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RESEARCH REPORT

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An on-line school-based substance use harm reduction programme: The Illicit Project randomized controlled trial results

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Abstract

Aims: The aim of this study was to measure the effectiveness of an on-line, neuroscience-based harm reduction intervention (The Illicit Project) on substance use, harms and knowledge over a 12-month period.

Design: We used a two-arm cluster-randomized controlled trial.

Setting: The study was conducted at eight secondary schools across New South Wales, Australia.

Participants: A total of 950 (mean age = 15.9; standard deviation = 0.68) in grades 10–12 at participating schools in 2020 took part.

Intervention and comparator: The Illicit Project intervention group (schools = five, *n* = 681) received an on-line, universal substance use and harm reduction programme over three classes. The active control group (schools = three, *n* = 269) received school-based health education as usual.

Measurements: Self-report questionnaires assessed primary [alcohol, nicotine, cannabis, 3,4-methylenedioxymethamphetamine (MDMA), cocaine and prescription drug misuse] and secondary outcomes (alcohol-related harms and drug literacy) at baseline and the 6- and 12-month follow-up assessment.

Findings: Approximately 63% (*n* = 595) of the sample completed the 12-month follow-up assessment, including 58% of the intervention group (*n* = 396/679) and 66% of the active control group (*n* = 179/271). Participants in the intervention group had slower annual increases in binge drinking [odds ratio (OR) = 0.33, 95% confidence interval (CI) = 0.12–0.89], nicotine use (OR = 0.80, 95% CI = 0.52–1.23), MDMA use (OR = 0.14, 95% CI = 0.02–1.00), cocaine use (OR = 0.06, 95% CI = 0.01–0.64) and prescription drug misuse (OR = 0.07, 95% CI = 0.01–0.54) compared with the active control group. There was limited evidence of an intervention effect on cannabis use and alcohol-related harm ($P > 0.5$). The secondary outcomes showed that the intervention group maintained higher levels of drug literacy knowledge ($\beta = 3.71$, 95% CI = 1.86–5.56) and harm reduction help-seeking skills ($\beta = 1.55$, 95% CI = 0.62–2.48) compared with the active control group.

Conclusion: The Illicit Project (an on-line, neuroscience-based substance use harm reduction intervention) was effective in slowing the uptake of risky substance use and

improving drug literacy skills among late secondary school students in Australia, compared with school-based health education as usual.

KEYWORDS
Adolescence, alcohol, harm reduction, prevention, schools, substance use

INTRODUCTION

Adolescence is a dynamic developmental period that marks the onset and escalation of substance use and mental health disorders [1, 2]. In Australia, substance use and mental health disorders are among the leading causes of disease burden among young people [3]; they have been growing substantially during the past decade [4] and made worse by the COVID-19 pandemic [5–7]. Early onset and regular substance use can have sustained behavioural and neurobiological consequences, including increased risk of dependence, comorbid mental illness and overall functional decline [4, 8]. Although current cohorts of young people are delaying substance use initiation compared to previous cohorts, the rate of escalation of use from late adolescence to young adulthood remains high [9, 10]. Preventing the initiation and escalation of risky substance use is a critical public health priority, and incremental improvement during adolescence can deliver long-lasting dividends into adulthood.

The extant literature identifies three key stages to deliver effective substance use interventions: the inoculation phase (occurs prior to experimentation), the early relevance phase (during initial exposure) and the later relevance phase (when prevalence of use is increasing [11]). Currently, the large preponderance of programmes target early adolescents (aged 13–15 years), which traditionally encompassed the inoculation and early relevant phases [12]; however, owing to global delays in the onset of alcohol and illicit substance use, these programmes now cover the inoculation phase only. To date, there are currently few effective programmes targeting adolescents in the early and later relevance phases (aged 16–20 years; [13,14]), marking a considerable gap in evidence-based harm minimization. The majority of young people receive no substance use education in their final years of school, despite this representing the age of initial exposure and escalation to substances [15,16].

The most effective universal prevention programmes, such as OurFutures [17] and Life Skills Training [18], follow the social influence theory of behaviour change and aim to build harm minimization skills. Such programmes are typically delivered to adolescents before the average age of first-time use, and leverage positive peer role modelling and normative education to promote abstinence. The leading systematic reviews and meta-analyses report reductions in harm and risky substance use (e.g. reductions in the frequency and volume of substance use); however, few programmes are effective in delaying life-time use and/or achieving abstinence [14–17, 19]. These findings suggest that programmes could benefit from directly targeting these higher-risk outcomes and engaging young people in content that has the strongest evidence base. Harm reduction education, being education that aims to reduce the preventable harms of recreational drug use, is a progressive and effective approach that attempts to prevent both the proximal and distal physiological, psychological and related behavioural harms of substance use [20]. Harm reduction strategies have been successful in reducing overdose deaths and the spread of bloodborne viruses among active drug-using populations; however, it has not been broadly examined in the prevention or educational setting [11]. A universal harm reduction programme can provide context-relevant strategies to reduce harms associated with recreational drug use and differs from targeted harm reduction strategies deployed in a treatment setting, which targets select drug-using populations. The potential efficacy of this approach in building credibility to engage young people warrants investigation, and adapting universal harm reduction to the education space may help young people avoid the known harms of recreational substance use [21]. On-line interventions enable careful control and preservation of programme messages and present a low-risk and feasible model to evaluate this new approach. On-line health interventions are rising in popularity, as they are able to overcome accessibility and implementation challenges of traditional programmes while maintaining programme fidelity at scale [13, 22]. On-line programme components and minimal teacher training associated with high uptake among schools can increase adoption and implementation sustainability [23].

The Illicit Project is a universal, on-line neuroscience-based harm reduction programme that aims to upskill young people in strategies that prevent recreational substance use harm while promoting self-help and wellbeing. The programme leverages reputable neuroscience teaching on brain development and neuroplasticity to educate young people about the impact of substance use on the brain and empower them to make positive health decisions. To align with school curriculums, the content revolves largely around alcohol, cannabis and 3,4-methylenedioxymethamphetamine (MDMA) use; however, the frameworks can be generalized to other substance use behaviours (e.g. set, setting and drug framework, brain development frameworks and brain addiction models). A feasibility pilot study conducted in schools and youth centres in 2018 confirmed that the programme content is acceptable and credible among teachers, students and health professionals [24]. The programme was transitioned on-line in 2019, following a participatory co-design process whereby young people were not only consulted throughout the process, but designed key segments of the programme [25]. This study aims to evaluate the effectiveness of The Illicit Project over 12 months, the official trial end-point. We hypothesize that compared to health education as usual, The Illicit Project would be more effective in reducing risky substance use and alcohol-related harms and increasing drug literacy knowledge and self-help skills. To our knowledge, this is the first clinical trial of an on-line harm reduction programme delivered in the last

years of school that assesses outcomes over the average age of initial exposure to alcohol.

METHODS

Design

A cluster-randomized controlled trial was conducted in secondary schools across New South Wales, Australia in 2020–21. There was a 1:1 school allocation ratio, and participants in the intervention group completed The Illicit Project during three in-class lessons spanning a 6-week period in 2020; participants in the active control group completed health education as normal, which is mandatory for all year 10 students in New South Wales. All participants completed self-report surveys at baseline, 6 and 12 months post-baseline, and the intervention group completed an additional evaluation survey immediately post-intervention. Ethics approval for the study was received from the University of Sydney Human Research Ethics Committee (2020/053) and the State Education Research Applications Process (2020237), and details of the protocol have been reported [25]. The trial follows the Consolidated Standards of Reporting Trials (CONSORT) statement and was prospectively registered with the Australian and New Zealand Clinical Trials Registry (ACTRN12620000805976).

Participants and procedure

Nine schools with students in grades 10 and 11 (aged 15–19 years) agreed to take part in the study. Block randomization into the intervention or active control group was conducted at the school level by an independent statistician to avoid contamination between individual participants [26]. Both passive parental and active student consents were required for participation, and one school required active parental consent to adhere to internal policies. The on-line data collection platform, REDCap, was used to generate unique identifiers for each participant to enable data linkage while ensuring confidentiality and to send survey links to the students' school e-mail accounts [27]. Five schools were randomly allocated to the intervention group and four schools were randomly allocated to the active control group. The final baseline sample included 950 participants from eight schools.

Intervention

The Illicit Project is a three-class, on-line intervention which aims to teach young people the basics of neuroscience and practical strategies to reduce substance use-related harm and promote self-help. The intervention was informed by several large neuroscience reviews led by the programme developer (J.D.) [28-31], extensive reviews of effective intervention components conducted by the research team [14,22,32-37], rigorous co-design with young people and consultations with teachers/health educators [25]. The three interactive modules (Alcohol and the Developing Brain; MDMA, Cannabis and Harm Reduction; and Mental Health and Wellbeing) employ neuroscience teachings to empower young people to nurture and respect their developing brains by positive psychology relevant to the dynamic social and neurobiological period of adolescence. The programme adopts strengths-based learning, which is grounded in harm reduction principles that encourage rapid skill development [20], corrects misinformation regarding the prevalence of substance use and helps to build resilience in young people to withstand peer pressure [38,39]. Through interactive activities, case studies and peer role modelling of culturally and sexually diverse young people, the programme aims to promote diversity and inclusion of all young people. The web-based programme can be accessed via www.theillicitproject.com.

Active control group

Schools in the active control group implemented health education as usual, including a combination of the Health and Physical Education curriculum (all grade 10 students), the Life Ready curriculum (grades 11 and 12 students attending state schools) or other school-dependent extra-curricular programmes (grades 11 and 12 students attending independent schools).

Outcomes

This paper reports the pre-specified primary outcomes (substance use) and secondary outcomes (alcohol harms, drug literacy levels) during the 12-month period post-baseline, the primary trial end-point. All included measures are well-validated scales that reflect developmentally relevant patterns of consumption.

Primary outcomes

Weekly binge alcohol use

Past 6-month engagement in weekly binge drinking (defined as consuming more than five standard drinks per occasion) was quantified as weekly binge drinking (yes/no). This question was similar to the Alcohol, Smoking and Substance Use Involvement Screening Test (ASSIST [40]).

Cannabis use

Past 6-month frequency of cannabis use was quantified as monthly use (yes/no).

MDMA use

Recent MDMA/ecstasy use was quantified as any past 6-month use (yes/no) adapted from the Australian National Drug Strategy Household Survey (NDSHS) [41].

Nicotine use

Recent nicotine use, including cigarette smoking or vape use, was quantified as any past 6-month use (yes/no) adapted from the Australia NDSHS [41].

Cocaine use

Recent cocaine use was quantified as any past 6-month use (yes/no) adapted from the Australian NDSHS [41].

Prescription medication misuse

Recent non-medical prescription drug use (for example, dexamphetamine) was quantified as any past 6-month use (yes/no).

Secondary outcomes

Alcohol-related harms

Alcohol-related harms were measured by the 18-item Rutgers Alcohol Problem Index scale [42], and dichotomized into those experiencing more than one harm (yes/no).

Drug literacy (knowledge)

A drug literacy knowledge score was measured through summing responses from a 20-item true or false knowledge scale measuring knowledge of how different substances affect the body, adapted from the School Health and Alcohol Harm Reduction Project [43]. Participants responded to items such as 'you can do things like take a shower or eat food to sober up more quickly'. The scale demonstrates acceptable internal consistency (knowledge scale $\alpha = 0.73$).

Drug literacy (skills)

Drug literacy skills is a score reflecting an individual's self-efficacy to reduce substance use-related harms and seek help. A total drug literacy skills score was measured through summing responses from a six-item self-efficacy scale where students completed items such as how confident are you in 'identifying substance use issues and understanding when it's time to seek help?' or 'discussing the risks associated with drug use with your parents' on a five-point Likert scale, ranging from not at all to extremely, for a total score out of 30. The scale demonstrates low, albeit acceptable internal consistency (attitudes scale $\alpha = 0.64$).

Programme evaluation

Students randomized to the intervention group completed an evaluation survey immediately post-intervention, providing feedback on how relevant, interesting and engaging the programme was. Students provided an overall rating of the programme from 'very good' to 'very poor' and supplied their most and least favourite elements. Inductive analytical techniques were used to allow key themes to emerge, which were summarized based on the frequency and significance of the response.

Sample size

Sample size was determined by power calculations for cluster-randomized controlled trials (RCTs) using multi-level mixed-effect regression models [44]. To achieve 80% power and a standardized between-group mean difference of 0.3 ($P = 0.05$) during the 12-month trial, this study required three schools per arm, with at least 60 students per school. We expected 10% school dropout and the average year group size to be 100 students, therefore we aimed to recruit eight schools and 800 students to the study. The intraclass correlation coefficient for participants in the same school was 0.027. The student sample size targets were met and the study was fully powered.

Statistical analyses

Multi-level mixed-effects regression modelling were used to determine the effects of the intervention over a 12-month period. The hierarchical data follow level 1 (repeated measures over time), nested within level 2 (each student) and nested within level 3 (each school). As per our a-priori analysis plan [25], there is one main effect for the difference between groups at baseline (group main effect) and one main effect for the change in the control group over time (time main effect), and the intervention effectiveness was reported as a group × time interaction term, comparing the growth trajectories of the intervention group during the 12-month period. To increase accuracy, data from all three assessments (baseline, 6 and 12 months) were incorporated, and the best-fitting model for time was linear, representing growth from baseline to the 12-month follow-up. The interaction terms for binary outcomes (alcohol, cannabis, nicotine, MDMA, cocaine and prescription drug misuse and alcohol-related harm) were modelled via the logit link function, and the odds were calculated by exponentiating the regression coefficient. The continuous outcomes (drug literacy knowledge and skills) were modelled via a linear mixed-effect growth model with all three time-points. All models included both a random intercept at the individual level and the school level, and a random slope at the individual level was added when it improved the model parsimony or fit. In addition, discrete models predicting probabilities of primary outcomes at the 12-month follow-up were presented as coefficients. Full information maximum likelihood procedures were used to manage missing data, whereby all available data were included in the model estimates under the assumption that data were missing at random. Multiple imputation was conducted to explore the impact of missing data on the robustness of the findings. For each outcome, 40 imputed data sets were created. Covariates associated with missingness or the outcome were included in the imputed model, including sex, age, baseline grades and baseline substance use outcomes. Descriptive statistics were run on baseline variables and to determine whether baseline outcomes predict missingness at follow-up, χ^2 tests for categorical outcomes, one-way analysis of variance for continuous outcomes and Mann–Whitney *U* for non-normally distributed continuous outcomes were conducted. All analyses were conducted in Stata version 17 [45] using the intention-to-treat sample.

RESULTS

Participant characteristics and attrition

The final sample included 950 students from eight schools [mean age = 15.9 years, standard deviation (SD) = 0.68, 60% female, 94% born in Australia]; see Table 1 for baseline characteristics of the sample and Figure 1 for the CONSORT flow diagram illustrating recruitment and retention. Approximately 63% (n = 595) of the sample completed the 12-month follow-up assessment, including 58% of the intervention group (n = 396/679) and 66% the active control group (n = 179/271). After randomization, but prior to baseline data collection, one school withdrew from the active control group due to scheduling issues. Missing data analyses suggested that missingness was more likely among individuals in the intervention group (OR = 0.88, 95% CI = 0.66–0.99), among males (OR = 2.3, 95% CI = 1.88–3.14) and individuals who binge drink alcohol ($\chi^2_{(1)}$ = 4.42) (P = 0.04). No other baseline variables predicted missingness at follow-up. See Table 2 for the prevalence of outcome variables over time and Supporting information, Figure S1 for a visual illustration of the outcomes over time.

Intervention effects

Primary outcomes

Table 3 presents the results from the multi-level mixed-effect regression models for each primary outcome. Compared to controls, students in the intervention group showed significantly slower annual growth in binge drinking, recent MDMA use, recent cocaine use and prescription drug misuse during the trial. This was consistent with the model-predicted estimate for binge drinking (OR = 0.14, 95% CI = 0.03–0.80) and prescription drug misuse (OR = 0.07, 95% CI = 0.01–0.54), although uncertainty was introduced for predicted probability of MDMA use (OR = 0.24, 95% CI = 0.05–1.15) and cocaine use (OR = 0.20, 95% CI = 0.03–1.12) There was less certain evidence that the intervention slowed the yearly growth in cannabis and nicotine use, both in the growth model (see Table 3) and at the final end-point (P > 0.05).

Multiple imputation analysis examined the robustness of the primary results using 40 imputed data sets. Results showed the intervention slowed annual weekly binge drinking, cocaine use and prescription drug misuse compared to the active control group. The imputed results were inconclusive regarding the intervention effect on monthly cannabis use (OR = 0.77), nicotine use (OR = 0.96) and MDMA use (OR = 0.68) and harm reduction and help-seeking skills (β = 0.06), given the wide confidence intervals (see Table 3).

Secondary outcomes

Table 4 presents the results from the multi-level mixed-effect regression analysis for the secondary outcomes. Students in the intervention group maintained higher levels of drug literacy knowledge, harm reduction and help-seeking scores during the trial. There was little evidence of an intervention effect on alcohol-related harms, which was consistent with the predicted probability at the final end-point (OR = 1.68, 95% CI = 0.82–3.5). The multiply imputed results are

TABLE 1 Baseline characteristics of the sample.

	The Illicit Project	Control	Total sample N = 950
Total	679	271	950
Gender (F)	455/679 (67%)	140/271 (52%)	595/950 (63%)
Mean age (SD)	15.8 (0.6)	16.1 (0.7)	15.9 (0.7)
Average grades			
90–100%	12%	13%	12%
80–89%	29%	29%	29%
70–79%	24%	28%	25%
60–69%	14%	15%	15%
59% or below	21%	15%	19%
Year group			
Year 10	71%	54%	67%
Year 11	11%	26%	15%
Year 12	18%	20%	18%
School type			
Independent	2	0	2
State	3	3	6

Abbreviations: F = female; SD = standard deviation.

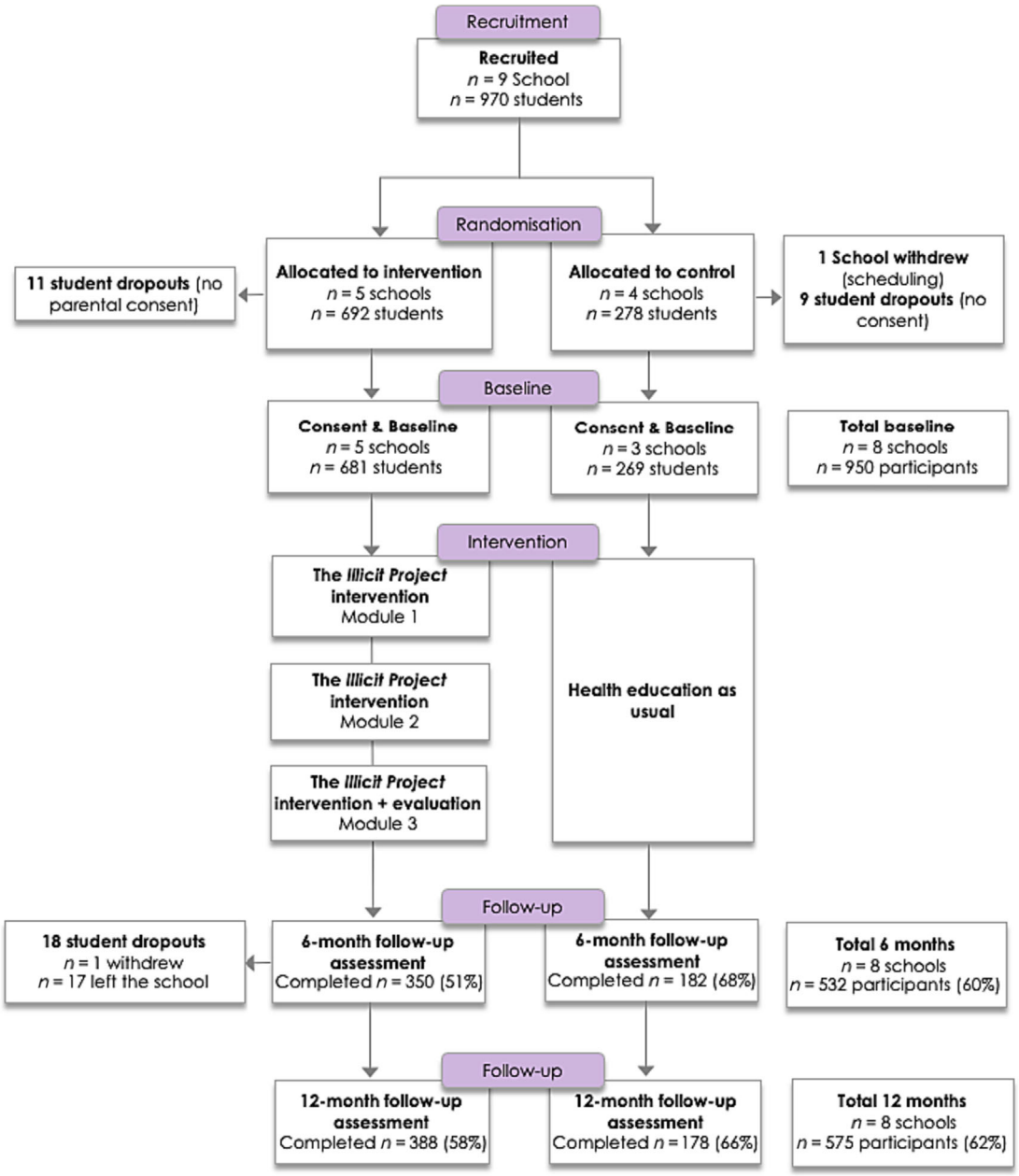

FIGURE 1 Consolidated Standards of Reporting Trials (CONSORT) flow-chart of participant recruitment and retention.

largely in line with these findings; however, wider confidence intervals indicates that these findings are less robust to the impact of missing data.

Programme evaluation

A total of 275 participants in the intervention group completed the evaluation survey. More than three-quarters (78%) agreed that they felt more equipped to make better choices concerning drinking and substance use after completing the programme, 76% agreed that they had learnt a lot more about the dangers of drinking and taking drugs, 76% agreed that the neuroscience information was interesting, 74% agreed that the content was relevant to their lives and the delivery was engaging and more than two-thirds (70%) agreed that they plan to use the information learnt in the programme in their own lives. More than two-thirds (72%) of students provided an overall rating of the programme as good or very good. A summary of students most and least favourite elements of the programme are included in Table 5.

DISCUSSION

This study demonstrates for the first time, to our knowledge, that a neuroscience-based harm reduction programme delivered during the last years of secondary school (aged 16–19 years) can have positive

TABLE 2 Primary and secondary outcome prevalence over time.

Outcomes	Time-point	Intervention prevalence	Control prevalence
Primary outcomes			
Weekly binge	Baseline	23/671 (3%)	16/271 (6%)
	6 months	18/354 (5%)	19/177 (11%)
	12 months	7/387 (2%)	17/174 (10%)
Monthly cannabis use	Baseline	60/675 (9%)	25/265 (9%)
	6 months	26/324 (7%)	16/177 (9%)
	12 months	16/392 (4%)	16/178 (9%)
Nicotine product use	Baseline	148/675 (22%)	73/269 (26%)
	6 months	81/350 (23%)	61/174 (36%)
	12 months	79/390 (20%)	47/177 (27%)
MDMA use	Baseline	37/675 (6%)	15/269 (6%)
	6 months	7/350 (2%)	16/174 (9%)
	12 months	6/390 (2%)	7/170 (4%)
Cocaine use	Baseline	21/675 (3%)	6/263 (2%)
	6 months	10/350 (3%)	9/174 (5%)
	12 months	6/390 (2%)	8/177 (5%)
Methamphetamine use	Baseline	12/675 (2%)	7/269 (3%)
	6 months	3/350 (1%)	5/174 (3%)
	12 months	4/390 (1%)	5/177 (3%)
Non-medical prescription substance use	Baseline	37/675 (5%)	10/269 (4%)
	6 months	17/350 (5%)	6/174 (3%)
	12 months	9/390 (2%)	9/177 (5%)
Secondary outcomes			
Alcohol harms	Baseline	209/674 (31%)	125/276 (44%)
	6 months	95/356 (27%)	76/178 (43%)
	12 months	96/396 (24%)	57/179 (32%)
Mean drug literacy knowledge (SD)	Baseline	18.4 (8.8)	20.8 (8.3)
	6 months	21.8 (8.3)	20.6 (9.1)
	12 months	20.9 (8.1)	21.4 (8.3)
Mean drug literacy skills (SD)	Baseline	19.5 (5.4)	20.3 (5.2)
	6 months	20.7 (5.3)	20.3 (5.7)
	12 months	20.5 (5.4)	19.5 (5.3)

Notes: Baseline n = 950; 6 months n = 532; 12 months n = 575.
Abbreviations: SD = standard deviation; MDMA = 3,4-methylenedioxymethamphetamine.

sustained effects on substance use outcomes over 12 months. The Illicit Project is a novel, on-line intervention that targets high-risk patterns of substance use behaviour and encourages early help-seeking and friendship support. The intervention was effective in reducing the frequency of binge drinking, MDMA use, cocaine use and prescription drug misuse while improving drug literacy knowledge, help-seeking and harm reduction skills. However, further replication of the results is required, given the low retention rates and wide CIs in the sensitivity analyses.

In comparison to a recent meta-analysis assessing the average effect size of prevention programmes on alcohol use outcomes during short-term follow-up, the results of this study suggest that The Illicit Project is associated with a larger overall effect on risky alcohol use, imparting a 67% risk reduction compared to the average small-to-moderate effect size of other programmes (for example, Cohen's d = 0.13, 95% CI = 0.07–0.19) [15,46,47]. Notably, the majority of established programmes target younger adolescents and follow-up typically concludes at approximately 16 years, when prevalence is low. Nonetheless, the larger effect sizes demonstrated in the current study align with another consistent finding that programmes targeting adolescents aged more than 14 years produce large effects on drinking outcomes, and can be used to supplement or 'boost' the effects of programmes delivered during early and mid-adolescence [23]. The Illicit Project's large positive impact on substance use outcomes, such

TABLE 3 Effectiveness of the programme on primary outcomes over 12 months.

Multi-level logistic regression models	OR	95% CI	*P*-value
Weekly binge drinking			
Group effect	0.99	0.11–8.76	0.99
Time effect	1.91	0.92–3.96	0.08
Group × time	0.33	0.12–0.89	0.03
Imputed analysis			
Group effect	0.74	0.29–1.91	0.54
Time effect	2.06	1.20–3.55	0.01
Group × time	0.41	0.17–1.00	0.05
Monthly cannabis use			
Group effect	1.04	0.36–3.01	0.94
Time effect	0.82	0.46–1.45	0.50
Group × time	0.83	0.40–1.7	0.62
Imputed analysis			
Group effect	1.02	0.49–2.13	0.96
Time effect	1.09	0.65–1.85	0.74
Group × time	0.77	0.35–1.72	0.52
Any nicotine use			
Group effect	0.80	0.25–2.53	0.70
Time effect	1.29	0.91–1.84	0.15
Group × time	0.80	0.52–1.23	0.30
Imputed analysis			
Group effect	0.50	0.24–1.00	0.05
Time effect	1.12	0.79–1.59	0.52
Group × time	0.96	0.63–1.46	0.83
Any MDMA use			
Group effect	1.01	0.30–3.38	0.99
Time effect	0.77	0.21–2.82	0.70
Group × time	0.14	0.02–1.00	0.05
Imputed analysis			
Group effect	0.82	0.47–1.43	0.48
Time effect	0.90	0.61–1.32	0.60
Group × time	0.68	0.39–1.19	0.18
Any cocaine use			
Group effect	4.35	0.52–36.32	0.17
Time effect	11.52	1.56–86.48	0.02
Group × time	0.06	0.01–0.64	0.02
Imputed analysis			
Group effect	1.42	0.46–4.53	0.55
Time effect	1.94	1.00–3.77	0.05
Group × time	0.50	0.22–1.11	0.08
Any prescription drug misuse			
Group effect	2.94	0.66–13.15	0.16
Time effect	2.22	0.45–11.05	0.33
Group × time	0.07	0.01–0.54	0.01
Imputed analysis			
Group effect	2.19	0.76–6.29	0.14

TABLE 3 (Continued)

Multi-level logistic regression models	OR	95% CI	*P*-value
Time effect	1.23	0.65–2.31	0.51
Group × time	0.45	0.21–0.98	0.04

Notes: Baseline *n* = 950; 6 months *n* = 532; 12 months *n* = 575.
Abbreviations: MDMA= 3,4-methylenedioxymethamphetamine; OR = odds ratio; CI = confidence interval.

TABLE 4 Effectiveness of the programme on secondary outcomes over 12 months.

Multi-level logistic regression models	OR	95% CI	*P*-value
Alcohol harms			
Group effect	0.38	0.14–1.06	0.06
Time effect	0.41	0.19–0.86	0.02
Group × time	1.52	0.62–3.71	0.36
Imputed analysis			
Group effect	0.31	0.12–0.82	0.02
Time effect	1.27	0.74–2.17	0.39
Group × time	1.46	0.79–3.05	0.31
Multi-level linear regression models	**β**	**95% CI**	***P*-value**
Drug literacy (knowledge)			
Group effect	−3.27	−6.02 to −0.52	0.02
Time effect	−0.69	−2.24 to 0.86	0.38
Group × time	3.71	1.86–5.56	< 0.01
Imputed analysis			
Group effect	−1.86	−3.29 to −0.43	0.01
Time effect	0.16	−0.61 to 0.93	0.68
Group × time	0.91	−0.07–1.89	0.07
Drug literacy (help-seeking and harm reduction skills)			
Group effect	−0.96	−2.18 to 0.24	0.12
Time effect	−0.90	−1.68 to −0.12	0.02
Group × time	1.55	0.62–2.48	< 0.01
Imputed analysis			
Group effect	−0.28	1.00–0.44	0.45
Time effect	−0.15	−0.65 to 0.34	0.54
Group × time	0.06	−0.53 to 0.95	0.85

Notes: Baseline *n* = 950; 6 months *n* = 532; 12 months *n* = 575.
Abbreviations: OR = odds ratio; CI = confidence interval.

as an approximate 86% reduction in the odds of MDMA use and 94% reduction in the odds of cocaine use during late adolescence, compares favourably to a recent meta-analysis and umbrella review of school-based prevention programmes which report programmes to have an average 17% risk reduction (RR) for illicit substance outcomes (RR = 0.83, 95% CI = 0.69–0.99) [15,48]. Nonetheless, the sensitivity analyses showed wider CIs which introduces uncertainty into these results, and further studies are required.

TABLE 5 Qualitative feedback on The Illicit Project.

Theme	Quotes
Favourite element of the programme	
Interest in neuroscience	'Learning about the science behind the drugs and alcohol and how they can affect your body and especially the long-term effects on your brain'
	'I liked learning about how different parts of the brain are affected when drinking alcohol'
Credibility of the science and peer voice	'The statistic as it showed me that taking drugs and drinking is not as popular as I thought which makes me more confident towards making decisions towards my choices'
	'I liked how the personal testimonies made it especially relevant and rooted in real life. I liked how the information we were learning came from prominent experts and we could see this was credible evidence'
Engaging and interactive content	'My favourite part of the programme was the detail and animations that made it clearer to understand. It was highly engaging which made it enjoyable to watch'
	'The graphics allowed for significant engagement within the topic'
Areas for improvement	
Length and repetition	'My least favourite of the programme was the length of it. Maybe shortening it with the same amount of information would be great'
	'My least favourite part was the extended response questions, which were boring to do on my own'
Granularity and amount of information	'I feel as though the modules could be more spread out so that it is not a huge influx of information'
	'The programme as a whole was very long and I have a short attention span so I could not process all the information'
Functional features of the programme	'My suggestion would be to add a feature where you would be able to pause and return to the session from the part you were up to rather than the beginning'
	'We had tech issues so we had to do it all with the class, made the process unenjoyable and very long'

Developmentally appropriate substance use education is essential. Most people who first try an illicit substance do so out of curiosity (69%), and those who continue to use report doing so because they enjoy it (71%) [49]. It is therefore important to meet young people where they are developmentally, and use science to credibly address the outcomes that substances are perceived to deliver by young people. There are three key cognitive traits that tend to underlie risk adolescent behaviours: delay discounting, response inhibition and sensation-seeking and urgency [50]. Leveraging the power of neuroscience may be a credible and compelling method to engage high-risk students in health promotion. Positive psychology delivered by neuroscience teachings may be a key mechanism behind the effects of the programme, engaging not only those who are abstaining from substance use, but also individuals who have initiated recreational substance use and seek relevant and credible information. There is mounting evidence that harm reduction education is effective and credible in reducing the harms of substances among adolescents [20,51], and is particularly relevant for older adolescents and young adults who are undergoing initial exposure to substances.

In the context of implementation science and programme up-scale, there remains a question of the suitability of on-line interventions in engaging a diverse range of learners in complex health campaigns. A meta-analysis found that college students with low motivation to learn preferred face-to-face interventions over on-line interventions, whereas motivated/independent learners demonstrated a preference for on-line delivery and self-paced learning [23,52]. This suggests that greater facilitator involvement may help to improve programme completion among less academically engaged students and, by extension, some learners with more complex needs may benefit from a hands-on, peer-delivered format. This raises the importance of implementation trials, whereby various modes of programme delivery can be explored and customized to target a given group more effectively.

The results of this trial must be interpreted within the context of several limitations. First, the trial was conducted during the COVID-19 pandemic under lockdown conditions, where young people were reportedly less social and engaged in lower-than-usual substance use [6]. This may have reduced the likelihood of detecting intervention effects on key outcomes, which is further supported by the lower-than-usual time main effect for many outcomes of interest. In addition, COVID-19 may have negatively impacted retention, and hence missing data (approximately 38%) are a key limitation of this trial. Further studies with larger sample sizes and schools committed to helping improve retention rates are needed. Another limitation is the absence of teacher fidelity scores which reduces transparency of the intervention delivery modality, and although the programme is delivered on-line to preserve the core components of the intervention, one school reported significant technical issues which impeded delivery of some programme elements and may have reduced the likelihood of detecting programme effects. Finally, majority female sampling highlights the need for future research to explore potential gender differences and recruit a more diverse sample.

This large multi-site clinical trial is the first, to our knowledge, to support the effectiveness of an on-line harm reduction intervention in reducing risky substance use in late adolescence. Further research is needed to expand upon these results with improved retention rates and over a longer period of time; however, this trial supports harm reduction as an engaging and efficacious method to reduce risky substance use during late adolescence. With the liberalization of attitudes towards cannabis and other substances globally, it is important to strive towards more innovative, engaging and effective harm reduction interventions for the next generation of young people.

TRIAL REGISTRATION

Australian New Zealand Clinical Trials Registry (ACTRN12620000805976). Open access publishing facilitated by The University of Sydney, as part of the Wiley - The University of Sydney agreement via the Council of Australian University Librarians.

AUTHOR CONTRIBUTIONS

Jennifer Debenham: Conceptualization (equal); data curation (lead); formal analysis (lead); funding acquisition (equal); investigation (equal); methodology (equal); project administration (lead); resources (equal); writing—original draft (lead); writing—review and editing (lead). **Louise Birrell:** Conceptualization (equal); data curation (supporting); funding acquisition (equal); investigation (equal); methodology (equal); project administration (supporting); resources (equal); supervision (equal); validation (equal); writing—original draft (supporting); writing—review and editing (supporting). **Katrina E. Champion:** Conceptualization (equal); data curation (supporting); formal analysis (supporting); funding acquisition (equal); investigation (equal); methodology (equal); project administration (supporting); resources (equal); supervision (equal); validation (equal); writing—original draft (supporting); writing—review and editing (supporting). **Nicola Newton:** Conceptualization (equal); data curation (supporting); formal analysis (supporting); funding acquisition (equal); investigation (equal); methodology (equal); project administration (equal); resources (equal); supervision (equal); validation (equal); writing—original draft (supporting); writing—review and editing (supporting).

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DECLARATION OF INTERESTS

J.D. is the developer of The Illicit Project intervention, which is freely available for schools to access.

DATA AVAILABILITY STATEMENT

Research data are not shared.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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