Cannabis use and the mental health of young people

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Objective: To review the evidence on the mental health and psychosocial consequences of rising rates of cannabis use among young people in developed countries.
Method: This paper critically reviews epidemiological evidence on the following psychosocial consequences of adolescent cannabis use: cannabis dependence; the use of heroin and cocaine; educational underachievement; and psychosis. Leading electronic databases such as PubMed have been searched to identify large-scale longitudinal studies of representative samples of adolescents and young adults conducted in developed societies over the past 20 years.
Results: Cannabis is a drug of dependence, the risk of which increases with decreasing age of initiation. Cannabis dependence in young people predicts increased risks of using other illicit drugs, underperforming in school, and reporting psychotic symptoms. Uncertainty remains about which of these relationships are causal although the evidence is growing that cannabis is a contributory cause of psychotic symptoms.
Conclusions: We face major challenges in communicating with young people about the most probable risks of cannabis use (dependence, educational underachievement and psychosis) given uncertainties about these risks and polarized community views about the policies that should be adopted to reduce them.
Key words: adolescence, cannabis use, dependence, marijuana smoking, psychosis.

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Cannabis is a relatively 'new' recreational drug that first began to be used by large numbers of young people in developed societies in the early 1970s. In the subsequent 30 years the proportion of young people who have used cannabis has steadily increased while the age of first use has declined [1]. Typically, cannabis use begins in mid-adolescence [1], an important psychosocial transition when misadventures can have potentially large adverse effects on a young person's life chances. Considerable community concern about adolescent cannabis use has been prompted by associations between cannabis use and the use of other more hazardous illicit drugs such as heroin and cocaine [2], poor educational outcomes [3] and psychosis [1].

This paper critically reviews epidemiological evidence to answer the following questions about the psychosocial consequences of adolescent cannabis use: Is there a cannabis dependence syndrome? Is cannabis a 'gateway drug' to the use of heroin and cocaine? What role does cannabis use play in educational underachievement? What role does cannabis use play in the precipitation and exacerbation of psychosis?

Leading electronic databases such as PubMed have been searched using combinations of the following key search terms: cannabis use; marijuana abuse; marijuana smoking; dependence; adolescence; mental health; psychosis; schizophrenia; educational outcomes; and the gateway hypothesis. Earlier papers cited in articles identified in these databases were also collected. A preference has been given to reviewing large-scale longitudinal

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studies of representative samples of adolescents and young adults conducted in developed societies over the past 20 years. Only the most important of these individual studies are cited; readers are referred to recent reviews for more detailed evidence. Selected references from monographs, edited works, and technical reports on longitudinal studies on drug use, adolescent problem behaviour, and trends in cannabis potency are also included.

Challenges in assessing the health effects of cannabis

To assess whether these adverse health effects are causally related to cannabis use we need longitudinal studies of the developmental effects of cannabis and other drug use in adolescence on psychosocial outcomes in young adulthood. These studies need to address the fact that young people who use cannabis differ from their peers in various ways, particularly in their use of alcohol, tobacco and other illicit drugs, and in their personal characteristics (e.g. parental characteristics, impulsivity, academic performance, antisocial traits etc.), which increases their likelihood of experiencing many of the adverse outcomes that have been attributed to cannabis use [4].

This paper reviews evidence from longitudinal studies on the most important of the harms attributed to cannabis use: cannabis dependence; whether cannabis is a 'gateway drug' to the use of heroin and cocaine; what role cannabis plays in educational underachievement; and the role that cannabis plays in the precipitation of psychosis.

Cannabis dependence

For much of the 1960s and 1970s cannabis was not regarded as a drug of dependence because it did not seem to produce a withdrawal syndrome like that seen in alcohol and opioid dependence. Scepticism has declined as: the number of people requesting help to stop using cannabis has increased [1]; evidence has emerged that animals and humans develop tolerance to the effects of delta-9-tetrahydrocannabinol (THC) [5–9]; and observational studies of regular users have described a cannabis withdrawal syndrome that includes anxiety, insomnia, appetite disturbance and depression [10–13].

Epidemiological studies of cannabis dependence

In epidemiological studies conducted in the US in the early 1980s [14] and 1990s [15] approximately 4% of the US population met DSM-III criteria for cannabis abuse or dependence at some time in their lives. Surveys using similar methods in Australia, Canada and New Zealand have produced similar estimates of cannabis abuse and dependence [16–19]. The risk of developing dependence is approximately one in 10 for those who have ever used cannabis [15] and perhaps as high as one in two for daily users [20]. The risk is higher for people with a history of poor academic achievement, deviant behaviour in childhood and adolescence, nonconformity and rebelliousness, personal distress and maladjustment, poor parental relationships, and a parental history of drug and alcohol problems [21–24].

Only a minority of those who meet criteria for cannabis dependence in community surveys report seeking treatment. But among the minority of dependent users who do seek help after failing to quit unassisted [25,26], many report cognitive, mood and motivational impairments that interfere with work performance [10,25]. Cannabis-dependent adolescents [27] in substance abuse treatment services also report withdrawal symptoms [27,28].

Evaluations [10,11,25] of psychological interventions for cannabis dependence report abstinence rates of 20–40% at the end of treatment, with substantial rates of relapse thereafter [25]. Nonetheless, treatment substantially reduces use and problems among those who do not succeed in quitting, an outcome that is similar to that for treatment for dependence on alcohol and other substances [25].

Is cannabis a gateway drug?

Surveys of adolescent drug use in the US and elsewhere over the past 30 years have consistently shown the following relationships between cannabis use and the use of other illicit drugs, such as heroin and cocaine [29].

First, most American adolescents who have tried cocaine and heroin have first used alcohol, tobacco and cannabis in that order [30,31]. Second, regular cannabis users are most likely to use heroin and cocaine [32,33]. Third, those who began to use alcohol and tobacco at an early age were the most likely to use cannabis and early cannabis users were, in turn, more likely to use hallucinogens and 'pills' (amphetamines and tranquillizers), cocaine and heroin [31,32,34,35].

Three explanations are often suggested of these patterns: (i) that users of cannabis are more likely to use other illicit drugs because they obtain cannabis from the same black market and hence have more opportunities to use other illicit drugs; (ii) that those who use cannabis at an early age are more likely for other reasons to use other illicit drugs; and (iii) that the pharmacological effects of cannabis increase an adolescent's propensity to use other illicit drugs.

The social environmental hypothesis

There is evidence that cannabis users have more opportunities to use other illicit drugs [36,37]. Wagner and Anthony [38] found that young cannabis users were much more likely to report an opportunity to use cocaine and reported these opportunities at an earlier age. Fergusson and Horwood [39] found that affiliating with peers who used these drugs predicted an increased risk of using them but it did not wholly explain the relationship between cannabis and other illicit drug use.

Is the gateway pattern explained by personal propensities to use drugs?

The association between regular cannabis use and the use of other illicit drugs could also arise from the selective recruitment into early cannabis use of socially deviant young people who have a high likelihood of using cocaine and heroin [39]. The observed sequence of drug involvement, on this hypothesis, would simply reflect the availability and societal disapproval of the different drugs [34], and cannabis and heroin use would be common consequences of pre-existing propensities to use drugs [40,41].

The selective recruitment hypothesis is supported by substantial correlations between nonconforming adolescent behaviours, such as, dropping out of high school, delinquency, and early alcohol and illicit drug use [42,43] and the fact that regular cannabis users are more likely than their peers to report these behaviours [21,22,24,44–47]. A simulation study has also provided support for the common cause hypothesis. Morral *et al.* [29] showed by means of computer modelling of a population of young adults that a common cause model would reproduce all three relationships between cannabis and other illicit drug use described above.

The selective recruitment hypothesis has been tested in longitudinal studies by assessing whether cannabis use predicts the use of heroin and cocaine after statistically controlling for differences between cannabis users and non-users in personal characteristics that preceded their cannabis use [39]. In one of the earliest such studies, Yamaguchi and Kandel [48] found that the relationship between cannabis use and 'harder' illicit drug use was reduced but still persisted after statistically controlling for pre-existing adolescent behaviours and attitudes, interpersonal factors and the age of initiation into drug use [48]. Fergusson and colleagues have more comprehensively tested the hypothesis in a prospective study of 990 New Zealand children who were followed from birth to age 21 years [37,39]. Fergusson and Horwood [39] found a dose–response relationship between the frequency of cannabis use by age 16 and problem use of cannabis, alcohol and other substances by age 18. Adjustment for family and personal differences between users and non-users substantially reduced but did not eliminate the relationships between early cannabis use and the use of other illicit drugs. Fergusson and Horwood [39] and Fergusson *et al.* [2] reported similar results in a subsequent follow-up of this birth cohort [39].

Is there a shared genetic vulnerability to drug dependence?

Twin studies suggest that the association between cannabis and other illicit drug use may be explained by a shared genetic contribution to dependence on alcohol, cannabis, tobacco and other drugs [49]. Lynskey *et al.* [50] have recently used twin data to test this genetic explanation of the 'gateway' pattern. They examined the relationship between cannabis and other illicit drug use in 136 monozygotic and 175 dizygotic twin pairs in which one twin had, and the other twin had not, used cannabis before the age of 17 years. If the association is due to shared genetic vulnerability to dependence, then there should be no difference in the use of other illicit drugs between monozygotic twins who did and did not use cannabis before age 17. Lynskey *et al.* found that the twin who had used cannabis before age 17, was more likely to have used sedatives, hallucinogens, stimulants and opioids than their co-twin who had not. These relationships persisted after controlling for other non-shared environmental factors that predicted an increased risk of developing drug abuse or dependence.

Pharmacological explanations of the gateway pattern

Animal studies suggest a number of ways in which the pharmacological effects of regular cannabis use could predispose to the use of other illicit drugs by producing changes in the brain that sensitize users to the effects of other drugs [51]. Cannabis, cocaine, and heroin all act on the dopaminergic mediated 'reward centre' in the nucleus accumbens [52]. The cannabinoid and opioid systems in the brain interact with each other [53] and animal studies have also suggested that the self-administration of cannabinoids 'primes' animals to self-administer opioids [54,55]. The major uncertainty about the relevance of these animal studies to adolescent drug use is that these effects were produced by high doses of cannabinoids given intravenously. They may be most relevant to that minority of adolescents who expose themselves to very

high doses of THC by using cannabis on a daily basis from an early age [56].

The effects of delaying gateway drug use

If cannabis use somehow causes the use of other illicit drugs then delaying adolescent cannabis use should reduce the use of other illicit drugs [57]. There is some evidence that interventions that prevent or delay tobacco and alcohol use also reduce cannabis use [58] but no studies have so far been shown that delaying cannabis use reduces the use of other illicit drugs. It may be difficult to obtain such evidence because the most effective prevention programs produce very modest reductions in cannabis use and the rarity of other illicit drug use in representative samples of youth [59] means that very large sample sizes are needed to detect the small effects that modest delays in cannabis use may have on the use of other illicit drugs.

An overall evaluation of the gateway hypothesis

The strong association between regular and early cannabis use and other illicit drug use has persisted in studies that have controlled for potential common causes that may explain the association and animal studies provide some biological plausibility for a causal relationship between cannabis and other types of illicit drug use. Nonetheless, the role of cannabis in the pattern of illicit drug use remains controversial because it is difficult to exclude the hypothesis that it is due to the common characteristics of those who use cannabis and other drugs. The finding of a simulation study that supported the common causal explanation has to be weighed against a number of well-controlled longitudinal studies which suggest that selective recruitment to cannabis use does not wholly explain the association between cannabis use and the use of other illicit drugs; and a discordant twin study which suggests that shared genes and environment do not wholly explain the association.

Adolescent educational performance

A major parental concern is that adolescent cannabis use impairs educational performance and increases the risk of discontinuing education by interfering with learning [60]. Cross-sectional surveys typically find associations between cannabis use and poor educational attainment among school children and youth (see Lynskey and Hall [3] for a review). The simplest explanation is that cannabis use is one of the causes of poor educational performance [61]. A second possible explanation is that heavy cannabis use is a *consequence* of poor educational attainment. This is supported by evidence that poor school performance is a risk factor for cannabis use [47,62–65]. These two hypotheses could both be true [66] if poor school performance increases the risks of using cannabis, which in turn worsens school performance. A third hypothesis is that cannabis use and poor educational attainment are reflections of common factors that increase the risk of both early cannabis use and poor educational performance (e.g. ADHD, externalizing disorders, cognitive impairment). This hypothesis is supported by the fact that the risk factors and life pathways for early cannabis use overlap with those for poor educational performance [47,67,68].

These explanations can only be distinguished in prospective studies of young people [4,69] that can provide answers to the question: do young people who use cannabis have poorer educational outcomes than those who do not, when we allow for the fact that cannabis users are more likely to have a history of poor school performance and other characteristics before they used cannabis?

Longitudinal studies have generally shown that early cannabis use predicts early school leaving. The hypothesis that cannabis use is a cause of poor educational performance has been supported by the persistence of the relationship after statistically controlling for differences between cannabis users and non-users [41,62,66,70–72]. It seems probable that the impaired educational performance of adolescent cannabis users is attributable to a combination of pre-existing poor educational attainment, acute cognitive impairment from cannabis intoxication, affiliation with peers who reject school, and early transitions to adulthood without adequate preparation [3].

Cannabis use and psychosis

Cannabis use and psychotic symptoms and disorders are associated in the general population [73–75] and in clinical populations [76–80]. The major hypotheses offered to explain this association have been: (i) that cannabis use precipitates schizophrenia in people who are otherwise vulnerable to the disorder; (ii) cannabis use is a form of self-medication for schizophrenia; and (iii) that the association arises from uncontrolled residual confounding by variables that predict an increased risk of cannabis use and of schizophrenia [4,81,82].

The Swedish conscript study

The earliest evidence that cannabis use may precipitate schizophrenia came from a 15-year prospective study

of 50 465 Swedish conscripts [83]. Andreasson *et al*. found a dose–response relationship between the risk of schizophrenia and the number of times cannabis reportedly had been used by age 18. These risks were reduced after statistical adjustment for potentially confounding variables (a psychiatric diagnosis at age 18, and parental divorce) but the relationships remained statistically significant.

Zammit *et al*. [84] followed the Swedish cohort study over a 27-year period and improved on the earlier study by providing more complete coverage of cases in the register and better statistical control of confounding variables, that included other drug use, IQ, and social integration. They also found a dose–response relationship between the frequency of cannabis use at age 18 and the risk of schizophrenia during the 27-year follow-up that persisted after statistically controlling for the effects of potential confounding factors. The authors estimated that 13% of cases of schizophrenia would be averted if cannabis use were prevented.

van Os *et al*. supported Zammit *et al*.'s findings in a 3-year longitudinal study of a community sample of 4848 young people in the Netherlands [85]. van Os *et al*. found that cannabis use at baseline predicted an increased risk of psychotic symptoms during the follow-up period in individuals who had not reported symptoms at baseline. There was a dose–response relationship between frequency of cannabis use at baseline and risk of psychotic symptoms during the follow-up. These relationships persisted when they statistically controlled for the effects of other drug use. The relationship between cannabis use and psychotic symptoms was stronger for cases with more severe psychotic symptoms. People who reported psychotic symptoms at baseline were also more likely to develop schizophrenia if they used cannabis than were individuals who did not. van Os *et al*. estimated the attributable risk of cannabis to psychosis at 13% for psychotic symptoms and 50% for cases with psychotic disorders that required psychiatric treatment.

Henquet *et al*. [86] substantially replicated the results of the Swedish and Dutch studies in a 4-year follow-up of a cohort of 2437 German adolescents and young adults between 1995 and 1999. They found a dose–response relationship between self-reported cannabis use at baseline and the likelihood of reporting psychotic symptoms. Young people who reported psychotic symptoms at baseline were much more likely to experience psychotic symptoms at follow-up if they used cannabis than cannabis-using peers with no such history.

The results of the European cohort studies have been confirmed in two smaller New Zealand birth cohorts. Arseneault *et al*. [87] found a relationship between cannabis use by age 15 and an increased risk of psychotic symptoms by age 26 in a prospective study of a New Zealand birth cohort (n = 759). Fergusson *et al*. [88] have reported a longitudinal study of the relationship between cannabis dependence at age 18 and the number of psychotic symptoms reported at age 21 in the Christchurch birth cohort in New Zealand. Fergusson *et al*. adjusted for a large number of potential confounding variables and found that cannabis dependence at age 18 predicted an increased risk of psychotic symptoms at age 21 years (RR of 2.3). This association was smaller but still significant after adjustment for potential confounders (RR of 1.8).

The self-medication hypothesis

The self-medication hypothesis was not supported in the van Os or Henquet studies. Neither found that early psychotic symptoms predicted an increased risk of using cannabis (as the hypothesis requires). Their negative results were supported by Verdoux *et al*. [89] who examined the temporal relationship between cannabis use and psychotic symptoms using an experience sampling method in 79 college students over 7 consecutive days. Verdoux *et al*. found that users reported more unusual perceptions after cannabis use and there was no relationship between reporting unusual experiences and using cannabis, as would be expected if self-medication explained the relationship between cannabis use and psychosis. This evidence does not rule out the possibility that people with psychosis use cannabis to control some of their symptoms or improve their mood but it makes it unlikely that self-medication wholly explains the relationship between cannabis use and psychosis.

Summary

Different studies have used different ways of assessing cannabis use and psychotic symptoms; few studies have assessed psychosis using diagnostic criteria, or attempted to distinguish between schizophrenia and affective psychoses. Despite the heterogeneity of methods and definitions of psychosis, there is reasonably consistent evidence from prospective studies that frequent cannabis use predicts an increased risk of psychotic symptoms and psychosis that is not explained by potential confounders such as other drug use. The relationship has also been stronger in people who have a personal or family history of schizophrenia which one recent study suggests may be explained by an interaction between a genetic vulnerability to psychosis and cannabis use [87,89,90].

A casual relationship has some biological plausibility in that the cannabinoid and dopaminergic neurotransmitter systems interact in animals; a provocation study has shown that THC produces a dose-dependent increase in psychotic symptoms under double-blind placebo conditions [91]; and Caspi *et al.* [92] have shown an interaction between an allele of the catechol-o-methyltransferase and psychotogenic effects of cannabis. The detailed nature of any relationship between cannabis use and psychosis awaits further research.

The issue of cannabis potency

It is sometimes claimed that cannabis now is a 'different drug' from that used in the 1970s and early 1980s [93,94]. The US is the only country that has analysed the THC content of cannabis products over the past three decades. These data show an increase in THC content from 1.5% in the early 1970s to 3.3% in the mid-1980s to 4.4% in 1998 [95,96].

The increase in average THC content has overshadowed another important determinant of exposure to THC, a sharp decline in the age of initiation of cannabis use between 1970 and 2000, and a consequent increase in rates of regular cannabis use (see [1], chapter 10). These changes in patterns of use have increased both the amount of THC consumed, and the duration of such consumption, among adolescent cannabis users [93], thereby increasing their risk of dependence, poor educational performance and psychotic symptoms.

Summing up

Adolescent cannabis users can become dependent on cannabis. The risk is lower than that for alcohol, nicotine and opiates but 10% is not trivial and the risk is higher for young people who start at a younger age.

Young people who become dependent on cannabis are at increased risk of using other illicit drugs, performing poorly at school and leaving early without completing qualifications, and experiencing psychotic symptoms. It remains controversial which of these associations between regular cannabis use and adverse outcomes are causal. The most controversial relationship is that between the regular use of cannabis and the use of other illicit drugs where the choice is between a common causal explanation (whether due to shared personal characteristics, shared environments or shared genes or combinations thereof) and a causal explanation in terms of either drug markets or the pharmacological effects of cannabis. The evidence for a causal relationship is stronger for educational underachievement and the risk of psychotic symptoms. A number of longitudinal studies have found that these relationships persist when controlling for plausible confounding variables and both relationships are biologically plausible in that cannabis intoxication acutely impairs cognitive function and increases psychotic symptoms, especially in people with a personal history of such symptoms. Confidence in a causal relationship will increase as larger and better-controlled longitudinal studies are reported on these relationships.

These findings raise a major challenge for health education of young people about the risks of cannabis use. Arguably, we have a moral obligation to alert young people to these risks. The major challenge will be in finding effective ways of communicating with young people about the most probable psychosocial harms of cannabis use (dependence, educational underachievement and psychosis) given the continuing debate about the causal interpretation of these risks and polarized community views about whether we should continue to criminalize cannabis use [1].

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