Effectiveness of the 'Healthy School and Drugs' prevention programme on adolescents' substance use: a randomized clustered trial


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Effectiveness of the ‘Healthy School and Drugs’ prevention programme on adolescents’ substance use: a randomized clustered trial

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ABSTRACT

Aim To evaluate the effectiveness of the Healthy School and Drugs programme on alcohol, tobacco and marijuana use among Dutch early adolescents. Design Randomized clustered trial with two intervention conditions (i.e. e-learning and integral). Setting General population of 11–15-year-old adolescents in the Netherlands. Participants A total of 3784 students of 23 Dutch secondary schools. Measurements Structured digital questionnaires were administered pre-intervention and at 32 months follow-up. The primary outcome measures were new incidences of alcohol (life-time and 1-month prevalence), tobacco (life-time and 1-month prevalence) and marijuana use (life-time prevalence). Findings Main effect analyses showed no programme effects on incidences of alcohol consumption (life-time prevalence: e-learning condition: $B = 0.102$, $P = 0.549$; integral condition: $B = -0.157$, $P = 0.351$; 1-month prevalence: e-learning condition: $B = 0.191$, $P = 0.288$; integral condition: $B = -0.140$, $P = 0.445$), tobacco consumption (life-time prevalence: e-learning condition: $B = 0.164$, $P = 0.444$; integral condition: $B = 0.160$, $P = 0.119$; 1-month prevalence: e-learning condition: $B = 0.088$, $P = 0.746$; integral condition: $B = 0.261$, $P = 0.093$), or marijuana consumption (life-time prevalence: e-learning condition: $B = 0.070$, $P = 0.732$; integral condition: $B = 0.186$, $P = 0.214$). Conclusion The non-significant impact of the Healthy School and Drugs programme (a Dutch school-based prevention programme for early adolescents) on incidences of alcohol, tobacco and marijuana use indicates that the programme is either ineffective or implemented inadequately.

Keywords Alcohol use, early adolescents, marijuana use, prevention, randomized clustered trial, tobacco use.

INTRODUCTION

Prevention programmes are often implemented as tools to reduce prevalence rates of substance use in early adolescents. One of the most popular and widely used Dutch prevention programmes is ‘The Healthy School and Drugs (HSD)’ programme, which aims at preventing, postponing or reducing excessive substance use among early adolescents in secondary schools. Approximately 75% of all secondary schools in the Netherlands annually carry out (parts of) the HSD programme. The implementation is handled and supervised by the regional institutions for treatment and care of drug addiction (ITCD) or the Municipal Health Services (MHS). It is one of the few school-based Dutch national prevention programmes of which the effectiveness was previously tested, in a quasi-experimental study [1]. Although beneficial effects were found for alcohol and tobacco use the effects were small, which is common for universal school-based prevention programmes [2–5]. Since the study of Cuijpers and colleagues [1], many changes have been made in both materials (e.g. e-learning modules have been implemented) and content (e.g. renewed marijuana module) of the HSD programme. Therefore, our aim was to perform a novel, more stringent test—based on a randomized clustered trial (RCT)—of the effects of the renewed HSD programme on adolescents’ substance use.
In many trials, research teams are involved in or control the delivery of (parts of) the programme themselves (e.g. [6,7]). The results of such an efficacy trial, however, cannot be translated readily to everyday practice because, after initial implementation, programme delivery is usually taken over and carried out by local professionals. For example, an efficacious Swedish prevention programme called ‘Örebro Prevention Programme’ (ÖPP) [8] was recently re-tested in an effectiveness trial (i.e. under ‘real world’ circumstances). Findings then indicated that ÖPP did not seem to postpone or reduce alcohol use among Swedish adolescents [9]. This emphasizes the importance of conducting an effectiveness trial of prevention programmes as they are implemented in practice.

Many Dutch schools direct their preventive efforts at students (i.e. through education and information). Recently, a previous Dutch prevention trial (PAS) has shown that a multi-component approach can be more effective than a single component approach in reducing alcohol use among adolescents [7,10]. However, Foxcroft & Tsertsvadze [11], in their review on universal multi-component prevention programmes for alcohol misuse, concluded that except for PAS there is little evidence that multi-component programmes are more effective than single-component programmes. To examine if solely relying upon the education of adolescents within the HSD programme is enough for preventive effects, or that the multi-component approach of the HSD programme is necessary to obtain preventive effects, we compared two intervention conditions (i.e. e-learning and integral condition) to a control group in our RCT.

The two intervention conditions were compared to the regular curriculum of Dutch secondary schools in an RCT including 3784 adolescents. We expected that adolescents in the intervention conditions, relative to controls, would be less likely to engage in alcohol, tobacco and marijuana use at 32 months follow-up. Moreover, because the integral HSD programme focuses upon the home and school environment in addition to the individual education of students, and because the study of Koning and colleagues already showed that a multi-component programme targeting both adolescents and their parents was more effective compared to a programme targeting only adolescents or their parents [7,10], we expected that HSD effects would be more pronounced in the integral than in the e-learning condition.

**METHOD**

**Design and procedure**

Of the 123 eligible secondary schools (i.e. schools with no recent involvement in the HSD programme) that were invited, 23 schools including a total of 3784 adolescents agreed to participate (see study protocol: [12]). In collaboration with the schools’ headmasters, we informed the adolescents’ parents annually about study goals. This was achieved by means of a letter in which we also notified parents that they could refuse or terminate participation of their child in the study at any time. Approval for the design and data collection procedures was obtained from the ethics committee of the Faculty of Social Sciences, Radboud University Nijmegen (ECG03072008).

**Sample size**

We estimated our targeted sample size based on a small effect size ($d$) of 0.15 [13] in Stata [14]. We based our effect size on other prevention studies on adolescent substance use that generally have small effects [2–5]. To detect small intervention effects ($d = 0.15$), a sample size of $n = 698$ adolescents per condition was required at the end of the study (at 32 months follow-up) for testing the hypothesis of superior effectiveness in a two-sided independent $t$-test at alpha = 0.05 and a power of (1-beta) = 0.80. We corrected this sample size for 5% attrition at each time-point, which resulted in a number of 815 participants. Lastly, we corrected for the fact that our data were clustered (i.e. adolescents were nested within schools) by multiplying this number by 1.3 (cf. [15–17]). Considering these corrections, at least $n = 1060$ adolescents per condition had to be included in the study.

**Randomization**

After initial recruitment and enrolment in the trial, randomization took place at the school level, to avoid contamination between conditions (cf. [7]). An independent statistician performed the allocation before baseline assessment and randomly assigned the 23 schools to either the control condition, e-learning condition or integral condition. Randomization was carried out using a blocked randomization scheme (block size 6), and was stratified by the level of education that the schools offered. The random allocation to conditions was as follows: control condition (seven schools), e-learning condition (seven schools) and integral condition (nine schools). Directly after randomization, but before the intervention took place, a baseline assessment (T0) was carried out among all first-grade students between January and March 2009. The first follow-up (T1) was carried out between September and November 2009, the second (T2) between September and November 2010 and the third (T3) between September and December 2011. Adolescents completed a digital questionnaire during school hours in the presence of a teacher and a research assistant. Adolescents were informed that their data
would be processed anonymously; respondent-specific codes were used to link the data from one time-point to the next. Because adolescents did not know beforehand when the questionnaires would be administered, we can assume that non-response was random (e.g. due to illness or leaving school).

Participants

Twenty-three secondary schools, including 3784 first-grade students, were selected to participate (see Fig. 1). At T0, a total of 3542 first-grade students took part in the study; 229 adolescents (6.1%) were absent during data collection and 13 participants (0.3%) were declined participation by their parents. The T0 sample ($n = 3542$) included 49.4% boys ($n = 1750$). Participants ranged in age from 11 to 15 years [mean = 13.01, standard deviation (SD) = 0.49]. In total, 24.6% of these adolescents received pre-university education ($n = 871$), 18.9% received higher general education ($n = 668$), 9.7% received a combination of pre-university education and higher general education ($n = 343$), 24.1% received lower general education ($n = 855$) and 22.7% received lower vocational education ($n = 805$). The majority of the participants were of Dutch descent (96%).

Loss to follow-up

Of the total of 3784 randomized participants, 3542 (93.6%) completed the baseline assessment (T0). In total,
3215 participants of the T0 sample (90.8% of 3542) participated in the programme and completed the follow-up assessment after 8 months (T1). The response rate for the 20 months follow-up (T2) was 82.3% (n = 2915 out of n = 3542). Just before the 32-month follow-up (T3), one school from the control condition and one school from the e-learning condition dropped out of the study due to practical considerations. As adolescents were included by school participation, all students of these schools were lost to follow-up. A total of 2340 adolescents of the remaining 21 schools participated at T3 (response rate out of n = 3542 = 66.1%). We conducted logistic regression analyses with loss to follow-up as DV to examine attrition effects at T3 for sex, age, educational level, ethnicity and condition (we excluded schools that withdrew from the effectiveness trial, as student attrition was a consequence of school attrition). Adolescents lost to follow-up were less likely to be in pre-university education and more likely to be in higher general education or a combination of pre-university education and higher general education [odds ratio (OR) = 1.13, 95% confidence interval (CI) = 1.07, 1.20, P < 0.0001] compared to adolescents who completed the 32-month follow-up assessment. Nagelkerke R² for the regression model was 0.015. No differences in loss to follow-up were found for the demographics sex, age and ethnicity. Furthermore, no differences in loss to follow-up were found between the three conditions.

Intervention

The primary goal of both the intervention conditions was to prevent (or postpone) the onset of use of alcohol, tobacco and marijuana. The e-learning condition only targeted the education part of the HSD programme, in which adolescents are educated on alcohol, tobacco and marijuana use. The integral condition targeted the whole multi-component structure of the HSD programme.

Control condition

An agreement was reached with the control schools that they would not start any substance-related interventions in our target group throughout the study period. Because many schools in the Netherlands have employed basic initiatives to decrease or prevent substance use, they were allowed to continue their ‘business-as-usual’ activities.

e-Learning condition

The participants in this condition received an e-learning module about alcohol (four lessons) between April and July 2009, tobacco (three lessons) between April and July 2010 and marijuana (three lessons) between April and July 2011. The lessons are based on the ASE model [18–22] and the social cognitive theory [23]. The ASE components are embedded in the modules in that the lessons are focused upon increasing knowledge about substances, aim to tutor adolescents about risks concerning substance use and preparing adolescents for coping with group pressure by training their refusal skills (i.e. increasing self-efficacy). The lessons consist of small films, animations and several types of interactive tasks. Also, adolescents are able to discuss relevant topics or to exchange their opinions through chatrooms and forums. The lessons are designed to gradually increase adolescents’ skills in responsibly dealing with substances. For more details on the e-learning modules and their theoretical basis see [12].

Integral condition

As well as the digital e-learning modules, the participants in the integral condition received three additional intervention components (i.e. parental participation, regulation and monitoring and counselling). The parental participation component consists of a plenary parental meeting for the parents of participating students and was planned in the first year of the intervention at school in collaboration with the ITCD or MHS. During this meeting, information was provided on the HSD programme and substance use. Specifically, characteristics and risks of substance use, opinions on substance use and education in the home setting with respect to substance use were discussed. The regulation component concerned the school standard and subsequent rules regarding substance use behaviours of students and school personnel, and was planned in the second year. Examples of rules regarding substance use concern alcohol use at school parties or if and where adolescents are allowed to smoke at school. If a school in the integral condition lacked such regulation, one was created in cooperation with the ITCD or MHS. Finally, the monitoring and counselling component consisted of a training session for school personnel on signalling and guiding problematic substance use among individual adolescents, which was also scheduled in the second year and provided by the ITCD or MHS. During this training session, practical information was provided on how to recognize problematic use in adolescents and on how to efficiently support these adolescents in and outside the school setting. For more details on the integral components see [12].

Measures

Alcohol use

Alcohol use was assessed through two different outcomes. Life-time prevalence indicated whether adolescents had ever consumed a glass of alcohol in their life
Table 1  Similarities and differences on adolescent demographics at baseline (n = 3542).

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>e-Learning</th>
<th>Integral</th>
<th>Test result</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Boys</td>
<td>613 (51.5)</td>
<td>596 (48.7)</td>
<td>541 (48.0)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Girls</td>
<td>578 (48.5)</td>
<td>629 (51.3)</td>
<td>585 (52.0)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age Mean (SD)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>12.92 (0.44)</td>
<td>13.04 (0.50)</td>
<td>13.08 (0.53)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ethnicity</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dutch</td>
<td>1152 (96.7)</td>
<td>1180 (96.3)</td>
<td>1070 (95.0)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-Dutch</td>
<td>39 (3.3)</td>
<td>45 (3.7)</td>
<td>56 (5.0)</td>
<td>χ²(1) = 3.14</td>
<td>0.208</td>
</tr>
<tr>
<td>Education</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>139 (11.7)</td>
<td>337 (27.5)</td>
<td>329 (29.2)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>164 (13.8)</td>
<td>374 (30.5)</td>
<td>317 (28.2)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>341 (28.6)</td>
<td>186 (15.2)</td>
<td>141 (12.5)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>178 (14.9)</td>
<td>9 (0.7)</td>
<td>156 (13.9)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>369 (31.0)</td>
<td>319 (26.0)</td>
<td>183 (16.3)</td>
<td>χ²(8) = 479.88</td>
<td>&lt; 0.0001</td>
</tr>
</tbody>
</table>

Education: 1 = lower vocational education, 2 = lower general education, 3 = higher general education, 4 = combination higher general education and pre-university education, 5 = pre-university education. SD = standard deviation.

(‘yes’ = 1 and ‘no’ = 0) and 1-month prevalence was inquired through the question: ‘How often have you consumed alcohol in the past 4 weeks?’ [24]. Response options were 1 = ‘I did not consume alcohol’, 2 = ‘1–3 days in the past 4 weeks’, 3 = ‘1–2 days per week’, 4 = ‘3–4 days per week’, 5 = ‘5–6 days per week’ and 6 = ‘every day’. Adolescents who responded in categories 2–9 were categorized as drinking in the past month (= 1) and adolescents who responded in category 1 were categorized as not drinking in the past month (= 0). Dichotomous measures are clinically useful and allow us to calculate important outcome measures (i.e. number needed to treat; [25]), which should be reported according to the Consolidated Standards Of Reporting Trials (CONSORT) guidelines [26,27].

Tobacco use

Tobacco use was assessed according to life-time prevalence and 1-month prevalence. Life-time prevalence of tobacco use was measured with a single item on a nine-point scale, ranging from 1 = ‘I never smoked, not even a puff’ to 9 = ‘I smoke at least once a day’ [28]. Adolescents who responded in categories 2–9 were categorized as having tried smoking before (= 1) and adolescents who responded in category 1 were categorized as never having tried smoking (= 0) [29]. The 1-month prevalence was measured by asking the adolescents how many cigarettes they had smoked in the past 4 weeks. Adolescents answered this question on an eight-point scale ranging from 1 = ‘I never smoked’ to 8 = ‘more than 20 cigarettes per day’. Adolescents who had smoked in the past 4 weeks were assigned the number 1 and the adolescents who did not smoke in this period were assigned the number 0.

Marijuana use

Marijuana use was measured on the basis of life-time prevalence of use through a single item: ‘Have you ever used marijuana?’ [30]. Adolescents could report ‘yes’ (= 1) or ‘no’ (= 0).

Strategy of analyses

We performed χ² tests and F-tests to investigate whether randomization had resulted in an equal distribution of demographics across the three conditions. Uneven distribution across the three study conditions was found in terms of age and level of education (Table 1). These variables, including sex and ethnicity, were therefore included as covariates in all subsequent analyses. To correct for the potential non-independence (complexity) as well as clustering of the data, the TYPE=COMPLEX procedure in Mplus was used [31].

Data were analysed in accordance with the intention-to-treat principle, using Mplus version 6.1 [32]. To ascertain the impact of the programme on the onset of substance use, a selection of the study cohort was required. We selected the adolescents who, at baseline, had never consumed a glass of alcohol (n = 2499), never smoked (n = 2709) or never used marijuana (n = 3415). Missing data were handled by multiple imputation (MI), using the Markov chain Monte Carlo (MCMC) method [33]. For the main analyses, we compared each of the experimental conditions with the control condition. Logistic regression analysis was used with the binary outcome (1 = case, 0 = not a case) as dependent variable and the treatment dummies as independent variables, while adjusting for both the confounders and the clustered data. Presented are the standardized regression coefficients.

RESULTS

Covariates

Sex, age, educational level and ethnicity were predominantly unrelated to substance use outcomes. Exceptions
Marijuana use (Tobacco use outcomes in all programme conditions. Results involved null findings across all time-points for all users due to the minimum variance on life-time prevalence at baseline. Results involved null findings across all time-points for all baseline.

Table 2 Numbers and percentages of alcohol, tobacco and marijuana use at follow-up (T3) per condition among never users at baseline.

<table>
<thead>
<tr>
<th></th>
<th>Control (n = 521)</th>
<th>e-Learning (n = 563)</th>
<th>Integral (n = 543)</th>
<th>Total (n = 1627)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Alcohol use (n = 2499)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Life-time prevalence</td>
<td>n (%)</td>
<td>364 (69.9)</td>
<td>407 (72.3)</td>
<td>370 (68.1)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>248 (47.7)</td>
<td>299 (53.1)</td>
<td>251 (46.2)</td>
</tr>
<tr>
<td><strong>Tobacco use (n = 2709)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Life-time prevalence</td>
<td>n (%)</td>
<td>189 (32.9)</td>
<td>238 (37.8)</td>
<td>233 (39.0)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>81 (14.1)</td>
<td>100 (15.8)</td>
<td>117 (19.6)</td>
</tr>
<tr>
<td><strong>Marijuana use (n = 3415)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Life-time prevalence</td>
<td>n (%)</td>
<td>103 (15.6)</td>
<td>137 (17.3)</td>
<td>152 (19.7)</td>
</tr>
</tbody>
</table>

The sample sizes in the left column refer to the selection of never users at baseline (T0), the sample sizes in the rows refer to the number of never users at T0 that completed T3. The percentages presented are relative to the sample sizes in the rows above.

were, first, a significant effect of age on 1-month prevalence of drinking (B = 0.214, P = 0.046), indicating that older adolescents were more likely to report drinking in the past month. Secondly, lower educational levels were associated with higher chances of life-time drinking (B = -0.070, P = 0.045), life-time smoking (B = -0.101, P = 0.007) and 1-month prevalence for smoking (B = -0.114, P = 0.029).

Programme effects on drinking, smoking and marijuana use

Table 2 presents all substance use outcomes at follow-up for both the e-learning and the integral condition. Table 3 presents the results of the intervention on the substance use outcomes for both intervention conditions. We found no significant effects for either of the programme conditions on any of the outcomes for drinking, smoking and marijuana use.*†

DISCUSSION

In contrast to both our expectations and a previous quasi-experimental study on HSD [1], neither the e-learning nor the integral intervention prevented the onset of alcohol, tobacco or marijuana use. The differences in results between our study and that of Cuijpers and colleagues [1] might be explained by our study design. The allocation to research conditions is, by definition, not at random in a quasi-experimental design and therefore potentially induces a bias towards a favourable evaluation of HSD effects. Secondly, the intervention schools of the Cuijpers study were already very actively involved in prevention activities and thus more experienced, which may have enabled their intervention to be more effective. In contrast, the schools in the present study were selected only if they had no HSD experience in the previous 2 years. Thirdly, the Cuijpers study was carried out 10 years before the current study. That decade witnessed the implementation of many societal campaigns and preventive efforts aimed at diminishing alcohol use, correlating with a drop in adolescents’ substance use in this time-period [15,17,34].

Many universal school-based prevention programmes produce small effects, but effect sizes still depend upon programme content and context (e.g. [3,35–38]). With respect to programme content, social influence programmes that cover broader-based personal and social skills training combined with knowledge and normative elements seem to be most effective [2,4,37,39–49]. Although these elements are combined in the HSD programme, the actual skills training in the programme is limited (i.e. exclusively aimed at refusal skills) and

*For reasons of parsimony, we have not reported the statistics of the other two time-points and the other outcomes that have been measured and included in our trial registration in the present paper. Briefly, we found no effects of the presently reported outcomes on T1 and T2 either, and there were no significant effects on either one of the three time-points of any of the programme conditions on weekly drinking and binge drinking. Any information on all outcomes at all time-points can be obtained through the first author.

†As testing prevention effects among baseline ‘never users’ only is a very conservative test, we also checked if the intervention was effective for adolescents who reported sporadic experience at baseline. To this end, we selected the adolescents who were ‘less than weekly drinkers’ (n = 3220) and ‘less than daily smokers’ (n = 3382) at baseline. We were unable to select a subsample of marijuana users due to the minimum variance on life-time prevalence at baseline. Results involved null findings across all time-points for all outcomes in all programme conditions.
minimal (i.e. practice solely embedded in e-learning modules). Also, more intense programmes may exert stronger effects in reducing adolescent substance use behaviour [4,11,38,43,48,50–53]. There are indications that at least 10 sessions are necessary in order to obtain programme effects [4,54,55]. The lessons of the HSD programme, in contrast, consist of four sessions on alcohol, three on tobacco and three on marijuana provided in 3 consecutive years. In addition, interactive methods have beneficial effects over non-interactive methods [4,42–44,48,51,56,57], and interaction between students is of key importance [4,57]. It might be that the interactive modules (i.e. chat rooms and forums) used in the HSD e-learning lessons do not sufficiently evoke discussion, role-playing and interaction between adolescents [58]. Embedding more traditional (i.e. classical) methods or components, in which trained adults successfully guide and stimulate student interactions, might benefit the programme [42,47,51].

Finally, in light of the programme context, targeting multiple contexts seems to have beneficial effects over targeting one specific context (e.g. [3,36,59–62]). A recent Dutch RCT showed that combining the alcohol module of the HSD programme with a structured parental meeting, in which parental rule-setting behaviour was encouraged as an effective strategy, helped to reduce adolescents’ alcohol use [7,10]. When offered separately, neither the alcohol module nor the structured parental meeting was effective. Although our lack of results in the e-learning condition corresponds with Koning and colleagues [7], the parental meetings used in both studies are clearly different. The parental meeting of Koning et al. [7] was integrated in the first general parental meeting of the school year, which is generally visited by all parents. Also, the parental meeting of Koning and colleagues was more structured and protocolized.

Remarkably, even though not significant, there is a negative trend with respect to the influence of the HSD programme on incidence of tobacco use. Although prevention efforts aim to reduce risk behaviours, it is not uncommon that these efforts sometimes produce iatrogenic effects [36,63–65]. An explanation might be the presence of a contagion effect between peers. Research shows that adolescents are more likely to start smoking when more of their friends or peers smoke [66–69]. It could be that more adolescents started smoking because more peers smoked in their school surroundings. It is still mostly unclear, however, if specific prevention programmes or components are accountable for these negative effects, and more research is needed on possible iatrogenic effects of substance use prevention.

Limitations and implications

A first limitation concerns the imbalances between conditions regarding age and level of education at baseline. We were forced to adjust for these potential confounding variables in all analyses. Considering the impact of age and education on the outcome measures, a next step might be to vary dosage, readability and comprehension level of the programme by age and educational level. Secondly, our use of self-reports might have led to measurement errors, due to situational and cognitive influences [70]. To overcome these influences and to optimize measurement validity, we guaranteed full confidentiality (anonymity) to our participants [7,71,72], and we asked adolescents if they ever tried a specific substance, which one might expect participants to recall reliably. Also, we used short time-intervals in order to reduce recall bias [73,74]. Thirdly, adolescents who were retained in our study were more likely to pursue a high education level than those lost to follow-up. However, besides school withdrawal, attrition was limited and not related to condition. Also, we analysed all participants in the condition to which they were allocated. Therefore, it seems unlikely that our attrition affected study conclusions. Fourthly, there is a possibility that the study was slightly underpowered in order to detect small effects for alcohol and

Table 3 Effects of the e-learning and integral conditions on substance use outcomes at follow-up (T3) among never users at baseline.

<table>
<thead>
<tr>
<th></th>
<th>e-Learning</th>
<th></th>
<th></th>
<th>Integral</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>B</td>
<td>SE B</td>
<td>P value</td>
<td>B</td>
<td>SE B</td>
<td>P value</td>
</tr>
<tr>
<td>Alcohol use (n = 2499)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Life-time prevalence</td>
<td>0.102</td>
<td>0.170</td>
<td>0.549</td>
<td>−0.157</td>
<td>0.168</td>
<td>0.351</td>
</tr>
<tr>
<td>1-month prevalence</td>
<td>0.191</td>
<td>0.180</td>
<td>0.288</td>
<td>−0.140</td>
<td>0.183</td>
<td>0.445</td>
</tr>
<tr>
<td>Tobacco use (n = 2709)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Life-time prevalence</td>
<td>0.164</td>
<td>0.214</td>
<td>0.444</td>
<td>0.160</td>
<td>0.103</td>
<td>0.119</td>
</tr>
<tr>
<td>1-month prevalence</td>
<td>0.088</td>
<td>0.273</td>
<td>0.746</td>
<td>0.261</td>
<td>0.156</td>
<td>0.093</td>
</tr>
<tr>
<td>Marijuana use (n = 3415)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Life-time prevalence</td>
<td>0.070</td>
<td>0.204</td>
<td>0.732</td>
<td>0.186</td>
<td>0.150</td>
<td>0.214</td>
</tr>
</tbody>
</table>

Reference group = control condition. Adjusted for sex, age, education, ethnicity and cluster effects. B = standardized logistic regression coefficient.
tobacco use due to our selection of never users at baseline. However, with a more lenient selection (i.e., less than weekly drinkers and less than daily smokers) and sufficient power we also did not find any effects of the HSD programme. Filthly, at the start of our study, approximately 60% of all secondary schools conducted HSD activities. As we included only schools that had no experience with HSD in the previous 2 years, a selection effect occurred, and caution is warranted when generalizing our results. Other unmeasured school level variables, such as proportion of students coming from low versus middle or high socio-economic backgrounds within a school, may also have impacted the results. Finally, only short-term effects of the marijuana module were measured in the present study.

The present findings indicate that the HSD programme, as it is currently implemented, is ineffective. Based on our findings, we cannot infer whether it is the content, the implementation or both the content and implementation that need adjustment. Future evidence-based research is necessary to further direct the re-development of the HSD programme. Based on previous knowledge, we suggest that a more intense (i.e., more sessions) and skill-focused intervention method is necessary in order to effectively lower substance use in early adolescence [4, 7, 11, 38, 43, 48, 50–53]. The HSD programme might benefit from attention for the rule-setting behaviour in the family context [7, 10] and the expansion of skill-training elements. Secondly, the HSD programme is a universal school-based prevention programme. There are indications that selective prevention programmes targeting ‘at risk’ populations produce more effect than universal programmes [6, 75–77]. This might indicate that the programme could benefit from a more selective approach. Finally, given that cognitive abilities and the corresponding capability to make responsible decisions are only fully developed in late adolescence [78–80], one might wonder whether cognitive methods, such as the ones that are included in the e-learning modules of the HSD programme, adequately match the cognitive development of early adolescents.

Clinical trial registration
NTR1516.

Declaration of interests
None.

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References