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COMMENTARY

Cannabis use and symptom experience amongst people with mental illness: a commentary on Degenhardt *et al.*

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A high proportion of people who have a serious mental illness also use non-prescribed psychoactive drugs. This association is perhaps most apparent, and possibly also has the greatest implications for health, in relation to tobacco use. In fact recognition of the special relationship between mental illness and smoking was recently reflected in exemption of psychiatric units from legislation to ban smoking in enclosed public spaces in the UK (UK Smoking Law Resource Centre, 2007). The prevalence of tobacco use has generally decreased in most European, North American and Australasian countries, however, use of other psychoactive drugs, has not followed this pattern (Advisory Council on the Misuse of Drugs, 2006). Cannabis use in particular is widespread, both in the general population but especially so amongst people with serious and enduring mental illness, particularly psychotic illness. Recognition of the particular coincidence of cannabis use with psychotic illness amongst psychiatric patients was one of the observations that precipitated current debate around the possible aetiological role of cannabis use in relation to incidence of schizophrenia (Thornicroft, 1990; Hall, 2006; Macleod *et al.* 2006).

This debate continues and, as with many other instances where policy and evidence collide, sometimes may be informed more by ideological than scientific considerations (Strang *et al.* 2000; Davey Smith *et al.* 2001). However, aside from the question of the effect of cannabis use on the incidence of schizophrenic – or more broadly psychotic – illness there is the other important issue of its effect on clinical course and prognosis of established disease. It is this latter issue that is the focus of the study by Louisa Degenhardt and colleagues in this issue of *Psychological Medicine* (Degenhardt *et al.* 2007). More specifically, Degenhardt and co-workers considered a particular question; amongst people with established psychotic illness who also use cannabis what is the temporal association between cannabis use and illness symptoms? They found clear evidence that use of cannabis was associated with a subsequent increase in psychotic symptoms. Cannabis use was also associated with increased depressive symptoms, although this latter association was weaker ($p=0{\cdot}07$, compared to $p=0{\cdot}05$).

The authors' interest in the questions explored in their study relates, in part, to the 'reverse causality' explanation for the association between cannabis use and mental illness. This holds that causality runs more from psychosis to cannabis use than vice versa, perhaps because people with mental illness use cannabis to in some way ameliorate the unpleasant aspects of their illness experience. A simplistic representation of this hypothesis, but one testable in a prospective study, is to examine whether cannabis use appears to increase following increased symptom experience or whether symptoms increase following cannabis use amongst people with psychotic illness. The hypothesis is simplistic in the sense that cannabis use may provide other effects to users aside

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from those on psychotic (or depressive) symptoms. These effects might derive from the psychopharmacology of the drug itself or may be related more to the social milieu around use. It is also relevant that the ability of cannabis use to precipitate unusual thoughts and perceptions in users is not, generally, in question (Hall & Solowij, 1998). These effects are typically acute, that is they disappear on sustained abstinence from cannabis. However, regular cannabis users excrete detectable drug metabolites for up to a month after abstinence and 'acute' (i.e. self-limiting) psychoactive effects may also be apparent over a prolonged period (Hall & Solowij, 1998; Wolff *et al*. 1999). Degenhardt and colleagues are clear on this point in their paper; amongst their group of relatively regular cannabis users assessed regularly, all the effects seen may have been acute effects.

It might even be thought surprising if increased use of cannabis were not followed by increased psychotic symptoms – given this well-known acute effect of cannabis use. Nevertheless this study provides additional interesting evidence on the relation between cannabis use and mental state in people with mental illness. If such use genuinely reflected self-medication then one might predict that it would increase following periods where users felt worse. Instead, lower (rather than higher) depressive symptom scores at one assessment were associated with higher subsequent use of cannabis. Scores on the psychotic symptom scale showed a similar, albeit weaker, relation. Strikingly, current amphetamine use was strongly and relatively substantially associated with lower symptoms of depression. Clearly, psychotic and depressive symptoms are only one aspect of psychological, physical and social well-being but the suggestion from these data is that people with mental illness may use psychoactive drugs when they feel better rather than when they feel worse. As the authors assert, this does not seem in keeping with the simple self-medication hypothesis.

It is perhaps useful to consider wider evidence relating to this question and some of the general issues around interpreting associations between reports of cannabis use and reports of psychological symptoms in observational studies. If one wants to establish the primary direction of causality between mental illness and cannabis use then ideally, one needs to take a sample of people in which neither have occurred yet and follow-up these people to see which phenotype is apparent first. Evidence from the New Zealand birth cohorts, the studies that to date have published the most relevant data on this question, clearly show that both children with psychological problems and those that report psychotic-like symptoms have a heightened risk of later reporting cannabis use (Fergusson *et al*. 1993; Arseneault *et al*. 2002). This has also been shown in older adolescents (Henquet *et al*. 2005). However, these pieces of evidence do not settle the issue. The fact that a child who reports psychotic-like symptoms at age 11 is more likely to report cannabis use at 15 or 18 does not mean that psychosis necessarily causes cannabis use. The other general sources of non-causal (even prospective) associations in observational epidemiology need to be considered (Davey Smith & Ebrahim, 2002). The first is measurement bias, where the apparent association between two things is spurious and merely reflects the way this association was studied. It is not impossible that some people who are more (or less) inclined to talk about their experience of odd thoughts and perceptions are also more (or less) inclined to report cannabis use (Macleod *et al*. 2005). The problem is possibly more serious in relation to associations between cannabis use and other outcomes more obviously subject to notions of social desirability – antisocial behaviour for example. However, there has perhaps been a general reluctance to acknowledge the possibility that reporting bias may be as much of an issue in the epidemiology of drug use as it is in other areas of epidemiology (Macleod *et al*. 2002, 2005). Possibly this reluctance relates to the widespread reliance on uncorroborated self-report in the field, or to the feeling that suggestions of reporting bias question the truthfulness of young people's accounts or even to a belief that objective alternative measures of acceptable validity are not available. It is also true that reporting bias of this nature is probably less of an issue in studies of psychiatric patients where drug use and talking about symptoms are more commonplace, compared to the situation in general population studies.

Confounding is usually the most serious source of causal misattribution in observational

epidemiology (Davey Smith & Ebrahim, 2002). Taking the example of the association between psychotic symptoms in childhood and cannabis use in adolescence, this may arise because both of these outcomes have common antecedents – possibly lying in early life disadvantage. Degenhardt and colleagues took considerable care to adjust for obvious potential confounders of the association between cannabis use and symptom experience in their study. The well-known limitations of statistical adjustment aside (Phillips & Davey Smith, 1991), there is no strong suspicion that the symptom increases they observed following increased cannabis use were a product of confounding by any measured factor. Nevertheless, it is important to remember that the only reliable way to fully address this question is through random allocation of exposure status in an experimental design, or alternatively to use an instrumental variable that re-creates this condition (Davey Smith & Ebrahim, 2002).

Given these difficulties inherent in quantitative observational studies of cannabis use and its relation to mental state some may be tempted to suggest that qualitative research is needed to tease out the processes underlying this complicated picture. A small number of studies, recently reviewed, have asked people with psychosis who also use drugs (including cannabis) their reasons for drug use (Gregg *et al.* 2007) Social reasons were most frequently cited along with the pursuit of intoxication as a relief from dysphoria. Conscious attempts to alleviate psychotic symptoms were cited less often. Personal accounts of lived experience may be valuable in this context if, for example, they shed light on apparently paradoxical observations (such as why a substantial proportion of people with psychotic illness might choose to use a psychotogenic drug). Such value notwithstanding, however, qualitative studies can be misleading when attempting to clarify causal processes. Individuals may be well able to rationalize their experience but are not necessarily best placed to explain it. People with coronary heart disease, for example, often attribute a primary causal role for their illness to psychological stress, whereas other objective evidence suggests that the roots of their coronary pathology lie elsewhere (Macleod *et al.* 2002; Wainwright & Calnan, 2002).

What then are the implications of this paper, for our understanding of the relationship between cannabis use and mental health; for how we try to help people with mental illness who may choose to use cannabis and for the future research projects we might undertake? Issues of interpretation aside, Degenhardt and colleagues make the important point that the effects they observed were very small. A substantial change in cannabis use from no use to daily use was associated with an increased psychotic symptom score that was only 3% (2% in the adjusted model) of the possible total score. As with many symptom scales, translating such a change into clinical significance is very difficult. Given this apparently small effect, are we justified in trying to prevent or reduce cannabis use amongst our mentally ill patients – particularly since, rather than merely being a reflection of poor judgement, their cannabis use may afford them some perceived benefit?

In my view the answer to this question is 'yes'. The first point is that it is unfortunate that discussions of the health implications of cannabis use have become mired in the single issue of effects on psychotic symptoms. This is perhaps understandable; schizophrenia, in particular, is a dreadful illness that is substantially unexplained and ineffectively treated – small wonder therefore that any suggestion of a modifiable environmental cause attracts a certain amount of enthusiasm and 'wish bias' (Wynder *et al.* 1990). However, irrespective of the possibility that cannabis use may cause or exacerbate psychosis most users smoke cannabis with tobacco and their use of the former may both lead to and reinforce their use of the latter (Amos *et al.* 2004; Patton *et al.* 2005). The deleterious health consequences of tobacco use are well established. Add to this the fact that for most people in most places cannabis use will increase risk of criminalization and all its attendant health and social consequences. There is thus a strong case for advising and attempting to help people stop or reduce their cannabis use. This case is particularly strong amongst people with serious mental illness whose risk of physical health problems – especially cardiovascular disease – is high. A significant part of this heightened risk probably relates to drug use, particularly tobacco, use (Casey & Hansen, 2003; Hennekens *et al.* 2005). As acknowledged above, people

with mental illness may perceive benefits from their cannabis use – even if these are not readily apparent to health workers. However, this seems likely to be true, at least initially, in relation to use of any drug by any drug user. The justification for prevention therefore seems the same as it is in relation to any behaviour where increased risk of harm seems to outweigh any likely benefit.

This conclusion has direct implications for the future research agenda. Other than supporting Degenhardt and colleagues' call for bigger observational studies with better, more complete, more objective measures (along with the more imaginative use of instrumental variables) we also need experimental evaluations of preventive interventions. Like all preventive interventions these technologies should be cost-effective, acceptable to the people receiving them and should cause more net good than harm. We need such studies both in the general population and in populations of people with mental illness. Through this approach we can clarify the best ways to help people generally, and people with mental illness particularly to reduce their use of cannabis and other drugs. Moreover, by utilizing the power of the experimental design to overcome confounding we can further our understanding of the true basis of the association between cannabis use and psychosis.

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Declaration of Interest

None.

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