/Ecstasy-web.pdf	Not produced in the UK
International Drug Policy Consortium UK https://idpc.net/ From google search	MDMA specific information: A guide to MDMA harm reduction https://idpc.net/alerts/2015/02/a-guide-to-mdma-harm-reduction	News article
Pivot Point Australia https://pivotpoint.org.au/ From google search	MDMA specific information: MDMA: Avoid an overdose and stay safe https://pivotpoint.org.au/avoid-an-overdose-and-stay-safe/	Not produced in the UK
PsyCareUK UK https://www.psycareuk.org/ Stakeholder recommendation	Generic information: Harm reduction https://www.psycareuk.org/harm-reduction/ Tips for Staying Safe at Festivals & Events[a] https://www.psycareuk.org/tips-for-staying-safe-at-festivals-events/	NO MDMA specific information

PsychonautWIKI German https://psychonautwiki.org/ Link from The Psychedelic Society and The Loop	MDMA specific information: MDMA https://psychonautwiki.org/wiki/MDMA	Not produced in the UK
RollSafe USA https://rollsafe.org/ Link from PsyCareUK, TripSit, The Psychedelic Society and The Loop leaflet	MDMA specific information: How to take MDMA (Molly/Ecstasy) https://rollsafe.org/how-to-take-mdma/ Generic information: Drug harm reduction: List of what you should know https://rollsafe.org/drug-harm-reduction/ (link to MDMA above)	Not produced in the UK
The Conversation Australia https://theconversation.com/ From google search	MDMA specific information: My friends are taking MDMA at raves and music festivals. IS it safe? https://theconversation.com/my-friends-are-taking-mdma-at-raves-and-music-festivals-is-it-safe-122128	Not produced in the UK
TripSit Not stated https://combo.tripsit.me/ Link from PsyCareUK and The Loop leaflet	MDMA specific information: MDMA https://wiki.tripsit.me/wiki/MDMA#Harm_Reduction MDMA Factsheet https://drugs.tripsit.me/mdma	Geographical origins of website not reported
WEDINOS UK https://www.wedinos.org Stakeholder recommendation	Generic information: Harm reduction advice https://www.wedinos.org/harm-reduction-advice	NO MDMA specific information

Figures

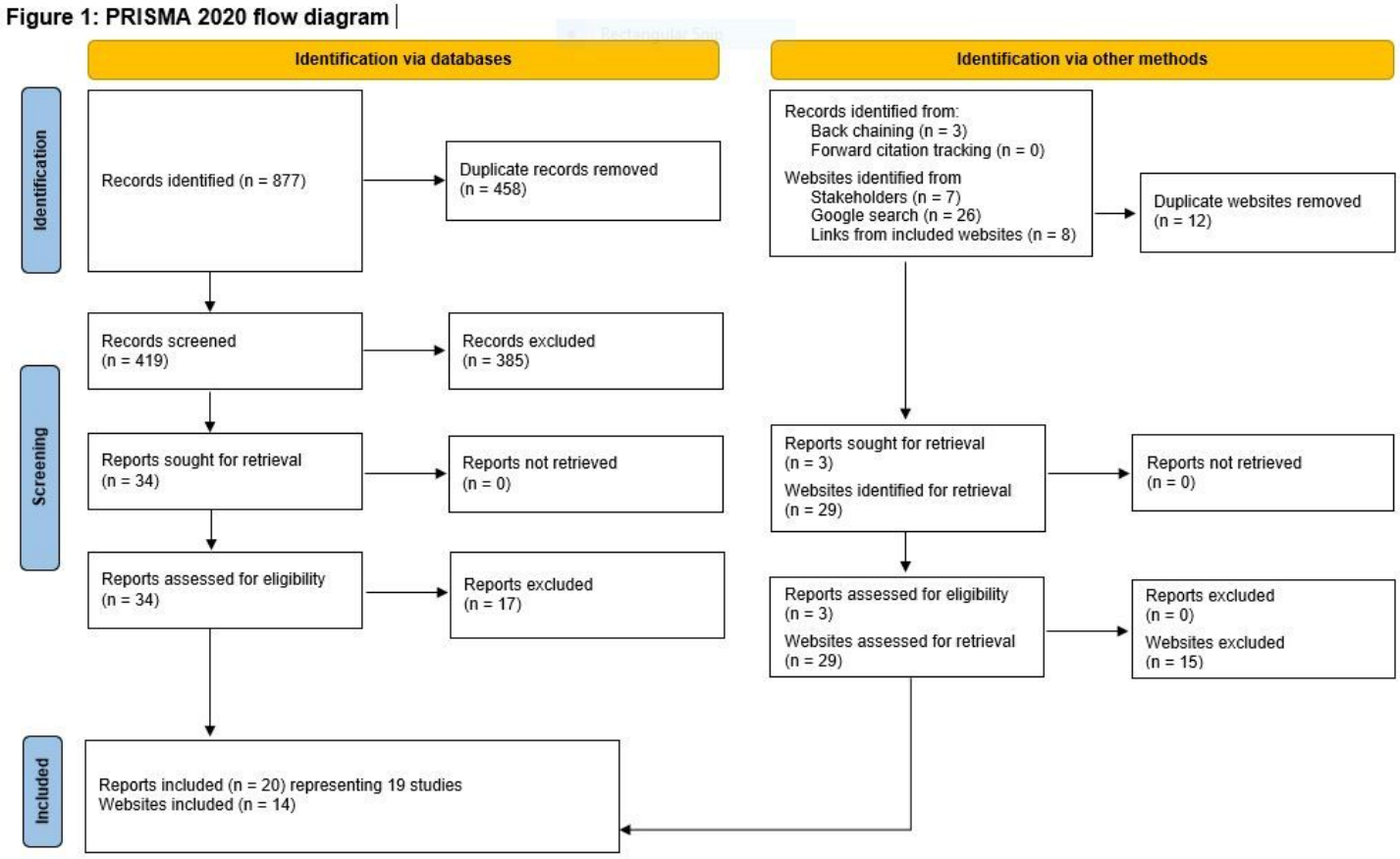

Figure 1

See image above for figure legend.