Psychological and social sequelae of cannabis and other illicit drug use by young people: a systematic review of longitudinal, general population studies

John Macleod, Rachel Oakes, Alex Copello, Ilana Crome, Matthias Egger, Mathew Hickman, Thomas Oppenkowski, Helen Stokes-Lampard, George Davey Smith

Summary

Background Use of illicit drugs, particularly cannabis, by young people is widespread and is associated with several types of psychological and social harm. These relations might not be causal. Causal relations would suggest that recreational drug use is a substantial public health problem. Non-causal relations would suggest that harm-reduction policy based on prevention of drug use is unlikely to produce improvements in public health. Cross-sectional evidence cannot clarify questions of causality; longitudinal or interventional evidence is needed. Past reviews have generally been non-systematic, have often included cross-sectional data, and have underappreciated the extent of methodological problems associated with interpretation.

Methods We did a systematic review of general population longitudinal studies reporting associations between illicit drug use by young people and psychosocial harm.

Findings We identified 48 relevant studies, of which 16 were of higher quality and provided the most robust evidence. Fairly consistent associations were noted between cannabis use and both lower educational attainment and increased reported use of other illicit drugs. Less consistent associations were noted between cannabis use and both psychological health problems and problematic behaviour. All these associations seemed to be explicable in terms of non-causal mechanisms.

Interpretation Available evidence does not strongly support an important causal relation between cannabis use by young people and psychosocial harm, but cannot exclude the possibility that such a relation exists. The lack of evidence of robust causal relations prevents the attribution of public health detriments to illicit drug use. In view of the extent of illicit drug use, better evidence is needed.

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See Commentary page 1568

Departments of Primary Care and General Practice (J Macleod PhD, R Oakes BSc, T Oppenkowski MSocSci, H Stokes-Lampard MRCGP) **and Psychology** (A I Copello PhD)**, University of Birmingham, Birmingham, UK; Academic Psychiatry Unit, Keele University, Stoke on Trent, UK** (Prof I Crome MD)**; Department of Social Medicine, University of Bristol, Bristol, UK** (Prof M Egger MD, Prof G Davey Smith DSc)**; Department of Social and Preventive Medicine, University of Berne, Berne, Switzerland** (Prof M Egger)**; and Centre for Research on Drugs and Health Behaviour, Social Science and Medicine, Imperial College, London, UK** (M Hickman PhD)

Correspondence to: Dr John Macleod, Department of Primary Care and General Practice, Primary Care Clinical Sciences and Learning Centre building, University of Birmingham, Edgbaston, Birmingham B15 2TT, UK
(e-mail: j.a.macleod@bham.ac.uk)

Introduction

The use of illicit drugs amongst young people seems to be widespread and may be increasing.[1] Cannabis is the most widely used illicit substance, although use of psychostimulants also appears quite common; use of opiates seems less common. Most of these drug users do not access drug treatment services and the consequences of their drug use are unclear. Physical health problems aside, there are concerns that illicit drug use, particularly cannabis use, could cause psychological and social problems.[2] Cannabis use has been shown to be associated with psychological health problems, use of other illegal drugs, reduced educational attainment, and antisocial behaviour.[2] The causal basis of these associations has not been established. If associations are non-causal, harm-reduction policies based on the prevention of drug use are likely to be ineffective. Conversely, a causal association could mean that "recreational" illicit drug use, in view of its apparent extent, represents an important, and substantially hidden, public health problem.

Causal explanations for associations between drug use and psychosocial harm compete with three alternative explanations: reverse causation, where drug use is a consequence, rather than a cause, of psychosocial problems; bias, where the association is an artifact of study methodology; and confounding, when drug use is associated with other factors that predispose to psychosocial problems.

A causal relation between drug use and psychosocial harm could plausibly be mediated by two principal mechanisms: directly, through neurophysiological pathways, or indirectly, through involvement in the criminal culture and commerce associated with use of an illegal substance.[3,4] Past reviews of the relevant evidence have often been non-systematic and have used restricted search strategies. Much evidence is cross-sectional and derives from highly selected samples. Such evidence is limited as a basis for inferring true causal relations and their possible relevance to public health. We therefore undertook a systematic review of general population, longitudinal studies relating illicit drug use by young people to subsequent psychological and social harm.

Methods

Search strategy and selection criteria

We searched the general electronic databases MEDLINE, EMBASE, CINAHL, PsycLIT, and Web of Science, and the specialist databases of the Lindesmith Center, DrugScope, US National Institute on Drug Abuse and Substance Abuse and Mental Health Services Administration, and Addiction Abstracts, with an agreed battery of search terms (available from the authors) in July, 2000. This search was updated in July, 2001, and again in June, 2003. Addiction Abstracts was hand-searched for the period not covered by the electronic database. Key individuals in the specialty of addictions

	Participants and setting*	Drug exposure measures†	Other measures‡	Main findings§
National Longitudinal Study on Adolescent Health[6,7]	National representative sample of 7–12th grade students sampled from 80 high schools and their "feeder" schools in the USA. Recruited in 1995. 79% of schools selected agreed to participate. 75% of eligible students in these schools (n=90118) completed a self-completion questionnaire. Random sub-sample of these selected for follow-up home interview in 1996, 79·5% of these (12118) contacted	Self-reported frequency of cannabis and other drug use via standard instrument. Categorical scale derived from these data	Cigarette smoking, alcohol use, sex, family structure, parent education, age, ethnic origin	Cannabis use associated with violent behaviour (tobacco and alcohol use show similar associations)
The Boston Schools Project[8,9]	1925 students from three public schools in Boston, USA, recruited aged 14–15 years in 1969 and studied yearly until 1973. Surveyed again in 1981. 79% (1521) had complete follow-up	Self-reported frequency of cannabis and other drug use via standard instrument. Categorical scale derived from these data	Socialisation, grade point average, self-reported physical and psychological health problems	Adolescent cannabis use associated with adult drug use. Little apparent association between use and psychological health or work related factors
The Children in the Community Project[10,11,12]	Population-based sample of families in New York State, USA. 976 participants aged 5–10 years at recruitment in 1975. 709 followed up until age 27 years	Self-reported frequency of cannabis and other drug use via standard instrument. Categorical scale derived from these data	Personality factors, family factors, parental drug use, sibling factors, peer factors, licit drug use; all self-reported via standard instruments	Little apparent association between cannabis use and either depression or anxiety. Association between cannabis use and antisocial personality although lower reported delinquency. Lower frequency of cannabis use associated with better parenting, higher frequency with unemployment and lone parenthood
The Central Harlem Study[13,14]	Population based sample of black adolescents recruited in 1968–69 from Central Harlem, New York City, USA. Initial sample of 668 age 12–17 years. 392 (59%) followed up till 1990	Cumulative use index based on self report of lifetime use (more than once) of nine classes of substance (marijuana, LSD, cocaine, heroin, methadone, "uppers", "downers", inhalants, alcohol)	Lifestyle and health behaviours, social ties and networks, adult social attainment	Cannabis and cocaine use associated with greater reported psychological problems. Associations with opiate use inconsistent
The Christchurch Health and Development Study[15–19]	Birth cohort of 1265 children born in Christchurch, New Zealand, during mid-1977. Reassessed regularly until age 21 years. 80% had complete follow-up	Self-reported frequency of cannabis use via standard instrument. Categorical scale derived from these data	Licit drug use, family background and parental factors, childhood behaviour, early problem behaviour, early psychological problems, educational history, cognitive ability, peer affiliations, antisocial behaviour, social environment, history of sexual abuse; generally self-reported, some use of official records	Cannabis use associated with lower educational attainment, greater use of other illicit drugs, poorer psychological health, and greater involvement in antisocial behaviour
Dunedin Multi-disciplinary Health and Development Study[20–22]	Birth cohort of all children born in Dunedin, New Zealand between April 1, 1972, and March 31, 1973, who were still resident locally when the study began in 1975. 1649 children born during study recruitment period, 1139 of these still resident locally at age 3 years, 1037 of these successfully recruited to study (91%). Reassessed regularly until age 26 years. 96% of survivors had complete follow-up	Self-reported frequency of cannabis use via standard instrument. Categorical scale derived from these data	Perinatal assessment, early physical health and development, physical and psychological health in childhood, emotional and educational development, social and family environment, cognitive abilities, adolescent physical and psychological health, licit drug use, antisocial behaviour; generally self-reported, some use of official records	Cannabis use associated with greater reported psychological problems. Similar associations with tobacco and alcohol use
East Harlem Study[23]	1332 African-American and Puerto Rican adolescents (mean age 14 years at recruitment) from 11 schools in East Harlem, New York City in 1990. 66% followed up 5 years later	Self-reported frequency of cannabis and other drug use via standard instrument. Categorical scale derived from these data	Adolescent personality attributes, family relationship characteristics, peer factors, residential area, acculturation measures	Cannabis use associated with later licit and illicit drug problems and with problem behaviours in participant, siblings and peers
The LA Schools Study[24–27]	1634 students in grades 7, 8, and 9 recruited from 11 schools in Los Angeles, USA in 1976. Assessed regularly over the subsequent 21 years. 477 (30%) had complete follow-up	Self-reported frequency of cannabis and other drug use via standard instrument. Categorical scale derived from these data	Social conformity, family formation, deviant behaviour, sexual behaviour, educational pursuits, livelihood pursuits, mental health including depression, social integration and conformity, relationship quality, divorce,	Drug use (generally judged as a latent variable dominated by cannabis use) associated with lower educational commitment. Little apparent association with psychological problems other than increased reported symptoms with cocaine use.

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	Participants and setting*	Drug exposure measures†	Other measures‡	Main findings§
			sensation seeking, parental support, academic aspiration, parental drug problems, psychological distress	Drug use associated with greater involvement in drug crime, lower involvement in violent crime, and higher income in young adulthood
New York Schools Study[28,29]	1636 adolescents enrolled in New York State public secondary schools in 1971. Aged 15 years at recruitment. Interviewed again in 1980, 1984, and 1990. 1160 (71%) had complete follow-up	Self-reported frequency of cannabis and other drug use via standard instrument. Categorical scale derived from these data	Income, marital status, education level, ethnic origin, peer activity, employment history, self-assessed health	Initiation of drug use usually follows an orderly sequence from tobacco and alcohol, through cannabis to other drugs. Drug use associated with higher income in early adulthood, lower income in later adulthood
National Collaborative Perinatal Project (NCPP)[30]	Sub-sample of NCPP cohort (birth cohort followed till age 7 years); African-American participants in Philadelphia contacted again at age 24 years and again at 26 years. About 70% (380) of target sub-sample had complete follow-up	Self-reported frequency of cannabis and other drug use via standard instrument. Categorical scale derived from these data	Perinatal and early life environmental factors, early health and development, academic performance, school behaviour and adjustment (from school records), personality, social integration, reported illness symptoms, reported antisocial behaviour and sexual behaviour	Cannabis use associated with antisocial personality and reports of criminal offences
National Longitudinal Survey of Youth[31,32]	National representative sample of 12686 young people (aged 14–21 years) from the non-institutionalised civilian segment of the US population, recruited in 1979. Ongoing regular assessment with about 90% retention	Self-reported frequency of cannabis and other drug use via standard instrument. Categorical scale derived from these data (questions about drug use were added in 1984)	Alcohol use, educational attainment, ethnic origin, family background, parental factors, cognitive function, religion, employment history, social position	Cannabis and cocaine use associated with problematic interpersonal relationships. No apparent association with income
Pittsburgh Youth Study[33]	School based sample of 850 boys from public schools in Pittsburgh. Mean age 13. 25 years at recruitment, followed up until mean age 18·5 years.	Self-reported frequency of cannabis and other drug use via standard instrument. Categorical scale derived from these data. Parent/teacher reports used to corroborate reports in some instances	Antisocial behaviour and conduct disorders, psychological symptoms, relations with parents, neighbourhood factors, sexual behaviour, educational attainment	Cannabis use associated with violent behaviour
Project Alert[34,35]	4500 adolescents from 30 junior high and middle schools in California and Oregon participating in evaluation of a preventive intervention. Mean age of participants at baseline 13 years, followed up for 4 years	Self-reported frequency of cannabis and other drug use via standard instrument. Categorical scale derived from these data. Salivary cotinine used to validate reported tobacco use (suggested to participants that sample could also be tested for cannabis—it was not, but this suggestion may have influenced validity of reported cannabis use)	Family and parental factors, social position and environment, employment history, educational history, anti-social behaviour, peer factors, religiosity	Cannabis use associated with lower educational attainment. No association with violent behaviour
South Eastern Public schools study[36]	Four longitudinal surveys within the US SE public schools. Participants recruited in grades 6–8 in 1985–87 and followed up till 1993–94. 1392 subjects (55·1%) had complete follow up	Indicator variable derived from self reported age of initiation of use of cannabis and other illicit drugs	Ethnicity, parental factors, educational attainment from combination of self-report and official records	Cannabis use associated with lower educational attainment. Similar but weaker association with tobacco use, no association with alcohol use
Swedish Military Conscripts study[37–39]	Different subgroups of 50 465 Swedish men age 18–20 years conscripted for national military service in 1969–70. Follow-up in official records to 1986, recently extended to 1996	Self-reported frequency of cannabis and other drug use via standard instrument. Categorical scale derived from these data (90% of sample provided usable data)	Social position, licit drug use, parental and family factors, behavioural factors, psychological factors	Cannabis use associated with later injection drug use (association between use of other illicit drugs and injection much stronger). Cannabis use associated with incidence of clinical schizophrenia. Cannabis use not associated with increased mortality by middle adulthood after adjustment—specific mortality from suicide not reported
Woodlawn study[40,41]	1242 African-American 1st grade students starting school in 1966–76 in a disadvantaged inner-city neighbourhood of Chicago. Follow-up assessments in 1976–77 and 1992–94. (84% of original cohort located, 96% of those interviewed)	Self-reported frequency of cannabis and other drug use via standard instrument. Categorical scale derived from these data	Licit drug use, family factors, parental factors, behavioural development, psychological problems, social integration, sexual behaviour, anti-social behaviour, educational history, employment history religiosity	Cannabis use not associated with reported suicidal thoughts or attempts

*In some instances data on completeness of follow=up not reported. †"Standard instrument" means some details of validation given. ‡Main groups of other measures as reported, for complete list see individual publications. §Main findings related to psychosocial outcomes reported as of June 2003, only prospective associations noted (ie, those where exposure assessment preceded outcome assessment).

Table 1: **Description of studies reviewed in detail**

(details available on request) were asked to identify evidence unlikely to be found through the other sources. Both published and unpublished evidence, along with that not published in English (which was translated), was judged.

We included all prospective studies based in the general population that measured use of any illicit drug by individuals aged 25 years or younger at the time of use and related these data to any measure of psychological or social harm assessed subsequently.

Quality assessment

Quality assessment was undertaken after initial searches in July, 2000. Two reviewers assessed methodological quality of studies independently against set criteria (sample size and representativeness, age at recruitment, duration and completeness of follow-up, apparent validity and reliability of exposure and outcome measures, and degree of adjustment for potential confounding factors). Formal quantitative quality scoring was not used, since it can be misleading and give a false sense of objectivity.[5]

Reviewers made an independent overall assessment of study quality based on the above criteria, and assigned studies to categories of higher quality, uncertain quality, or lower quality. Studies were judged to be of higher quality if the probability of selection bias seemed low, exposure to drugs was assessed with a validated instrument, follow-up was over several years, and analyses were adjusted for important confounding factors. Validity and relevance of psychosocial outcome measurement was also considered. Initial agreement between reviewers was high (weighted $\kappa>0{\cdot}9$). Reviewers then discussed, and agreed, which studies of higher or uncertain quality warranted more detailed consideration. Corresponding authors on papers deriving from these studies were contacted and asked to supply any relevant unpublished data.

We assessed the potential for quantitative synthesis of study results against criteria for combinability. Results were also summarised descriptively.

Role of the funding source

The sponsors of the study had no role in study design, data collection, data synthesis, data interpretation, or writing of the report

Results

We located more than 200 publications deriving from 48 longitudinal studies reporting associations between drug use by young people and psychological or social outcomes. Five studies were not published in English. All studies were observational. All had published results in peer-reviewed journals; however, some additional publications in books and unpublished papers were identified through personal contact. Many studies used composite measures of illicit drug use, making it impossible to infer effects of specific drugs. Most drug-specific results related to use of cannabis. Many studies reported substantial losses to follow-up and made either no, or little, attempt to adjust estimates for possible confounding factors. 16 studies were classified as of higher methodological quality (table 1). The remaining 32 studies are summarised, in terms of their ostensible findings and with a brief methodological critique, in table 2. All studies were judged, but appraisal was focused on evidence from the 16 in table 1.

Recruitment strategies, and thus the precise relation of the study population to the general population, varied substantially (tables 1 and 2). In all studies, exposure to illicit drugs was measured through uncorroborated self-report. Although some measures were similar across studies, no two studies measured either illicit drug exposure or psychosocial outcome in the same way. Additionally, potential confounding factors were inconsistently assessed across studies. Because of these considerations, we felt that quantitative synthesis (meta-analysis) was likely to be misleading and did not attempt to do this.[76]

We report our principal findings on relations between cannabis use and educational attainment, use of other drugs, psychological health, antisocial behaviour, and other social problems. Illustrative crude and adjusted effect estimates in relation to these outcomes are described in table 3. Findings on relations between use of other illicit drugs and psychosocial problems are also summarised. Key publications are cited; a full list of publications is available on request.

Cannabis use was consistently associated with reduced educational attainment. Most relevant studies indexed this outcome through objective and apparently valid measures. The strength and magnitude of the association varied. Adjustment of estimates for potential confounding factors generally led to their attenuation, which was often substantial.

Cannabis use was consistently associated with use of other drugs. In all but one relevant study, other drug use was indexed by uncorroborated self-report (in one study, use of injected drugs was corroborated by inspection of injection sites).[37] The strength and magnitude of these associations varied, although in one study, both were substantial.[15] In this study, as with most studies, the outcome reported was other drug use, rather than drug problems. Adjustment of estimates for potential confounding factors generally led to their attenuation.

Cannabis use was inconsistently associated with psychological problems. Some studies found no association, although others reported associations between increased use and increased problems. Within these latter studies, patterns of association with specific psychological problems were inconsistent. In most studies, psychological problems were indexed through self-report of symptoms, some assessed according to standard diagnostic criteria. The outcome was clinical mental illness (schizophrenia) in only one study.[38] This report also mentioned a crude association between cannabis use and mortality from suicide, but did not report actual estimates.[39] A crude association with all-cause mortality disappeared on adjustment for confounding factors. Adjustment of other estimates of increased psychological problems for potential confounding factors generally led to their attenuation, which was often substantial.

Cannabis use was inconsistently associated with antisocial or otherwise problematic behaviour. In most studies these outcomes were indexed through uncorroborated self-report. In some studies corroboration was sought from other sources. In studies that did report associations between greater use and behavioural problems, adjustment of estimates for potential confounding factors generally led to their attenuation, often substantially so.

Evidence of effect modification according to sex and ethnic origin (where these were reported separately) was inconsistent across studies. Cannabis use at a younger age was consistently associated with greater subsequent problems.

Two studies reported associations between use of cocaine and opiates and subsequent psychological

	Participants and setting	Main relevant findings*	Comments*
Studies reporting outcomes related to general drug exposure			
Sadava 1973, Canada[42]	College "freshmen"	Low expectations of goal attainment and more "pro-drug" attitudes associated with drug problems	Probable selection bias, limited adjustment for confounding, significance of outcome measures unclear
Annis 1975, Canada[43]	High school students	Use of both licit and illicit drugs positively associated with school dropout from official records	No adjustment for confounding
Benson 1984 and 1985, Sweden[44,45]	Male military conscripts	Drug use associated with higher rates of criminality, health problems and mortality as ascertained from official records	Crude exposure measurement and no adjustment for confounding
Friedman 1987, USA[46]	Volunteer high school students reporting drug use	Drug use and self-reported psychological distress higher amongst this sample than in a reference cohort	Probable selection bias, little adjustment for confounding, arguably a case-control study
Choquet 1988, France[47]	High school students	Drug use associated with higher self-reported health problems and use of health services	No adjustment for confounding in analyses reported
Farrell 1993, USA[48]	High school students	Drug use associated with lower self-reported emotional restraint in a reciprocal manner	Probable selection bias, limited adjustment for confounding, significance of outcome measure unclear
Huizinga 1994, USA[49]	"High risk" youths	Positive association between drug use and self-reported antisocial behaviour	This association is alluded to in text though actual analyses are not presented. Impossible to critically appraise
Sanford 1994, Canada[50]	Population based sample of adolescents	Heavy drug use associated with a greater risk of reporting work-force involvement (as opposed to continued schooling)	Potential selection bias due to large loss to follow-up
Schulenberg 1994, USA[51]	High school students	Drug use and lower grade point average positively associated with later self-reported drug use	Focus of the surveys is on patterns and antecedents, rather than consequences, of drug use
Anthony 1995, USA[52]	Population based sample of adolescents reporting drug use	Earlier drug use associated with greater risk of developing later self-reported drug problems	Possible selection bias and limited adjustment for confounding. Focus of the epidemiological catchment area programme (of which this was a sub-study) is on the descriptive epidemiology of mental illness in the community rather than the consequences of drug use.
Farrington 1995, UK[53]	"Working-class" male school children.	Positive association between drug use and measures of anti-social behaviour derived from self-report, school-reports and official records	Specific relation between drug exposure and subsequent behavioural outcomes not reported. Focus of the study is on antecedents of "delinquency". Drug use is reported as part of the delinquency spectrum
Krohn 1997, USA[54]	"High risk" school children.	Drug use positively associated with earlier school leaving, earlier independent living and earlier parenthood—particularly among women	Possible selection bias. Limited adjustment for confounding
Luthar 1997, USA[55]	High school students	Drug use associated with increased risk of self-reported depression, maladjustment and internalising of problems	Small study, short follow-up limited adjustment for confounding
Stanton 1997, USA[56]	Black adolescents recruited from an HIV risk reduction project	Drug use weakly associated with self-reported risky sex, fighting, and weapon carrying	Possible selection bias, limited adjustment for confounding
Rao 2000, USA[57]	Female high school students	Substance use disorder positively associated with self-reported depression	Possible selection bias, small sample, limited adjustment for confounding
Weiser 2002, Israel[58]	Male military conscripts	Drug abuse associated with doubling of risk of schizophrenia	Drug abuse only assessed in high risk sub-sample, limited adjustment for confounding†
Studies reporting outcomes related to specific drug exposure			
Epstein 1984, Israel[59]	High school students	Alcohol and tobacco use associated with earlier sexual intercourse and earlier leaving of education. Cannabis use also reported to be associated with the latter (analyses not shown)	Small study, no adjustment for confounding. Since latter analyses not reported impossible to critically appraise in this regard
Kaplan 1986, USA[60]	High school students	Early cannabis use along with use associated with self-reported psychological distress, associated with greater reported escalation of use and later psychological distress	Potential selection bias. Focus of the study is not on consequences of drug use
Tubman 1990, USA[61]	Children of "middle class" families	Alcohol, tobacco and cannabis use all positively associated with self-reported symptoms of psychological distress.	Small study, possible selection bias, focus on antecedents rather than consequences of drug use
Scheier 1991, USA[62]	High school students in drug prevention programme	Cannabis use positively associated with risk of use of other illicit drugs and with socially negative attitudes	Probable selection bias, limited adjustment for confounding
Hammer 1992, Norway[63]	"High risk" adolescents	Cannabis use positively associated with self-reported symptoms of psychological distress	Possible selection bias, limited adjustment for confounding
Degonda 1993, Switzerland[64]	Population based sample of young adults	Cannabis use positively associated with self-reported symptoms of agoraphobia and social phobia	Possible selection bias, limited adjustment for confounding
Romero 1995, Spain[65]	High school students	Cannabis use inconsistently associated with different dimensions of self-reported self-esteem	Loss to follow-up not reported, limited adjustment for confounding, relevance of outcome unclear
Andrews 1997, USA[66]	Adolescents responding to an advertisement	Tobacco and cannabis use associated with lower academic motivation in a reciprocal manner.	Self-selected sample with high loss to follow-up Limited control of confounding
Patton 1997, Australia[67]	High school students	Frequent cannabis use strongly positively associated with reported risk of self-harm in females. Weak, negative association in males.	Short follow-up, limited adjustment for confounding
Hansell 1991 and White 1998, USA[68,69]	Telephone survey of adolescents	Cannabis and cocaine use associated with higher self-reported aggression and psychological distress	Possible selection bias, limited adjustment for confounding, relevance of outcome measures unclear

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	Participants and setting	Main relevant findings*	Comments*
Costello 1999, USA[70]	"High risk" adolescents	Alcohol, tobacco, cannabis, and other drug use positively associated with self-reported psychological distress and behavioural problems	Probable selection bias, limited adjustment for confounding
Duncan 1999, USA[71]	"High-risk" adolescents	Alcohol, tobacco, and cannabis use all positively associated with risky sexual behaviour. Association strongest for tobacco	Small sample, possible selection bias, limited adjustment for confounding
Perkonigg 1999, Germany[72]	Population based sample of adolescents	Cannabis use and dependence were generally sustained over the follow-up period	Focus of publications to date from this study has not been consequences of drug use
Huertas 1999, Spain[73]	High school students	Cannabis, alcohol, and tobacco use positively associated with poorer school performance	No adjustment for confounding
Braun 2000, USA[74]	Population based sample of adolescents	Cannabis and tobacco use weakly associated with lower income and less prestigious employment. Association stronger with tobacco and amongst white participants	Possible selection bias, limited adjustment for relevant confounders (focus of the study is on development of cardiovascular risk)
Brook 2002, Colombia[75]	Population based sample of adolescents	Cannabis use associated with risky sexual behaviours	Limited adjustment for confounding†

*Summaries and comments are based on evidence available following initial searches and quality assessment in 2000, except †study identified through subsequent searches or contact with experts.

Table 2: **Summary of other studies identified in review listed in chronological order of relevant publications**

symptoms; results were mixed.[13,14,24] Amphetamines and ecstasy (3,4-methylenedioxymethamphetamine, MDMA) seem to be widely used illicit drugs.[1] We identified no studies meeting our selection criteria that reported effects of either amphetamine or ecstasy use.

Discussion

In this review, we found little evidence from longitudinal studies in the general population about the outcomes of exposure to any illicit drugs other than cannabis. We confirmed the existence of evidence of associations between cannabis use and psychosocial harm; however, the extent and strength of this evidence seemed less than is perhaps sometimes assumed. Furthermore, the causal nature of these associations is far from clear. Some seem to fulfil at least some of the traditional criteria for establishing causality.[79] They are fairly consistent; cause seems to precede effect, and a plausible mechanism can be advanced. The criterion of specificity of association was less consistently fulfilled. In several studies (tables 1 and 2) tobacco and alcohol showed similar associations as cannabis with psychosocial outcomes. This finding does not suggest a causal mechanism mediated through drug-specific neurophysiological effects or involvement in criminalised commerce, since tobacco and alcohol have distinct neurophysiological effects, and they are not illegal. Existence of a dose-response relation, in which magnitude of the outcome varies with magnitude of the exposure is another criterion often invoked. In many studies, existence of such a relation was impossible to assess since only binary exposure categories were examined. Where effects of more than two exposure categories were reported, a graded association with outcome from higher to lower exposure was sometimes noted. Interpretation of these gradients was complicated by the fact that in almost all studies, frequency of drug use, rather than dose, was assessed. Quantity used was probably closely related to frequency, and frequency measures allowed inference of extent of drug involvement, which is of relevance to social mechanisms of causation.

However, empirical evidence has shown that associations can fulfil these criteria, and still be unlikely to

	Measure of cannabis use and measure of outcome	Crude estimate	Adjusted estimate
Outcome/study			
Educational attainment			
Christchurch[16]	Any use before age 15 years and odds ratio for school dropout	8·1 (4·3–15·0)	3·1 (1·2–7·9)
Project Alert[34]	One point increase on frequency of use scale and odds ratio for school dropout	1·68 (p<0·001)	1·13 ("not significant")
Australian schools*[77]	Weekly use at ages 15, 16, and 17 years and odds ratio for early school leaving	6·8 (2·8–1·6) 3·2 (1·4–7·3) 1·8 (0·69–4·6)	5·6 (2·0–1·5) 2·2 (0·91–6·0) 1·1 (0·40–2·9)
Use of other drugs			
Swedish conscripts[37]	Report that cannabis "most used illicit drug" and odds ratio for later injection drug use	6·8 (4·9–9·4)	3·3 (1·9–5·9)
Christchurch[15]	Weekly use and odds ratio for use of any other drug	142·8 (92·3–222·9)	59·2 (36·0–97·5)
Psychological health			
Christchurch[16,19]	Any use before age 15 years and odds ratio for reported anxiety, depression or suicidal thoughts	2·7(1·3–4·1) 2·9(1·6–5·1) 3·6(2·1–6·1)	1·2 (0·5–2·8) 1·4 (0·7–2·7) 1·4 (0·7–2·8)
	Cannabis dependence at age 18 years and rate ratio for reported psychotic symptoms	2·3 (1·7–3·2)	1·8 (1·2–2·6)
Dunedin[21]	Any use at age 15 years and odds ratio for any mental disorder (sexes combined) Any use at age 18 years and odds ratio for any mental disorder in males and in females	2·69† 3·59† 1·54†	0·97 (0·59–1·60) 2·00 (1·29–3·09) 0·75 (0·47–1·17)
Swedish conscripts[38]	Use on more than 50 occasions and odds ratio for clinical diagnosis of schizophrenia	6·7 (4·5–10·0)	3·1 (1·7–5·5)
Australian schools*[78]	Daily use at age 15 years and odds ratio for reported depression in males and in females	1·9 (0·93–3·8) 8·6 (4·2–18·0)	1·1 (0·55–2·6) 5·6 (2·6–12·0)
Antisocial behaviour			
Christchurch[16]	Any use before age 15 years and odds ratios for conduct disorder, reported offending and police contact	7·0 (4·3–11·4) 5·7 (3·3–10·0) 4·8 (2·5–9·3)	1·0 (0·5–2·1) 0·8 (0·6–2·7) 2·1 (0·9–4·8)

*Study summarised in table 2, relevant results published subsequent to initial quality assessment. †95% CIs were not reported. Adjustment factors for individual estimates are not given. Measures available are described in table 1, but adjustments did not necessarily include the full range of available measures.

Table 3: **Crude and adjusted estimates of effects of cannabis use on selected psychosocial outcomes**

be causal.[80,81] Alternative explanations of reverse causation, bias, and confounding are discussed.

Psychosocial problems might be more a cause than a consequence of cannabis use, especially with regard to associations between use and mental illness. Some studies adjusted for psychological symptoms reported at baseline or excluded incident problems occurring during early follow-up. Nevertheless, unreported or subclinical psychological problems might have preceded and precipitated cannabis use. Individuals with a pre-existing tendency to experience psychological difficulties might have a greater inclination to develop problematic patterns of drug use (for example, depressed individuals are more likely to start smoking tobacco and less likely to stop than those who are not depressed).[82] Cannabis use might also exacerbate existing predispositions to psychological problems.

Exposure to cannabis use and experience of psychosocial problems might have been associated with both study recruitment and retention leading to selection bias that could affect the apparent association between cannabis use and harm. Measurement bias is another possibility. Some empirical evidence suggests reasonable validity of self-reported drug use, although other evidence shows that in some situations, especially general population studies in which the drug-use status of participants has not been previously recorded, this method can be unreliable.[83,84] Random misclassification of drug-use status will simply lead to dilution of apparent effects, but systematic misclassification, especially when it affects both exposure and outcome measurement, can generate spurious effects. For example, an individual may have a general tendency to value either conformist or non-conformist, behaviour, and this tendency may influence their reporting. In this situation one would expect artefactual associations between greater reported use of cannabis and greater reported use of other drugs or other non-conformist behaviours. Since most associations of cannabis use with use of other drugs, and with antisocial behaviour, are based exclusively on self-reported measures, the effect of this type of bias must be considered. In other contexts, reporting bias has been shown to be capable of generating strong and substantial associations between measures that, individually, seem to have high validity.[81]

Discounting confounding is probably the most serious interpretational challenge in observational epidemiology.[85] Both cannabis use and adverse psychosocial outcomes seem to share common antecedents related to various forms of childhood adversity, and factors relating to peer-group and family.[86,87] The relation between cannabis use and harm might simply reflect these associations; cannabis use could be a marker, rather than a cause, of a life trajectory more likely to involve adverse outcomes.

There are no completely reliable means to identify confounded associations within observational data, and instances where apparently robust observational evidence has later been shown to be seriously misleading are common.[85] The importance of this issue to the epidemiology of drug use might have been underestimated. In particular, the extent to which confounding can be overcome through statistical adjustment seems to have been overestimated. Adjustment is useful, but its power to abolish the confounded component of an association depends on the completeness and precision of measurement of the confounders.[88] Only three studies[16,20,30] included in our analysis had any prospectively measured indices of the early life factors that may covary with both cannabis use and harm. It seems unlikely that even these measures were complete or precise.

Unmeasured, as well as measured, potential confounders can be taken into account through techniques such as fixed effects regression and latent variable modelling.[17,89] These approaches allow more sophisticated adjustment. The main value of adjustment is to allow the comparison of adjusted with unadjusted estimates, but few studies provided both of these estimates. The most informative examples of those that did are summarised in table 3. Attenuation of estimates towards the null value, on adjustment, suggests confounding by the adjustment factor. In this situation, residual confounding can be assumed to be present. Unchanged or strengthened estimates suggest that confounding by the factor adjusted for is unlikely—confounding by another factor is still possible. In table 3, almost all adjusted estimates are substantially attenuated towards the null value. With attenuation of this relative magnitude even small degrees of measurement imprecision in the confounders could account for the residual effects.

Sensitivity analyses are another means to explore the possibility of confounding. A recent application of this principle to North American data showed that confounding by a factor termed "propensity for drug use" could explain associations between cannabis use and use of other drugs.[90] Both environmental and genetic factors could underlie such a propensity.[91]

Further evidence against a simple causal explanation for associations between cannabis use and psychosocial harm relates to population patterns of the outcomes in question. For example, incidence of schizophrenia seems to be strongly associated with cannabis exposure over a fairly short period (four-fold to five-fold relative risks over follow-up of 10–30 years). Cannabis use appears to have increased substantially amongst young people over the past 30 years, from around 10% reporting ever use in 1969–70, to around 50% reporting ever use in 2001, in Britain and Sweden.[1,38] If the relation between use and schizophrenia were truly causal and if the relative risk was around five-fold then the incidence of schizophrenia should have more than doubled since 1970. However population trends in schizophrenia incidence suggest that incidence has either been stable or slightly decreased over the relevant time period.[92,93]

The above considerations suggest that a non-causal explanation is possible for most associations between cannabis exposure and both psychological and social harm. It is important to clarify these questions, and evidence meeting this requirement could come from several sources. Birth cohorts provide the ideal prospective design within which to investigate the role of early life factors.[94] They are expensive and time consuming, and ensuring complete follow-up is challenging. However two of the studies we identified successfully adopted this design.[15,20] Other ongoing birth cohorts whose participants are now entering adolescence exist.[95] These studies could provide valuable information, especially if they incorporated approaches to measurement other than those completely reliant on uncorroborated self-report.

The principle of "Mendelian randomisation" is proving useful in cardiovascular and cancer epidemiology.[96] If level of exposure to a putative environmental cause is substantially affected by a particular genetic polymorphism, then analysis of effect by genotype is unlikely to be confounded by environmental factors. Study of polymorphisms affecting neuroreceptor affinity for the psychoactive components of cannabis may have potential in this regard.[97] The statistical power is generally

low in such studies, however, and sample sizes need to be large.[98,99] Finally, experimental studies are the traditional approach to overcoming problems of selection bias and confounding. If experimental reduction in cannabis exposure were associated with reductions in psychosocial harm, this would be stronger evidence for a true causal relation. Currently, this approach is limited by the absence of interventions that substantially or reliably reduce exposure to cannabis.[100] Concerns have been expressed about the public health effects of ecstasy use;[101] the same principles should guide research to provide evidence relating to this drug. Evidence on public health effects of opiate use seems likely to be most feasibly obtained through follow-up of population-based cohorts of opiate users.[102]

In this review we did not consider physical health outcomes. Clearly, some types of illicit drug use lead to serious physical harm, but the extent of this problem outside known treatment populations is unclear. It is probable that cannabis use is associated with some physical harm, since most users apparently smoke the drug with tobacco. Intermittent use confined to adolescence or early adulthood might have small effects, but data confirming that this pattern of use predominates, or measuring the prevalence of other usage patterns, are limited. Little reassurance is available from the evidence we identified. Only one study reported mortality up to middle adulthood and found no increase with cannabis use, however the same study showed no mortality increase associated with tobacco use.[39]

Drug policy is sometimes justified on the basis of a causal relation between drug use and psychosocial harm. We have shown that evidence for this relation is not strong. However it would be naive to assume that scientific evidence is generally an important determinant of policy, especially in this area.[103,104]

No search strategy can ensure identification of all relevant evidence. Our search was the most comprehensive of any we are aware of in this field and was recently updated. However, it is probable that we missed some potentially relevant evidence. Given the general issues of interpretation we have discussed, it seems unlikely that such omissions would have substantially altered our conclusions. Our quality assessment was inevitably subjective; however, we undertook it as a guide to readers and to make the task of the review more manageable. We contacted only authors of higher-quality studies to identify further evidence, although again it seems unlikely that this procedure introduced substantial bias.

Despite widespread concern, we have found no strong evidence that use of cannabis in itself has important consequences for psychological or social health. This finding is not equivalent to the conclusion that use of cannabis is harmless in psychosocial terms; problems with the available evidence render it equally unable to support this proposition. Better evidence is needed in relation to cannabis, which is widely used, and in relation to other drugs that, although less widely used, might have important effects.

Contributors

J Macleod, A Copello, I Crome, M Egger, M Hickman, and G Davey Smith devised the search strategy. Electronic searches, expert contact, and retrieval of references were undertaken by R Oakes and T Oppenkowski. Hand searches were undertaken by J Macleod and I Crome. Quality assessment was undertaken by J Macleod, M Egger, and H Stokes-Lampard. Data synthesis and interpretation was discussed by J Macleod, A Copello, I Crome, M Egger, M Hickman, H Stokes-Lampard, and G Davey Smith. J Macleod wrote the first draft of this report, all authors contributed to the final draft.

Conflict of interest statement

None declared.

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