Does integrated academic and health education prevent substance use? Systematic review and meta-analyses

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Abstract

Background: Prevention of substance (alcohol, tobacco, illegal/legal drug) use in adolescents is a public health priority. As the scope for school-based health education is constrained in school timetables, interventions integrating academic and health education have gained traction in the UK and elsewhere, though evidence for their effectiveness remains unclear. We sought to synthesize the effectiveness of interventions integrating academic and health education for the prevention of substance use.

Methods: We searched 19 databases between November and December 2015, among other methods. We included randomized trials of interventions integrating academic and health education targeting school students aged 4–18 and reporting substance use outcomes. We excluded interventions for specific health-related subpopulations (e.g., children with behavioural difficulties). Data were extracted independently in duplicate. Outcomes were synthesized by school key stage (KS) using multilevel meta-analyses, for substance use, overall and by type.

Results: We identified 7 trials reporting substance use. Interventions reduced substance use generally in years 7–9 (KS3) based on 5 evaluations ($d = -0.09$, 95% CI $[-0.17, -0.01]$, $I^2 = 35\%$), as well as in years 10–11 (KS4) based on 3 evaluations ($d = -0.06$, $[-0.09, -0.02]$; $I^2 = 0\%$). Interventions were broadly effective for reducing specific alcohol, tobacco, and drug use in both KS groups.

Conclusions: Evidence quality was highly variable. Findings for years 3–6 and 12–13 could not be meta-analysed, and we could not assess publication bias. Interventions appear to have a small but significant effect reducing substance use. Specific methods of integrating academic and health education remain poorly understood.

KEYWORDS
child social development, health education, substance use, systematic review

1 | INTRODUCTION

Prevention of alcohol, tobacco, and illegal or legal drug use (henceforth termed substance use) as children move into adolescence remains a public health priority in the UK and internationally. Early initiation of alcohol use and excessive drinking are linked to later heavy drinking and alcohol-related harms (Hingson, Heeren, & Edwards, 2008; Viner & Taylor, 2007) and poor health (World Health Organization, 2007).

Alcohol use among young people is associated with truancy, exclusion, and poor attainment, as well as unsafe sexual behaviour, unintended pregnancies, youth offending, accidents/injuries, and violence (Masterman & Kelly, 2003). Preventing young people from taking up tobacco smoking is another key public health objective with 80,000 deaths in the UK alone due to smoking each year (Department of Health, 2010). Of smokers, 40% start in secondary school (Dunstan, 2012) and early initiation is associated with heavier and more enduring...
smoking and greater mortality (Hibell et al., 2011; Secretary of State for Health, Secretary of State for Scotland, Secretary of State for Wales, & Secretary of State for Northern Ireland, 1998). Early initiation and frequent use of “soft” drugs may be a potential pathway to more problematic drug use in later life (Ferguson, Boden, & Horwood, 2006). Among UK 15- to 16-year-olds, 25% have used cannabis and 9% have used other illicit drugs (Hibell et al., 2011). Drugs such as cannabis and ecstasy are associated with increased risk of mental health problems, particularly among frequent users (Ferguson et al., 2006; Hall, 2006; Moore et al., 2007; Parrott, Lees, Garnham, Jones, & Wesnes, 1998). Young people’s drug use is also associated with accidental injury, self-harm, suicide (Beautrais, Joyce, & Mulder, 1999; Charlton, Kelly, Dunnell, Evans, & Jenkins, 1993; J. Thomas et al., 2007), and other “problem” behaviours (Calafat et al., 2009; Drugs Strategy Directorate, 2002; Jayakody, Sinha, Curtis, Roberts, & Viner, 2005; Jessor, Donovan, & Costa, 1994). Finally, harms accruing to young people as a result of substance use are an important driver of health inequalities (Droomers, Schrijvers, Casswell, & Mackenbach, 2003; Dunstan, 2012).

Existing systematic reviews suggest that school curriculum-based health interventions can reduce alcohol consumption (Foxcroft & Tsertsvadze, 2012), tobacco smoking (Thomas & Perera, 2006), and drug use (Faggiano et al., 2005). Given an increasing focus in state-provided education on “accountability” and performance metrics for core academic subjects, health education, including that relating to the prevention of substance use, is increasingly difficult to deliver within busy school timetables (PSHE Association, 2013). In this context, many schools deliver health education in other subjects, integrating it with academic learning (Fornby et al., 2011). This may be an appropriate modality of delivery even in schools with dedicated time to health education. That is, even without the marginalization of health education, this approach may be more effective because it could allow for larger doses (Fornby et al., 2011; Pearson et al., 2015); it may be less prone to student resistance to health messages (Kupersmidt, Scull, & Benson, 2012); and it may enable synergy and reinforcements between lessons provided in different subjects (Bier, Zwarun, & Warren, 2011). On the other hand, integration may lead to delivery by school staff less qualified, confident, or willing to address specific health issues, who may not be qualified teachers, or who offer only a cursory treatment of health topics. Existing UK interventions aiming to integrate health and academic education (The British Heart Foundation, 2014; Wright & Ainsworth, 2008) have not been informed by existing theory or evidence, which may limit their effectiveness. For example, the British Heart Foundation’s “Money to Burn” and the Ariel Trust’s “Plastered” interventions incorporate education about the risks, respectively, of smoking and drinking into mathematics lessons. Money to Burn includes activities such as calculating how much a smoker would typically spend on cigarettes, whereas Plastered includes activities calculating units of alcohol consumed and presenting statistics on attitudes to alcohol, as a basis for whole-class discussions about the harmful consequences of alcohol consumption. An additional question arising in school-based interventions is at which developmental period these interventions might be most effective. In England, key stages (KS) describe each age-related phase of schooling. KS2 includes school years 3–6 (age 7–11 years), KS3 includes years 7 to 9 (age 11–14 years), KS4 includes years 10 and 11 (age 14–16 years), and KS5 includes years 12 and 13 (age 16–18 years).

No systematic review has examined the effectiveness of interventions integrating health and academic education. Existing reviews relating to school-based interventions (Faggiano et al., 2005; Farrington & Ttofi, 2010; Foxcroft & Tsertsvadze, 2012; Hahn et al., 2007; R. E. Thomas & Perera, 2006; Vreeman & Carroll, 2007), some of which are now quite old, largely focus on interventions in specific health education lessons or their international equivalents. Because of such lessons increasingly being squeezed from school timetables, there is an urgent need for a systematic review to synthesize evidence for interventions that integrate academic and health education by developmental stage, and our review meets this need with a focus on substance use.

2 | METHODS

A protocol for this systematic review and meta-analyses was registered on PROSPERO (https://www.crd.york.ac.uk/prospERO/), as CRD42015026464. The work reported in this paper was part of a larger evidence synthesis project looking at various aspects of interventions integrating academic and health education.

We included randomized controlled trials of school-based health curriculum interventions integrating health and academic education, where a majority of participants were school students aged 4–18 years. Academic education was defined as education in specific academic subjects, literacy, numeracy, or study skills. Operationalizing “integration” was challenging. We judged that to be included, study reports must have been explicit that the intervention aimed to integrate health and academic education, either in the form of health education being woven into one or more existing mainstream school subjects (such as the example presented in Section 1 where education on smoking and alcohol were woven into existing timetabled mathematics lessons) or of distinctive health education lessons also including academic content (for example, a social and emotional skills curriculum aiming to prevent violence which also included education aiming to improve literacy or study skills). That is, interventions could either incorporate health education into academic lessons or featured health education lessons that also included academic education. In the element of the review...
reported here, we included evaluations measuring outcomes relating to substance use: tobacco smoking, alcohol use, or legal or illegal drug use. We did not restrict our focus to interventions seeking to alter substance use as their only or main objective because our preliminary scoping work indicated that many interventions integrating academic and health education may take a "whole-child" approach, where substance use is one outcome of interest out of several. We did not restrict our studies by date of research or publication, or language, nor did we restrict our searches.

Because our interest was in mainstream education, we excluded interventions that targeted specific subpopulations defined in terms of health outcomes such as children with autism, children with learning disabilities, or children with known behavioural problems. We also excluded interventions which were delivered in mainstreet subject lessons without any attempt at integrating health and academic education; trained teachers in classroom management without student curriculum components; or were delivered exclusively outside of classrooms. We did not include outcomes relating to attitudes or knowledge, preferring instead estimates of actual use.

We undertook searches for this review between November 18 and December 22, 2015. We searched 19 electronic bibliographic databases and 32 websites and contacted subject experts. A full description of electronic searches undertaken can be found in Online File 1.

An exclusion criteria worksheet, informed by our inclusion criteria and with guidance notes, was prepared and piloted by four reviewers (GJM, TT, AF, CB), who screened 50 references in pairs on title and abstracts until achieving a 90% agreement rate, after which single reviewers each screened discrete subsets of the full set of references. After pairs of reviewers screened each set of abstracts in the pilot screening phase, they discussed decisions. This process was invaluable because, despite being guided by clear inclusion criteria, decisions about whether an intervention did or did not aim to integrate health and academic education were not always easy. The definition of integration, in terms of full integration of health content into existing academic lessons or partial integration whereby new health lessons also included some academic content, was also helpful in making clear decisions about which studies to include or exclude. Full reports were obtained for those references not excluding based on title and abstract. Again, reviewers piloted the procedure for screening full reports working in pairs screening 50 reports and discussing any differences until a 90% agreement rate was reached. CB reviewed all studies identified as potentially included in the review as a final check to determine inclusion.

We extracted data using a modified version of an existing tool (Peersman, Oliver, & Oakley, 1997) including items on study location, intervention description, description of integration, intervention development, timing of intervention and evaluation, target population description, provider and organization characteristics, research questions or hypotheses, sampling methods and sample size at baseline and follow-up, sociodemographic characteristics of participants at baseline and any follow-ups, and data collection and analysis. Trials were assessed for risk of bias using a modified version of questions suggested in the Cochrane Handbook for Systematic Reviews of Interventions (Higgins & Green, 2011). Data from all studies were extracted and appraised by two reviewers in parallel and independently, before meeting to agree details.

Effect sizes from included study reports concerning substance use (tobacco smoking, alcohol, or drugs) as defined in the protocol were extracted into a Microsoft Excel spreadsheet and converted into standardized mean differences (Cohen’s d) using all available information as presented for each study. Because all evaluations were cluster randomized trials, some baseline imbalance on individual participant characteristics was likely. Thus, we used effect estimates adjusted for covariates when these were presented alongside unadjusted estimates. Negative effect sizes indicate a reduction in substance use.

Most studies reported several substance use outcomes at several measurement time-points. As indicated in the protocol, we used multilevel meta-analysis as set out by Cheung (2014) and van den Noortgate, López-López, Marín-Martínez, and Sánchez-Meca (2015) with random effects at both the outcome and study level. Multilevel meta-analysis accounts for dependencies between outcomes from the same study by partitioning the variance (tau-squared) between outcomes into a within-study level and a between-study level. The final effect size estimate includes all information that the multiple effect size estimates contribute while correcting for the nonindependence of multiple effect size estimates from each study and presented an estimate of I² between studies for heterogeneity.

Because outcomes were measured at different points in students’ developmental trajectory, we created a “matrix” of KS against type of outcome. We then meta-analysed findings within each cell of the matrix where appropriate, for example, substance use for students in KS3. We considered omnibus outcomes (e.g., count of substances used, any substance use), alcohol outcomes, tobacco smoking outcomes, and drug use outcomes separately and then as a combined model to examine the global impact of these interventions on substance use. Were we to have had 10 or more studies in any comparison, we would have used funnel plots to investigate the presence of small-study bias.

The funder of the study had no role in study design, data collection, data analysis, data interpretation, or reporting. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

3 | RESULTS

A total of 78,451 references were identified from the searches. Of these, 1,472 (2%) were identified as duplicates. The remaining 76,979 references were screened on title and abstract and, of these, 76,277 (99%) were excluded using the criteria listed in the protocol. Of the 702 remaining reports, 12 were unobtainable and 690 full-text reports were screened, of which 628 were excluded. Of the remaining 62 reports of 16 different evaluations included in the overall project, seven outcome evaluations reported across 12 papers specifically addressed substance use and are reviewed here; the remaining papers reported other outcomes relevant to the larger review. See Figure 1 for the review flowchart. In total, the included studies represent data from 89 schools and approximately 7,013 students. Trial-level average cluster sizes ranged from 36 students to 103 students, with a median of 83 students across trials.
3.1 | Included studies

Included studies are described in Table 1. All included studies were randomized controlled trials. In each trial, the comparator was treatment as usual. All trials randomized at the school level. One evaluation was conducted in the UK (Kids, Adults Together, KAT [Segrott et al., 2015]) and one in Australia (Gatehouse [Bond, Patton, et al., 2004]), whereas all others were conducted in the United States.

Trials varied in length of follow-up time. One intervention, KAT (Segrott et al., 2015), only evaluated outcomes in the same period as the intervention was administered, whereas two evaluations followed up participants for 3 years (Gatehouse [Bond et al., 2004]; Infused Life Skills Training, I-LST [Smith, Swisher, Vicary, & Bechtel, 2004]). The remaining four evaluations included follow-ups between 5 and 8 years from baseline. Study populations in most evaluations drew from different year cohorts at baseline. Students in the trials of KAT and Linking the Interests of Families and Teachers (LIFT) were largely drawn from years 5 and 6. The Hawaii evaluation of Positive Action (Beets et al., 2009) included students in years 2 or 3 at baseline, as did the evaluation of Raising Healthy Children (RHC; Catalano et al., 2003). Unusually, the evaluation of Gatehouse (Bond et al., 2004; Bond, Patton, et al., 2004; Patton et al., 2006) included students in one cohort from year 9 through year 11, and also surveyed three consecutive cohorts of year 9 students at the end of one intervention year. Positive Action Chicago (Lewis et al., 2013; Li et al., 2011) recruited students in year 4, and I-LST (Smith et al., 2004) recruited students in year 8.

3.2 | Quality of included studies

Quality was variable between studies. For many of the items, studies did not report sufficient information to enable judgment. Ratings by item are reported in Table 2. Three evaluations, KAT (Segrott et al., 2015), LIFT (DeGarmo, Eddy, Reid, & Fetrow, 2009; Eddy, Reid, & Fetrow, 2000; Reid, Eddy, Fetrow, & Stoolmiller, 1999), and Positive Action Chicago (Bavarian et al., 2013; Lewis, 2012; Lewis et al., 2012; Lewis et al., 2013; Li et al., 2011) all presented enough information to appraise these evaluations as having a low risk of bias in randomization sequence generation. Positive Action Chicago used random number generators, whereas LIFT drew allocations from a hat (Reid et al., 1999). KAT used optimal allocation to determine the randomization sequence (Segrott et al., 2015). The remaining four evaluations had unclear risk of bias. None of the included evaluations stated if or how allocation was concealed, thus preventing a determination as to risk of bias in this domain. Although blinding is often difficult in trials of school interventions, blinding of outcome assessors is often possible and may reduce ascertainment bias. Only one evaluation, LIFT (DeGarmo et al., 2009; Reid et al., 1999), provided enough information to judge whether any blinding occurred. In this evaluation, outcome assessors were blind to allocation. All evaluations were judged as having relatively low or balanced attrition where this was relevant to outcome assessment (complete outcome data domain). Trial protocols were rarely available, thus precluding determinations as to risk of bias on selection reporting. All evaluations except for one (RHC) reported in text methods to account for clustering, and all evaluations took steps to reduce other forms of bias. In two evaluations (LIFT and KAT), it was unclear if a suitable control group had been recruited.

3.3 | Substance use in KS2

Of the three evaluations presenting substance use outcomes for KS2, one evaluation, Positive Action Chicago (Li et al., 2011), presented an omnibus outcome comparing counts of substances used. Both KAT (Segrott et al., 2015) and Positive Action Hawaii (Beets et al., 2009) presented outcomes relating to alcohol use. In addition, Positive Action Hawaii (Beets et al., 2009) presented outcomes relating to tobacco smoking and drug use. We did not undertake a meta-analysis for substance use outcomes in KS2.

At the end of the third intervention year (corresponding to year 6), intervention students in the Positive Action Chicago trial (Li et al., 2011) had a lower count of types of substance use compared to control students (IRR = 0.69, 95% CI [0.50, 0.97]). In the Positive Action Hawaii trial (Beets et al., 2009), intervention students reported fewer substances used (IRR = 0.41, 90% CI [0.25, 0.66]), but differences between groups were not significant for teacher reports (0.66, [0.30, 1.45]). Intervention students were less likely to report ever having used alcohol than control students (OR = 0.48, 90% CI [0.34, 0.68]) and less likely to report having ever been drunk (0.30, [0.15, 0.57]), but teacher reports on student alcohol use were not significant (0.81, [0.41, 1.58]). As with alcohol, intervention students in year 6 in the Positive Action Hawaii trial (Beets et al., 2009) reported being less likely to have ever smoked tobacco than control students (OR = 0.52, 90% CI [0.31,
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<tr>
<th>Intervention description</th>
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<tr>
<td>Infused Life Skills Training (I-LST)</td>
<td>USA</td>
<td>3 schools, 297 students (IG: 3 schools, 201 students (CG) Students enrolled starting year 8 and followed up over 3 years 45.6% female, 54.4% male 96.6% White 32.5% qualify for free/reduced lunch</td>
<td>Teachers were trained in the regular life skills curriculum with additional information on integration and embedding lessons in different disciplines. Teachers supported one another in multi-disciplinary teams.</td>
<td>LST interventions were first established as tobacco prevention intervention. Different studies of LST interventions, when applied to different areas, were also found to be successful in reducing alcohol and other substance use. However, findings have been contested, and the need for testing of different models of LST delivery inspired the I-LST intervention and its study.</td>
<td>I-LST aims to promote social skills, personal self-management skills, and drug resistance skills, all for reduced substance use. Core components include: self-image and self-improvement; decision-making; smoking, marijuana and alcohol myths and realities; smoking and advertising awareness; coping with anxiety; communication skills; social skills; and assertiveness. Lessons are integrated into the existing curriculum.</td>
<td>Participating teachers delivering I-LST develop a matrix of LST principles that are then mapped onto curricular content areas. The hypothesis is that the I-LST curriculum achieves dual objectives of both LST and the usual academic subject. “In this way, more teachers can provide the LST lessons, allowing for repeated exposure to the constructs in a variety of topics and eliminating the necessity for time set aside for prevention in an already burdened curriculum.” (Vicary et al., 2006; p. 328)</td>
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<td>Kids, Adults Together (KAT)</td>
<td>UK</td>
<td>5 schools, of which 3 remained in trial, 172 students (IG: 4 schools, 152 students (CG) Students enrolled in years 5 and 6 (some year 4 due to mixed-year classrooms) and followed up after one term 51.9% female, 47.8% male (0.3% missing) 81.3% White, 22% Black or Black British, 4.2% mixed-race, 7.3%</td>
<td>Teachers, supported by the KAT organizer</td>
<td>The KAT intervention was derived from an Australian predecessor (P-KAT) that focused more broadly on substance misuse (vs. only alcohol). The intervention was developed by the “programme organizer” and a working group, of which two members were head teachers from the two</td>
<td>The KAT intervention aims to reduce drinking and antisocial behaviours in young people. It has three components: 1. A classroom component in which students learn material and prepare presentations for a parent evening, 2. A parent evening in which students take turns presenting their lessons to parents</td>
<td>The classroom component integrates lessons around the effects and consequences of alcohol use into various classes. For example: in literacy classes, in addition to learning about alcohol, students also learn how to collect data; in art classes, learning is tied into development of skills in arts and...</td>
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<td>Linking the Interests of Families and Teachers (LIFT)</td>
<td>USA</td>
<td>3 schools, 214 students (IG); 3 schools, 147 students (CG)</td>
<td>Provided by teachers who received 40 hr of training</td>
<td>Due to rising levels of delinquency, in the 1990s, school-based interventions to reduce delinquency were created. LIFT was one such intervention. The authors refer to the existence of scientific literature and clinical knowledge around antisocial behaviours that informed the development of the intervention.</td>
<td>The LIFT intervention has classroom and playground components as well as a parent training intervention. It aims to reduce antecedents of violence and delinquency in children. The classroom component is 1 hr, twice per week, for 10 weeks. Each class had the following structure: lecture and role play around social and problem-solving skills and small- and large-group skill practice. The playground component involves free play in the playground and skills review and presentation of daily rewards. In the skills review, negative behaviours are noted and subtracted from positive ones, which</td>
<td>The fifth grade classroom component also develops study skills that align with the fifth grade curricula.</td>
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<td>DeGarmo, 2009</td>
<td>DeGarmo et al., 2009</td>
<td>Students enrolled in year 6 and followed up over 7 years</td>
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<td>Eddy, 2003</td>
<td>Eddy et al., 2003</td>
<td>12% mother less than high school graduate, 8% father less than high school graduate; 36% mother unemployed, 10% father unemployed; 22% single-parent families; 18% receiving benefits; 20% less than $15,000/year in early 1990s</td>
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<td>Eddy, 2003</td>
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<td>49% female, 51% male</td>
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<td>86% White, 14% ethnic minority</td>
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<td>6.4% low on Family Affluence Scale, 33.0% medium, 52.8% high, 7.8% missing</td>
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<td>Positive Action Chicago Lewis, 2012 (Lewis et al., 2012)</td>
<td>USA</td>
<td>7 schools, ~240 students (IG), 7 schools, ~260 students (CG)</td>
<td>83% receiving free lunch and staff team</td>
<td>Positive Action is grounded in the theories of self-concept, particularly Self-Esteem Enhancement Theory, which suggests that people inherently want to feel good, and will use cognitive, affective and behavioural strategies to help achieve and sustain this feeling. Thus, the programme's classroom curriculum introduces motivation and opportunities for students to feel good about themselves, plus ecological supports to sustain it. Authors also mentioned the shifts in curriculum following the &quot;No Child Left Behind&quot; Act of 2001, which are rewarded. In the parent component, LIFT instructors meet with parents from 10–15 families once per week for 6 weeks. Parents are given home activities for the week to reflect their children's curriculum and have their own lecture and role plays.</td>
<td>Positive Action is a social-emotional and character development intervention aimed at encouraging positive behaviours through positive thoughts and actions. Students are given 140 lessons, each 15–20 min, throughout the school year by their teachers. Lessons cover six units: self-concept; positive actions for mind and body; positive social-emotional actions; managing oneself; being honest with oneself; and continually improving oneself. Teachers receive training and principals at participating schools receive a &quot;school climate kit&quot; in which they are provided with directions to support the core elements of the Positive Action curriculum throughout the school.</td>
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| Positive Action Hawaii Beets, 2009 (Beets et al., 2009) | USA | 10 schools, 976 students (IG); 10 schools, 738 students (CG) | Provided by teachers, supported by a "school climate coordinator" and staff team | Positive Action recognizes the relationship between students' academic performance, their learning and life skills, and their behaviours. The methods of education used in Positive Action promote active learning and learning skills development alongside behaviour change. Students are encouraged to solidify academic learning by applying it to real-life scenarios. For example, unit two on positive actions for the mind and body, emphasizes thinking skills, problem solving, and study skills. Teachers are also encouraged to tie lessons into academic content. | | |

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<td>Raising Healthy Children (RHC)</td>
<td>USA</td>
<td>5 schools, 497 students (IG); 5 schools, 441 students (CG)</td>
<td>Teachers deliver the intervention supported by school-home coordinators</td>
<td>placed huge emphasis on standardized test performance, squeezing out non-academic curricula. There has also been a movement towards integrated interventions that involve families and communities. Positive Action was developed to address all of those aspects.</td>
<td>RHC is guided by the social development model, which emphasizes the importance of early intervention, prior to the onset of antisocial behaviours, and individual, family, and community (including school and peer influences) characteristics</td>
<td>RHC is a four-component intervention that promotes positive youth development by targeting risk and protective factors at different stages of development. The components are (a) school intervention strategies (staff and teacher development and monthly coaching of teachers); (b) student intervention strategies (after-school tutoring and study clubs in grades 4–6, and group-based workshops in secondary school. These are for academic achievement, prosocial bonding, teaching refusal skills and developing prosocial beliefs around healthy behaviours); (c) peer intervention strategies (through classroom instruction and annual summer camps in primary school and social skills booster retreats in secondary schools. For social–emotional learning and developing problem-solving skills); and (d) family intervention strategies (parenting workshops to increase parenting skills, decrease familial conflict, clarify family standards and expectations around substance use, and to practice peer resistance skills).</td>
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Staff are trained to promote reading as part of school intervention strategies. Also, in grades 4–6, there are after-school study groups and group-based workshops in secondary school, all of which aim to increase academic achievement.
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<td>The Gatehouse Project</td>
<td>Australia</td>
<td>Longitudinal cohort: 2 districts, 12 schools, 1335 students (IG); 2 districts, 14 schools, 1343 students (CG)</td>
<td>Experienced educators developed the intervention. They became facilitators of the intervention and then acted as liaisons between the schools and the intervention. Teachers provided the intervention supported by a school adolescent health team.</td>
<td>The intervention was developed to address shortcomings in school health promotion, building on intervention that emphasise whole-school change. The Gatehouse Project is in line with the health promoting schools framework. The conceptual framework drew on adolescent risks and incorporated work on attachment and social support theories.</td>
<td>The Gatehouse Project is a school health promotion intervention that includes both institutional- and individual-level components. The intervention aims to: build a sense of security and trust in students; enhance skills and opportunities for good communication; and build a sense of positive regard through participation in school life. The teaching curriculum is delivered over each term in normal classes. It focuses on cognitive and interpersonal skills that underlie emotional well-being relevant to teenagers. At the institutional level, a school-based adolescent health team (comprised of administrators, teachers and community members) is established to identify risks in the school and create of strategies to address these risks.</td>
<td>Teaching resources are delivered in usual English, health, or personal development classes. The intervention also adopts a critical literacy approach. Concepts are also taught using literature, poetry, song, film and visual materials. The integration of Gatehouse Project and normal curricula is intended to embed the work such that it could be continued beyond the project. There is a deliberate link made between the intervention's goals and academic goals.</td>
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<tr>
<td>Bond, 2004a</td>
<td></td>
<td>Students enrolled in Year 9, followed up for 3 years 53.2% female, 46.8% male 87.5% Australian-born 79.2% from two-parent family; 24.2% speak language other than English at home</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bond, Thomas, et al., 2004</td>
<td></td>
<td>1999 cross-section: 1158 students (IG), 1428 students (CG)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patton, 2006</td>
<td></td>
<td>Students enrolled in year 9, followed up for 1 year 55% female, 45% male 88% Australian-born 79.2% from two-parent family; 22% speak language other than English at home</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bond, 2004b</td>
<td></td>
<td>2001 cross-section: 966 students (IG), 1497 students (CG)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patton et al., 2006</td>
<td></td>
<td>Students enrolled in year 9, followed up for 1 year 54% female, 46% male 90% Australian-born 78% from two-parent family; 19% speak language other than English at home</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
for all substance use outcomes. Findings from meta-
tobacco smoking, and drug use (including marijuana separately), and
et al., 2005). We undertook separate meta-
2004), Positive Action Chicago (Lewis et al., 2012) and RHC (Brown
same five evaluations: Gatehouse (Bond, Patton, et al., 2004; Bond,
hol, tobacco smoking and drug use outcomes were reported by the
these, Gatehouse (Patton et al., 2006) and Positive Action Chicago
Gatehouse (Bond, Patton, et al., 2004; Bond, Thomas, et al., 2004; Patton et al., 2006), LIFT, I-
LST (Smith et al., 2004), Positive Action Chicago (Lewis et al., 2012), and RHC (Brown, Catalano, Fleming, Haggerty, & Abbott, 2005). Of
Gatehouse (Patton et al., 2006) and Positive Action Chicago
(Lewis et al., 2012) reported omnibus substance use outcomes. Alco-
hol, tobacco smoking and drug use outcomes were reported by the
same five evaluations: Gatehouse (Bond, Patton, et al., 2004; Bond,Thomas, et al., 2004; Patton et al., 2006), LIFT, I-
LST (Smith et al., 2004), Positive Action Chicago (Lewis et al., 2012) and RHC (Brown et al., 2005). We undertook separate meta-analyses for alcohol use, tobacco smoking, and drug use (including marijuana separately), and for all substance use outcomes. Findings from meta-analyses are
summarized in Table 3. A pooled analysis across all substance use out-
comes, including 55 effect sizes from five evaluations, suggested a
small but statistically significant global effect of these interventions
(−0.09, [−0.17, −0.01]), albeit with some between-studies heterogene-
ity ($I^2 = 35\%$; see Figure 2). Interventions integrating academic and
health education had an effect of borderline statistical significance in
reducing alcohol use among students in KS3 ($d = −0.11$, $95\%$ CI
$[−0.23, 0.004]$). However, this analysis, which included 23 effect sizes
across five evaluations, had substantial between-studies heterogeneity
($I^2 = 54\%$). Included evaluations drew on diverse follow-up times, with
a clearer picture of effectiveness from evaluations of Positive Action Chi-
obgo (Lewis et al., 2012) and LIFT (Eddy, Reid, Stoolmiller, & Fetrow, 2003), both of which had longer follow-ups in KS3 (i.e., an ear-
lier start point for the intervention). Moreover, frequency of use esti-
mates were not available for RHC in KS2. Meta-analyses were not
indicative of an effect of these interventions for tobacco smoking
(−0.05, [−0.12, 0.02]), based on 13 effect sizes from five evaluations.
However, these interventions were effective in reducing drug use
(−0.07, [−0.14, −0.01]) and marijuana use (−0.10, [−0.16, −0.04]).
Unlike the meta-analysis of alcohol outcomes, meta-analyses for
tobacco smoking and drug use all had negligible between-studies het-
erogeneity ($I^2 = 0\%$). We did not undertake meta-analysis for omnibus
substance use outcomes alone given that only two evaluations would
have been included. The two evaluations measuring omnibus sub-
stance use outcomes in KS3 related to different interventions and fol-
low-up periods. In Gatehouse, intervention recipients in year 9 were
not different in substance use patterns compared to control recipients
at the end of the first intervention year for each of the first ($OR = 0.92$
$[0.7, 1.2]$), second ($0.84$, $[0.61, 1.18]$), and third ($0.85$, $[0.65,$
$1.12]$) cohorts (Patton et al., 2006). However, in Positive Action Chi-
obgo (Lewis et al., 2012), intervention participants in year 9 used fewer

### TABLE 2 Risk of bias judgments for included studies

<table>
<thead>
<tr>
<th>Intervention name</th>
<th>Random generation of allocation sequence</th>
<th>Concealed allocation</th>
<th>Blinding</th>
<th>Complete outcome data</th>
<th>Reporting not selective</th>
<th>Accounted for clustering</th>
<th>Reduced other forms of bias</th>
<th>Suitable control group</th>
</tr>
</thead>
<tbody>
<tr>
<td>I-LST</td>
<td>NC</td>
<td>NS</td>
<td>NS</td>
<td>Yes</td>
<td>NC</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>KAT</td>
<td>Yes</td>
<td>NS</td>
<td>NS</td>
<td>Yes</td>
<td>NC</td>
<td>Yes</td>
<td>Yes</td>
<td>NC</td>
</tr>
<tr>
<td>LIFT</td>
<td>Yes</td>
<td>NS</td>
<td>NS</td>
<td>Yes</td>
<td>NC</td>
<td>Yes</td>
<td>Yes</td>
<td>NC</td>
</tr>
<tr>
<td>Positive Action Hawaii</td>
<td>NC</td>
<td>NS</td>
<td>NS</td>
<td>Yes</td>
<td>NC</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Positive Action Chicago</td>
<td>Yes</td>
<td>NS</td>
<td>NS</td>
<td>Yes</td>
<td>NC</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>RHC</td>
<td>NC</td>
<td>NS</td>
<td>NS</td>
<td>Yes</td>
<td>NC</td>
<td>Yes</td>
<td>Yes</td>
<td>NC</td>
</tr>
<tr>
<td>Gatehouse</td>
<td>NC</td>
<td>NS</td>
<td>NS</td>
<td>Yes</td>
<td>NC</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
</tbody>
</table>

Note. I-LST = Infused Life Skills Training; KAT = Kids, Adults Together; LIFT = Linking the Interests of Families and Teachers; NC = not clear; NS = not stated.

### 3.4 Substance use in KS3

Five evaluations reported outcomes relating to substance use in KS3: Gatehouse (Bond, Patton, et al., 2004; Patton et al., 2006), LIFT, I-
LST (Smith et al., 2004), Positive Action Chicago (Lewis et al., 2012), and RHC (Brown, Catalano, Fleming, Haggerty, & Abbott, 2005). Of
these, Gatehouse (Patton et al., 2006) and Positive Action Chicago
(Lewis et al., 2012) reported omnibus substance use outcomes. Alco-
hol, tobacco smoking and drug use outcomes were reported by the
same five evaluations: Gatehouse (Bond, Patton, et al., 2004; Bond,Thomas, et al., 2004; Patton et al., 2006), LIFT, I-
LST (Smith et al., 2004), Positive Action Chicago (Lewis et al., 2012) and RHC (Brown et al., 2005). We undertook separate meta-analyses for alcohol use, tobacco smoking, and drug use (including marijuana separately), and for all substance use outcomes. Findings from meta-analyses are
summarized in Table 3. A pooled analysis across all substance use out-
comes, including 55 effect sizes from five evaluations, suggested a
small but statistically significant global effect of these interventions
(−0.09, [−0.17, −0.01]), albeit with some between-studies heterogene-
ity ($I^2 = 35\%$; see Figure 2). Interventions integrating academic and
health education had an effect of borderline statistical significance in
reducing alcohol use among students in KS3 ($d = −0.11$, $95\%$ CI
$[−0.23, 0.004]$). However, this analysis, which included 23 effect sizes
across five evaluations, had substantial between-studies heterogeneity
($I^2 = 54\%$). Included evaluations drew on diverse follow-up times, with
a clearer picture of effectiveness from evaluations of Positive Action Chi-
obgo (Lewis et al., 2012) and LIFT (Eddy, Reid, Stoolmiller, & Fetrow, 2003), both of which had longer follow-ups in KS3 (i.e., an ear-
lier start point for the intervention). Moreover, frequency of use esti-
mates were not available for RHC in KS2. Meta-analyses were not
indicative of an effect of these interventions for tobacco smoking
(−0.05, [−0.12, 0.02]), based on 13 effect sizes from five evaluations.
However, these interventions were effective in reducing drug use
(−0.07, [−0.14, −0.01]) and marijuana use (−0.10, [−0.16, −0.04]).
Unlike the meta-analysis of alcohol outcomes, meta-analyses for
tobacco smoking and drug use all had negligible between-studies het-
erogeneity ($I^2 = 0\%$). We did not undertake meta-analysis for omnibus
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have been included. The two evaluations measuring omnibus sub-
stance use outcomes in KS3 related to different interventions and fol-
low-up periods. In Gatehouse, intervention recipients in year 9 were
not different in substance use patterns compared to control recipients
at the end of the first intervention year for each of the first ($OR = 0.92$
$[0.7, 1.2]$), second ($0.84$, $[0.61, 1.18]$), and third ($0.85$, $[0.65,$
$1.12]$) cohorts (Patton et al., 2006). However, in Positive Action Chi-
obgo (Lewis et al., 2012), intervention participants in year 9 used fewer

### TABLE 3 Meta-analyses of substance use outcomes

<table>
<thead>
<tr>
<th>Key stage</th>
<th>Outcome</th>
<th>k (n)</th>
<th>SMD [95% CI]</th>
<th>I$^2$, study-level (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>3</td>
<td>Alcohol</td>
<td>5 (23)</td>
<td>$−0.11$ [−0.23, 0.004]</td>
<td>54</td>
</tr>
<tr>
<td></td>
<td>Smoking</td>
<td>5 (13)</td>
<td>$−0.05$ [−0.12, 0.02]</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Illicit drug use: marijuana</td>
<td>5 (10)</td>
<td>$−0.10$ [−0.16, −0.04]</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Illicit drug use</td>
<td>5 (14)</td>
<td>$−0.07$ [−0.14, −0.01]</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>All drug use outcomes</td>
<td>5 (55)</td>
<td>$−0.09$ [−0.17, −0.01]</td>
<td>35</td>
</tr>
<tr>
<td>4</td>
<td>Alcohol</td>
<td>3 (15)</td>
<td>$−0.01$ [−0.09, 0.06]</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Smoking</td>
<td>3 (9)</td>
<td>$−0.08$ [−0.15, −0.01]</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Illicit drug use: marijuana</td>
<td>3 (10)</td>
<td>$−0.10$ [−0.17, −0.03]</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>All drug use outcomes</td>
<td>3 (34)</td>
<td>$−0.06$ [−0.09, −0.02]</td>
<td>0</td>
</tr>
</tbody>
</table>
substances ($g = -0.29, 95\% CI [-0.51, -0.08]) and less frequently ($-0.27, [-0.48, -0.05]) than control participants at the end of the sixth year.

3.5 | Substance use in KS4

Three evaluations reported outcomes relating to substance use in KS4: Gatehouse (Bond, Patton, et al., 2004; Bond, Thomas, et al., 2004), I-LST (Vicary et al., 2006), and RHC (Brown et al., 2005). All outcomes reported related to alcohol use, tobacco smoking, and drug use (namely, marijuana use). We undertook separate meta-analyses for alcohol use, smoking, and drug use (namely, marijuana use). We also undertook an overall meta-analysis of substance use outcomes in KS4. Findings from these meta-analyses are summarized in Table 3. Meta-analyses for alcohol use integrating 15 effect sizes from three evaluations did not suggest any impact on alcohol use ($d = -0.01, 95\% CI [-0.09, 0.06];$ see Figure 3). This analysis had some minor statistical heterogeneity, with a between-studies $I^2$ of 2\%. In contrast, meta-analyses for smoking integrating nine effect sizes from three evaluations suggested a small but statistically significant effect of these interventions in reducing smoking ($-0.08, [-0.15, -0.01]; I^2 = 0\%$). Interventions also appeared to have a positive effect in reducing marijuana use ($-0.10, [-0.17, -0.03]), based on 10 effect sizes from three evaluations. A pooled analysis integrating all 34 effect sizes from the three evaluations suggested a small but significant global effect of these interventions in reducing substance use ($-0.06, [-0.09, -0.02]; I^2 = 0\%$).

3.6 | Substance use in KS5

Only LIFT (DeGarmo et al., 2009) presented findings in KS5, at the end of the eighth year from the start of the intervention. Participants in the original year 6 cohort from were significantly less likely to have initiated alcohol use (OR = 0.93, $p < .05$) or smoking (0.90, $p < .01$) and less likely to have initiated drug use at borderline statistical significance (OR = 0.91, $p < .10$).

4 | DISCUSSION

In this systematic review and meta-analysis, quality of evidence was highly variable. There was some evidence from meta-analyses that interventions were broadly effective for reducing substance use in KS3 and KS4, with more and stronger evidence in KS3. Effect sizes were small but of potential public health significance. For both estimates of global effects of these interventions, findings can be translated to represent that about 53\% of people receiving the intervention will have lower levels of substance use than people receiving the control group. Although this is a small individual-level effect, at the population level, the cumulative burden of ill health avoided may be large. Our findings regarding the specific developmental periods in which interventions are effective are especially interesting given trajectories of harmful substance use, where early prevention of substance use could decrease the risk of harmful patterns and sequelae of drug use in later adolescence and adulthood.

Our findings reflect the positive findings from previous systematic reviews on substance use prevention in schools and extend this to
interventions integrating health and academic education, suggesting that these have the potential to achieve significant population-level health benefits if delivered at scale. A landmark review on alcohol use prevention in schools did not pool study estimates but authors concluded that interventions had the potential to be effective (Foxcroft & Tsertsvadze, 2012). Our meta-analyses found specific evidence of effectiveness in KS3 but not KS4. Similarly, a systematic review of school-based tobacco prevention programmes found evidence for interventions preventing initiation of smoking (Thomas & Perera, 2006). Although our analysis combined all smoking outcomes, we were able to find evidence for effectiveness in reducing smoking in KS4. Again, the magnitude of effects was small but of potential public health significance at a population level. A recent systematic review on peer-led interventions to reduce alcohol, tobacco, and drug use in young people, while focused on ages 11 to 21, similarly found significant reductions in these outcomes, adding to the plausibility of our findings (MacArthur, Harrison, Caldwell, Hickman, & Campbell, 2016). Finally, a major systematic review on illicit drug use prevention in schools found “small but consistent” effects (Faggiano et al., 2005); like in our meta-analyses, review authors predominantly included marijuana use outcomes. Our findings reflect theirs in sum and substance, but we were able to locate effects more specifically as occurring in KS3 and KS4, with weaker evidence supporting effectiveness in KS2.

Our interest was in interventions that integrate academic and health education. Most interventions reviewed undertook integration as a practical way to introduce health materials into a school day, with very few acknowledging integration as central to intervention theory of change. This made searching for this evidence especially challenging. It is likely that we missed some potentially relevant studies, as integration may not have been apparent in titles or abstracts. Determining whether studies found in our searches should be included or not was also sometimes difficult. All study reports of included studies explicitly described some form of integration between health and academic content, but the extent and clarity of this description varied enormously. It is possible that we excluded studies of interventions where in practice health education was sometimes or always delivered in academic lessons but where this was not mentioned as part of the design of the intervention in study reports, or where interventions introduced new health lessons some of which included academic learning objectives, but where this level of detail was omitted from study reports. Despite this risk of excluding potentially relevant studies and thereby reducing the sensitivity of our screening, we judged that restricting inclusion to studies of interventions where integration was explicitly described as part of the design of the intervention was the only way to ensure the review had a specificity of focus and avoided an unworkable situation where screening decisions required detailed examination of intervention materials or lengthy discussion with authors.

![FIGURE 3 Substance use outcomes in KS4. I-LST = Infused Life Skills Training](colour figure can be viewed at wileyonlinelibrary.com)
We were also unable to assess publication bias. Anecdotally, reviewers also noted that there were a considerable number of quasi-experimental studies that may have provided useful insights but were excluded due to our inclusion only of RCTs. Inclusion of nonrandomized trials may have also been beneficial here or would warrant further study in the future. Our "matrix"-based meta-analysis method had both strengths and limitations. One strength is that it could examine effects in specific developmental phases of relevance to educators and intervention implementers. However, one limitation is that it involved combining estimates across a diversity of follow-up times. The few studies included in each meta-analysis precluded examination of heterogeneity by follow-up time.

In terms of policy, this intervention type presents great promise as a means of addressing health in school systems that are overwhelmingly focused on academic attainment and school timetables and in which health education is increasingly being squeezed out and to enhance existing provision where dedicated time for health education still exists. It is possible that these interventions may work in part by improving health-related knowledge and skills and also by improving school engagement through the enhancement of relationships between students and teachers and by breaking down boundaries between different subjects and between classrooms and the wider school environment. Interventions such as Positive Action that aimed to improve such relationships yielded a consistent pattern in achieving reductions in substance use.

However, our findings also suggest that integrative interventions, although attractive as a means to deliver health, social and emotional learning in the context of school systems, overwhelmingly focused on educational attainment are not necessarily a panacea. Study quality varied and was often unclear, and more evaluations are needed across the range of key stages to better understand the effectiveness of these interventions in preventing substance use. In addition, evaluators should make an effort to understand subgroup effects more specifically. Although some evaluations (namely, the evaluations of Positive Action) considered subgroup effects, more careful attention to moderation by school-level characteristics could yield useful knowledge about context-intervention fit.

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Authors have no conflicts of interest or financial interests to disclose.

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**REFERENCES**


