

Adverse and other unintended consequences of setting-based interventions to prevent illicit drug use: A systematic review of reviews

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Abstract

This article explores adverse and unintended consequences (AUCs) of setting-based public health interventions to prevent illicit drug use, including the mechanisms leading to these AUCs. Additionally, the reporting of AUCs in systematic reviews was assessed. Therefore, we conducted a systematic review of reviews and searched four big databases were searched. We included systematic reviews concerned with setting-based interventions to prevent illicit drug use. We used AMSTAR 2 to rate the overall confidence of the results presented in the reviews. Data on study characteristics, types and mechanisms of AUCs were extracted. An a priori categorisation of consequences drew on the WHO-INTEGRATE framework, and the categorisation of mechanisms on the Behaviour Change Wheel. For reviews reporting AUCs, the same information was also retrieved from relevant primary studies. Findings were synthesised narratively and in tables. Finally, we included 72 reviews, of which 18 reported on AUCs. From these, 11 primary studies were identified. Most of the reviews and primary studies were conducted in educational settings. The most prevalent AUCs reported in systematic reviews and primary studies were paradoxical health effects (i.e. increase of drug use). Potential mechanisms discussed primarily focussed on the change though social norms and practices. Changes of knowledge and perception were also mentioned. Concluding, the identified reviews and primary studies paid insufficient attention to AUCs of public health interventions to prevent illicit drug use. Where reported, it was mostly as an afterthought and narrowly framed as health related. No mentions of potential broader social consequences were found.

Keywords

Primary prevention, substance abuse, adverse effects, systematic review

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Introduction

Illicit drug use represents a major public health challenge. This can lead to substance addiction, a chronic and often relapsing behavioural disorder with medical and social implications for individuals, families and society at large.^{1–3} Primary prevention tends to focus on reducing or delaying first use or on preventing the transition from experimental use to addiction.^{4–6} According to the international standards on drug use prevention by the United Nations Office on Drugs and Crime (UNODC) and the World Health Organisation (WHO), setting-based approaches such as those concerned with families, schools, universities, communities and workplaces are of particular importance in making individuals less vulnerable to drug use and associated risky behaviours.⁶

Interventions aiming to prevent illicit drug use, as well as public health interventions in general, need to balance intended (or unintended) beneficial effects against any adverse effects. To do so, decision makers need to take into consideration adverse or unintended consequences (AUCs) – where unintended consequences could be beneficial or

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harmful – resulting from public health interventions, so that harm can be prevented or mitigated. Importantly, they need to take into account that AUCs are not limited to health but might become manifest in multiple other areas or sectors (e.g. social consequences, economic consequences).⁷ However, uncertainties remain regarding how to identify AUCs of public health interventions in a comprehensive manner^{8,9} and how to evaluate them best.¹⁰

The documentation of adverse events is well established in trials of clinical interventions, but even here, studies have shown that these are often insufficiently reported or underreported.^{11,12} In fact, the ability of short-term clinical trials to detect a broad range of adverse events is limited, and studies are usually powered for efficacy, but do not have sufficient power to detect adverse events.^{13–15} In contrast, the AUCs of public health interventions are very rarely studied and poorly reported.^{11,12,16} In recent years, researchers have begun to identify and describe harms and to suggest typologies or classifications of such harms^{7,17}; these imply that the potential impact of harmful effects caused by public health interventions may be considerable.^{14,18}

As the majority of adults with illicit drug use problems start using drugs during their adolescence, most prevention efforts are concerned with settings where young people live, learn or socialise (e.g. schools, family).^{4,19,20} Multi-component interventions aiming to prevent or stop young people from using illicit drugs tend to be complex and interact with the characteristics of the settings in which they are implemented^{21,22} representing a range of sources of uncertainty.^{22,23} It is important to take these complexities and sources of uncertainty into account and to acknowledge the multitude of intended and unintended consequences when planning or evaluating setting-based interventions to prevent illicit drug use.²⁴

Therefore, this systematic review of reviews has the primary objective to assess and categorise the AUCs of setting-based interventions to prevent illicit drug use, and to describe the mechanisms examined or hypothesised to lead to them. As a secondary objective, this study seeks to assess the reporting of AUCs in systematic reviews and to describe differences in the reporting of AUCs.

Methods

We conducted a systematic review of reviews of setting-based interventions to prevent illicit drug use and additionally retrieved relevant primary studies reported in the identified reviews. We used an unregistered predefined protocol.

Definitions and terminology

We use the term ‘adverse or unintended consequences’ or AUCs to describe events that were noticeable or observable

and are assumed to be related to the intervention of interest. These AUCs are not necessarily health-related but may extend beyond health (e.g. economic, social, environmental). The judgement of whether an AUC is beneficial or adverse, will be made by taking the perspective of the affected individuals and/or the researchers reporting on the consequence into account. It is often not possible to establish or rule out a causal relationship between an AUC and the intervention of interest (e.g. when a suicide occurs in the intervention arm of a school-based drug education intervention), so we consider every observed AUC as potentially caused by the intervention.

For the purposes of this review, the term ‘illicit drug use’ refers to the use of psychoactive substances outside of their legitimate use for medical or scientific purposes.⁶ We will focus on psychoactive substances such as cannabis, inhalants (e.g. nitrous oxide often called ‘laughing gas’, nitrides often called ‘poppers’), and new psychoactive substances (so-called ‘legal highs’ or ‘smart drugs’). Although considered illegal in some jurisdictions, this review will not address drugs such as coffee/caffeine, tobacco/nicotine or alcohol.

Search methods for identification of studies

Searches of articles published up to 14 June 2020 in MEDLINE, EMBASE, the Cochrane Library and Epistemonikos were performed, using two linked blocks of key terms associated with (1) illicit drug use and (2) setting-based prevention. Results were limited to systematic reviews and meta-analysis. The search strategy was adapted for each database (see Supplemental Appendix Tables 1 and 2). The language was restricted to English and German. Citations of included systematic reviews were subsequently hand-searched for additional relevant studies.

Identification of eligible systematic reviews

Screening of titles and abstracts and screening of full texts was initially performed according to predefined inclusion and exclusion criteria regarding Population, Intervention, Comparison and Study design (Table 1). All eligible systematic reviews were subsequently screened for reporting on AUCs, that is, outcomes. The corresponding full-texts of all primary studies reporting on AUCs were retrieved and assessed for eligibility (Table 1). Screening was performed independently by two researchers (JS, RB) using the software Rayyan.²⁵ Any discrepancies were discussed and resolved by consensus.

Data extraction and management

Data extraction was performed by one author (RB) using a pre-defined form and checked by a second author (JMS) for accuracy and comprehensiveness. The following information

Table 1. Eligibility criteria for reviews.

	Inclusion criteria	Exclusion criteria				
Population	<ul style="list-style-type: none"> Humans of any age who are not currently consuming any illicit drugs (e.g. marijuana, hashish, heroin, opium, opioids, cocaine, amphetamine, methamphetamine, benzodiazepine, ketamine, lysergic acid diethylamide, mescaline, psilocybin, inhalants) or are consuming these but are not dependent on them yet 	<ul style="list-style-type: none"> Humans who are addicted to one or more illicit drugs 				
Intervention	<ul style="list-style-type: none"> Setting-based interventions (e.g. in schools, families, workplaces, communities, neighbourhoods) to prevent illicit drug use No intervention 	<ul style="list-style-type: none"> Interventions to treat or support people using illicit drugs in healthcare settings (e.g. hospital, psychiatric institution) Interventions to prevent only tobacco or alcohol consumption or prevent any other form of addiction (e.g. gambling) Secondary and tertiary prevention of illicit drug use as well as harm reduction programmes 				
Comparison	<ul style="list-style-type: none"> Any other setting-based intervention to prevent illicit drug use Any other intervention to prevent illicit drug use 	<ul style="list-style-type: none"> None excluded 				
Outcome	<ul style="list-style-type: none"> Health-related intended or unintended events, effects or consequences (e.g. metabolic outcomes, mental health outcomes, effectiveness outcomes) Non health-related intended or unintended events, effects or consequences (e.g. changes in behaviours, educational outcomes, environmental outcomes) 	<ul style="list-style-type: none"> Studies only reporting economic measures (e.g. cost-effectiveness) 				
Study designs	<table border="0"> <tr> <td>For reviews</td> <td> <ul style="list-style-type: none"> Systematic reviews (of quantitative and/or qualitative studies) assessing the effects of setting-based interventions to prevent illicit drug use </td> </tr> <tr> <td>For primary studies</td> <td> <ul style="list-style-type: none"> All empirical study designs (e.g. epidemiological studies, qualitative studies) </td> </tr> </table>	For reviews	<ul style="list-style-type: none"> Systematic reviews (of quantitative and/or qualitative studies) assessing the effects of setting-based interventions to prevent illicit drug use 	For primary studies	<ul style="list-style-type: none"> All empirical study designs (e.g. epidemiological studies, qualitative studies) 	<ul style="list-style-type: none"> The study is not a systematic review or meta-analysis Mathematical modelling studies
For reviews	<ul style="list-style-type: none"> Systematic reviews (of quantitative and/or qualitative studies) assessing the effects of setting-based interventions to prevent illicit drug use 					
For primary studies	<ul style="list-style-type: none"> All empirical study designs (e.g. epidemiological studies, qualitative studies) 					

was extracted for systematic reviews and primary studies: (1) general information about the study (i.e. title, reference, publication year), (2) objective of the study and study characteristics, (3) approach to assessing the quality of included studies, (4) whether or not the study reports on AUCs, (5) the type, scope and scale of the AUCs (6) the reported mechanism leading to the observed effects, (7) conflicts of interest statements and funding sources. We extracted the following additional information for included primary studies: (1) characteristics of the intervention under investigation, (2) characteristics of the population and context.

Authors of included studies were contacted and requested to provide any missing data. Where the data available or provided was insufficient to decide on eligibility, the study was excluded.

Quality assessment

The confidence in the results of eligible systematic reviews was assessed using the AMSTAR 2 checklist and rating

scheme.²⁶ We did not conduct a risk of bias or quality assessment of primary studies.

Data analysis

The assessment and analysis of the type, scope, scale and potential mechanisms leading to the AUCs from systematic reviews and primary studies was done independently by two authors (JMS, RB); conflicts were resolved through discussion. Findings are presented narratively and through tables.

Classification of AUCs. We classified AUCs according to their type and scope (e.g. adverse health-related effects such as injuries; or beneficial social outcomes such as reduced unemployment rates). We used the WHO-INTEGRATE framework, an evidence-to-decision framework,^{27–29} as it explores public health interventions from a complexity perspective going beyond health effects and explicitly considering societal consequences. We directly

applied the six criteria of the framework as first-order domains but adapted the so-called sub-criteria of the framework as second-order domains (Table 2). Whenever the classification of a given AUC was unclear or if it fitted into more than one domain of the adapted WHO-INTEGRATE framework, this conflict was resolved through discussion within the research group.

Classification of mechanisms leading to AUCs. Where potential mechanisms of AUCs were reported or discussed, these were categorised using a framework based on the Behaviour Change Wheel (BCW).³⁰ The BCW was chosen as it is the most widely used approach for examining behaviour change and its influences at individual as well as societal levels. For the purposes of classifying mechanisms, we focussed on the nine intervention functions of the BCW and derived potential mechanisms leading to AUCs (e.g. through restrictions, through improving skills and abilities, through changing perceptions and attitudes) (Table 3). In Table 3 we present an adapted version of the proposed framework.

Assessment of the reporting of AUCs in systematic reviews. We used data on the year of publication (before/after the year 2010) as well as AMSTAR 2 rating of the systematic reviews to identify differences in the reporting of AUCs over time and according to systematic review quality. The year 2010 was chosen as the first PRISMA statement was published 2009 and the authors encourage to also consider adverse effects in systematic reviews.³¹ We assumed that this publication has changed the reporting within systematic reviews and that the implementation might have taken some time. Additionally, we investigated whether the reviews specified AUCs as an outcome of interest (in the Methods section) and whether they reported AUCs in the Results or Discussion section.

Results

Characteristics of included reviews and studies

After the removal of duplicates, the literature searches identified 2422 records. The full texts of 162 records were reviewed in more detail and 72 reviews met the criteria for inclusion (see Supplemental Appendix Table 3 for a list of excluded references). A total of 18 systematic reviews reported on AUCs of setting-based interventions to prevent illicit drug use (see Table 4)^{4,32–48}; from these 11 eligible primary studies were retrieved (see Table 5).^{49–59} The PRISMA flow-chart³¹ visualising this process is presented in Figure 1.

Reviews. Seventy two reviews were included. Of these 34 investigated interventions based in an educational setting (pre-school, school and higher education),^{4,34,35,39–41,44,46,48,60–84} three in a family setting,^{85–87}

three in a community setting,^{37,88,89} one in a church⁹⁰ and 31 in multiple settings.^{32,33,36,38,42,43,45,47,91–113} Most reviews used the age of participants as an inclusion criterion, resulting in 62 studies focussed on children and adolescents.^{4,32–41,43–48,60–70,72–85,87,89,92–95,97–107,110,113} The types of interventions varied between the reviews but mostly focussed on educational interventions ($n=16$)^{32,34,40,47,61,62,64,66,67,70,72,75,77,81,83,110} or included multiple interventions ($n=42$).^{4,33,36–39,41–44,46,48,60,65,68,69,71,73,74,76,78–80,82,84,85,87,88,90,95–100,103–105,107,108,111,113} Some interventions employed computer-based approaches to prevent substance abuse ($n=4$).^{47,94,109,112} Some of the included reviews focussed on interventions in certain countries, especially the United States ($n=18$).^{46,61,62,66,67,70,72–74,77,83,88,90,95,96,101,106,111} Detailed characteristics of all included reviews are presented in Supplemental Appendix Table 4. The subset of 18 reviews reporting on AUCs is presented in Table 4.

The overall confidence in the results of 56 out of 72 reviews was rated ‘critically low’,^{32–34,37,40–48,61–73,77–81,83–91,94–96,99–101,103–113} 10 reviews were rated ‘low’,^{60,74–76,82,92,93,98,102} one was rated ‘moderate’,³⁹ while six reviews were rated ‘high’^{4,35,36,38,45,97} (see detailed assessment in Supplemental Appendix Table 5). The five reviews rated ‘high’ were mostly Cochrane reviews,^{36,38,45,97} with one being a regular peer-reviewed publication.³⁵ Reviews performed most poorly concerning the following AMSTAR 2 items:

- Reporting sources of funding for included studies (36 out of 72)
- Use of satisfactory risk of bias assessment (42 out of 72)
- Establishing review methods prior to review conduct (54 out of 72)
- Justification for excluding individual studies (65 out of 72)

Primary studies. In total 11 primary studies^{49–59} reported AUCs of interventions aiming to prevent drug abuse. Nine primary studies were concerned with multi-component interventions.^{49–55,57,58} These interventions sought to prevent and reduce the consumption of multiple drugs (illicit drugs, tobacco, alcohol). All interventions, apart from two implemented in multiple settings,^{56,57} were based in schools ($n=9/11$).^{49–55,58,59} Ten out of 11 studies assessed educational interventions ($n=10/11$)^{49,51–59}, one study investigated multiple interventions (e.g. education, school regulation).⁵⁰ Characteristics of included primary studies are presented in Table 5.

Adverse and unintended consequences

All included reviews and primary studies were analysed using the a priori frameworks described in the method

Table 2. Framework used to categorise consequences.

WHO-INTEGRATE framework domains used to derive consequences ^{27,29}	Classification categories for identified consequences	Definition and description
Health-related consequences	Physical health and well-being	This domain captures consequences for the physical health and well-being of individuals and populations, including related behavioural, environmental or metabolic risk factors as well as the risk of accidents and being affected by violence.
	Psychosocial health and well-being	This domain includes consequences for mental health and well-being, including risk- and protective factors and practices, quality of life and social well-being.
Human and fundamental rights consequences	Human and fundamental rights	This domain covers consequences for all human and fundamental rights, including the right to physical integrity, autonomy, self-determination or privacy.
	Acceptability	This category captures consequences regarding the acceptability of the intervention in the target population as well as other affected populations. Acceptability includes the willingness to implement, adhere to or enforce the intervention.
Consequences related to acceptability and adherence	Adherence and compliance	This category describes the degree to which a population targetted by an intervention adheres to or refuses to comply with the intervention.
	Health-related equality and equity	This category covers the consequences regarding relative and absolute inequalities – whether assessed neutrally or judged with respect to their fairness – in health-related outcomes, as well as the relative capabilities of individuals to achieve health.
Consequences for equality and equity	Socio-economic equality and equity	This domain captures consequences for social outcomes and participation of individuals and groups, including aspects such as household income, housing and education. It furthermore captures consequences regarding the availability, accessibility, acceptability and quality of social services aiming to contribute to social outcomes and participation.
	Societal implications	This domain captures consequences for social outcomes and participation of individuals and groups, including aspects such as household income, housing and education. It furthermore captures consequences regarding the availability, accessibility, acceptability and quality of social services aiming to contribute to social outcomes and participation.
Societal implications	Social outcomes and participation	This domain captures consequences for social outcomes and participation of individuals and groups, including aspects such as household income, housing and education. It furthermore captures consequences regarding the availability, accessibility, acceptability and quality of social services aiming to contribute to social outcomes and participation.
	Communities and social cohesion	This category captures consequences for communities, including social cohesion, solidarity and the risk of social and political division. This includes consequences affecting actors and institutions of civil society, social life and culture which contribute to the functioning of communities.
	Social norms and values	This category covers consequences regarding social norms and values, including the social roles and role expectations of individuals within a given society or community and their identities.
Financial and economic considerations	Financial consequences	This domain captures consequences regarding financial costs, available financial resources, and budgetary implications regarding the intervention itself, as well as individuals (micro level), stakeholder groups or institutions affected by the intervention (meso level) or the society and their institutions (macro level). The financial consequences can, but do not necessarily lead to economic consequences (e.g. bankruptcy of businesses)
	Resource-related consequences	This domain addresses consequences for the availability, accessibility, affordability and quality of non-financial resources, such as devices and products, human resources, and infrastructure, beyond the health system. It captures these consequences for individuals (micro level), stakeholder groups or institutions affected by the intervention (meso level) or the society and their institutions (macro level).
	Economic consequences	This domain captures consequences for economic activities (e.g. producing, distributing, and consuming goods and services), for the economic situation (e.g. poverty, bankruptcy), as well as the stability, resilience, and sustainability of the economic activities and the economic situation. This includes individuals (micro level) and stakeholder groups or institutions (meso level) in their role as economic actors (e.g. in the form of employees or businesses), as well as the local, regional, national or supranational economy as a whole (macro level).
Health system consequences	Access to and utilisation of healthcare	This domain captures consequences regarding the availability, accessibility, acceptability and quality of preventative and curative health services and institutions.
	Health system functioning	This domain addresses how the intervention interacts (synergistically or adversely) with other interventions in the same setting or population and other not directly-related components of the health system.
Environmental consequences	Energy consumption and greenhouse gas emissions	This domain addresses consequences for energy consumption and energy efficiency as well as consequences regarding changes in the discharge of fossil carbon dioxide, methane and other greenhouse gases.
	Availability and quality of air, land and water	This domain captures different consequences regarding the quality (incl. risk of contamination) and availability (where applicable) of surface and ground water, land, soil, air and atmosphere.
	Animals, ecosystems and biodiversity	This domain captures the consequences regarding animal health and well-being (beyond their direct implications for human health and their economic value and function), integrity and functioning of ecosystems and (natural) biodiversity.

Table 3. Framework used to categorise mechanisms.

Behaviour Change Wheel categories used to derive mechanisms ³⁰	Mechanisms	Description
BHW-framework in general	Through changing behaviours	A measure leads to changes in behaviour, which affect health or other outcomes of interest (e.g. changes in smoking behaviour, practicing unsafe sex, diet changes).
	Through affecting metabolic or physiological reactions	A measure leads to metabolic changes, which affect health or other outcomes of interest (e.g. changes in immune response, metabolic changes affecting atherosclerosis).
Restrictions	Through restricting practices, goods or services	A consequence may arise implementing or lifting restrictions leading to reduced or increased the opportunity to engage in behaviour practices as well as to provide or utilise goods or services.
Education and training	Through increasing knowledge or understanding	A consequence may arise through changes in knowledge, understanding or skills based on new information as well as opportunities to train skills, as well as the lack thereof. This can include false, inadequate or overgeneralised information, leading to an erroneous knowledge or understanding as well as the consequences of not receiving information or training.
Training	Through improving skills and abilities	A consequence may arise through improving skills and abilities. These changes can be based on training or knowledge transfer.
Persuasion	Through changing perceptions and attitudes	A consequence may arise through changes in perceptions and attitudes, as well as through knowledge or information which evokes an emotional response regarding diseases and disorders (incl. risk factors), as well as individuals affected by them. Changes in the perception of individuals or populations affected by a disease or disorder includes public stigma, self-stigma and label avoidance, changes in the perceived severity or susceptibility, and risk compensation.
	Through affecting psychological reactions	A consequence may arise through psychological reactions or effects, which affect health or other outcomes of interest (e.g. experiencing a stress reaction or anxiety following a test result).
Incentivisation and coercion	Through providing financial, economic or social incentives (or disincentives)	A consequence may arise from (dis)incentives and the reaction to them. Incentives refers to the expectation of gain or rewards, which could be financial, economic or social. Disincentives refer to the expectation in cost or punishment.
Environmental restructuring (environmental context)	Through changing environmental exposures	A consequence may arise through changes in environmental exposures, which directly affects health or other outcomes of interest (e.g. higher risk of accidents, exposure to pollutants, exposure to infectious agents). Environmental is defined broadly, it includes factors such as exposure to air, atmosphere, food, water, chemicals, physical agents, microbiological pathogens, noise, vibration, radiation, temperature, etc.; as well as factors increasing the risk of being affected by accidents and violence.
	Through triggering automated responses	A consequence may arise from (intended or unintended) alterations of the environment in a way that trigger automatic cognitive processes leading to changes in practices. This includes changes in the saliency of and cognitive load associated with practices or goods.
	Through changing the availability, accessibility or quality of goods or services	A consequence may arise through the availability, accessibility, affordability or quality in goods or services.
Environmental restructuring (social context) modelling	Through changing social practices and norms	A consequence may arise through changes in individual behaviours and social practices (rooted in social norms and values) through (i) copying the action of other individuals in an ambiguous social situations where people are unable to determine the appropriate mode of behaviour (social proof), (ii) providing examples for people to aspire to or imitate (modelling), or (iii) through imitating the social practices in a social group and incorporating the norms, values and social practices associated with them (habit formation). These can lead to changes in the perception of norms and values within a community, as well as the identities of individuals and the roles of individuals within a community.
Enablement	Through empowering individuals and communities	A consequence may arise through empowering or disempowering individuals and thereby enabling or hinder them to act in a specific way (e.g. through building up confidence).

section. The results of the categorisation are presented verbally in the following text and tables. The text passages which were used to assign a category of the framework are presented in the Supplemental Appendix.

Among 18 reviews reporting on AUCs, an increase in substance use (no differentiation between illicit drugs, alcohol, or tobacco) was the most prevalent AUC ($n=8/18$).^{4,34,39-41,46-48} Similarly, an increase of illicit drug consumption was frequently reported ($n=4/18$).^{37,38,43,44}

Table 4. Characteristics of review reporting on AUCs.

Study ID [Ref. No.]	Confidence in results (AMSTAR 2 rating)	Objective/rationale	Outcome of interest	Target population	Setting	AUCs specified as outcome of interest under methods?	Reported AUCs	Type(s) of AUCs	Reported mechanisms
<i>Reviews focussing on educational interventions</i>									
Berberian et al. ³²	Critically low	Assessing the effectiveness of school-based drug abuse prevention programmes	Substance use (multiple)	Students	Multiple	No	'Overidentification with ex-addicts' in the intervention group ^b	Social norms and values	Through changing social practices and norms
Hansen ³⁴	Critically low	Reviewing the state of knowledge on what is effective in achieving substance abuse prevention	Substance use (multiple)	Adolescents	Educational settings	No	Increased substance use (i.e. alcohol, cannabis, tobacco) ^a	Psychosocial health and well-being	Through changing social practices and norms; Through increasing knowledge or understanding
Mellanby et al. ⁴⁰	Critically low	Evaluating school-based health education programmes which have set out to compare the effects of peers or adults delivering the same material	Substance use (multiple)	Students	School	No	Increased substance use (i.e. alcohol) ^a	Psychosocial health and well-being	Not reporting or discussing mechanisms
White and Pitts ⁴⁷	Critically low	Assessing effectiveness of interventions directed at the prevention or reduction of use of illicit substances by young people or those directed at reducing harm caused by continuing use	Substance use (multiple)	Children/young people (aged 8–25 years)	Multiple	No	Increased substance use ^a	Psychosocial health and well-being	Not reporting or discussing mechanisms
<i>Reviews focussing on multiple interventions</i>									
Bröning et al. ³³	Critically low	Assessing evaluations of selective preventive interventions in childhood and adolescence targeted at this specific group	Substance use (multiple)	Children and adolescent (and their families)	Multiple	Yes	No relevant AUCs identified by the review ^{a,b}	-	-
Faggiano et al. ⁴	High	Assessing the effectiveness of universal school-based interventions in reducing drug use compared to usual curricular activities or no intervention	Illicit drug use	Students	School	Yes	Increased substance drug use (i.e. marijuana, other drug, alcohol) ^{a,b}	Psychosocial health and well-being	Chance finding
Langford et al. ³⁶	High	Assessing the effectiveness of the Health Promoting Schools (HPS) framework in improving the health and well-being of students and their academic achievement	Substance use (multiple)	Students (aged 4–18 years)	Multiple	Yes	No relevant AUCs identified by the review ^{a,b}	-	-
Lin et al. ³⁷	Critically low	Assessing the impact of comprehensive community initiatives on population-level child, youth, and family outcomes	Substance use (multiple)	Children and youth	Community	No	Increased illicit drug use (i.e. inhalants, MDMA, Ecstasy) ^a	Psychosocial health and well-being	Not reporting or discussing mechanisms
MacArthur et al. ³⁹	Moderate	Assessing the effect of peer-led interventions that sought to prevent tobacco, alcohol and/or drug use	Substance use (multiple)	Students	School	No	Increased substance use ^a	Psychosocial health and well-being	Through changing social practices and norms

(continued)

Table 4. (Continued)

Study ID [Ref. No.]	Confidence in results (AMSTAR 2 rating)	Objective/rationale	Outcome of interest	Target population	Setting	AUCs specified as outcome of interest under methods?	Reported AUCs	Type(s) of AUCs	Reported mechanisms
MacArthur et al. ³⁸	High	Assessing the effects of interventions implemented up to 18 year of age for the primary or secondary prevention of multiple risk behaviours among young people.	Substance use (multiple)	Children and adolescents (aged up to 18 years)	Multiple	Yes	Increased illicit drug use ^a	Psychosocial health and well-being	Chance finding
Onrust et al. ⁴¹	Critically low	Overview of the different universal and targeted substance use prevention programmes offered at school	Substance use (multiple)	Students	School	No	Increased substance use ^{a,b}	Psychosocial health and well-being	Through changing social practices and norms
Ruiz-Casares et al. ⁴²	Critically low	Assessing the quality of studies that have evaluated programmes for ethno-culturally diverse parents and adolescents that specifically address mental health promotion and prevention	Substance use (multiple)	Ethno-cultural populations	Multiple	No	No relevant AUCs identified by the review ^a	-	-
Snijder et al. ⁴³	Critically low	Assessing the effectiveness of substance use prevention programmes for Indigenous adolescents in the USA, Canada, Australia and New Zealand	Substance use (multiple)	Indigenous adolescents (aged 10–19 years)	Multiple	No	Increased illicit drug use ^a	Psychosocial health and well-being	Not reporting or discussing mechanisms
Soole et al. ⁴⁴	Critically low	Assessing the effectiveness of school-based drug prevention programmes in preventing illicit drug use	Substance use (multiple)	Students	School	No	Increased illicit drug use (i.e. marijuana and other illicit drugs) ^a	Psychosocial health and well-being	Not reporting or discussing mechanisms
Tobler et al. ⁴⁶	Critically low	Assessing effectiveness of different types of drug prevention programmes in USA and Canada	Substance use (multiple)	Students (grade 6–12)	School	No	Increased substance use ^{a,b}	Psychosocial health and well-being	Chance finding
Wilson et al. ⁴⁸	Critically low	Assessing the effectiveness of the subset of prevention practices that occur in schools or are implemented by school staff and are designed to reduce the occurrence of these problem behaviours	Substance use (multiple)	Students	School	No	Increased substance use ^{a,b}	Psychosocial health and well-being	Not reporting or discussing mechanisms
<i>Reviews focussing on other interventions</i>									
Hodder et al. ²⁵	High	Assessing whether universal school-based 'resilience' interventions are effective in reducing the prevalence of tobacco, alcohol, or illicit substance use by adolescents	Substance use (multiple)	Students	School	Yes	No AUCs identified by the review ^a	-	-
Thomas et al. ⁴⁵	High	Assessing the effectiveness of mentoring to prevent adolescent alcohol/drug use	Substance use (multiple)	Adolescents (aged 13–18)	Multiple	No	No AUCs identified by the review ^a	-	-

AUCs: adverse and other unintended consequences; n.s.: not specified.

^aReview reported AUCs in the Results section.^bReview discussed the presence or absence of AUCs.

Table 5. Characteristics of primary studies reporting on AUCs.

Study ID [Ref. No.]	Outcome of interest	Objective/rationale	Study design	Target population	Setting	AUCs specified as outcome of interest under methods?	Reported AUCs	Type(s) of AUCs	Reported mechanisms
<i>Primary studies focussing on educational interventions</i>									
Botvin et al. ⁴⁹	Illicit drug use	Assessing the effectiveness of a cognitive-behavioural substance abuse prevention approach	RCT	Students (eighth grade)	School	No	Increase of alcohol consumption in the teacher session ^{a,b}	Psychosocial health and well-being	Not reporting or discussing mechanisms
Dixon et al. ⁵¹	Substance use (multiple)	Assessing how a non-targeted group of ethnic minority youth might or might not benefit from a prevention intervention focussed on other cultural groups (keepin' it R.E.A.L. curriculum)	RCT	Students (seventh grade)	School	No	Increase of alcohol consumption among American Indian participants ^{a,b}	Psychosocial health and well-being	Through changing social practices and norms
Ellickson and Bell ⁵²	Illicit drug use	Results of Project ALERT, a multi-site, longitudinal test of a school-based prevention programme (curriculum)	RCT	Students (seventh grade)	School	No	Increased smoking in teen-led intervention ^{a,b}	Psychosocial health and well-being	Through changing social practices and norms
Furr-Holden et al. ⁵³	Illicit drug use	Assessing the potential early impact of two developmentally inspired universal preventive interventions on the risk of early-onset alcohol, inhalant, tobacco, and illegal drug use through early adolescence	RCT	Students (first grade)	School	No	Potential increase of drug use ^a	Psychosocial health and well-being	Chance finding
Hansen et al. ⁵⁵	Illicit drug use	Assessing the efficacy of two drug abuse prevention curricula in preventing the onset of tobacco, alcohol and marijuana use among adolescents (Project SMART)	RCT	Students	School	No	Increase of drug consumption in the affective intervention ^{a,b}	Psychosocial health and well-being	Through changing perceptions and attitudes; Chance finding
Hansen and Graham ⁵⁴	Illicit drug use	Assessing the efficacy of two strategies (i.e. refusal skill training, change in normative perceptions) for preventing the onset of alcohol, marijuana and tobacco	RCT	Students	School	No	Increase of marijuana consumption in the peer pressure resistance group ^{a,b}	Psychosocial health and well-being	Through changing social practices and norms; Through changing perceptions and attitudes

(continued)

Table 5. (Continued)

Study ID [Ref. No.]	Outcome of interest	Objective/rationale	Study design	Target population	Setting	AUCs specified as outcome of interest under methods?	Reported AUCs	Type(s) of AUCs	Reported mechanisms
Hawkins et al. ⁵⁶	Substance use (multiple)	Assessing whether the Communities That Care (CTC) prevention system reduced levels of risk and adolescent problem behaviours community wide 8 year after implementation of CTC	Community-randomised trial	Students (5th–12th grade)	Multiple	No	Increase of ecstasy consumption among 12th graders ^{a,b}	Psychosocial health and well-being	Chance finding
Jalling et al. ⁵⁷	Substance use (multiple)	Assessing the effects of parent programmes (Comet and ParentSteps) on measures of antisocial behaviour when given under real world conditions to parents of at-risk adolescents	RCT	Adolescents (aged 12–18) and parents	Multiple	Yes	Increased risk of drug use ^{a,b}	Psychosocial health and well-being	Chance finding
Sánchez et al. ⁵⁸	Illicit drug use	Assessing the fidelity of implementation within a treatment effectiveness trial of the Reconnecting Youth (RY) prevention programme	RCT	Teacher	School	No	Increase of marihuana use in the teacher led intervention ^{a,b}	Psychosocial health and well-being	Not reporting or discussing mechanisms
Valente et al. ⁵⁹	Illicit drug use	Assessing whether a social network tailored substance abuse prevention programme can reduce substance use among high-risk adolescents without creating deviancy training (iatrogenic effects)	RCT	Students	School	No	Increased drug consumption in the network curriculum interventions ^{a,b}	Psychosocial health and well-being	Through changing social practices and norms
<i>Primary studies focussing on multiple interventions</i>									
Cuijpers et al. ⁵⁰	Substance use (multiple)	Assesses the effects of the 'Healthy School and Drugs' project, a Dutch school-based drug prevention project	Quasi-experimental	Students (aged 12–18)	School	No	Increased drug consumption in the intervention group ^{a,b}	Psychosocial health and well-being	Not reporting or discussing mechanisms

AUCs: adverse or other unintended consequences.

^aStudy reported AUCs in the Results section.

^bStudy discussed the presence or absence of AUCs.

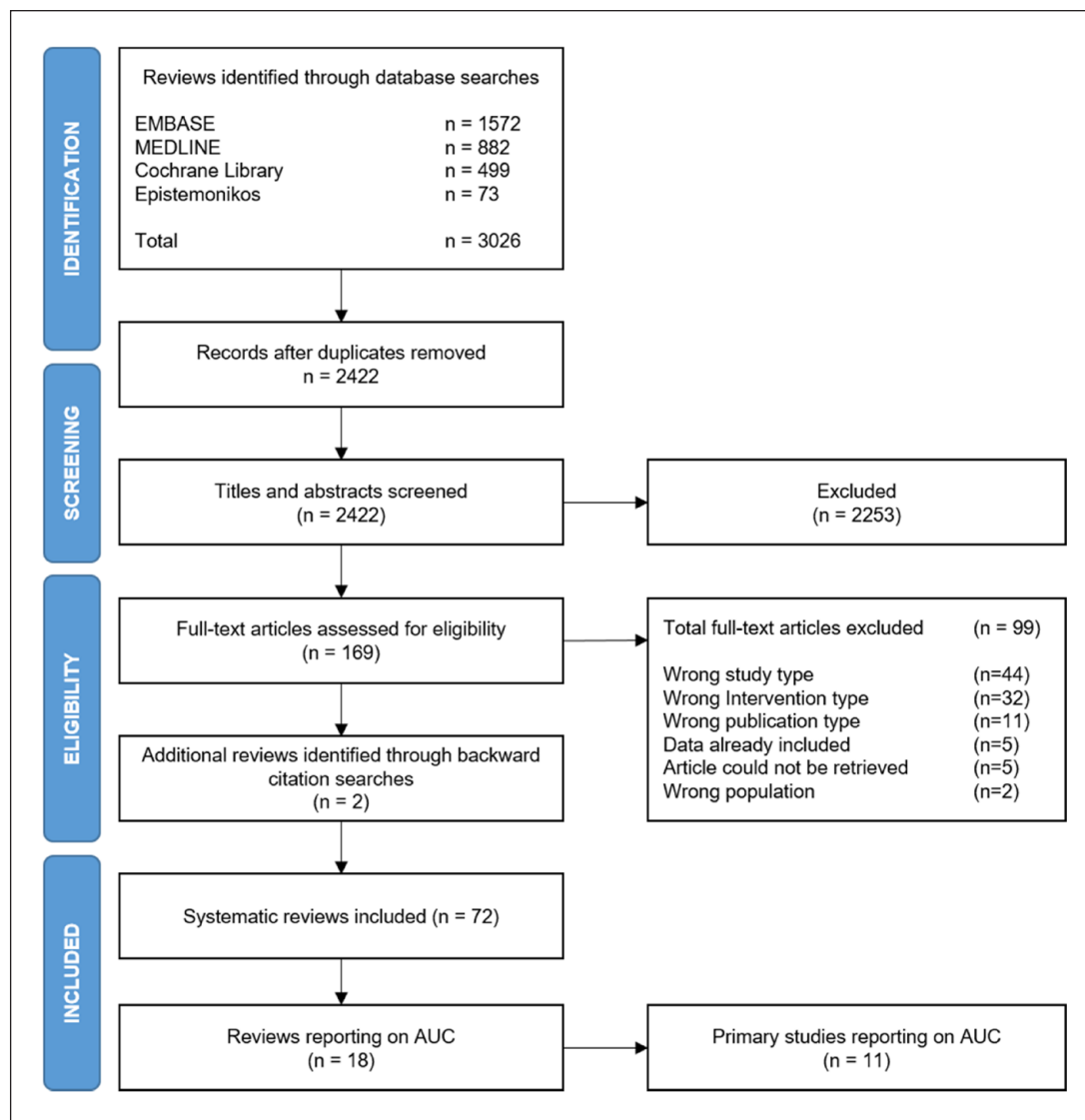


Figure 1. PRISMA flow-chart.³¹

Both AUCs were assessed as an effect on the outcome of interest with an unexpected negative or paradoxical direction. Even though the AUCs described above do not imply an established disorder, we categorised these under ‘Psychosocial health and well-being’.

Only one review reported on a different AUC, describing a change in expectations regarding drug consumption among some of the participants (i.e. positive drug and alcohol expectations) through identifying with ex-addicts and was therefore categorised under ‘Social norms and values’.³²

Five reviews did not observe any AUCs related to illicit drug prevention in the school setting, but did report AUCs in other settings or in other substance prevention interventions.^{33,35,36,42,45}

Among 11 primary studies retrieved from the included reviews and reporting AUCs, an increase in substance

consumption (drug use included) was most prevalent ($n=8/11$).^{50,53–59} Other AUCs were an increase in alcohol consumption ($n=2/11$)^{49,51} and smoking ($n=1/11$).⁵² Therefore, all AUCs reported in primary studies were categorised under ‘Psychosocial health and well-being’.

Mechanisms leading to AUCs. Mechanisms were only reported in a minority of the identified reviews ($n=7/18$). The mechanisms described were most often categorised as ‘Through changing social practices and norms’ ($n=6/18$).^{32,34,36,39–41} Authors discussed the interaction of social norms, peer pressure, deviance training, ethno-cultural backgrounds and personal beliefs. AUCs were then described as a potential consequence of supposedly unfavourable interactions. Some reviews considered the observed AUCs a ‘Chance finding/bias’ ($n=3/18$)^{4,38,46} as a result of statistical effects or design issues. One review discussed the potential effects of the

Table 6. Comparison of selected review characteristics.

	No. of reviews reporting on AUCS	No. of reviews not reporting on AUCS	Odds ratio (95% confidence interval)
Published before 2010 (reference category)	7	14	1.82 (0.59–5.61)
Published after 2010	11	40	
Low or critically low AMSTAR 2 rating (reference category)	12	53	0.04 (0.004–0.34)
High or moderate AMSTAR 2 rating	6	1	

AUCs: adverse or other unintended consequences.

delivered information/content as well as the didactic methods used³⁴ was therefore coded as the mechanism ‘Through increasing knowledge or understanding’.

A majority of the primary studies discussed mechanisms of AUCs ($n=8/11$). In 4 out of 11 primary studies the observed AUCs were described as a ‘Chance finding’,^{45,53,55–57} referring to the small number of participants and potential measurement error. Other mechanisms discussed were categorised as ‘Through changing social practices and norms’ ($n=4/11$)^{45,51,52,54,59} based on discussions of group differences, social influence of teachers, ethno-cultural differences, peer influence and social acceptability in the primary studies. Two primary studies discussed the mechanism ‘Through changing perceptions and attitudes’,^{54,55} suggesting that misinformation and a change in perception might have led to AUCs.

Reporting of AUCs

Reporting and discussion of AUCs differed substantially in the identified reviews and primary studies. Most of the reviews ($n=64$) did not report or discuss any AUCs. Many of the 18 reviews and 11 primary studies reporting AUCs did not assess these as an outcome of interest, nor did they report them in the Results section.

We observed among the seven reviews with an AMSTAR 2 rating of ‘High’ or ‘Moderate’^{4,35,36,38,39,45,97} all but one⁹⁷ reported on AUCs but only three reviews referred to these AUCs in the discussion.^{4,36,39} The 65 reviews with a ‘Low’ or ‘Critically Low’ AMSTAR 2 rating varied in their reporting and discussion of AUCs. Only 11 reviews^{33,34,37,40–44,46–48} with such rating reported AUCs and six discussed these findings^{33,34,40,41,46,48} (see Table 6). Therefore, studies with a higher AMSTAR 2 rating were found to be more likely to report on AUCs. We also observed a higher rate of AUCs reported in reviews published before 2010 compared to reviews published after or in the same year (see Table 6). The complexity and scope of the discussion differed between the studies. Some reviews ($n=7/18$)^{4,34,39–41,46,48} and primary studies ($n=7/11$)^{45,51,54–59} reported AUCs in the results section and briefly discussed these finding but only a fraction considered AUCs as an outcome of interest (i.e. five reviews,^{4,33,35,36,38} one primary study^{45,57}). Several studies

specifically referred to the occurrence of AUCs as a chance finding and did not expand on the possibility that the AUC might be causally related to the intervention under investigation.

Discussion

This systematic review of reviews assessed AUCs of setting-based interventions to prevent illicit drug use and explored the mechanisms leading to these AUCs, as reported or assumed in the included studies. We found that the majority of the reported AUCs were paradoxical health consequences and a few broader societal consequences, that is, the intervention led to an unintended increase rather than the intended decrease in drug use, and identification with ex-addicts. Potential mechanisms discussed primarily focussed on the change though social norms and practices, but knowledge as well as understanding and the change of perception were also mentioned.

The social mechanisms leading to unintended deviant behaviour caused by prevention or treatment interventions are often referred to as ‘deviancy training’.^{16,93,114,115} This phenomenon describes that group interventions may lead to AUCs or generate harms by promoting interaction between people who are in higher behavioural risk groups and change the perception of social norms.^{115,116} As discussed by Lorenc and Oliver,⁷ social norms and contexts play a role with regards to AUCs but are often neglected in the evaluation of health interventions.

Additionally, this systematic review of reviews described differences in the reporting of these AUCs across included reviews. Reviews with a higher AMSTAR 2 rating, especially Cochrane reviews, reported AUCs more often than reviews with a lower AMSTAR 2 rating; similarly, more recent reviews (i.e. those published after 2010) were more likely to examine AUCs.

The majority of reviews or studies did not anticipate the occurrence of AUCs (e.g. AUCs specified as an outcome of interest under Methods section) or discussed these findings extensively. Most of these AUCs could, however, have been anticipated. Different strategies to do so or at least acknowledge the possibility of AUCs in public health interventions (e.g. dark logic models) have been discussed by multiple authors.^{93,117,118} Acknowledging the broader

social and environmental context as the complex system in which individuals and interventions interact plays a key role in trying to understand the potential mechanisms leading to AUCs.^{21,22,24} As discussed by Morell¹¹⁷ and Oliver et al.,^{9,10} stakeholders initiating evaluations tend to prefer a ‘narrative of success’⁹ which might lead to a publication bias, explaining the low reporting of AUCs across studies. The lack of reported harms requires careful interpretation as reasons may be diverse. AUCs might not have occurred (actual null event), not have been investigated or might have been observed but not reported (reporting bias).¹⁴ Additionally, the reporting of AUCs in systematic reviews depends on the reporting of AUCs in primary studies. Even in clinical research reporting of AUCs is an important issue as reporting guidelines exist but AUCs are nevertheless not reported in all cases.^{14,24,119}

Strengths and limitations

To the knowledge of the authors, this review made use of the best available a priori frameworks to categorise AUCs and potential mechanisms. This allowed us to systematically investigate AUCs and identify potential gaps in the available data. Both consequences and mechanisms were examined not only from an individual and biomedical but also from a societal perspective. We used a predefined protocol to conduct this review and used a standardised review approach.

Despite these efforts, this review and its findings can only be as good as the underlying evidence base. The reporting and exploration of AUCs was scarce and in most cases focussed on individual health rather than society at large. It is likely, that further AUCs or mechanisms leading to them were not identified and/or not reported in the primary studies. This is not doing justice to the scope of AUCs and the likely mechanisms leading to AUCs.

Conclusion

All health interventions potentially lead to AUCs. However, while it is widely accepted that clinical interventions lead to AUCs or complications, this is not always the case for public health interventions.^{7,24} Safety studies or harm reviews are often conducted in clinical research (i.e. health technology assessments, safety trials, real-world trials) but have not yet been established to the same degree in the broader health sciences.^{7,18,24} When primary studies fail to assess AUCs, these cannot be documented in subsequent reviews. Existing tools like the Cochrane Handbook for Systematic Reviews of Interventions¹²⁰ or the PRISMA Harms Checklist¹²¹ as well as dark logic models⁹³ informed by existing frameworks (e.g. WHO-INTEGRATE²⁷) can be useful tools in the planning and evaluation of public health interventions as these to highlight the complexity of public health interventions and can help to acknowledge

the occurrence of AUCs. Systematic reviews and primary studies evaluating certain interventions (especially such in complex systems) should be aware of different types of AUCs, the scope of the AUCs and potential mechanisms so that these can be assessed systematically.^{7,24} These frameworks could also be used to develop study protocols so that AUCs can be assessed systematically taking multiple domains/categories into account, which is particularly important in public health interventions, as these tend to be complex and integrate multiple factors consequently aggravating the anticipation of potential AUCs. This is important as AUCs will most probably not be identified if one is not searching for it or at least considering the existence of such consequences.

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Significance for public health

This review is one of the very few that presents adverse and unintended consequences (AUCs) of setting-based interventions to prevent illicit drug use and uses a priori frameworks to categorise them and explore possible mechanisms. This allowed us to systematically examine AUCs and identify potential gaps in the available data. Both consequences and mechanisms were examined not only from an individual and biomedical perspective but also from a societal perspective. This review promotes the importance of recognising AUCs in the design, implementation and evaluation of public health interventions.

Supplemental material

Supplemental material for this article is available online.

References

1. The European Commission. *Polydrug use: patterns and responses*. Luxembourg: Publications Office of the European Union; 2009.
2. The European Commission. *Health and social responses to drug problems: a European guide*. Luxembourg: Publications Office of the European Union; 2017.
3. Leshner AI. Drug abuse and addiction treatment research. The next generation. *Arch Gen Psychiatry* 1997; 54: 691–694.
4. Faggiano F, Minozzi S, Versino E, et al. Universal school-based prevention for illicit drug use. *Cochrane Database Syst Rev* 2014; 2014: CD003020.

5. Kempf C, Llorca P-M, Pizon F, et al. What's new in addiction prevention in young people: a literature review of the last years of research. *Front Psychol* 2017; 8: 1131.
6. United Nations Office on Drugs and Crime (UNODC) & World Health Organization (WHO). International standards on drug use prevention, https://www.unodc.org/documents/prevention/standards_180412.pdf (2018, accessed 25 March 2021).
7. Lorenc T and Oliver K. Adverse effects of public health interventions: a conceptual framework. *J Epidemiol Community Health* 2014; 68: 288–290.
8. Lee LM. Public health ethics theory: review and path to convergence. *J Law Med Ethics* 2012; 40: 85–98.
9. Oliver K, Lorenc T, Tinkler J, et al. Understanding the unintended consequences of public health policies: the views of policymakers and evaluators. *BMC Public Health* 2019; 19: 1057.
10. Oliver K, Lorenc T and Tinkler J. Evaluating unintended consequences: new insights into solving practical, ethical and political challenges of evaluation. *Evaluation* 2020; 26: 61–75.
11. Bibawy H, Cossu A, Cogan S, et al. Reporting of harms and adverse events in otolaryngology journals. *Otolaryngol Head Neck Surg* 2009; 140(2): 241–244.
12. Lee PE, Fischer HD, Rochon PA, et al. Published randomized controlled trials of drug therapy for dementia often lack complete data on harm. *J Clin Epidemiol* 2008; 61(11): 1152–1160.
13. Loke YK, Price D and Herxheimer A. Systematic reviews of adverse effects: framework for a structured approach. *BMC Med Res Methodol* 2007; 7: 32.
14. Zorzela L, Golder S, Liu Y, et al. Quality of reporting in systematic reviews of adverse events: systematic review. *BMJ* 2014; 348: f7668.
15. Parsons R, Golder S and Watt I. More than one-third of systematic reviews did not fully report the adverse events outcome. *J Clin Epidemiol* 2019; 108: 95–101.
16. Allen-Scott LK, Hatfield JM and McIntyre L. A scoping review of unintended harm associated with public health interventions: towards a typology and an understanding of underlying factors. *Int J Public Health* 2014; 59: 3–14.
17. Gould MS, Marrocco FA, Kleinman M, et al. Evaluating iatrogenic risk of youth suicide screening programs: a randomized controlled trial. *JAMA* 2005; 293: 1635–1643.
18. Rosenthal S and Chen R. The reporting sensitivities of two passive surveillance systems for vaccine adverse events. *Am J Public Health* 1995; 85: 1706–1709.
19. Griffin KW and Botvin GJ. Evidence-based interventions for preventing substance use disorders in adolescents. *Child Adolesc Psychiatr Clin N Am* 2010; 19: 505–526.
20. Mittelmark MB. Unintended effects in settings-based health promotion. *Scand J Public Health* 2014; 42: 17–24.
21. Hawe P, Shiell A and Riley T. Theorising interventions as events in systems. *Am J Community Psychol* 2009; 43: 267–276.
22. Moore GF, Evans RE, Hawkins J, et al. From complex social interventions to interventions in complex social systems: future directions and unresolved questions for intervention development and evaluation. *Evaluation* 2019; 25: 23–45.
23. Moore GF, Evans RE, Hawkins J, et al. All interventions are complex, but some are more complex than others: using iCAT_SR to assess complexity. *Cochrane Database Syst Rev* 2017; 7: ED000122.
24. Bonell C, Jamal F, Melendez-Torres GJ, et al. 'Dark logic': theorising the harmful consequences of public health interventions. *J Epidemiol Community Health* 2015; 69: 95–98.
25. Ouzzani M, Hammady H, Fedorowicz Z, et al. Rayyan-a web and mobile app for systematic reviews. *Syst Rev* 2016; 5: 210.
26. Shea BJ, Reeves BC, Wells G, et al. AMSTAR 2: a critical appraisal tool for systematic reviews that include randomised or non-randomised studies of healthcare interventions, or both. *BMJ* 2017; 358: j4008.
27. Rehfuss EA, Stratil JM, Scheel IB, et al. The WHO-INTEGRATE evidence to decision framework version 1.0: integrating WHO norms and values and a complexity perspective. *BMJ Glob Health* 2019; 4: e000844.
28. Stratil JM, Baltussen R, Scheel I, et al. Development of the WHO-INTEGRATE evidence-to-decision framework: an overview of systematic reviews of decision criteria for health decision-making. *Cost Eff Resour Alloc* 2020; 18: 8.
29. Stratil JM, Paudel D, Setty KE, et al. Advancing the WHO-INTEGRATE framework as a tool for evidence-informed, deliberative decision-making processes: exploring the views of developers and users of WHO Guidelines. *Int J Health Policy Manag* 2022; 11: 629–641.
30. Michie S, van Stralen MM and West R. The behaviour change wheel: a new method for characterising and designing behaviour change interventions. *Implement Sci* 2011; 6: 42.
31. Liberati A, Altman DG, Tetzlaff J, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate healthcare interventions: explanation and elaboration. *BMJ* 2009; 339: b2700.
32. Berberian RM, Gross C, Lovejoy J, et al. The effectiveness of drug education programs: a critical review. *Health Educ Monogr* 1976; 4: 377–398.
33. Bröning S, Kumpfer K, Kruse K, et al. Selective prevention programs for children from substance-affected families: a comprehensive systematic review. *Subst Abuse Treat Prev Policy* 2012; 7: 23.
34. Hansen WB. School-based substance abuse prevention: a review of the state of the art in curriculum, 1980-1990. *Health Educ Res* 1992; 7: 403–430.
35. Hodder RK, Freund M, Wolfenden L, et al. Systematic review of universal school-based 'resilience' interventions targeting adolescent tobacco, alcohol or illicit substance use: a meta-analysis. *Prev Med* 2017; 100: 248–268.
36. Langford R, Bonell CP, Jones HE, et al. The WHO Health Promoting School framework for improving the health and well-being of students and their academic achievement. *Cochrane Database Syst Rev* 2014; 4: CD008958.
37. Lin ES, Flanagan SK, Varga SM, et al. The impact of comprehensive community initiatives on population-level child, youth, and family outcomes: a systematic review. *Am J Community Psychol* 2020; 65: 479–503.
38. MacArthur G, Caldwell DM, Redmore J, et al. Individual-, family-, and school-level interventions targeting multiple risk behaviours in young people. *Cochrane Database Syst Rev* 2018; 10: CD009927.

39. MacArthur GJ, Harrison S, Caldwell DM, et al. Peer-led interventions to prevent tobacco, alcohol and/or drug use among young people aged 11-21 years: a systematic review and meta-analysis. *Addiction* 2016; 111(3): 391–407.
40. Mellanby AR, Rees JB and Tripp JH. Peer-led and adult-led school health education: a critical review of available comparative research. *Health Educ Res* 2000; 15(5): 533–545.
41. Onrust SA, Otten R, Lammers J, et al. School-based programmes to reduce and prevent substance use in different age groups: what works for whom? Systematic review and meta-regression analysis. *Clin Psychol Rev* 2016; 44: 45–59.
42. Ruiz-Casares M, Drummond JD, Beeman I, et al. Parenting for the promotion of adolescent mental health: a scoping review of programmes targeting ethnoculturally diverse families. *Health Soc Care Community* 2017; 25: 743–757.
43. Snijder M, Stapinski L, Lees B, et al. Preventing substance use among indigenous adolescents in the USA, Canada, Australia and New Zealand: a systematic review of the literature. *Prev Sci* 2020; 21: 65–85.
44. Soole DW, Mazerolle L and Rombouts S. School-based drug prevention programs: a review of what works. *Aust N Z J Criminol* 2008; 41: 259–286.
45. Thomas RE, Lorenzetti D and Spragins W. Mentoring adolescents to prevent drug and alcohol use. *Cochrane Database Syst Rev* 2011; 11: CD007381.
46. Tobler NS, Roona MR, Ochshorn P, et al. School-based adolescent drug prevention programs: 1998 meta-analysis. *J Prim Prev* 2000; 20: 275–336.
47. White D and Pitts M. Educating young people about drugs: a systematic review. *Addiction* 1998; 93: 1475–1487.
48. Wilson DB, Gottfredson DC and Najaka SS. School-based prevention of problem behaviors: a meta-analysis. *J Quant Criminol* 2001; 17: 247–272.
49. Botvin GJ, Baker E, Filazzola AD, et al. A cognitive-behavioral approach to substance abuse prevention: one-year follow-up. *Addict Behav* 1990; 15: 47–63.
50. Cuijpers P, Jonkers R, de Weerd I, et al. The effects of drug abuse prevention at school: the ‘Healthy School and Drugs’ project. *Addiction* 2002; 97: 67–73.
51. Dixon AL, Yabiku ST, Okamoto SK, et al. The efficacy of a multicultural prevention intervention among urban American Indian youth in the southwest U.S. *J Prim Prev* 2007; 28: 547–568.
52. Ellickson PL and Bell RM. Drug prevention in junior high: a multi-site longitudinal test. *Science* 1990; 247: 1299–1305.
53. Furr-Holden CDM, Ialongo NS, Anthony JC, et al. Developmentally inspired drug prevention: middle school outcomes in a school-based randomized prevention trial. *Drug Alcohol Depend* 2004; 73: 149–158.
54. Hansen WB and Graham JW. Preventing alcohol, marijuana, and cigarette use among adolescents: peer pressure resistance training versus establishing conservative norms. *Prev Med* 1991; 20: 414–430.
55. Hansen WB, Johnson CA, Flay BR, et al. Affective and social influences approaches to the prevention of multiple substance abuse among seventh grade students: results from project SMART. *Prev Med* 1988; 17: 135–154.
56. Hawkins JD, Oesterle S, Brown EC, et al. Youth problem behaviors 8 years after implementing the communities that care prevention system: a community-randomized trial. *JAMA Pediatr* 2014; 168: 122–129.
57. Jalling C, Bodin M, Romelsjö A, et al. Parent programs for reducing adolescent’s antisocial behavior and substance use: a randomized controlled trial. *J Child Fam Stud* 2016; 25: 811–826.
58. Sanchez V, Steckler A, Nitirat P, et al. Fidelity of implementation in a treatment effectiveness trial of reconnecting youth. *Health Educ Res* 2006; 22: 95–107.
59. Valente TW, Ritt-Olson A, Stacy A, et al. Peer acceleration: effects of a social network tailored substance abuse prevention program among high-risk adolescents. *Addiction* 2007; 102: 1804–1815.
60. Agabio R, Trincas G, Floris F, et al. A systematic review of school-based alcohol and other drug prevention programs. *Clin Pract Epidemiol Ment Health* 2015; 11(Suppl 1 M6): 102–112.
61. Bangert-Drowns RL. The effects of school-based substance abuse education-meta-analysis. *J Drug Educ* 1988; 18: 243–264.
62. Bruvold WH. A meta-analysis of the California school-based risk reduction program. *J Drug Educ* 1990; 20(2): 139–152.
63. Champion KE, Newton NC, Barrett EL, et al. A systematic review of school-based alcohol and other drug prevention programs facilitated by computers or the internet. *Drug Alcohol Rev* 2013; 32: 115–123.
64. Cuijpers P. Peer-led and adult-led school drug prevention: a meta-analytic comparison. *J Drug Educ* 2002; 32: 107–119.
65. D’Onise K, Lynch JW, Sawyer MG, et al. Can preschool improve child health outcomes? a systematic review. *Soc Sci Med* 2010; 70: 1423–1440.
66. Dusenbury L, Falco M and Lake A. A review of the evaluation of 47 drug abuse prevention curricula available nationally. *J Sch Health* 1997; 67: 127–132.
67. Ennett ST, Tobler NS, Ringwalt CL, et al. How effective is drug abuse resistance education? A meta-analysis of Project DARE outcome evaluations. *Am J Public Health* 1994; 84: 1394–1401.
68. Espada JP, González MT, Orgilés M, et al. Meta-analysis of the effectiveness of school substance abuse prevention programs in Spain. *Psicothema* 2015; 27: 5–12.
69. Fletcher A, Bonell C and Hargreaves J. School effects on young people’s drug use: a systematic review of intervention and observational studies. *J Adolesc Health* 2008; 42: 209–220.
70. Flynn AB, Falco M and Hocini S. Independent evaluation of middle school-based drug prevention curricula: a systematic review. *JAMA Pediatr* 2015; 169: 1046–1052.
71. Gottfredson DC and Wilson DB. Characteristics of effective school-based substance abuse prevention. *Prev Sci Off J Soc Prev Res* 2003; 4: 27–38.
72. Hopfer S, Davis D, Kam JA, et al. A review of elementary school-based substance use prevention programs: identifying program attributes. *J Drug Educ* 2010; 40(1): 11–36.
73. Lemstra M, Bennett N, Nannapaneni U, et al. A systematic review of school-based marijuana and alcohol prevention

- programs targeting adolescents aged 10–15. *Addict Res Theory* 2010; 18: 84–96.
74. Lize SE, Iachini AL, Tang W, et al. A meta-analysis of the effectiveness of interactive middle school cannabis prevention programs. *Prev Sci* 2017; 18: 50–60.
 75. Melendez-Torres GJ, Tancred T, Fletcher A, et al. Does integrated academic and health education prevent substance use? Systematic review and meta-analyses. *Child Care Health Dev* 2018; 44: 516–530.
 76. Newton NC, Champion KE, Slade T, et al. A systematic review of combined student- and parent-based programs to prevent alcohol and other drug use among adolescents. *Drug Alcohol Rev* 2017; 36(3): 337–351.
 77. Pan W and Bai H. A multivariate approach to a meta-analytic review of the effectiveness of the D.A.R.E. Program. *Int J Environ Res Public Health* 2009; 6: 267–277.
 78. Plotnikoff RC, Costigan SA, Kennedy SG, et al. Efficacy of interventions targeting alcohol, drug and smoking behaviors in university and college students: A review of randomized controlled trials. *J Am Coll Health* 2019; 67: 68–84.
 79. Porath-Waller AJ, Beasley E and Beirness DJ. A meta-analytic review of school-based prevention for cannabis use. *Health Educ Behav* 2010; 37: 709–723.
 80. Sussman S, Arriaza B and Grigsby TJ. Alcohol, tobacco, and other drug misuse prevention and cessation programming for alternative high school youth: a review. *J Sch Health* 2014; 84: 748–758.
 81. Tancred T, Papparini S, Melendez-Torres GJ, et al. Interventions integrating health and academic interventions to prevent substance use and violence: a systematic review and synthesis of process evaluations. *Syst Rev* 2018; 7: 227.
 82. Waller G, Finch T, Giles EL, et al. Exploring the factors affecting the implementation of tobacco and substance use interventions within a secondary school setting: a systematic review. *Implement Sci* 2017; 12: 130.
 83. West SL and O'Neal KK. Project D.A.R.E. Outcome effectiveness revisited. *Am J Public Health* 2004; 94: 1027–1029.
 84. Teesson M, Newton NC and Barrett EL. Australian school-based prevention programs for alcohol and other drugs: a systematic review. *Drug Alcohol Rev* 2012; 31(6): 731–736.
 85. Kao TS, Gibbs MB, Clemen-Stone S, et al. A comparison of family interventions to address adolescent risky behaviors: a literature review. *West J Nurs Res* 2013; 35: 611–637.
 86. Petrie J, Bunn F and Byrne G. Parenting programmes for preventing tobacco, alcohol or drugs misuse in children <18: a systematic review. *Health Educ Res* 2007; 22: 177–191.
 87. Van Ryzin MJ, Roseth CJ, Fosco GM, et al. A component-centered meta-analysis of family-based prevention programs for adolescent substance use. *Clin Psychol Rev* 2016; 45: 72–80.
 88. Hearod JB, Wetherill MS, Salvatore AL, et al. Community-based participatory intervention research with American Indian communities: what is the state of the science? *Curr Dev Nutr* 2019; 3: 39–52.
 89. Liddell J and Burnette CE. Culturally-informed interventions for substance abuse among indigenous youth in the United States: a review. *J Evid Inf Soc Work* 2017; 14: 329–359.
 90. Hankerson SH and Weissman MM. Church-based health programs for mental disorders among African Americans: a review. *Psychiatr Serv* 2012; 63: 243–249.
 91. Alexander CN, Robinson P and Rainforth M. Treating and preventing alcohol, nicotine, and drug abuse through transcendental meditation: a review and statistical meta-analysis. *Alcohol Treat Quart* 1994; 11: 13–87.
 92. Allen ML, Garcia-Huidobro D, Porta C, et al. Effective parenting interventions to reduce youth substance use: a systematic review. *Pediatrics* 2016; 138: 8.
 93. Bonell C, Dickson K, Hinds K, et al. *The effects of Positive Youth Development interventions on substance use, violence and inequalities: systematic review of theories of change, processes and outcomes*. Southampton: NIHR Journals Library; 2016.
 94. Champion KE, Newton NC and Teesson M. Prevention of alcohol and other drug use and related harm in the digital age: what does the evidence tell us? *Curr Opin Psychiatry* 2016; 29: 242–249.
 95. Durand Z, Cook A, Konishi M, et al. Alcohol and substance use prevention programs for youth in Hawaii and Pacific Islands: a literature review. *J Ethn Subst Abuse* 2016; 15: 240–251.
 96. Freudenberg N, Silver D, Carmona JM, et al. Health promotion in the city: a structured review of the literature on interventions to prevent heart disease, substance abuse, violence and HIV infection in US metropolitan areas, 1980-1995. *J Urban Health* 2000; 77: 443–457.
 97. Gates S, McCambridge J, Smith LA, et al. Interventions for prevention of drug use by young people delivered in non-school settings. *Cochrane Database Syst Rev* 2006; 1: CD005030.
 98. Hale DR, Fitzgerald-Yau N and Viner RM. A systematic review of effective interventions for reducing multiple health risk behaviors in adolescence. *Am J Public Health* 2014; 104: e19–e41.
 99. Jackson C, Geddes R, Haw S, et al. Interventions to prevent substance use and risky sexual behaviour in young people: a systematic review. *Addiction* 2012; 107: 733–747.
 100. Kuntsche S and Kuntsche E. Parent-based interventions for preventing or reducing adolescent substance use - a systematic literature review. *Clin Psychol Rev* 2016; 45: 89–101.
 101. Lauricella M, Valdez JK, Okamoto SK, et al. Culturally grounded prevention for minority youth populations: a systematic review of the literature. *J Prim Prev* 2016; 37(1): 11–32.
 102. Melendez-Torres GJ, Dickson K, Fletcher A, et al. Positive youth development programmes to reduce substance use in young people: systematic review. *Int J Drug Policy* 2016; 36: 95–103.
 103. Norberg MM, Kezelman S and Lim-Howe N. Primary prevention of cannabis use: a systematic review of randomized controlled trials. *PLoS One* 2013; 8: e53187.
 104. Pandey A, Hale D, Das S, et al. Effectiveness of universal self-regulation-based interventions in children and ado-

- lescents: a systematic review and meta-analysis. *JAMA Pediatr* 2018; 172: 566–575.
105. Salvo N, Bennett K, Cheung A, et al. Prevention of substance use in children/adolescents with mental disorders: a systematic review. *J Can Acad Child Adolesc Psychiatry* 2012; 21: 245–252.
 106. Simonton AJ, Young CC and Johnson KE. Physical activity interventions to decrease substance use in youth: a review of the literature. *Subst Use Misuse* 2018; 53: 2052–2068.
 107. Skara S and Sussman S. A review of 25 long-term adolescent tobacco and other drug use prevention program evaluations. *Prev Med* 2003; 37: 451–474.
 108. Stockings E, Bartlem K, Hall A, et al. Whole-of-community interventions to reduce population-level harms arising from alcohol and other drug use: a systematic review and meta-analysis. *Addiction* 2018; 113: 1984–2018.
 109. Tait RJ, Spijkerman R and Riper H. Internet and computer based interventions for cannabis use: a meta-analysis. *Drug Alcohol Depend* 2013; 133(2): 295–304.
 110. Valdez ES, Skobic I, Valdez L, et al. Youth participatory action research for youth substance use prevention: a systematic review. *Subst Use Misuse* 2020; 55: 314–328.
 111. Walsh ML and Baldwin JA. American Indian substance abuse prevention efforts: a review of programs, 2003–2013. *Am Indian Alsk Native Ment Health Res* 2015; 22: 41–68.
 112. Wood SK, Eckley L, Hughes K, et al. Computer-based programmes for the prevention and management of illicit recreational drug use: a systematic review. *Addict Behav* 2014; 39: 30–38.
 113. Shek DT and Yu L. A review of validated youth prevention and positive youth development programs in Asia. *Int J Adolesc Med Health* 2011; 23(4): 317–324.
 114. Moos RH. Iatrogenic effects of psychosocial interventions for substance use disorders: prevalence, predictors, prevention. *Addiction* 2005; 100(5): 595–604.
 115. Dishion TJ, McCord J and Poulin F. When interventions harm: peer groups and problem behavior. *Am Psychol* 1999; 54: 755–764.
 116. Kaminer Y. Challenges and opportunities of group therapy for adolescent substance abuse: a critical review. *Addict Behav* 2005; 30: 1765–1774.
 117. Morell JA. Systematic iteration between model and methodology: a proposed approach to evaluating unintended consequences. *Eval Program Plann* 2018; 68: 243–252.
 118. Jabeen S. Unintended outcomes evaluation approach: a plausible way to evaluate unintended outcomes of social development programmes. *Eval Program Plann* 2018; 68: 262–274.
 119. Golder S, Loke YK, Wright K, et al. Reporting of adverse events in published and unpublished studies of health care interventions: a systematic review. *PLoS Med* 2016; 13: e1002127.
 120. Higgins J, Thomas J and Chandler J (eds.). *Cochrane handbook for systematic reviews of interventions*. Chichester: John Wiley & Sons; 2019.
 121. Zorzela L, Loke YK, Ioannidis JP, et al. PRISMA harms checklist: improving harms reporting in systematic reviews. *BMJ* 2016; 352: i157.