Addiction
FOR DEBATE
doi:10.1111/j.1360-0443.2009.02846.x

How ideology shapes the evidence and the policy: what do we know about cannabis use and what should we do?

John Macleod & Matthew Hickman

Department of Social Medicine, University of Bristol, Bristol, UK

ABSTRACT

In the United Kingdom, as in many places, cannabis use is considered substantially within a criminal justice rather than a public health paradigm with prevention policy embodied in the Misuse of Drugs Act. In 2002 the maximum custodial sentence tariff for cannabis possession under the Act was reduced from 5 to 2 years. Vigorous and vociferous public debate followed this decision, centred principally on the question of whether cannabis use caused schizophrenia. It was suggested that new and compelling evidence supporting this hypothesis had emerged since the re-classification decision was made, meaning that the decision should be reconsidered. The re-classification decision was reversed in 2008. We consider whether the strength of evidence on the psychological harms of cannabis has changed substantially and discuss the factors that may have influenced recent public discourse and policy decisions. We also consider evidence for other harms of cannabis use and public health implications of preventing cannabis use. We conclude that the strongest evidence of a possible causal relation between cannabis use and schizophrenia emerged more than 20 years ago and that the strength of more recent evidence may have been overstated—for a number of possible reasons. We also conclude that cannabis use is almost certainly harmful, mainly because of its intimate relation to tobacco use. The most rational policy on cannabis from a public health perspective would seem to be one able to achieve the benefit of reduced use in the population while minimizing social and other costs of the policy itself. Prohibition, whatever the sentence tariff associated with it, seems unlikely to fulfil these criteria.

Keywords Cannabis, evidence, public health, schizophrenia.

Correspondence to: Matthew Hickman, Department of Social Medicine, University of Bristol, Canynge Hall, Whatley Road, Bristol B58 2PS, UK.
E-mail: matthew.hickman@bristol.ac.uk
Submitted 16 July 2009; initial review completed 2 September 2009; final version accepted 19 October 2009

INTRODUCTION

Around half of adults in the United Kingdom (including the last Home Secretary) report that they have tried cannabis, with approximately a fifth of young adults reporting regular use [1,2]. Prohibition is the principal policy intended to prevent cannabis use in the United Kingdom. Use has been illegal since 1928 and until 2002 was considered within Class B of the 1971 Misuse of Drugs Act, a classification meaning that possession offences attract a maximum tariff of 5 years imprisonment (although in practice few convictions result in this disposal). In 2002, mainly in an attempt to re-focus criminal justice resources, cannabis was re-classified within class C, reducing the maximum custodial sentence for possession to 2 years. The sentence tariff for supply offences (up to 14 years imprisonment and/or an unlimited fine) is identical within classifications B and C [3]. A surprisingly vociferous public debate (considering the magnitude of this relatively minor legislative change) on the wisdom of re-classification then ensued, involving doctors and researchers, mental health lobby groups, pro- and anti-drugs campaigners, politicians and the police (e.g. BBC News, 5 February 2008: 'Cannabis Now Three Times Stronger', http://news.bbc.co.uk/1/hi/uk/7227651.stm; BBC panorama programme, 'Cannabis: What teenagers need to know', 19 June 2005, http://news.bbc.co.uk/1/hi/programmes/panorama/4082196.stm). At the centre of this debate was a single prominent health issue: whether or not cannabis use caused serious mental illness, in particular schizophrenia. To many it appeared self-evident that if the answer to this question was 'yes', then

cannabis use should be prohibited in the most vigorous terms and re-classification should be reversed. Data from several studies of associations between cannabis use and a range of psychological outcomes were published around this time and publicized widely [4–7]. Several commentators have presented these studies as representing a new, growing and increasingly compelling evidence base of the psychological harms of cannabis use (e.g. *Independent on Sunday*, 18 March 2007: leading article, 'Cannabis a retraction', http://www.independent.co.uk/opinion/leading-articles/leading-article-cannabis-a-retraction-440665.html). Indeed, to question the strength of the evidence that cannabis causes schizophrenia seems equivalent to some to encouraging the use of cannabis by young people (e.g. Melanie Phillips, 'The Cabinet's cannabis cabaret', *Daily Mail*, 23 July 2007, http://www.melaniephillips.com/articles-new/?p=526). Against this background of apparent widespread opposition to a 'softer' stance on cannabis use, the decision to re-classify cannabis was reversed in 2008 (http://www.homeoffice.gov.uk/drugs/drugs-law/cannabis-reclassification/.).

HARMS OF CANNABIS

The use of cannabis has long been thought to be associated with psychotic illness, and in the 1980s evidence emerged from Sweden of an association between cannabis use and hospitalization for schizophrenia among military conscripts [8]. This is still the only prospective general population study where a link between cannabis use and clinical schizophrenia (as opposed to reports of symptoms that may relate to risk of schizophrenia) has been demonstrated. In 2004 we published a systematic review of evidence from prospective observational studies on harms associated with illicit drug use by young people [9]. Most of this evidence related to cannabis use and showed a consistent, non-specific association between the most extreme category of cannabis exposure considered and a wide range of adverse psychosocial outcomes. The most common psychological outcomes considered in these studies were self-reports of unusual thought and perceptions ('psychotic symptoms') measured using various questionnaires. Unlike in the Swedish conscripts study, where records of admission to hospital with a diagnosis of schizophrenia were used as the study end-point, the relationship of these questionnaire reports to clinical outcomes is unknown. Our review included all the studies published by 2004 that met our inclusion criteria. We concluded that evidence for a causal basis for these associations was not strong and that many factors, including their non-specific nature, pointed to the probable influence of residual confounding and other types of bias. We also stated that it was possible that cannabis *did* cause schizophrenia and that the absence of strong evidence for this effect should not be seen as evidence of absence. Our review attracted the criticism that we may have overemphasized the limitations of observational research [10]. Our counter to this argument is that underestimation of these limitations in relation to several recent studies, much more methodologically robust than those relating cannabis use to psychosis, has led to some of the most important mistakes (and the health consequences of these mistakes) in recent epidemiological history [11,12].

There have now been several systematic reviews of this evidence base that between them have considered all the relevant prospective evidence published to date and that have come to conclusions very similar to our own [13,14]. That is, that a causal link between cannabis use and psychosis is one possible explanation for a relatively consistent association between the two. Where the reviews have differed is in the emphasis they have placed on the possibility of non-causal explanations [15,16].

We continue to take the view that evidence that cannabis use causes schizophrenia is neither very new nor, by normal criteria, particularly compelling. This question is important; schizophrenia is an enormously costly public health problem in both human and material terms [17]. Its causes are poorly understood, no effective prevention exists and treatment has limited effect. None the less, premature adoption of a particular aetiological hypothesis may narrow research and funding which may not be in the best interests of public health or individual patients. This is another lesson that past experience should have taught us. For instance, commitment to a psychological theory of the aetiology of peptic ulcer led to investment of vast resources in years of largely fruitless research effort to little public health benefit and distracted most researchers from discovery of the true physical cause of this once common disease and development of effective treatment [18].

However, the harmfulness (beyond reasonable doubt) of cannabis use should not be at issue [19]. Aside from the question of health risks of cannabis smoke alone [20,21], the relatively poor combustion properties of cannabis mean that to facilitate use through smoking (the most common means of ingestion), most people mix cannabis with tobacco [22]. This exposure to generally unfiltered tobacco smoke seems a clear and relatively unambiguous harm of cannabis use, albeit one that is difficult to quantify precisely [23]. Moreover, a proportion of cannabis users appear to become dependent upon the drug and seek help increasingly to overcome this addiction [24–26]. Why so many commentators have chosen to focus not on these harms, but on the issue of cannabis and schizophrenia, is an interesting question in itself. There are several possible answers.

OVERSTATEMENT OF THE EVIDENCE THAT CANNABIS CAUSES SCHIZOPHRENIA

It is a natural tendency of most researchers to overstate the strength of their own work in relation to their favourite causal hypotheses; this near-universal phenomenon among researchers is referred to generally as 'wish bias' [27]. Moreover, as we have stated above, schizophrenia is an important and poorly understood disease [17]. In fact, given this important disease burden and our relative lack of understanding of the processes that generate it, it might seem surprising that schizophrenia research does not feature more prominently on the funding agenda [28]. This may have led many with an interest in schizophrenia, whether academic, clinical or personal, to talk up any new (and old) evidence around possible aetiology. While this tendency is perfectly understandable, its potential drawbacks are those discussed above. A further consideration that may be relevant is that in the ongoing debate around drug control, anti-prohibition arguments have often been framed in terms of overstatement of the strength of evidence for the harmless nature of cannabis use. Possibly this has led those ideologically opposed to the anti-prohibitionist position to overstate evidence for cannabis harm.

Other factors may also have been important. Cannabis use is often associated with poorer treatment outcomes among psychotic and schizophrenic patients [29], and some clinicians may have taken this evidence of a possible influence on prognosis as providing further support for the hypothesized influence on incidence. Here we are not considering evidence for an influence of cannabis use on schizophrenia prognosis, although its interpretation is no less difficult than evidence of influence on aetiology. The important general epidemiological point, however, is that factors that influence disease aetiology are not necessarily the same as those that influence disease prognosis which is why, conventionally, they are considered separately.

Some studies around cannabis and psychosis seem to have caught the public imagination mainly because they appear to exemplify biological processes long assumed to be of general importance, albeit with little prior empirical support for this assumption. This is especially true for possible evidence of gene–environment interactions; the idea that risk of particular environmental exposures depends substantially upon whether an individual carries a particular 'disease susceptibility' gene. For example, some evidence suggested a possible interaction between early cannabis use and a variant of the catechol-o-methyl transferase gene on risk of psychotic symptoms [5,30]. Popular science documentaries in the United Kingdom have featured individuals undergoing genetic testing to see if they had the 'psychosis gene'—the implication being that if they did not, they could use cannabis with impunity. Other possible gene–environment interactions in the field of mental illness have been published recently —the most widely publicized and debated probably being the proposed interaction between the polymorphism in the serotonin transporter gene and stressful life events in relation to risk of depression [31]. Several leading geneticists and epidemiologists have argued that, rather than evidencing any substantive causal effects, these studies demonstrate many of the pitfalls around studying gene–environment interactions [32–36]. Concern has also been voiced that premature acceptance of the face validity of some of this evidence may have led to inappropriate and unhealthy changes in research funding policy [35].

ATTRIBUTABLE RISK AND IMPACT OF PREVENTION

The above arguments aside if, by way of a thought experiment, we assume that cannabis does cause schizophrenia, we can then estimate how much of schizophrenia is caused by cannabis using a simple calculation based on prevalence of cannabis use and relative risk of schizophrenia associated with use [1]. Some studies have done this and estimated attributable risks of around 50% [4]. Such estimates seem unlikely to be valid, as if the attributable risk was genuinely this high then we would expect to have seen increases in schizophrenia prevalence by now, which have not been apparent [37,3]. In contrast, if the attributable risk is around 10% then increases in schizophrenia prevalence would still be expected (unless decreases in some other cause of schizophrenia had mirrored increases in cannabis use) but may be too small to yet be detectable [1]. We can also, within the same assumptions around causality, estimate the number of people whose cannabis use we would need to modify to a specified extent to prevent one additional case of schizophrenia. For example, our recent modelling suggests that we would need to prevent between 3000 and 5000 cases of heavy cannabis use among young men and women to prevent one case of schizophrenia and that four or five times more young people would need to avoid light cannabis use to prevent a single schizophrenia case [38]. Modelling is an inexact science, but this gives a picture of the realism of the aspiration of schizophrenia prevention based upon prevention of cannabis use. This aspiration should also be viewed in the context of evidence for the effectiveness of interventions intended to prevent cannabis use by young people. To date these appear to have, at best, modest effects. To be clear, what we are suggesting is *not* that prevention of cannabis use is pointless. Rather, based on available evidence, even if cannabis use does

cause schizophrenia, prevention of schizophrenia is unlikely to be the main objective motivating our cannabis prevention efforts.

EVIDENCE-BASED POLICY

In our view, the main reason to prevent cannabis use is to prevent young people smoking the tobacco they smoke typically with cannabis and whose continued use appears to be reinforced by their use of cannabis [39]. Further, preventing cannabis dependence is an important goal; and as long as cannabis use continues to be prohibited, preventing the criminalization of young people is also desirable. These appear to be the most tangible benefits of cannabis prevention policy and any policy option should be judged on evidence regarding how effectively it achieves these benefits compared to what it costs in human and social terms. Current policy is based upon prohibition and the question of whether this is embodied within class B as opposed to C of the relevant legislation is, in our view, a minor issue. The only important possible benefit of prohibition is prevention of cannabis use. There is little or no evidence that it effectively achieves this benefit. Patterns of cannabis use in the population appear to be independent of the policy surrounding use, and criminalizing individual cannabis users does not appear to modify their use in a healthy way [40,41].

OPTIONS FOR CHANGE

There have been several useful suggestions as to how we might begin to move towards an evidence-based cannabis policy considering all the relevant costs and benefits [26]. In our view, cannabis use should be reframed as a public health rather than criminal justice issue, and the important public health goal of prevention should be pursued within the same paradigm as is applied currently to the two substances that cause the most public health harm: tobacco and alcohol. This suggestion is, of course, neither radical nor new, and currently there appears little enthusiasm among politicians with elections on their minds to act on it. This should not lead us to avoid contentious questions while focusing debate upon politically safer issues.

Cannabis use might cause schizophrenia but, until we have better evidence, it is impossible to know whether it does and in our view jumping to premature conclusions does not help. We already know, however, that cannabis use is almost certainly harmful, that our main policy to reduce this harm in the United Kingdom seems not to be working and that the policy itself generates considerable material and social costs. Given that this is what we know, the question remains as to what we are going to do.

Declarations of interest

None.

References

1. Hickman M., Vickerman P., Macleod J., Kirkbride J., Jones P. B. Cannabis and schizophrenia: model projections of the impact of the rise in cannabis use on historical and future trends in schizophrenia in England and Wales. *Addiction* 2007; **102**: 597–606.
2. Aust R., Sharp C., Goulden C. *Prevalence of Drug Use: Key Findings from the 2001/2002 British Crime Survey*. Findings 182.London: Home Office; 2002.
3. Advisory Council on the Misuse of Drugs. *Cannabis: Classification and Public Health*. London: Advisory Council on the Misuse of Drugs; 2008. Available from http://drugs.homeoffice.gov.uk/publication-search/acmd/acmd-cannabis-report-2008 (accessed 26 November 2009)
4. van Os J., Bak M., Hanssen M., Bijl R. V., de Graaf R., Verdoux H. Cannabis use and psychosis: a longitudinal population-based study. *Am J Epidemiol* 2002; **156**: 319–27.
5. Arseneault L., Cannon M., Poulton R., Murray R., Caspi A., Moffitt T. E. Cannabis use in adolescence and risk for adult psychosis: longitudinal prospective study. *BMJ* 2002; **325**: 1212–3.
6. Fergusson D. M., Horwood L. J., Swain-Campbell N. R. Cannabis dependence and psychotic symptoms in young people. *Psychol Med* 2003; **33**: 15–21.
7. Henquet C., Krabbendam L., Spauwen J., Kaplan C., Lieb R., Wittchen H. U. *et al.* Prospective cohort study of cannabis use, predisposition for psychosis, and psychotic symptoms in young people. *BMJ* 2005; **330**: 11.
8. Andréasson S., Allebeck P., Engström A., Rydberg U. Cannabis and schizophrenia: a longitudinal study of Swedish conscripts. *Lancet* 1987; **330**: 1483–6.
9. Macleod J., Oakes R., Copello A., Crome I., Egger M., Hickman M. *et al.* The psychosocial consequences of use of cannabis and other illicit drugs: systematic review of longitudinal, general population studies. *Lancet* 2004; **363**: 1579–88.
10. Hall W. Is cannabis use psychotogenic? *Lancet* 2006; **367**: 193–5.
11. Lawlor D. A., Davey S. G., Ebrahim S. Commentary. The hormone replacement–coronary heart disease conundrum: is this the death of observational epidemiology? *Int J Epidemiol* 2004; **33**: 464–7.
12. Petitti D. Commentary. Hormone replacement therapy and coronary heart disease: four lessons. *Int J Epidemiol* 2004; **33**: 461–3.
13. Moore T. H., Zammit S., Lingford-Hughes A., Barnes T. R., Jones P. B., Burke M. *et al.* Systematic review of cannabis use and risk of developing psychotic or affective mental health outcomes. *Lancet* 2007; **370**: 319–28.
14. Arseneault L., Cannon M., Witton J., Murray R. M. Causal association between cannabis and psychosis: examination of the evidence. *Br J Psychiatry* 2004; **184**: 110–7.
15. Iversen L. Long-term effects of exposure to cannabis. *Curr Opin Pharmacol* 2005; **5**: 69–72.
16. Macleod J., Davey S. G., Hickman M. Does cannabis use cause schizophrenia? *Lancet* 2006; **367**: 1055.
17. Murray R., Jones P., Susser E., van Os J., Cannon M. *The Epidemiology of Schizophrenia*. Cambridge: Cambridge University Press.

18. Marshall B. J., Warren J. R. Unidentified curved bacilli in the stomach of patients with gastritis and peptic ulceration. *Lancet* 1984; **1**: 1311–5.
19. Hall W., Pacula R. *Cannabis Use and Dependence: Public Health and Public Policy*. Melbourne: Cambridge University Press; 2003.
20. Hashibe M., Morgenstern H., Cui Y., Tashkin D. P., Zhang Z. F., Cozen W. *et al.* Marijuana use and the risk of lung and upper aerodigestive tract cancers: results of a population-based case–control study. *Cancer Epidemiol Biomarkers Prev* 2006; **15**: 1829–34.
21. Tashkin D. P. Does smoking marijuana increase the risk of chronic obstructive pulmonary disease? *Can Med Assoc J* 2009; **180**: 797–8.
22. Robertson J. R., Miller P., Anderson R. Cannabis use in the community. *Br J Gen Pract* 1996; **46**: 671–4.
23. Patton G. C., Coffey C., Carlin J. B., Sawyer S. M., Lynskey M. Reverse gateways? Frequent cannabis use as a predictor of tobacco initiation and nicotine dependence. *Addiction* 2005; **100**: 1518–25.
24. Office of National Statistics (ONS). Psychiatric Morbidity Among Adults Living in Private Households, 2000. http://www.statistics.gov.uk/downloads/theme_health/psychmorb.pdf (accessed 26 November 2009).
25. Nordstrom B. R., Levin F. R. Treatment of cannabis use disorders: a review of the literature. *Am J Addict* 2007; **16**: 331–42.
26. Hall W. D. The contribution of research to the development of a national cannabis policy in Australia. *Addiction* 2008; **103**: 712–20.
27. Wynder E. L., Higgins I. T., Harris R. E. The wish bias. *J Clin Epidemiol* 1990; **43**: 619–21.
28. 1st European Conference on Schizophrenia Research—Perspectives from European Networks, September 2007, Germany. *Eur Arch Psychiatry Clin Neurosci* 2007; **257**: 1–40.
29. Linszen D. H., Dingemans P. M., Lenior M. E. Cannabis abuse and the course of recent-onset schizophrenic disorders. *Arch Gen Psychiatry* 1994; **51**: 273–9.
30. Caspi A., Moffitt T. E., Cannon M., McClay J., Murray R., Harrington H. *et al.* 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.
31. Caspi A., Sugden K., Moffitt T. E., Taylor A., Craig I. W., Harrington H. *et al.* Influence of life stress on depression: moderation by a polymorphism in the 5-HTT gene. *Science* 2003; **301**: 386–9.
32. Munafo M. R., Bowes L., Clark T. G., Flint J. Lack of association of the COMT (Val158/108 Met) gene and schizophrenia: a meta-analysis of case–control studies. *Mol Psychiatry* 2005; **10**: 765–70.
33. Munafo M. R., Durrant C., Lewis G., Flint J. Gene–environment interactions at the serotonin transporter locus. *Biol Psychiatry* 2009; **65**: 211–9.
34. Zammit S., Spurlock G., Williams H., Norton N., Williams N., O'Donovan M. C. *et al.* Genotype effects of CHRNA7, CNR1 and COMT in schizophrenia: interactions with tobacco and cannabis use. *Br J Psychiatry* 2007; **191**: 402–7.
35. Risch N., Herrell R., Lehner T., Liang K. Y., Eaves L., Hoh J. *et al.* Interaction between the serotonin transporter gene (5-HTTLPR), stressful life events, and risk of depression: a meta-analysis. *JAMA* 2009; **301**: 2462–71.
36. Zammit S., Owen M. J. Stressful life events, 5-HTT genotype and risk of depression. *Br J Psychiatry* 2006; **188**: 199–201.
37. Degenhardt L., Hall W., Lynskey M. Testing hypotheses about the relationship between cannabis use and psychosis. *Drug Alcohol Depend* 2003; **71**: 37–48.
38. Hickman M., Vickerman P., Macleod J., Lewis G., Zammit S., Kirkbride J. *et al.* If cannabis caused schizophrenia—how many cannabis users may need to be prevented in order to prevent one case of schizophrenia? England and Wales calculations. *Addiction* 2009; **104**: 1856–61.
39. Amos A., Wiltshire S., Bostock Y., Haw S., McNeill A. You can't go without a fag . . . you need it for your hash—a qualitative exploration of smoking, cannabis and young people. *Addiction* 2004; **99**: 77–81.
40. Fergusson D. M., Swain-Campbell N. R., Horwood L. J. Arrests and convictions for cannabis related offences in a New Zealand birth cohort. *Drug Alcohol Depend* 2003; **70**: 53–63.
41. Reinarman C., Cohen P. D., Kaal H. L. The limited relevance of drug policy: cannabis in Amsterdam and in San Francisco. *Am J Public Health* 2004; **94**: 836–42.