

What Are the Policy Implications of the Evidence on Cannabis and Psychosis?

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Objective: To explore the implications for mental health services, for health education about the risks of cannabis use, and for public policy toward cannabis use of observational evidence that cannabis use is a contributory cause of psychosis.

Method: Using comparative analyses of similar evidence for the harmful effects of alcohol, tobacco, and amphetamine use, we considered the relation between observational evidence and action on cannabis. We examined arguments on the grounds of public health prudence for discouraging cannabis use by young individuals. With the assumption that the relation may be causal, we considered recommendations for policy in mental health services, health education, and public policy toward cannabis.

Results: The observational evidence and biological plausibility of the hypothesis that cannabis is a contributory cause of psychosis is at least as strong as evidence for causal relations between heavy alcohol and amphetamine use and psychosis. On public health grounds, there is a good case for discouraging cannabis use among adolescents and young adults. It remains uncertain how best to discourage use and at whom campaigns to reduce cannabis use should be targeted.

Conclusions: We should discourage young adults seeking treatment in mental health services from using cannabis and inform them of the probable mental health risks of cannabis use, especially of early and frequent use. We must exercise caution in liberalizing cannabis laws in ways that may increase young individuals' access to cannabis, decrease their age of first use, or increase their frequency of cannabis use. We should consider the feasibility of reducing the availability of high-potency cannabis products.

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Clinical Implication

- Screening all patients with psychoses and advising those who use cannabis to stop should discourage cannabis use among the clients of mental health services and reduce the number of cannabis-related psychoses.

Limitations

- There is an absence of research evidence on how to best persuade young individuals with psychoses to stop using cannabis.
- There is also an absence of research on how to best assist those who would like to stop but find it difficult to do so.

Key Words: *cannabis use, psychosis, policy, mental health services, health education, penalties*

Interpretations of the relation between cannabis use and psychosis have often been refracted through the appraisers' preexisting views on whether cannabis use by adults should or should not attract criminal penalties. To justify their position, those who favour a continuation of criminal penalties often invoke evidence for a causal role of cannabis in psychosis (for example, the Australian Prime Minister, John Howard, 2005; 1) whereas those who favour more liberal policies toward cannabis have generally been sceptical about such evidence (2–4). In each case, the prior policy has shaped the appraisal of the evidence, rather than the evidence informing the policy.

We have separated our review of the evidence (5) from our discussion of its policy implications to reduce the impact of preexisting policy on our appraisal of the evidence. We approach the policy implications of the evidence in 2 steps. We begin by asking whether there is sufficient evidence to warrant the inference that cannabis is a contributory cause of psychosis in young adults. Although we argue that it is more likely than not that cannabis is a contributory cause of psychosis, we believe that, on the grounds of prudence, sceptics should be prepared to allow for the possibility that the relation may well be causal and thus support health education alerting young individuals to this possibility. Given this view, we then contemplate which policies we should consider adopting to reduce any psychotogenic effects of cannabis use.

We consider the policy issues under 3 broad headings, in increasing order of contention. We begin with the least controversial question: How should we respond to young individuals with psychoses who use cannabis? Second, we ask 2 interrelated questions: What should we tell young individuals about the mental health risks of cannabis use? How can we do so in a way that is likely to dissuade them from using cannabis in ways that increase these risks? Finally, we address the most contentious issue that is often at the forefront of the cannabis policy debate: How should the evidence on cannabis and psychosis affect legal policies toward cannabis use? More specifically, we consider whether jurisdictions that still impose criminal penalties for cannabis use should reject proposals to liberalize existing policies, for example, by imposing civil rather than criminal penalties for cannabis use or by legalizing the production, sale, and use of cannabis. We also examine whether jurisdictions that have liberalized cannabis policies

should consider reimposing criminal sanctions against cannabis use.

Making Causal Inferences From Observational Data

As summarized elsewhere, there is observational evidence from large longitudinal studies in several different countries that young adults who regularly use cannabis are at increased risk of developing psychosis (5–8). These studies have noted several important things:

1. Cannabis users report more psychotic symptoms and have higher rates of diagnosed psychosis than individuals who have not used cannabis.
2. The risk of psychosis and psychotic symptoms increases with the frequency of use and is greater if individuals begin using cannabis at an earlier age.
3. Individuals with a personal or family history of psychotic symptoms appear to be more likely to develop psychotic symptoms if they use cannabis.
4. These relations usually persist after controlling for a range of potentially confounding variables, such as personal characteristics, other types of drug use, and a family history of psychiatric disorder.

The major uncertainty about the evidence arises from the fact that individuals are not randomly assigned to use cannabis or not; we cannot be certain that the baseline risk of psychosis in the 2 groups was the same before they began to use cannabis (7,9). The 2 most plausible alternative explanations for the association between cannabis use and psychosis are:

1. That psychosis is caused by uncontrolled confounding, for example, the use of other drugs such as psychostimulants and alcohol that are more likely to be used by regular cannabis users, or by a genetic vulnerability to psychosis that also increases the risk of cannabis use (10).
2. That cannabis use is a symptom of emerging psychosis.

The epidemiologic studies to date have attempted to address these forms of confounding by measuring and statistically adjusting for other drug use, personal characteristics that predict psychosis risk, and a personal history of psychotic symptoms (11–15). The logic of this approach is that the relation between cannabis use and psychosis is unlikely to be explained by confounding of any of these variables if the association persists after controlling for them. The number of assessed confounding variables varies between studies, as do the specific variables that have been statistically controlled for. One recent study has used fixed effects regression methods in an attempt to control for unmeasured confounders (12).

Abbreviations used in this article

COMT	catechol-O-methyltransferase
RR	relative risk
SIDS	sudden infant death syndrome
SSRI	selective serotonin reuptake inhibitor
THC	delta-9-tetrahydrocannabinol

We think it is unlikely that these (or any other unmeasured) confounding variables explain the associations between cannabis use and psychosis. The better-controlled studies, which have controlled for personal characteristics and other drug use, have still found such a relation. Those who continue to assert the possibility of uncontrolled confounding must identify plausible confounding variables for which these studies have not adequately controlled so that they can be controlled for in future studies (16).

We also give weight to the following evidence for the biological plausibility of a causal relation between cannabis use and psychosis:

1. The principal psychoactive ingredient of cannabis, THC, acts on the CB₁ cannabinoid receptor in the brain (17). The cannabinoid system interacts with dopaminergic neurotransmission, which has been implicated in the production of psychotic symptoms (17).
2. There is more recent direct evidence that the cannabinoid system may be disturbed in patients with schizophrenia and related psychotic disorders (18–20).
3. In a double-blind provocation study, D'Souza and colleagues showed that intravenous THC increases positive and negative psychotic symptoms in a dose dependent way in patients and healthy volunteers with no history of psychosis (21).
4. Caspi and others reported a strong interaction between cannabis use and a common polymorphism in the COMT gene, which is implicated in dopaminergic neurotransmission (22).

We think that the best explanation for the evidence from prospective epidemiologic studies is that cannabis use precipitates schizophrenia in individuals who are vulnerable because of a personal or family history of schizophrenia (23). This hypothesis is consistent with the stress–diathesis model of schizophrenia (24,25) and with evidence that a genetic vulnerability to psychosis increases the risk that cannabis users will develop psychosis (22, 26–28). A vulnerability hypothesis is also consistent with several facts: the overall RR of developing schizophrenia is modest if cannabis is used (RR 2 to 3); the incidence of treated schizophrenia did not obviously increase during the 1970s and 1980s (29), when there were substantial increases in cannabis use among young adults in Australia and North America (30); and individuals with psychosis who have used cannabis have, on average, an earlier age of onset of their disorders (31,32).

A Comparative Evaluation of the Evidence

It is useful to compare the strength of the evidence on cannabis and psychosis with that of observational evidence on the relations between adverse health effects and other types of drug

use. Such comparisons facilitate more consistent, even-handed appraisals of the comparative strengths and weaknesses of evidence on the adverse effects of different drugs (33).

Some commentators (1) have drawn analogies to the debate in the early 1960s (34,35) about whether the epidemiologic evidence on associations between cigarette smoking and lung cancer was sufficient to warrant public health campaigns to discourage smoking. The eventual consensus, that cigarette smoking was a cause of lung cancer, heart disease, and chronic obstructive pulmonary disease, depended on observational evidence from large cohort studies in the absence of any pathophysiologic explanation of how cigarette smoking caused any of these diseases (36, 37). These commentators correctly argue that the evidence for the psychotogenicity of cannabis also depends on observational evidence from cohort studies (1). The major difference is that the effect size was far stronger for cigarette smoking and lung cancer (RR 12 for a smoker of 20 cigarettes daily) than it is for cannabis and psychosis (RR 2 to 3).

A more relevant comparison may be between the evidence on the psychotogenicity of alcohol and amphetamines and that of cannabis. Evidence that heavy alcohol use causes psychosis is considerably weaker than evidence for the psychotogenicity of cannabis. Evidence of alcohol-induced psychosis consists largely of case series of delirium tremens in severely alcohol dependent individuals undergoing alcohol withdrawal (38). One very old experimental study deliberately induced delirium tremens by the abrupt cessation of drinking, under controlled conditions in a hospital ward, after several weeks of sustained heavy drinking (39). There are also case series of psychotic disorders (alcoholic hallucinosis) that reportedly occur in heavy consumers of alcohol, but the status of this entity is uncertain (38,40).

The evidence that heavy amphetamine use can induce psychosis is stronger than the evidence that alcohol can induce psychosis. The initial observations were derived from 200 case studies of heavy amphetamine users who developed paranoid psychoses after sustained periods of heavy amphetamine use and whose disorders remitted within days to a week of abstinence from amphetamines (41). The case study evidence was later supported by the experimental reproduction of psychoses in amphetamine users (42) and healthy volunteers (43). These studies, which would now be considered unethical, involved administering chronically high doses of amphetamines to drug users in treatment (42) and to medical students (44). More recently, associations between the frequency of amphetamine injection and the frequency and severity of psychotic symptoms have been reported among amphetamine users (45). A causal relation is supported by animal evidence

that amphetamines and cocaine have major effects on dopaminergic neurotransmission (44).

It is useful to consider the relative frequency of cannabis- and amphetamine-related psychotic episodes. In Australia, despite the fact that the prevalence of amphetamine use is about one-fifth that of cannabis use, more hospital stays for psychotic episodes are attributed to amphetamine use than to cannabis use (46). The differences are even more marked when the relative number of cannabis and amphetamine users is taken into account. A recent study estimated that among users of these drugs, and depending on the considered age group, the rates were between 2.5 and 11 times greater for amphetamine users (46).

In summary, the evidence for a causal relation between cannabis use and psychosis is not as strong as that for cigarette smoking and lung cancer because the association is much weaker (RR 2 to 3, compared with 12 or greater). The evidence that cannabis is a contributory cause of psychosis is arguably stronger than the evidence for the psychogenicity of alcohol. The epidemiologic evidence for cannabis' role is also arguably more extensive than the evidence for a relation between amphetamine use and psychosis; however, the magnitude of the relation between drug use and psychosis is weaker for cannabis (two- to threefold) than it is for stimulant drugs (elevenfold) (47).

Evidence and Policy: A Public Health Case for Prudence

How strong must the evidence for a causal relation between cannabis and psychosis be before we are justified in taking action? If the standard of proof we require for action is beyond reasonable doubt, as is demanded in criminal cases, then we would find it difficult to make any policy decisions according to the available evidence. If, however, we are prepared to act on the balance of probabilities (more likely than not), some policy action is warranted (33). The latter standard is arguably what is used in judging the adverse effects of pharmaceutical drugs. If we had similar evidence of an association between using a pharmaceutical drug and an adverse effect, the drug would either be withdrawn from the market or would only be prescribed with clear warnings about the risk to patients and prescribers. This, for example, has been the response to what some argue is weaker evidence of increased suicide risk after the initiation of SSRI antidepressants (48).

There are important differences in the way we regulate pharmaceuticals, compared with some recreational drugs. We generally (and we would argue appropriately) use caution when responding to evidence of harm caused by therapeutic drugs. As a society, we are less concerned about voluntarily assumed risks from using alcohol and tobacco. We generally allow adults to decide whether or not to take these risks,

whereas we prohibit the use of these drugs by minors. As critics of contemporary cannabis policy argue, cannabis is a conspicuous exception to this policy because the penalty of imprisonment prohibits adults in developed countries from using cannabis. Below, we discuss how we think the evidence on cannabis and psychosis should affect the debate about the legal prohibition of cannabis use by adults.

If uncertain, we need to consider the possible costs and benefits of different policy actions. For example, the decision to advise parents to avoid putting infants to sleep in the prone position was advocated as a way of reducing SIDS on the grounds that this sleeping position was a strong risk factor for SIDS. The proposed behavioural change carried few risks and if incorrect, would not greatly inconvenience parents or their infants. Subsequent experience of a substantial reduction in SIDS deaths in countries that implemented this policy provided convincing proof, in the absence of any detailed understanding of the causal mechanism (49).

The same cautious reasoning suggests that it is good policy to encourage young individuals to avoid using cannabis or to at the least delay their use until early adulthood (1). Assuming, for the moment, that we know how to do this, if the relation is truly causal, the public health gain (probably a 10% reduction in schizophrenia incidence), would arguably offset the foregone pleasure among those young individuals who either did not use cannabis or delayed using it until they were young adults. A reduction in cannabis use among incident cases of psychosis would also provide some evidence for the effectiveness of this policy. However, for the same reasons that have made it difficult to decide whether the increased prevalence of cannabis use among youth has produced an increased incidence of schizophrenia, any reduction may be difficult to discern (30). This argument makes a good case for discouraging cannabis use among young individuals, but it leaves room for disagreement about the best method of achieving this goal in particular population groups. It is to these latter questions that we now turn.

Responding to Cannabis Use Among Individuals With Psychosis

The implications of the evidence are probably least controversial for mental health services that treat young individuals with psychoses, among whom there are high rates of regular cannabis use (50). Even if we believe that the relation between cannabis use and psychosis is not causal, there is still reasonable evidence that individuals with psychoses who are regular cannabis users have more positive symptoms, more frequent relapses, and require more hospitalization (51,52). It is accordingly wise to encourage young individuals with psychotic symptoms who use cannabis to stop or, at the very least, to encourage them reduce their frequency of use. If we were

able to reduce cannabis use among patients with schizophrenia we could discover whether their disorders improved and whether their risk of relapse decreased.

The major challenges with this strategy are to find ways to persuade individuals with schizophrenia to stop doing something they enjoy and to help those who want to stop using cannabis but find it difficult to do so. Recent evaluations of psychological interventions for cannabis dependence in individuals without psychoses report modest rates of abstinence at the end of treatment (20% to 40%) and substantial rates of relapse thereafter (53). Nonetheless, treatment still substantially reduces cannabis use and problems even among those who do not succeed in quitting, which is not very different from the outcome of treatment for alcohol and other drug dependence (54). However, many individuals with schizophrenia have characteristics that predict a poor outcome: they lack social support, they may be cognitively impaired, they are often unemployed, and they do not comply with treatment (55,56). There are very few controlled outcome studies of substance abuse treatment in schizophrenia (57). A recent Cochrane review identified only 6 relevant studies, 4 of which were small (58) and found no clear evidence that supported any type of substance abuse treatment in schizophrenia over standard care. The development of more effective pharmacologic and psychological methods of treatment for cannabis dependence should be a research priority (60).

Informing Young Individuals About the Mental Health Risks of Cannabis Use

Finding effective and palatable ways of explaining the psychotogenic effects of cannabis use to young individuals is a major public health challenge. In addition to a possible increased risk of psychosis, young individuals also need to be informed about the risks of becoming dependent on cannabis, impairing their educational achievement, and increasing their risk of depression (61,62). These risks have often been overshadowed in the public debate about cannabis use. Such risks add weight to the above argument for discouraging cannabis use among young individuals.

It is difficult to provide credible advice to young individuals on the mental health risks of cannabis use because of the polarized views of the health risks of cannabis expressed in the larger cannabis policy debate. As argued above, community debates about whether cannabis use should continue to be a criminal offence increase the prominence of conflicting messages about the association of cannabis with psychosis. This will probably increase skepticism among young individuals about which information they should heed (and perhaps some young individuals will justify their own behaviour by downplaying reasonable advice).

We need to be realistic about the practical impacts of educational messages (63,64). Reviews of the evidence on the effectiveness of school-based drug education suggest that small, statistically significant reductions in cannabis use may be observed in well-conducted programs, but the effects are small (64–66). These programs primarily impart knowledge rather than change behaviour (64). They are also more likely to influence less frequent cannabis users (66) rather than heavier users who are at greater risk of psychotic symptoms. Some argue that there is more value in programs aimed at smaller, targeted groups of individuals at higher risk (67).

There are also intergenerational differences of opinion about the risks of cannabis use (68), and there may well be different views about how information should be presented to discourage its use. The political imperative has been to loudly and publicly express community concern, preferably through high-profile, mass media campaigns. At times, this is presented by educators who seem indifferent to how young individuals will perceive the communication.

Mass media and school-based campaigns must deal with youth skepticism about health advice from adults. Adolescents are exquisitely sensitive to what they see as a parental double standard of disapproving of cannabis use while using alcohol. They are also alert to what they see as dishonest information about cannabis because of a history of cannabis scare campaigns. These responses create a youth audience skeptical about the information on the mental health risks of cannabis.

It is foolhardy to suggest simple solutions to the question of what advice should be given to young individuals. The nature and delivery of the advice must differ for different groups facing different levels of risk (69). The best way to deliver the advice will depend on good social marketing research on the preexisting views of young individuals (70).

We believe that general health education about drug use and mental health should include the risks of cannabis use (71). This should explain the mental health risks of regular intoxication with alcohol and cannabis as well as defining the known high-risk groups, such as those with a family history of psychosis and those who have had bad experiences with cannabis and alcohol. Such education needs to be directed at cannabis users and also at their peers so that young individuals can encourage their affected peers to cease cannabis use or to seek help.

It will be a major challenge to frame the magnitude of the risk of psychosis from cannabis use. Any individual's risk increases from about 7 in 1000 to 14 in 1000 (72), but psychosis has serious consequences for vulnerable individuals. It is tempting for parents and health educators to play up the risk, arguing that everyone is at risk because it is difficult to predict which young individuals are most vulnerable. We doubt this

strategy; it may be interpreted as an exaggeration of the risk and may undermine the credibility of the message.

Psychosis and Cannabis Policy

The implicit assumption that if we accept cannabis as a contributory cause of psychosis then we should continue to prohibit cannabis use and even increase the rigour with which this policy is enforced is a major obstacle to a more comprehensive cannabis policy (73). The following statement illustrates this slippage between evidence that cannabis causes psychosis and support for cannabis prohibition: “the appropriate question is: in the light of all that we know, should we recommend cannabis use to our youth or just wait and see until more evidence arises? Or is it wise to prohibit its use?” (1, p 358).

This framing of the relation between evidence and policy is an understandable response to the simplification of the policy debate by developed countries’ popular media: we should either legalize cannabis because its use is harmless or we should continue to prohibit it because it harms some users (74, 75). If this is how the policy choice we face is perceived it is understandable why advocates of more liberal cannabis policies have attacked the evidence that deprives them of their simplest and most compelling argument for cannabis law reform: that cannabis use is harmless.

As is argued in more detail elsewhere, it is illogical to prohibit cannabis use simply because it harms some users (75). If we prohibited cannabis use on these grounds we would be morally obliged to also prohibit alcohol and tobacco use. Advocates of cannabis prohibition should present criminal penalties as the best way to discourage cannabis use and to reduce the harm it causes. As a society, we must also consider the social costs of using criminal law to deter individuals from using cannabis. To decide whether the cost of prohibition is worth discouraging young individuals from using cannabis, information is needed about both the harms caused by cannabis and the social consequences of its prohibition (75).

The evidence on cannabis and psychosis should play a role in this societal decision because psychosis is a serious disorder that substantially affects the life chances of more severely affected young individuals (17). Nonetheless, we do not think that this health effect could or should be the sole basis of a social policy toward cannabis because if evidence of psychogenicity were a sufficient warrant for prohibition then we would be obliged to prohibit alcohol, which is also a probable contributory cause of psychosis.

Arguments for recriminalizing cannabis include the fact that it would simplify cannabis laws and make it easier to educate the community by sending a simple, strong message of disapproval about cannabis use and that, combined with criminal

penalties, it might deter more young individuals from using cannabis (73).

There are several arguments for the opposite side of the debate:

1. In jurisdictions that have substituted civil for criminal penalties for cannabis use, there is an absence of evidence that rates of use have been affected. For example, rates of cannabis use increased by the same amount in all Australian states during the early 1990s, despite differences in nominal legal penalties (76,77). This mirrors experience in the United States in the 1980s (78) and in The Netherlands in the early 1970s (79). Moreover, rates of cannabis use have declined in Australia since 1998, and the rate of decline has been much the same in all states and territories, regardless of penalties (80).
2. There are reasonable concerns about the social consequences of recriminalization. Reintroducing criminal penalties for an offence committed annually by 10% of Australian adults will lead either to a lack of law enforcement or to the selective enforcement of the law against social minorities or disadvantaged community groups (75).
3. A debate about penalties for cannabis use might intensify the existing polarization of opinion about the risks of cannabis. It might also distract us from considering policy options that might earn much wider public support, for example, effective health education of young individuals about the mental health risks of cannabis use.

Why Prohibition Is Not Enough

It seems likely that most developed countries’ governments will continue to prohibit cannabis use by adults, regardless of whether they do so by imposing criminal or civil penalties. It is clear that prohibiting cannabis use has not been enough to prevent the occurrence of cannabis-induced psychoses among young individuals, although it can be argued that the problem might have been worse in the absence of prohibition (75).

We must consider 2 possible contributions that law enforcement strategies may have unwittingly made to this outcome: creating incentives for black market producers to maximize the average potency of their cannabis products; and in the absence of regulation of an illicit market, allowing young individuals to have ready access to more potent forms of cannabis at an early age. Strategies enforcing the prohibition of cannabis cultivation by disrupting outdoor cannabis plantations may have contributed to the first problem by driving cannabis cultivation indoors and creating incentives for illegal producers to maximize their profit and reduce their risk of

detection by breeding and cultivating fewer indoor cannabis plants under conditions that maximize their THC content. The shift to indoor hydroponic cultivation has been one of the most generalized changes to cannabis production in several countries, including Canada, The Netherlands, and Australia.

If our reason for imposing criminal penalties on cannabis use is to reduce the aggregate social harm that cannabis use causes, our policies should also account for the potency of the cannabis products available to young individuals. One way to do so would be to consider the THC content when imposing legal sanctions on individuals caught growing and selling cannabis. This might, for example, mean imposing higher financial penalties and (or) custodial sentences on individuals who produce and distribute higher-potency cannabis seeds, plants, and products. It could also mean reducing the severity of penalties for individuals caught growing fewer plants of modest potency for their personal use. The main uncertainties with this proposal are the feasibility and cost of enforcing such laws because they would require assays of the THC content of confiscated cannabis. If such a policy were feasible, the collection of data on the THC content of black market cannabis products would be a useful byproduct of its implementation that could be used in health education (81).

Conclusions

The observational evidence for a causal relation between cannabis use and psychosis is at least as strong as observational evidence of associations between other types of drug use and adverse health outcomes, specifically, the relations between heavy alcohol and amphetamine use and psychosis. A causal relation is biologically plausible because the cannabinoids interact with dopaminergic neurotransmission, the cannabinoid system may be disturbed in psychosis, THC provokes psychotic symptoms, and there is suggestive evidence of an interaction between cannabis use and a genetic polymorphism that controls catecholamine transportation.

The clearest policy implication is that we should discourage cannabis use among the clients of mental health services, for example, by screening all patients with psychoses and advising those who use cannabis to stop or to reduce their use. More research is needed on how best to persuade them to stop and on better ways of assisting those who would like to stop but find it difficult to do so.

There is arguably an ethical imperative to inform young individuals of the probable mental health risks of cannabis use. To be cautious, young individuals should be discouraged from early and frequent use of cannabis, as they are for alcohol. The challenge will be to find credible and persuasive ways of doing this. This task could be complicated by the community debate about cannabis policy, with individuals' positions on this issue affecting their appraisals of the evidence. Political

imperatives to express community concern through mass media campaigns could be counterproductive if they also amplify current policy critics' expressions of skepticism about the evidence. The tobacco industry's success in undermining tobacco control policy suggests that raising doubts about the quality of the evidence for harmful effects is an effective way of reassuring users and ensuring they continue using the drug (82).

We should avoid making the common assumption that if the relation between cannabis use and psychosis is causal then we should continue to prohibit cannabis use and reverse the liberalization of penalties for cannabis use that has occurred in some countries. As we have argued, accepting a causal relation removes the strongest cause for liberalization—the absence of any harmful effects on users. Given the seriousness of psychotic disorders for the life chances of the young individuals who are affected by them, the evidence increases the case for caution in liberalizing cannabis laws in ways that might increase young individuals' access to cannabis, decrease their age of first use, or increase their frequency of cannabis use. The effect of the law on young individuals, however, is not the only outcome we should consider in framing our policies toward cannabis. The decision requires an analysis of the harms caused by current policy as much as it does the harms caused by cannabis use.

Even if our societies accept that some form of prohibition is the best policy toward cannabis, it has not been enough to prevent young individuals in developed societies from using high-potency cannabis products at an early age. We must take more action to reduce young individuals' access to high-potency cannabis products. This includes trialling the feasibility and efficacy of graduated penalties for producers and suppliers of cannabis products with higher THC content.

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References

1. De Irala K, Ruiz-Canela M, Martinez-Gonzalez MA. Causal relationship between cannabis use and psychotic symptoms or depression. Should we wait and see? A public health perspective. *Med Sci Monit* 2005;12:RA355–8.
2. Grotenhermen F. How to prevent cannabis-induced psychological distress . . . in politicians. *Lancet* 2004;363:1568–9.
3. Mirken B and Earleywine M. The cannabis and psychosis connection questioned: a comment on Fergusson et al. *Addiction* 2005;100:714–5.
4. Zimmer L, Morgan J. Marijuana myths, marijuana facts. A review of the scientific evidence. New York (NY): The Lindesmith Center; 1997.
5. Degenhardt LD, Hall W. Is cannabis a contributory cause of psychosis? *Can J Psychiatry* 2006;9:556–65.
6. Arseneault L, Cannon M, Witton J, Murray RM. Causal association between cannabis and psychosis: examination of the evidence. *Br J Psychiatry* 2004;184:110–7.
7. Fergusson DM, Poulton R, Smith PF, Boden JM. Cannabis and psychosis. *BMJ* 2006;332:172–6.
8. Semple DM, McIntosh AM, Lawrie SM. Cannabis as a risk factor for psychosis: a systematic review. *J Psychopharmacol* 2005;19:187–94.

9. MacLeod J, Oakes R, Copello A, Crome I, Egger M, Hickman M, and others. The psychological and social sequelae of cannabis and other illicit drug use by young people: a systematic review of longitudinal, general population studies. *Lancet* 2004;363:1579–88.
10. Weiser M, Noy, S. Interpreting the association between cannabis use and increased risk for schizophrenia. *Dialogues Clin Neurosci* 2005;7:81–5.
11. Fergusson DM, Horwood LJ, Swain-Campbell NR. Cannabis dependence and psychotic symptoms in young people. *Psychol Med* 2003;33:5–21.
12. Fergusson DM, Horwood LJ, Ridder EM. Tests of causal linkages between cannabis use and psychotic symptoms. *Addiction* 2005;100:354–66.
13. Henquet C, Krabbendam L, Spauwen J, Kaplan C, Lieb R, Wittchen HU, and others. Prospective cohort study of cannabis use, predisposition for psychosis, and psychotic symptoms in young people. *BMJ* 2005;330:11–4.
14. Van Os J, Bak M, Hanssen M, Bijl RV, de Graaf R, Verdoux H. Cannabis use and psychosis: a longitudinal population-based study. *Am J Epidemiol* 2002;156:319–27.
15. Zammit S, Allebeck P, Andreasson S, Lundberg I, Lewis G. Self reported cannabis use as a risk factor for schizophrenia in Swedish conscripts of 1969: historical cohort study. *BMJ* 2002;325:1199–1201.
16. Cook TD, Campbell DT. *Quasi-Experimentation: Design and Analysis Issues for Field Settings*. Chicago (IL): Rand McNally; 1979.
17. Hall W, Degenhardt L, Lynskey M. *The health and psychological consequences of cannabis use*. Canberra (AU): Australian Government Publishing Service; 2001.
18. Fritzsche M. Are cannabinoid receptor knockout mice animal models for schizophrenia? *Med Hypotheses* 2001;56:638–43.
19. Glass M. The role of cannabinoids in neurodegenerative diseases. *Prog Neuropsychopharmacol Biol Psychiatry* 2001;25:743–65.
20. Skosnik PD, Spatz-Glenn L, Park S. Cannabis use is associated with schizotypy and attentional dysinhibition. *Schizophr Res* 2001;48:83–92.
21. D'Souza C, Cho HS, Perry E, Krystal JH. Cannabinoid 'model' psychosis, dopamine-cannabinoid interactions and implications for schizophrenia. In: Castle DJ, Murray R, editors. *Marijuana and Madness*. Cambridge (UK): Cambridge University Press; 2004. p 142–65.
22. Caspi A, Moffitt TE, Cannon M, McClay J, Murray R, Harrington H, and others. Moderation of the effect of adolescent-onset cannabis use on adult psychosis by a functional polymorphism in the catechol-O-methyltransferase gene: Longitudinal evidence of a gene × environment interaction. *Biol Psychiatry* 2005;57:1117–27.
23. Hall W, Degenhardt L, Teesson M. Cannabis use and psychotic disorders: an update. *Drug Alcohol Rev* 2004;23:433–43.
24. Bromet EJ, Dew MA, Eaton W. Epidemiology of psychosis with special reference to schizophrenia. In: Zahner GEP, editors. *Textbook of psychiatric epidemiology*. New York (NY): Wiley-Liss; 1995. p 283–300.
25. Gottesman II. *Schizophrenia genesis: the origins of madness*. New York (NY): WH Freeman; 1991.
26. Arseneault L, Cannon M, Poulton R, Murray R, Caspi A, Morritt TE. Cannabis use in adolescence and risk for adult psychosis: longitudinal prospective study. *BMJ* 2002;325:1212–3.
27. McGuire PK, Jones P, Harvey I, Williams M, McGuffin P, Murray RM. Morbid risk of schizophrenia for relatives of patients with cannabis associated psychosis. *Schizophr Res* 1995;15:277–81.
28. Verdoux H, Gindre C, Sorbara F, Tournier M, Swendsen JD. Cannabis use and the expression of psychosis vulnerability in daily life. *Eur Psychiatry* 2002;17:180S–180S.
29. Der G, Gupta S, Murray RM. Is schizophrenia disappearing? *Lancet* 1990;335:513–6.
30. Donnelly N, Hall WD. *Patterns of cannabis use in Australia*. Canberra (AU): Australian Government Publishing Service; 1994. p 106.
31. Arendt M, Rosenberg R, Foldager L, Perto G, Munk-Jorgensen P. Cannabis-induced psychosis and subsequent schizophrenia-spectrum disorders: follow-up study of 535 incident cases. *Br J Psychiatry* 2005;187:510–5.
32. Barnes TRE, Mutsatsa H, Hutton SB, Watt HC, Joyce EM. Comorbid substance use and age of onset of schizophrenia *Br J Psychiatry* 2006;188:237–42.
33. Hall W. Assessing the health and psychological effects of cannabis use. In: Kalant H, Corrigall W, Hall W, Smart R, editors. *The health effects of cannabis*. Toronto (ON): Centre for Addiction and Mental Health; 1999. p 1–17.
34. Parascandola M. Cigarettes and the US Public Health Service in the 1950s. *Am J Public Health* 2001;91:196–205.
35. Talley C, Kushner HI, Sterk CE. Lung cancer, chronic disease, epidemiology, and medicine, 1948–1964. *J Hist Med Allied Sci* 2004;59:329–74.
36. Royal College of Physicians. *Smoking and Health*. London (UK): Pitman; 1962.
37. US Surgeon General. *Smoking and Health*. Washington (DC): US Department of Health, Education and Welfare; 1964.
38. Greenberg DM, Lee JWY. Psychotic manifestations of alcoholism. *Curr Psychiatry Rep* 2001;3:314–8.
39. Isbell H, Fraser HF, Wikler A, Belleville RE, Eisenmen AJ. An experimental study of the etiology of rum fits and delirium tremens. *Q J Stud Alcohol* 1955;16:1–33.
40. Lishman, WA. *Organic psychiatry: the psychological consequences of cerebral disorder*: 2nd ed. Oxford (UK): Blackwell Scientific Publication; 1987.
41. Connell PH. *Amphetamine psychosis*. Maudsley monograph number 5. London (UK): Chapman and Hall, Ltd; 1958.
42. Bell, D. The experimental reproduction of amphetamine psychosis. *Arch Gen Psychiatry* 1973;29:35–40.
43. Angrist B, Sathananthan G, Wilk S, Gershon S. Amphetamine psychosis: behavioral and biochemical aspects. *J Psychiatr Res* 1974;11:13–23.
44. Curran C, Byrappa N, McBride A. Stimulant psychosis: systematic review. *Br J Psychiatry* 2004;185:196–204.
45. Hall W, Hando J. *Patterns of illicit psychostimulant use in Australia*. In: Burrows D, Flaherty BA, MacAvoy M, editors. *Psychostimulant use in Australia*. Canberra (AU): Australian Government Publishing Service; 1993.
46. Degenhardt L, Roxburgh A, McKetin R. Hospital stays for drug related psychotic episodes in Australia, 1993–2004. *Med J Aust*. Forthcoming.
47. Degenhardt L, Hall WD. The association between psychosis and problematic drug use among Australian adults: findings from the National Survey of Mental Health and Well-Being. *Psychol Med* 2001;31:659–68.
48. Klein DF. The flawed basis for FDA post-marketing safety decisions: the example of antidepressants and children. *Neuropsychopharmacology* 2006;31:689–99.
49. Dwyer T, Ponsonby AL, Blizzard L, Newman NM, Cochrane JA. The contribution of changes in the prevalence of prone sleeping position to the decline in sudden infant death syndrome in Tasmania. *JAMA* 1995;273:783–9.
50. Green B, Young R, Kavanagh D. Cannabis use and misuse prevalence among people with psychosis. *Br J Psychiatry* 2005;187:306–13.
51. Linszen DH, Dingemans PM, Lenior ME. Cannabis abuse and the course of recent-onset schizophrenic disorders. *Arch Gen Psychiatry* 1994;51:273–9.
52. Grech A, Van Os J, Jones PB, Lewis SW, Murray RM. Cannabis use and outcome of recent onset psychosis. *Eur Psychiatry* 2005;20:349–53.
53. Roffman R, Stephens RS. *Cannabis dependence: its nature, consequences and treatment*. Cambridge (UK): Cambridge University Press; 2006.
54. Budney AJ, Moore BA. Development and consequences of cannabis dependence. *J Clin Pharmacol* 2002;42:28S–33S.
55. Kavanagh DJ. An intervention for substance abuse in schizophrenia. *Behav Change* 1995;12:20–30.
56. Mueser KT, Bellack AS, Blanchard JJ. Comorbidity of schizophrenia and substance abuse: implications for treatment. *J Consult Clin Psychol* 1992;60:845–56.
57. Lehman AF, Herron JD, Schwartz RP, Myers CP. Rehabilitation for adults with severe mental illness and substance use disorders: a clinical trial. *J Nerv Ment Dis* 1993;181:86–90.
58. Jeffery DP, Ley A, McLaren S, Siegfried N. Psychosocial treatment programmes for people with both severe mental illness and substance misuse (Cochrane Review). *The Cochrane Library*: volume 1. Chichester (UK): John Wiley and Sons, Ltd; 2004. Available: www.mrw.interscience.wiley.com/cochrane/clsystrev/articles/CD001088/frame.html Accessed 2006 February 2.
59. Jerrrell J, Ridgely M. Comparative effectiveness of three approaches to serving people with severe mental illness and substance abuse disorder. *J Nerv Ment Dis* 1995;183:566–76.
60. Ujike H, Morita Y. New perspectives in the studies on endocannabinoid and cannabis: cannabinoid receptors and schizophrenia. *J Pharmacol Sci* 2004;96:376–81.
61. Hall W. The mental health risks of adolescent cannabis use. *PLoS Med* 2006;3:e39.
62. Patton GC, Coffey C, Carlin JB, Degenhardt L, Lynskey M, Hall W. Cannabis use and mental health in young people: cohort study. *BMJ* 2002;325:1195–8.
63. Caulkins J, Pacula RL, Paddock S, Chiesa J. What we can—and cannot—expect from school-based drug prevention. *Drug Alcohol Rev* 2004;23:79–87.
64. White D, Pitts M. Educating young people about drugs: a systematic review. *Addiction* 1998;93:1475–87.
65. Tobler N, Lessard T, Marshall D, Ochshorn P, Roona M. Effectiveness of school-based drug prevention programs for marijuana use. *Sch Psychol Int* 1999;20:105–37.
66. Gorman DM. On the difference between statistical and practical significance in school-based drug abuse prevention. *Drugs Educ Prev Policy* 1995;2:275–83.
67. Gorman DM. Etiological theories and the primary prevention of drug use. *J Drug Issues* 1996;26:505–20.
68. Hall W, Nelson J. Correlates of the perceived health risks of marijuana use among Australian adults. *Drug Alcohol Rev* 1996;15:137–43.
69. Toumbourou J, Williams J, Waters E, Patton G. What do we know about preventing drug-related harm through social developmental intervention with children and young people? In: Stockwell T, Gruenewald P, Toumbourou J, Loxely W, editors. *Preventing harmful substance use: the evidence base for policy and practice*. Chichester (UK): John Wiley and Sons Ltd; 2004. p 87–100.
70. Grier S, Bryant CA. Social marketing in public health. *Annu Rev Public Health* 2005;26:319–39.
71. McBride N. A systematic review of school drug education. *Health Educ Res* 2003;18:729–42.
72. Saha S, Chant D, Welham J, McGrath J. A systematic review of the prevalence of schizophrenia. *PLoS Med* 2005;5:e141.
73. Cresswell A, Kearney S. Weak drug laws linked to madness. *The Australian* 2005 October 29;Sect 1:All-round Country (p 1).

74. Hall W. The recent Australian debate about the prohibition on cannabis use. *Addiction* 1997;92:1109–15.
75. Hall W, Pacula RL. Cannabis use and dependence: policy health and public policy. London (UK): Cambridge University Press; 2003.
76. Donnelly N, Hall W, Christie P. Effects of the Cannabis Expiation Notice Scheme on levels and patterns of cannabis use in South Australia: evidence from the National Drug Strategy Household Surveys 1985-1995. Canberra (AU): Australian Government Publishing Service; 1999. National Drug Strategy Research Monograph nr 37.
77. Williams J. The effects of price and policy on marijuana use: what can be learned from the Australian experience? *Health Econ* 2004;13:123–37.
78. Single EW. The impact of marijuana decriminalization: an update. *J Public Health Policy* 1989;10:456–66.
79. MacCoun RJ, Reuter P. Drug war heresies: learning from other vices, times, and places. Cambridge (UK): Cambridge University Press; 2001.
80. Australian Institute of Health and Welfare. Statistics on drug use in Australia 2004. Canberra (AU): Australian Institute of Health and Welfare; 2005. cat no PHE 62.
81. Hall W, Swift W. The THC content of cannabis in Australia: evidence and implications. *Aust N Z J Public Health* 2000;24:503–8.
82. Glantz SA, Slade J, Bero LA, Hanauer P, Barnes DE. *The Cigarette Papers*. Berkeley (CA): University of California Press; 1996.

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Résumé : Quelles sont les implications politiques des données probantes sur le cannabis et la psychose?

Objectif : Explorer les implications des données probantes d'observation, selon lesquelles l'usage du cannabis est une cause concurrente de la psychose, pour les services de santé mentale, l'éducation sanitaire sur les risques de l'usage du cannabis, et les politiques publiques sur l'usage du cannabis.

Méthode : Nous avons examiné la relation entre les données probantes d'observation et l'action à l'aide d'analyses comparatives de données probantes semblables sur les effets nocifs de l'usage d'alcool, de tabac et d'amphétamines. Nous avons examiné les arguments, pour des raisons de prudence en santé publique, en faveur de décourager l'usage du cannabis chez les jeunes personnes. Selon l'hypothèse que la relation puisse être causale, nous avons examiné les recommandations de politiques des services de santé mentale, d'éducation sanitaire, et les politiques publiques sur l'usage du cannabis.

Résultats : Les données probantes d'observation et la plausibilité biologique de l'hypothèse selon laquelle le cannabis est une cause concurrente de la psychose sont au moins aussi fortes que les données probantes sur les relations causales entre la consommation excessive d'alcool et d'amphétamines et la psychose. Pour des motifs de santé publique, il y a de bonnes raisons de décourager l'usage du cannabis chez les adolescents et les jeunes adultes. Reste à définir la meilleure façon de décourager l'usage et qui cibler par des campagnes de réduction de l'usage du cannabis.

Conclusions : Nous devrions décourager les jeunes adultes qui suivent un traitement dans les services de santé mentale d'utiliser le cannabis et les informer des risques probables de l'usage du cannabis pour la santé mentale, surtout de l'usage précoce et fréquent. Nous devons user de prudence en assouplissant les lois sur le cannabis de manière qui puisse accroître l'accès des jeunes au cannabis, diminuer l'âge de leur premier usage ou augmenter la fréquence de leur usage du cannabis. Nous devrions envisager la faisabilité de réduire la disponibilité des produits de cannabis très puissants.