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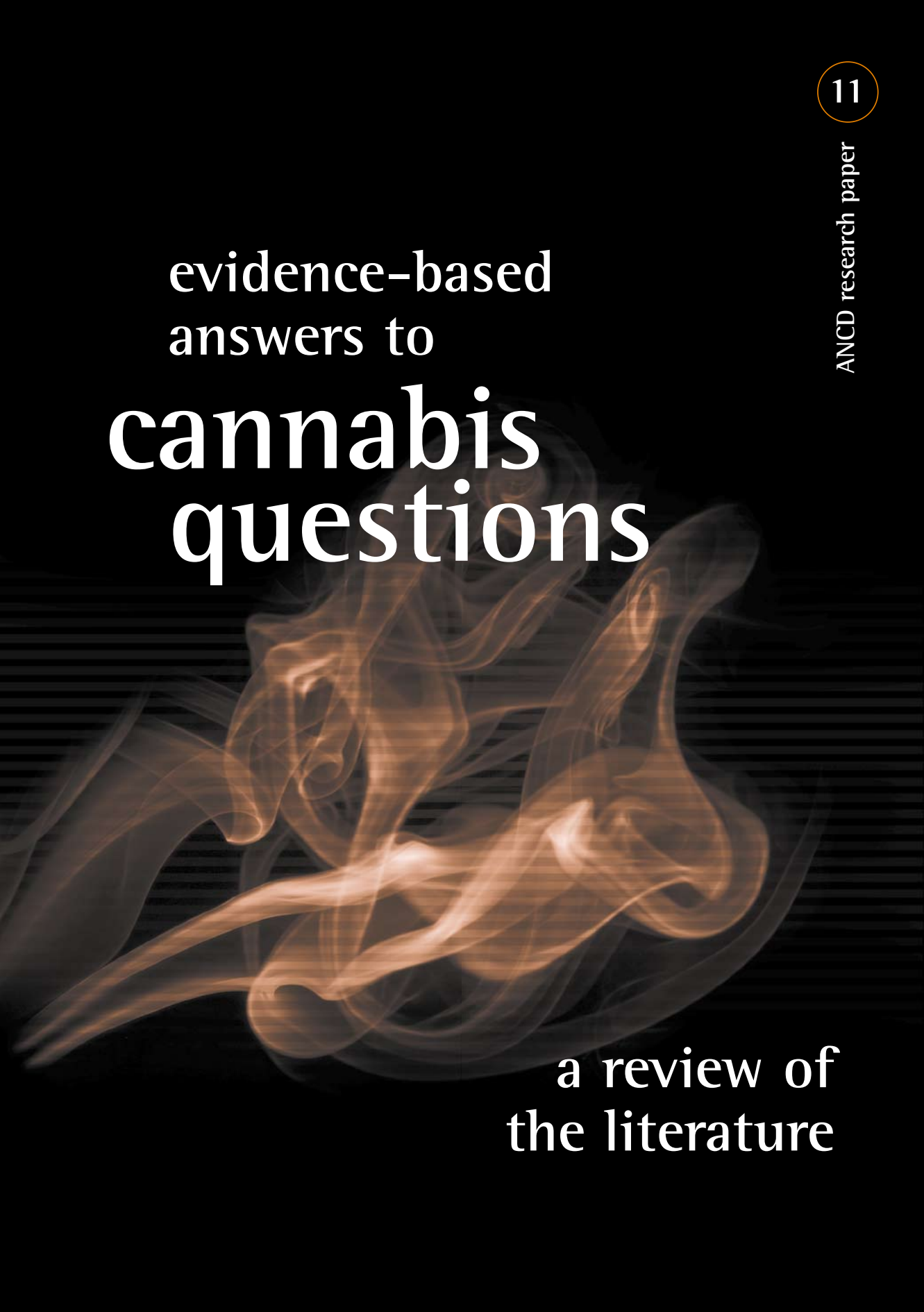
ANCD research paper

evidence-based answers to cannabis questions



a review of the literature

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evidence-based answers to cannabis questions

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Contents

Preamble

This brief review of the evidence answering key questions in relation to cannabis was commissioned by the Australian National Council on Drugs for an audience including media, politicians and their advisers, the alcohol and other drugs sector, and interested members of the community. This review of the current research and clinical literature reflects the status of the evidence to November 2004 and is supported by an even briefer 'plain English' version.

While the cannabis plant has been used both medicinally and recreationally for thousands of years, it was not until the early 19th century that the use of cannabis spread from China and the Middle East to the population of Europe. Widespread cannabis use emerged in Australia in the early 1970s and has been increasing since then. Today, cannabis remains the most commonly used illicit drug in Australia with an estimated five million people aged over 14 years having tried the drug. Typically, people begin using cannabis in their late teens or early twenties; thereafter, use steadily decreases. Most cannabis use is experimental or intermittent. However, it has been estimated that around one in ten people who try cannabis become dependent on it.

The literature on the health and psychosocial effects of cannabis has been reviewed according to the standard criteria for causal inference. These are:

- evidence that there is a relationship between cannabis use and a health outcome provided by one of the accepted types of research design (namely, case control, cross-sectional, cohort or experiment);
- evidence provided by a statistical test or confidence interval that the relationship is unlikely to be due to chance;
- evidence that drug use precedes the adverse effect (e.g. from a cohort study); and
- evidence, either from experiment or from observational studies with statistical or other form of control, that makes it unlikely that the relationship is due to some other variable related to both cannabis use and the adverse health effect.

This evidence was reviewed by three or more experts in the field and rated against these evidentiary standards. In this way the effects of the socio-political debate concerning the legalisation and harms of cannabis use, where the effects of cannabis use are subjected to significant problem inflation or deflation, are mitigated. As a result, the personal experiences of cannabis users, their families and treatment providers may not be supported by the scientific literature or may not yet have a sufficient standard of proof to warrant their inclusion in such a brief review.

In general, the evaluation of the health hazards of any drug is difficult for a number of reasons. First, causal inferences about the effects of drugs on human health are difficult to make, especially when the interval between use and alleged ill-effects is a long one. It takes time for adverse effects to develop and for research to identify such effects. Second, in making causal inferences there is a tension between the rigour and relevance of the evidence. The most rigorous evidence is provided by laboratory investigations using animals or in vitro preparations in which well-controlled drug doses are related to precisely specified biological outcomes. The relevance of this evidence to human disease is uncertain, because many inferences have to be made in linking the occurrence of specific biological effects in laboratory animals to the likely effects of human use. Epidemiological studies of relationships between drug use and human disease are of greater relevance to the appraisal of the health risks of human drug use, but by their nature are of reduced scientific rigour.

There are a number of additional difficulties in assessing the evidence related to cannabis use. Given the illicit nature, and therefore unregulated market, it is difficult to ascertain the amount of delta-9-tetrahydrocannabinol (THC) consumed by cannabis users in epidemiological studies and the effect of the stigma associated with reporting illicit drug use. In addition, as cannabis is often used with other substances, most commonly alcohol and tobacco, which also have adverse effects on health, it is difficult to distinguish the effects of cannabis from those of these substances without large case-control studies, which are yet to be available in any number.

There is a great deal of social and scientific research yet required to provide the level of proof necessary to fully understand the health effects, and the potential harms, associated with cannabis use.

Research process

The process of this review of the available literature to November 2004 is outlined below. The first stage was to identify the relevant peer-reviewed journal articles, monographs and reports. The strategy involved entering key words for all relevant questions posed in the review, using accepted thesaurus terms, into relevant databases. Around 700 articles were located from the following databases:

- Medline
- Embase
- PsycINFO
- PubMed
- Australasian Medical Index
- GrayLIT Network
- HEAPS
- Web of Science.

The results of the 2004 National Drug Strategy Household Survey were not included in this review as they were not published until 2005. The 2004 survey results do not affect the findings or conclusions contained in this review.

The second task was to audit the accessed literature in terms of relevance and quality. The project team has training and experience in the critical appraisal of the research literature according to the qualities of peer review, minimisation of bias and evidential support from well-conducted studies. Given the controversial nature of the health and psychosocial consequences of cannabis use, it was crucial to employ strict evidential standards when appraising the literature. We used the accepted model of evidential principles employed in recent comprehensive reviews on the health and psychological consequences of cannabis use, as outlined in the preamble to the report.

These include strength of association, consistency, specificity, biological gradient, biological plausibility and coherence.

In addition to thorough searches of the relevant current published literature (and where appropriate 'grey area' literature), standard criteria for causal inference described above were employed, evidential standards have been made explicit and clarification of issues with experts in the field was sought when required. Peer-reviewed journal articles and other relevant research were rated independently by three researchers according to the Agency for Health Care Policy and Research scales (where I = meta-analysis of multiple well-designed controlled studies; II = at least one well-designed experimental study; III = well-designed quasi-experimental studies; IV = well-designed non-experimental studies; and V = case reports and clinical examples).

The research was assessed for threats to validity such as non-randomisation and aspects of internal, external and construct validity, to ensure the weight and quality of evidence for any of the questions to be answered were assessed systematically, consistently and objectively. We felt that this approach would ensure that decision makers have access to the most valid and credible information currently available.

With regard to the use of 'grey literature', the Gray Literature Network notes that the United States Interagency Gray Literature Working Group's *Gray Information Functional Plan*, dated 18 January 1995, defines grey literature as 'foreign or domestic open source material that usually is available through specialised channels and may not enter normal channels or systems of publication, distribution, bibliographic control or acquisition by booksellers or subscription agents'.

A report by Jane Fountain reprinted by the Qualitative Drug Research Bulletin Board (http://qed.emcdda.eu.int/journal/bulletin27.shtml) concludes that the relatively hard-to-find, non-peer-reviewed grey literature is of value.

> 'Firstly, given the tight deadlines most research projects endure, the report will be topical and provide a valuable snapshot of the current situation, unlike a journal paper undergoing the slow process towards publication ... and during which the content cannot be published elsewhere. Secondly, whilst the research methods, findings and conclusions of a report are unendorsed by academia, it may raise urgent issues that merit further investigation and consideration in terms of health service development both within and outside the location studied. This is not to say that all grey literature can be uncritically accepted. A recent literature review conducted by the author concluded grey literature and a minority of research reports were well below the standard that is acceptable in academia. For instance, in some cases, conclusions and recommendations had little relationship to findings. Other reports made extravagant generalisations from interviews with a very small sample of informants, and lacked robust methods and sufficient detail of how the data were analysed. The reservations above do not apply to all grey literature, however, and more of the information it provides deserves to be in the public domain, especially as unpublished research reports give far more detail on the topic than is published in peer-reviewed journals.'

In line with these views, the only grey literature consulted for this review, apart from the GrayLIT Network to United States Government reports, was in topic areas where there are scant peer-reviewed publications, where the topic area is an emerging one and where the report is judged to be similar to the standard applied to international peer-reviewed journal articles. In addition to a number of government and parliamentary websites, both national and international, the grey literature reviewed includes the following reports.

- *Action Plan on Cannabis Research 2003–2006: Belgium, Germany, France, the Netherlands and Switzerland*. Final version June 2003, Steering Committee (*provided to JC as adviser to the group and used to assist in the identification of policy questions).*
- Papafotiou, K., Stough, C. and Nathan, P. (2002). *Detection of Cannabis-Induced Impairment with Sobriety Testing*. Commercial-in-confidence report to VicRoads.
- Longo, M.C. (2001). *The Prevalence and Role of Alcohol, Marijuana, Benzodiazepines and Stimulants in Drivers Injured in Road Crashes*. Doctoral Thesis, Department of Clinical and Experimental Pharmacology, University of Adelaide.
- Leach, D. and Dowell, A. (2002). *HS-GC Determination of Volatiles in some Cannabis Varieties.* Confidential report provided by Dr Andrew Katelaris.
- University of Mississippi National Center for the Development of Natural Products. (2003). *Quarterly Report: Potency Monitoring Project Report #882.*
- Lenton, S., Bennett, M. and Heale, P. (1999). *The Social Impact of a Minor Cannabis Offence under Strict Prohibition: the case of Western Australia.* National Centre for Research into the Prevention of Drug Abuse.

We believe that this review, therefore, takes into account the relevant peer-reviewed and high-quality grey literature published to the end of 2004 that inform the questions posed in the review. As we note in the preamble, this will not always reflect the personal experiences of cannabis users, their families and service providers, as there are many issues yet to be adequately researched.

1. How is cannabis used in Australia?

1.1 Patterns of use

Widespread cannabis use emerged in Australia in the early 1970s and has been increasing since then.[1] Today, cannabis remains the most commonly used illicit drug in Australia, with an estimated five million people aged 14 and above having tried the drug.[2] Typically, people begin using cannabis in their late teens or early twenties; thereafter, use steadily decreases.[3] While most cannabis use is experimental or intermittent, it has been estimated that around one in ten people who try cannabis become dependent on it.[4]

The best source of information on the prevalence of cannabis use in Australia comes from population surveys. The largest of these is the National Drug Strategy Household Survey series (NDSHS). According to the 2001 National Household Survey, around one-third (33.1%) of Australians aged 14 years and over reported that they had used cannabis at some point in their lives.[2] This proportion has remained relatively stable since 1993 but was marginally higher in 1998.[5] Due to changes in survey methodology, however, it is difficult to determine whether this small rise in reported use in 1998 represented actual changes in population use.[6]

Cannabis use in Australia is most prevalent among the young adult (20–29 years) and adolescent (14–19 years) age groups. In 2001, approximately three in five young adults (58.9%) and one in three adolescents (34.3%) reported using cannabis at least once in their life.[2] Less than one in three young adults (29.3%) and about one-quarter of adolescents (24.6%) reported using the drug recently (in the past 12 months). Around one in five recent users from both groups reported using the drug at least weekly; 19.1 per cent for adolescents and 21.1 per cent for young adults, respectively.[2]

Consistent with global trends and National Household Survey data,[7,8] surveys of Australian secondary school students indicate a rise in cannabis use in the 1990s. In a review of the literature, Donnelly and Hall (1994) found that 25–30 per cent of school-aged children (12–17 years) reported having used cannabis in the early 1990s.[9] While there appeared to be a slight increase in the 1996 Australian School Students' Alcohol and Drugs Survey (ASSADS),[10] the most recent ASSADS found that the prevalence of cannabis use decreased to levels observed in the early 1990s.[11]

Evidence suggests that higher proportions of people are beginning to use marijuana in their teens. Whereas around one-fifth of cannabis users born between 1940 and 1949 first used by age 18, about three-quarters of cannabis users born between 1970 and 1979 had used by the same age.[12,13] Furthermore, the average age at which people are beginning to use cannabis in Australia has dropped from 19.1 years in 1995 to 18.5 years in 2001.[2] This drop in the age of initiation is concerning because an earlier age of cannabis initiation is associated with an increased likelihood of regular use (for more detail on risk factors for dependence, see section 11). In turn, regular use at a young age is a risk factor for dependence and for other problems such as criminal activity and the use of other addictive drugs.[13–16]

In addition to age, there are other factors that increase the risks of using cannabis. People with lower education are more likely to become regular users.[17,18] As with most drugs, males are more likely than females to have tried cannabis and to use it more frequently.[2,14,19–21] A review of the literature also shows that unemployment is associated with an increased risk of cannabis dependence.[4]

Another issue of concern is the growing rates of cannabis use and associated problems in Indigenous Australian communities.[22,23] The 2001 National Household Survey found that cannabis use among Aboriginal and Torres Strait Islanders (ATSI) was higher than for the non-Indigenous population: 27 per cent of ATSI respondents reported using cannabis in the last 12 months compared to 13 per cent of non-Indigenous Australians. Cannabis use in Indigenous communities has received little research attention and the social and health impacts of cannabis use in such communities remain largely unknown. Surveys in the mid-1980s in the Northern Territory did not detect cannabis use among Indigenous peoples.[24] By 1999 cannabis use was reported in 55 per cent of males and 13 per cent of females in the same region.[23] A random sample of Indigenous peoples in two contiguous communities in Arnhem Land recently reported that 67 per cent of males and 22 per cent of females were current cannabis users.[25]

On a broader level, these figures highlight the importance of investigating cannabis use in ethnically diverse groups within the Australian population. Some recent research suggests that cannabis use is higher in Sydney youth of English-speaking background compared to those from Vietnamese- and Arabic-speaking backgrounds.[26] However, further investigation is needed to explain the reasons for such differences.

1.2 Types of cannabis used

There are three main forms of cannabis: marijuana, 'hashish' and 'hash oil'. Marijuana is the dried matter from the flowering tops and leaves of the plant. Levels of delta-9-tetrahydrocannabinol (THC), the main psychoactive component of cannabis, depend on the growing conditions and genetic strain of the plant. The flowering tops or 'heads' generally contain 5–14 per cent THC.[27] Leaf contains lower THC levels, ranging from 0.5 to 4 per cent, and cannabis resin, or 'hash', has 2–10 per cent THC, while 'hash oil' contains 16.5–60 per cent THC.[27] Hash and hash oil are not commonly used in Australia, with rates of use of 15.9 per cent and 6.5 per cent respectively.[2] They are found more often in India and Northern Africa, and then imported into Europe.

According to the 2001 National Household Survey, the most common way of using cannabis in Australia is smoking the heads (78.9%) and leaf (46.3%) of the plant. 'Skunk', a particularly potent form of heads, was reported to be smoked by around one in four cannabis users (23.7%), although it is not clear how they could be sure they were smoking this form. People aged 14–39 years were more likely to smoke the heads of the plant whereas older people (40+ years) were more likely to choose leaf.[2] This is evidence for the shifting preference in the younger generation of users for using the stronger parts of the plant.[2,12,28]

1.3 Use in conjunction with other drugs

The 2001 National Household Survey data indicate that cannabis is rarely used alone. Alcohol was commonly used in conjunction with cannabis (95.1%) and frequently with concurrent use of amphetamines (26%) and ecstasy (19.9%). Only 2.7 per cent reported not having used any other drug with cannabis.[2] While this survey did not assess concurrent tobacco use, cannabis users are more likely to be tobacco smokers than non-users (see section 10).

While there has been research on the combined effects of alcohol and cannabis on performing various tasks (e.g. driving), little research has been conducted on the reasons why this combination is so popular. Evidence from one controlled experimental study suggests that alcohol causes THC to be absorbed more rapidly into the blood plasma of the user.[29]

Cannabis users often report substituting cannabis for other drugs. Data from the Australian National Survey of Mental Health and Wellbeing (1997) found that three-quarters of recent cannabis users reported using alcohol when cannabis was not available.[30] This survey and other research among adolescent cannabis users found that current tobacco use was associated with cannabis abuse/dependence.[14,20,21,30,31]

1.4 Effects of different routes of administration

In Australia, cannabis is most often smoked. Within minutes of smoking, THC is absorbed into the bloodstream from the lungs,[32] resulting in a fairly immediate onset of a 'high'. The intensity of this 'high' depends on several factors, including the potency of cannabis, the method of use and the experience of the user.

Cannabis can be smoked through a 'joint', pipe or waterpipe. A 'joint' is a hand-rolled cigarette containing matter from the leaf, heads or resin of the cannabis plant. Other substances such as tobacco are often added to improve burning. Between inhalations, 30–80 per cent of the THC in the joint is lost in sidestream smoke.[33] A waterpipe or 'bong' uses water to cool the smoke before it is inhaled through a mouthpiece. While this minimises the amount of wasted smoke and enables maximum THC from the plant material to be recovered, larger amounts of carbon monoxide and tar are inhaled using this method compared to smoking a joint.[34] Although smoking the potent cannabis oil is rare in Australia, this may be done by adding a few drops to a joint or tobacco cigarette, or by heating the oil and inhaling the vapours.

As cannabis is fat-soluble, it is not suitable for injection. It can be eaten in cooked or baked foods, although this is uncommon in Australia. Compared to smoking it, eating cannabis produces a less intense high of longer duration. After eating, it can take 1–3 hours for psychoactive effects to occur because of the longer time it takes for THC to enter the bloodstream.[32] The delay between ingestion and the onset of acute effects makes it difficult for users to control the dose of THC consumed as compared to smoking where the psychoactive effects are more immediate.[35] Adding cannabis to infusions is also possible, but uncommon in Australia. This is practised regularly in India with the drinking of 'bhang' tea.[36]

With rising concerns about the health effects of cannabis smoke,[37,38] new methods of cannabis use have emerged that do not involve smoke inhalation. Vaporisers heat the cannabis and trap the tar and toxins in a chamber, allowing THC to be inhaled without the harmful smoke.[39,40] This method is relatively new and not widely used. Inhalers can also be used to deliver oral doses of THC. However, this method is also rare.[41]

1.5 Other issues with use

Data from the 2001 National Household Survey highlight the important role of the social group in the use of cannabis. For people who had tried cannabis at least once, the majority reported that up to a half of their friends or acquaintances had also tried the drug.

The most common place to use cannabis for recent users was either their own home or a friend's house (87.4%), with private parties being the second most common (42.9%). For those who had used recently, cannabis was usually obtained from friends or acquaintances (70.6%) compared with about one in seven who bought it from a dealer. Similarly, data from a Western Australian sample of 68 individuals with prior convictions for minor cannabis offences showed that family and friends were a common main source of supply for cannabis (44.8%), while purchasing from a dealer was less common (8.6%).[42]

2. What is the current legal status of cannabis in Australia?

The possession, use and supply of cannabis are illegal in Australia. At the national level, there is no uniform set of laws dealing with cannabis-related offences. Each State and Territory enacts its own legislation. While some jurisdictions enforce criminal penalties for cannabis possession, use and supply (New South Wales, Victoria, Tasmania and Queensland), others enact civil penalties for minor cannabis offences (South Australia, Northern Territory, the Australian Capital Territory and Western Australia). Conviction for a criminal offence attracts a criminal record and may be punishable by harsh penalties such as incarceration and major fines. In contrast, civil penalties do not result in a criminal record and are generally handled by lesser fines or mandatory treatment.

Despite differences in civil and criminal penalties for cannabis-related offences, all Australian States and Territories have implemented systems where non-violent, minor and early cannabis offenders are diverted from the legal system. Thus, in areas where cannabis-related activities are considered criminally punishable, it is rare for early offenders possessing small amounts of cannabis to receive a criminal conviction.

Cannabis cautioning schemes have been implemented in several States where minor early cannabis offenders (excluding dealers or violent offenders) are issued with a caution notice rather than face criminal proceedings. While all cautioning systems incorporate an educational component on the harms of cannabis, some also include mandatory counselling or more substantial treatment for repeat offenders (e.g. counselling, rehabilitation or detoxification).

Other States employ cannabis infringement notice systems where the payment of a fine precludes the offender from legal action or a criminal record. As with other diversionary measures, cannabis infringements do not apply to violent offenders, dealers or people with significant contact with the law. If the fine is not paid within a specified time, further legal measures are taken with the possibility of criminal conviction.

The table on the following page outlines the key features of current schemes for minor cannabis offences, not including possession of implements.[43]

Jurisdiction	Penalty
	Prohibition with civil penalty schemes (Infringement Notices)
SA (1987)	Less than 100 grams and no more than one plant (recently reduced from three). 60 days to expiate – adults only. Fines between $50 and $150, where failure to expiate usually results in a conviction.
ACT (1992)	Not more than 25 grams or five plants. 60 days to expiate – adults and juveniles. $100 fine, where failure to expiate does not usually lead to a conviction.
NT (1996)	Less than 50 grams and no more than two plants. 28 days to expiate – adults only. $100 fine, where failure to expiate results in a debt to the state but not conviction.
WA (2004)	Less than 30 grams and no more than two plants. 28 days to expiate – adults only. $100–$200 fine to expiate by payment of fines or attending a specified education session.
	Prohibition with cautioning and diversion to treatment
TAS (1998)	Less than 50 grams, plants excluded. Caution for first three offences.
VIC (1998)	Less than 50 grams, plants excluded. Up to two formal cautions, aged over 17 years.
NSW (2000)	Less than 15 grams. Statewide trial extended. Up to two formal cautions.
QLD (2001)	Less than 50 grams. Mandatory assessment and brief intervention session.

3. Why do people use cannabis?

3.1 What are the acute effects of cannabis?

The effects most commonly associated with cannabis use are the 'high' and an alteration of experiential awareness, characterised by physical and psychological sensations such as mild euphoria, relaxation, altered sense of time and heightened sensory perception, followed by drowsiness and a desire to sleep. Within minutes of smoking cannabis, the heart rate is increased by 20–50 per cent. Blood pressure is also altered, sometimes creating a light-headed feeling when the user changes posture from lying down to standing up. When used in a social setting, the high may cause contagious laughter, talkativeness and a drive to socialise. The heightened sensory perception that accompanies cannabis intoxication may intensify normal experiences such as eating, watching television or listening to music. Users may also experience loosening of association, fragmented thinking, enhanced creativity, heightened sexual experience and disturbed memory.[4,32,44]

Nevertheless, some people who consume cannabis report unpleasant experiences. The most common of these are anxiety, depersonalisation, depressive feelings and panic reactions.[4,32] These effects are more common in inexperienced users or those using for therapeutic purposes and may contribute to some people discontinuing use.[4] Users may experience hallucinations or delusions. This has led to debate about the existence of a toxic 'cannabis psychosis' or 'cannabis intoxication with psychotic features' that occurs for the duration of intoxication. However, if such a syndrome does exist, it is rare[4] (see section 6 for a detailed description of the relationship between cannabis and psychosis).

Most of the subjective effects of cannabis increase with dose.[45] This is not the case, however, for some effects. For example, small doses of THC may stimulate respiratory ventilation while larger doses produce respiratory suppression.[46] With heavy use over long periods of time, tolerance may develop to many of the acute effects, including the 'high'.[47,48]

In general, the acute effects of cannabis become evident within a few minutes of smoking and increase until they are felt most strongly after about two hours of use.[49] Psychological and behavioural effects usually dissipate four to six hours after use.[33] Experimental evidence, however, indicates that, following higher doses, some infrequent users report feeling significantly 'stoned' eight hours later.[49]

3.2 Evidence from surveys and other research

There is little research examining reported reasons and motives for cannabis use and this information is not usually collected by large population surveys such as the National Drug Strategy Household Survey. However, United States epidemiological research examining the role of attitudes and beliefs associated with cannabis use has found that lower levels of perceived risk and disapproval correlated strongly with higher rates of cannabis use.[18] Conversely, higher perceived risk and disapproval predicted decreases in cannabis use.[18]

Studies on smaller samples of cannabis users have found that people report a variety of reasons for use. For example, a survey of motivations for cannabis and alcohol use among a small group of American college students found that people used cannabis rather than alcohol for reasons of cognitive and perceptual expansion.[50] Conversely, social motivation was stronger for alcohol than cannabis. Women reported using cannabis over alcohol for the enhancement of positive mood; however, this difference was not found for males.[50] When an Australian sample of cannabis users was asked about the positive effects of cannabis use, most commonly reported effects were relaxation, heightening social enjoyment and euphoria.[51] Similarly, Hathaway (2003) found that the main reasons for use in a sample of regular users were relaxation and enhancement of recreational activities followed by stress and anxiety reduction.[52]

A common finding in these studies is that people report using cannabis for psychological reasons and to enhance positive mood or to escape negative mood. This is noteworthy because people who use for these reasons face an increased risk of persisting with cannabis use[53,54] and developing dependence.[55] Once cannabis dependence develops, people may continue to use for reasons other than those that prompted their initial use. For instance, dependent cannabis users may continue to use cannabis in order to relieve unpleasant withdrawal symptoms or to stop craving.[19,21,56]

Recent experimental research suggests that THC receptors are present in the parts of the brain associated with rewarding or reinforcing sensations.[57] Consequently, cannabis use may be associated with increased production of dopamine, a neurotransmitter produced by cells in these brain areas believed to be responsible for rewarding feelings. Other drugs of addiction such as alcohol, cocaine and amphetamines also interact with these neural pathways in a similar manner. This evidence suggests that cannabis and other drugs of potential abuse act on common areas of the brain. On a chemical level, the rewarding feelings that accompany the stimulated production of dopamine may be one of the reasons why people are attracted to using cannabis.

The emergence of new technologies has enabled a greater understanding of the brain mechanisms that underlie the acute effects of cannabis, particularly in the areas of mood, sense of time, attention and cognition. Of note are two experimental studies that utilised Positron Emission Tomography (PET) to explore the parts of the brain affected by cannabis.[58–60] PET allows investigators to examine regional Cerebral Blood Flow (rCBF), making it possible to determine whether blood flow to certain areas of the brain is increased or decreased during cannabis intoxication. The findings indicated that cannabis intake correlates with increased blood flow to parts of the brain that mediate mood and with decreased blood flow to brain areas associated with attention and cognition.[58–60]

4. Are greater amounts of cannabis being used and is it stronger now than it was in the 1970s?

4.1 Evidence for an increase in the amount of cannabis smoked

There are three factors that relate directly to the dose of THC delivered during cannabis use:

- the form of cannabis used (e.g. leaf, heads or resin);
- the way in which cannabis is delivered into the body (e.g. smoked or eaten); and
- the frequency with which the substance is used.

There is evidence that younger users prefer stronger forms of cannabis, typically heads, while older users tend to choose the less potent leaf of the plant. Data from the 1998 National Household Survey indicate that the preference for smoking heads over leaf was most pronounced in users between the ages of 14 and 29 years, with this trend dropping significantly in older age groups.[12]

The 1998 National Household Survey also shows a similar pattern in route of administration. While the use of waterpipes or 'bongs', rather than joints, predominated in younger users (14–19 years), this pattern steadily reverses with increasing age.[28] The use of joints moderately outweighed bongs in the 30–39 year age range, while those in the 40 years and over range reported the use of joints almost exclusively.[28] In this way younger users may be exposed to higher levels of THC than older users.[33,34]

Unfortunately, compared with studies of the prevalence of use, there are no longitudinal Australian data directly addressing the specific issue of whether the frequency or quantity of cannabis used has increased along with changes in the form of cannabis used and its route of administration. While there was an apparent increase in the proportion of people who had ever or recently used cannabis, especially among young people, in the early to mid-1990s (see section 1), it is not clear whether this translates to more frequent use or greater quantities used on each occasion. One possible indicator, however, that greater amounts of cannabis are being used among at least some younger people than previously is the fact that the age of cannabis initiation has decreased among young people. Early initiation to cannabis use is a known risk factor for persistent use and the risk of developing dependence (see section 11).

In sum, there are two important factors that contribute to a shift towards increased doses of THC in younger cannabis users. Firstly, the preference for smoking heads over leaf; and secondly, the tendency to deliver the smoke through a bong instead of a joint. This means that younger people are using more potent forms of the drug and exposing themselves to higher levels of THC.

While it is clear that younger cannabis users are using higher doses of the drug, it is important to note that the evidence for a shift in cannabis preference from leaf to heads and from joints to bongs is inferred from cross-sectional data. With this in mind, other explanations should not be ruled out. For instance, it may be the case that those in the older cohorts smoked heads when they were younger but changed to leaf as they grew older. Such an explanation can be validated only by following users for many years in a longitudinal study.

4.2 Evidence for change in strength (potency) of cannabis

There has been controversial speculation in Australia[61,62] and the United States[63] that the THC content of cannabis has increased up to thirty-fold during the past two decades, and that this has contributed to reported increases in cannabis-related harm, particularly in young regular users. Although this is a tempting argument, it is as yet unsubstantiated by research. In fact, cannabis potency monitoring has shown only small increases in THC over the past few decades.

Australia has no uniform program for the ongoing testing of cannabis THC content. Therefore, information is reliant on intermittent examination of cannabis seizures or small independent research studies. For example, while there was one isolated South Australian seizure of compressed heads with a THC content of 15 per cent,[64] a small study of other seizures of leaf and head from around the country indicated a lower THC content of 0.6–13 per cent, with the majority being 0.6–2.5 per cent THC.[65] A sample of 168 seizures in 1996 by Western Australian police found an average of 3.7 per cent THC content across all samples.[66] This figure almost doubled (6.4%) in the 59 sub-samples of heads.[66]

One recent study examined two batches of cannabis samples, the first from a controlled experimental crop and the second from the black market in New South Wales, South Australia and Queensland.[67] Results showed relatively low THC levels in the experimental crop of 0.19–5.05 per cent THC. [67] However, variations in THC content in the black market samples were considerable, ranging from 0.5 per cent to 22 per cent THC in a sample of hybrid cannabis.[67] Despite this, most samples contained below 5 per cent THC in the black market and 2 per cent THC in the experimental batches, respectively.[67]

Outside Australia, the New Zealand Government has monitored cannabis seizures since the mid-1970s. Between 1976 and 1996, there were no substantial increases in average THC content, which has remained at 2–4 per cent.[68]

To date, the best information on trends in cannabis THC levels has come from the Potency Monitoring Project at the University of Mississippi in the United States. Data derived from the mid-1970s up until late 2003 in 51,037 samples indicate that average cannabis potency has moderately increased.[27] However, some critics have argued that, due to improper storage of samples in the 1970s, THC contents may have been artificially low at the time of testing. [69] Between 1980 and 1997 THC content increased from 1.2 per cent to 4.2 per cent.[70] Cannabis samples (excluding hash and hash oil) analysed between May and August 2003 had average THC levels of 6.37 per cent[27] (see 1.2 for details on potency for different forms of cannabis). This finding suggests definite rises in cannabis THC content. However, over the last two decades, such increases are not consistent with claims of a thirty-fold increase. While Australia has not collected such comprehensive data, moderate changes as seen in the United States and New Zealand data are likely to be replicated in Australian trends given that, with isolated exceptions,[64] the majority of THC levels in studies of cannabis seizures have remained under 5 per cent.[65–67]

4.3 Hydroponic production

The term 'hydroponics' refers to the growing of a plant in an indoor environment under artificial light. A 2001 report by the Australian Bureau of Criminal Intelligence (ABCI) notes that growers may perceive this as an attractive cultivation method because higher yield can be obtained from fewer plants, light and soil conditions are held constant, information on growing procedure is readily available from hydroponic equipment retailers, and visibility of the cannabis crop is decreased.[71] Although hydroponic production usually occurs in private residences, there have been police seizures of large amounts of cannabis in warehouses.[71]

As yet, there has been no systematic investigation of whether hydroponic cannabis is stronger than naturally grown cannabis or whether it is associated with a different pattern of effects or harms. One concern about hydroponic production is that growers add potentially harmful chemicals, such as fertilisers, pesticides and hormones, to plants in a bid to increase crop potency.[72] Whether or not this practice is widespread remains speculative, while the long-term health effects of such exposure have not been researched. There has been recent speculation about headaches and migraines resulting from the smoking of hydroponic cannabis, in addition to concerns about possible associations with cannabis psychosis.[72]

Little is known about the percentage of the Australian cannabis market that is comprised of hydroponically grown cannabis. The 2001 ABCI report notes that approximately 90 per cent of seizures in South Australia in 2000–01 were hydroponically grown. In Tasmania, this figure was lower but still substantial at 38 per cent. Although these figures provide an indication that the domestic market proportion of hydroponically grown cannabis in Australia is substantial, more systematic evaluations that do not rely solely on seizure data are needed.

Although hydroponic production leads to higher yields from a smaller number of plants, high amounts of electricity are used in the process. One interesting consequence of this, also highlighted in the 2001 ABCI report, is electricity theft by growers. This is achieved by diverting electricity from other sources with specialised equipment to avoid detection.[71]

4.4 Domestically produced versus imported cannabis

The domestic cannabis market in Australia is substantial. Organised crime groups, including outlawed motorcycle gangs, are believed to control the large-scale production of Australian-grown cannabis.[71] Due to the ready supply of Australian-grown cannabis, it is unlikely that the importation of cannabis would be comparable to that of drugs that are not domestically produced, such as cocaine or heroin. This is because the associated risks of such a venture would not yield justifiable returns for importers who would be competing with a large domestic market.

Despite a domestically dominated market, there is evidence of modest cannabis importation into Australia. Seizures via parcel post and air passengers have generally been of small amounts. In 2000–01, 506 detections totalling 7.4 kilograms were made through the postal stream, while 313 detections with a total weight of 4.5 kilograms involved air passengers.[71] The largest seizures of imported cannabis have been made through sea cargo. Of the countries from which cannabis was sourced in 2000–01, China and South Africa made the largest contributions, totalling 49.3 and 9.8 kilograms respectively, with a reduction in seizures from Oceania.[71] It must be noted, however, that the majority of the Chinese exportation was of cannabis seeds, not intended for cultivation.[71] There have been no investigations or reports into whether imported cannabis is higher in potency than domestically produced cannabis. However, this would be unlikely given the evidence that THC levels of cannabis seizures in Australia do not differ dramatically from cannabis seizures in the United States or New Zealand.

5. What are the main health effects of cannabis?

5.1 Proven and possible short-term adverse health effects

Like many other psychoactive substances including alcohol, stimulants and opiates, cannabis use produces a period of acute intoxication which includes a range of psychological and physical changes in the body, commonly referred to as the 'high'. This state generally lasts from four to six hours after use and peaks at around two hours.[47] While there has been much research on the possible psychological and social consequences of short-term cannabis intoxication, such as heightened risk of car accidents (see section 13), psychosis and depression (see section 6), the literature on adverse physical health effects of short-term cannabis use is relatively small. Unlike other drugs of abuse such as heroin or cocaine, there have been no documented cases of death from cannabis overdose.[73] A recent review of the number and proportion of underlying causes of death for accidental drug-induced deaths in 1997–2001 indicated that cannabis use disorder was nominated in only 8 of the 5539 deaths (0.09%).[74]

Rather, literature on the short-term adverse health effects of cannabis use has primarily examined the role of the drug in triggering heart attack or in exacerbating symptoms of a pre-existing heart condition.

One of the most immediate physical effects of cannabis intoxication is an elevated heart rate of 20–50 per cent. This effect is more pronounced in occasional cannabis users because prolonged use builds a tolerance to this effect.[75–78] In addition, the smoke from cannabis contains dangerous compounds such as carbon monoxide. Although evidence suggests that increases in heart rate and absorption of harmful agents may increase the risks of heart attack in a small number of heavy users who persist into their late 40s,[79] this is not a likely short-term effect of occasional cannabis use in healthy individuals.[4] Despite this, cannabis use may have fairly immediate adverse cardiovascular effects in people who may not use the drug regularly but have pre-existing symptoms of cardiovascular disease. For instance, laboratory studies have tested the effects of cannabis use in individuals who suffer pain in the chest due to angina pectoris caused by a lack of blood supply to the coronary arteries.[80,81] Findings indicated that smoking a cannabis joint halved the amount of exercise time before chest pain occurred as compared with smoking a high nicotine cigarette or placebo cannabis cigarette.[80] In addition, heart rate increased by just over 40 per cent after smoking a cannabis joint.[80,81] On this basis, while short-term cannabis use may not pose a significant cardiovascular risk in healthy individuals, use of the drug is ill-advised in those who are prone to heart disease.

In sum, there is no evidence that short-term cannabis use can cause death from overdose. Adverse cardiovascular consequences arising from occasional use in healthy individuals are also unlikely. However, short-term cannabis use may be dangerous for persons who are predisposed to cardiovascular problems or have respiratory pathology.

5.2 Proven and possible long-term adverse health effects

Most of the adverse health consequences associated with cannabis use result from heavy use over the long term. The literature in this area has chiefly examined the possible links between prolonged cannabis use and cardiovascular disease,[82,83] cancer,[83–85] respiratory illness,[37,86–88] and impaired immune[89–91] and reproductive function.[89,92,93]

Only a few epidemiological studies have systematically examined the relationship between cannabis smoking and cardiovascular disease. The Kaiser Permanente Study of Cardiovascular Disease Mortality and Hospitalisations examined the health of 65,171 men and women between 1979 and 1985.[83] It found that neither current nor former cannabis use was associated with risk of circulatory disease death or hospitalisation for all cardiovascular diseases including stroke and heart disease. The major criticism of this study was that the young age of the sample (average 33 years at follow-up) made it unrepresentative of a group in which cardiovascular incidents are most common.[94]

A study of 6702 community residents who completed two surveys, each a year apart, found that daily cannabis use (during the one-year survey interval) was associated with a 2.2-fold increase of reported palpitations.[95] However, data were not collected on the temporal proximity of cannabis use, and the symptoms and palpitation reports were not medically verified.

Another study of 3882 people admitted to hospital for myocardial infarction found that, although a small proportion had used cannabis in the past year (3.5%), smoking cannabis was associated with a 4.8 times increased risk of myocardial infarction in the hour following use.[82] This risk substantially diminished after the first hour, consistent with lowering levels of carbon monoxide in the blood.[82] It must be noted that, compared to non-cannabis smokers, cannabis users in this sample had higher levels of obesity (43% versus 32%) and of cigarette smoking (68% versus 32%).[82] This suggests that cannabis use may be a rare trigger of heart attack, especially in the presence of other risk factors such as obesity and cigarette smoking.

Evidence suggests that cannabis smoke is carcinogenic and causes mutations in cells, raising the risks of cancer development in areas of the body exposed to cannabis smoke.[84,96] Despite this, the link between cannabis use and cancer is still debated. There have been case reports on the association between cannabis use and cancer of the tongue and lung,[97,98] head and neck,[99] and the upper respiratory tract.[85] Despite such reports, there has been a distinct lack of well-controlled studies on the issue.

In the only epidemiological study of the link between cannabis use and cancer, Sidney and colleagues (1997) found no relationship between cannabis use and head, neck or respiratory cancer.[83] However, some researchers have argued that the results of the study by Sidney and colleagues (1997) may have been compromised by the youth of the sample and the small number of regular cannabis users in the study – only 22 per cent reported regular cannabis use, which was assessed as use on six or more occasions.[100,101]

More convincingly, Zhang and colleagues (1999) compared 173 hospital cases of head and neck cancer with 176 controls (cancer-free blood donors at the same hospital) and found that, after controlling for tobacco use, age and sex, patients with head or neck cancer were 2.6 times more likely to have been cannabis users than those without cancer.[102] Those who had smoked cannabis more regularly and for a longer duration were at greatest risk. A recent study in the United States compared 407 adults with new cases of oral squamous cell carcinoma diagnosed across a 10-year period, with 615 age- and sex-matched adults recruited from the general population in the same area.[103] After accounting for factors such as alcohol and tobacco use, the study found that cannabis use was not associated with the disease. While there were no trends associated with frequency of duration of cannabis use, relatively few of the sample were long-term chronic users. The authors also did not include laryngeal cancers in their definition of oral cancer, which comprised a large proportion of cases in Zhang and colleagues' 1999 study.[102]

The effect of cannabis smoke on the airway system has received significant attention in the medical research literature. One reason for this is that the smoke of cannabis is similar to the smoke of tobacco in a number of ways (see section 10 for a review of the additive effects of cannabis and tobacco). For instance, both tobacco and cannabis smoke produce tar carrying many identical carcinogens.[79] The dangerous gas carbon monoxide is also present in both types of smoke.[79,104] Moreover, it has been found that when a joint is smoked as compared to a cigarette, the average puff is around two-thirds larger, inhalation is about one-third greater, and the breath is held approximately four times longer.[104] Consequently, a joint yielded around three times more tar and carbon monoxide than a cigarette.[104]

A number of medical studies have indicated that cannabis smoke causes respiratory inflammation even in relatively young habitual cannabis smokers who do not use tobacco.[87,105–107] Two observational studies, involving mucosal biopsies, also found that regular cannabis smokers exhibited many of the symptoms of chronic bronchitis.[104]

Recently Taylor and colleagues examined respiratory function in a New Zealand cohort followed from birth to 21 years.[37] The authors compared the lung function and symptoms of respiratory disease among cannabis-dependent people, tobacco smokers and non-smokers of tobacco and cannabis. The effects of cannabis dependence were roughly comparable to smoking 1–10 cigarettes per day. In comparison to the non-smoking group, cannabis-dependent individuals had higher rates of shortness of breath, wheezing, bronchial sputum and chest tightness after controlling for tobacco use. Taylor and colleagues (2002) conducted a further follow-up on this group at age 26 years and found that cannabis smoking produced minor decreases in lung function after controlling for the possible confounders of tobacco use, age and weight. Although these findings were marginal, the authors believed that, with continued cannabis use, lung function could further deteriorate.[38]

There has been concern that cannabis smoke, like tobacco smoke, may impair the function of the immune system, thereby heightening susceptibility to infectious diseases. If this were the case, it would place considerable pressure on the health system because of the widespread use of this drug.[100] Studies testing the effects of cannabinoids on blood cells (B-cells and T-cells) that fight infection and disease have produced mixed results. Although cannabinoids have been found to impair B-cell responses in mice, the findings in humans have failed to show that

cannabinoids trigger responses in B-cells that exceed the normal range.[91] While there have been reports of allergies being aggravated by cannabinoids in humans,[108] reviewers have expressed scepticism as to whether these reactions are caused by other contaminants of cannabis such as fungi or bacteria.[89] Similarly, while animal studies have found that cannabinoids reduce the functioning of T-cells, human studies have produced varied results.[108] The main criticism of the studies that found impaired T-cell functioning in humans was that such high cannabinoid levels were usually required that it is unlikely that humans would willingly use comparable amounts.[108]

Other research has examined the effects of cannabis smoke on macrophages – cells in the respiratory system that are first to attack foreign micro-organisms entering through the lungs. There is evidence that cannabis smoke reduces the ability of macrophages to inactivate infectious organisms such as staphylococcus[91] and candida[109] when placed in a test tube. Similar to the research on T-cells, these findings may not be applicable to human users because doses that have produced impairment in macrophage activity have usually been very high.[100] If cannabis were to lower immune function, the real impact remains unclear.

Studies testing whether heavy cannabis smokers face a heightened risk of infectious disease have been small, with samples of less than 100 individuals.[100] One epidemiological study found that cannabis-only smokers faced a greater risk of utilising health services for respiratory conditions.[110] It was not determined, however, whether these conditions were contagious or non-contagious.

The possibility that cannabis may lower immune functioning would be of particular concern to those suffering from diseases of the immune system, such as HIV. Large cohort studies that have followed HIV-infected males have failed to find an association between cannabis use and time taken to develop AIDS,[111] indicating that cannabis is unlikely to have marked effects on lowering immunity. Similarly, in a review of the literature, Hall and colleagues (2001) conclude that cannabis use is unlikely to be a source of major immune harm because of the absence of epidemics of infectious diseases among heavy cannabis users. However, the authors also note that it is difficult to rule out the possibility that heavy chronic cannabis use may result in slight immune impairments.[4]

Another concern is that cannabis use may have negative effects on the male reproductive system. Chronic cannabis administration in animals has been found to deplete testosterone, lower sperm count, decrease the ability of sperm to move quickly and cause increased sperm abnormalities.[92] Despite this, evidence in humans has been far less conclusive. Consistent with animal findings, one early study with male humans found reductions in testosterone, sperm movement and sperm count, as well as increased abnormalities.[112] These effects, however, were not replicated in a better controlled, larger study which found no differences in testosterone levels before and after three weeks of daily cannabis use.[93] This result is supported by other findings that testosterone levels generally fall within the normal range in human cannabis users.[113]

Two human endogenous cannabinoid receptors have been identified and cloned, CB1 and CB2. CB1 receptors are found primarily in the brain with additional sites in the genito-urinary system in males and females, while CB2 receptors are concentrated in the spleen and immune system. While cannabis does interact with oestrogen receptors, it has no direct effect on oestrogenic activity.[114] The acute administration of THC, however, has been shown to suppress the secretion of luteinising hormone (LH) in humans.[115] The LH response to THC is dictated by the stage of the menstrual cycle, such that a 30 per cent suppression of plasma LH levels occurs in the luteal phase but has no effect in the follicular stage or in post-menopausal women.[116] A study of 13 pregnant women who had consumed cannabis during pregnancy reported no significant changes in a range of circulating hormones.[117]

There is some evidence that cannabis may compromise female fertility with a modest association (OR 1.7) reported between cannabis use and infertility in a case-control study of 150 women with primary anovulatory infertility and 150 controls.[118] THC and anandamide have been shown to increase the duration of pregnancy and increase the frequency of stillbirth in rats.[119] While there have been few human studies, current understanding suggests that the endocannabinoid system is tightly modulated in gonadal tissues and during pregnancy. Cannabis exerts potent effects on this homeostasis and may be affecting embryo implantation and miscarriage.[114] It is clear, therefore, that cannabis-related substances are contraindicated in pregnancy, as are compounds that interact with endocannabinoid synthesis and metabolism.

5.3 Effects of cannabis on the foetus (unborn child)

Cannabis is the most commonly used illicit drug among women of reproductive age[120] and levels of self-reported cannabis use during pregnancy are relatively high compared with use of other illicit drugs. A US report published by the National Institute on Drug Abuse (1996) found that 2.9 per cent of pregnant mothers reported at least some cannabis use. This was around three times higher than for cocaine or crack usage.[121] The psychoactive component of cannabis, THC, crosses the placenta in humans and animals. This has been a source of concern because many psychoactive drugs that pass through the placenta, such as alcohol, cocaine and tobacco, are teratogenic. That is, these substances adversely affect the development of the human embryo.

High levels of maternal alcohol use during pregnancy can result in foetal alcohol syndrome, a condition characterised by permanent growth retardation, impaired mental capacities and abnormal facial features.[122] Prenatal use of cocaine is associated with an increased incidence of premature birth, growth retardation and impairments in several aspects of brain development.[123] Cigarette smoking during pregnancy has been associated with effects on foetal development including lowered IQ, poorer impulse control and poorer performance on tests requiring problem solving with visual stimuli.[120]

In a review of the literature, Hall and Pacula (2003) discuss several difficulties faced by researchers when designing studies on the possible teratogenic effects of cannabis use in humans. Firstly, cannabis use during pregnancy is a practice that is likely to be under-reported due to high levels of associated stigmatisation. Secondly, the low prevalence of both cannabis use during pregnancy and the incidence of negative foetal development make it difficult to discern differences in small samples. Thirdly, cannabis use commonly occurs in the context of other risk factors for disruptions in foetal development such as poor diet and cigarette use. This creates difficulty in isolating the effects of cannabis use.[100]

There is firm evidence that cannabis use during pregnancy is not associated with higher rates of foetal mortality.[120] Despite an early report of symptoms analogous to foetal alcohol syndrome in children of mothers who had used cannabis during pregnancy,[124] this finding has not been replicated in a number of well-designed studies.[125] The Maternal Health Practices and Child Development project (MHPCD), a longitudinal study of adolescents and their offspring in the United States, found that prenatal cannabis use was related to unexpected deficits in height at 6 years of age.[126] This finding contrasts with other well-designed longitudinal studies on maternal cannabis use that found no growth effects.[96,127,128] The reason for this difference may be that the MHPCD was conducted with a relatively young sample of low socio-economic status. This may have influenced living conditions, which in turn may have affected later growth.

The most robust finding in the literature is that cannabis use during pregnancy is associated with a minor reduction in birth weight, smaller than that related to maternal tobacco use.[125,129–131] The largest study to confirm this finding was conducted by Fergusson and colleagues (2002) in a sample of 12,000 pregnant women in England. [129] Similar to levels found in population surveys (e.g. NPHS, 1996), 2–3 per cent of the sample reported cannabis use during pregnancy. However, the authors suspect that this figure was artificially low due to under-reporting. After controlling for a large range of confounding factors such as cigarette smoking, alcohol consumption, use of other illicit drugs (e.g. cocaine) and the amount of coffee or tea imbibed, the study found that women who smoked cannabis at least once per week before and during pregnancy gave birth to infants weighing approximately 90 grams less than infants of non-cannabis smokers.[129]

Other research has focused on whether children exposed to cannabis in utero have a higher risk of acquiring lasting physical or psychological deficits which endure after birth. The most extensive evidence on this issue comes from the Ottawa Prospective Prenatal Study (OPPS), an ongoing longitudinal project that was initiated in 1978 examining the effects of prenatal exposure to cannabis from birth to adolescence in a predominantly middle-class sample.[127,132–136]

Results from the OPPS sample suggested that, shortly after birth, babies prenatally exposed to cannabis were more easily startled, had higher levels of tremors and had lower functioning visual systems compared with non-cannabis-exposed babies.[137] These effects, however, were no longer present one month after birth. This study contrasts with another conducted by Tennes and colleagues where such symptoms soon after birth were not found using the same measurement instruments as the OPPS team.[138]

At six and twelve months of age, cannabis-exposed children in the OPPS sample showed no impairments on tests of ability.[137] At 48 months, significantly lower scores in verbal ability and memory were associated with maternal cannabis use.[135] However, at 60 and 72 months, these deficits were not apparent. Rather, at 72 months, prenatal cannabis use predicted decreases in attention.[127] At age 9–12 years, while were no differences in overall IQ scores between children who had and had not been prenatally exposed to cannabis, prenatal cannabis exposure was associated with decreases in performance on individual tests of higher order problem solving and organisation skills.[137] A lack of association between overall IQ and prenatal cannabis use was also observed at 13–16 years of age. However, testing at these ages revealed significant impairments on tasks involving attention,[135] memory of visual stimuli, analysis and integrating concepts.[136]

A recent functional magnetic resonance imaging study with the OPPS cohort reported on the neurophysiological effects of prenatal cannabis exposure on response inhibition in 18–22 year olds.[139] This study demonstrated a plausible biological explanation (high levels of cannabis receptors in the developing brain, particularly the forebrain which is associated with higher cognitive functioning) and a dose response (a positive relationship between the amount of prenatal cannabis exposure and neuronal activity in the right premotor cortex). Similarly a study of the effects of prenatal cannabis and alcohol exposure on school achievement at age 10 years reported a significant association between second trimester cannabis use and reading comprehension and educational underachievement using structural equation modelling.[140]

Cannabis use has also been linked to the development of cancers in the children of cannabis-using mothers. Along with a number of other factors, cannabis use was examined as a risk factor in three case-control studies of childhood cancers. One study of acute non-lymphoblastic leukaemia found that mothers of cases were three times more likely to have used cannabis before and during pregnancy than mothers of controls.[141] Two other case-control studies reported an increased risk of rhabdomyosarcoma[142] and astrocytoma.[143] Hall and colleagues (2001) concluded that trends in the base rates of these cancers suggest that these studies may have produced a chance result.[4]

5.4 Potential therapeutic uses of cannabis

While much of the literature has centred on cannabis as a recreational drug, there is a long history of cannabis use for therapeutic purposes in Asia, India and the Middle East.[144,145] The earliest reports of cannabis being used as a medicine were about 5000 years ago from China, where it was recommended for a number of conditions including malaria, constipation and rheumatic pains.[146]

While information on the prevalence of cannabis use in the community for medicinal purposes has been scarce, a telephone survey conducted in Canada found that 2 per cent of respondents reported use for such reasons.[147] Growing awareness of the possible beneficial effects of cannabis has sparked medical research on cannabis in treating conditions such as nausea, weight loss, pain, neurological disorders, anxiety, glaucoma and asthma.

5.4.1 Cannabis as a treatment for chemotherapy-associated nausea

Intense nausea and vomiting are common adverse symptoms of chemotherapy and radiotherapy for the treatment of cancer. Due to the lack of universally effective treatments for chemotherapy-induced nausea, cannabis has been considered as a possible treatment option. Biological research has shed light on the association between cannabis and nausea, showing that there are cannabinoid receptors in brain areas that influence emesis, or the vomiting impulse.[79]

A number of randomised controlled trials (RCTs) have been conducted into the anti-emetic effects of cannabis. In an early study, Sallan and colleagues examined the effects of THC in a sample of 22 patients, most of whom were resistant to conventional anti-emetic agents. Findings indicated that THC was superior to placebo in reducing vomiting and this correlated with feelings of sedation and euphoria in the majority of patients.[148] These findings were supported in another RCT by Chan and colleagues in 1979, where 14 of 15 cancer patients had a reduction in nausea and vomiting after THC administration. The majority experienced sedation (12 of 15 patients) while around one-third (4 of 15 patients) had short-lived mild negative psychological reactions such as anxiety or unease.[149]

Since the early 1980s other RCTs have compared THC with other anti-emetic agents, most commonly prochlorperazine, in patients undergoing chemotherapy. While THC was generally found to be moderately more effective than prochlorperazine in smaller studies,[150,151] the largest and best designed study showed no difference between the two drugs.[152] Findings have also indicated that a combination of these drugs was more effective than either drug alone in reducing nausea and vomiting.[153] Although the majority of these studies found that THC produced a greater number of side effects than the other drug, these were generally short-lived and patients preferred THC to prochlorperazine.

More recently, the development of a class of drugs known as selective serotonin type 3 receptor agonists has significantly improved outcomes for chemotherapy patients.[79] Evidence suggests that these drugs can produce complete relief for nausea and vomiting in 75–90 per cent of chemotherapy cases compared with less than one-third of patients receiving THC.[79]

5.4.2 Cannabis as an appetite stimulator

Besides having effects on nausea and vomiting, cannabis has been found to simulate appetite and increase food intake. In one of the earliest studies, Hollister examined the effects of smoked cannabis in a group of fasting and non-fasting volunteers over 25 days in a residential laboratory setting. Cannabis smoking was found to increase the intake of calories and occasions of eating.[154] These appetite-stimulating effects have attracted special interest from researchers examining ways of reducing the dramatic weight loss in patients suffering from AIDS-related wasting, a condition that occurs as a result of AIDS-associated diseases or anti-retroviral drugs that suppress HIV. For instance, Beal and colleagues conducted a trial where synthetic THC was administered on a daily basis to 139 AIDS patients. Findings indicated that synthetic THC was significantly more effective than placebo in boosting appetite and decreasing nausea. In addition, there was a trend towards improved mood after THC administration and a tendency towards weight gain. Although THC caused more side effects than placebo, 75 per cent of these effects were mild or moderate. Most common side effects were euphoria, dizziness and thought abnormalities.[155]

5.4.3 Cannabis as a pain reliever

Another possible therapeutic use of cannabis is in the treatment of pain. In the brain, cannabinoids act on pathways that overlap with opiate receptors. It does appear, however, that cannabinoids have their own pain-relieving mechanisms that are separate from the opiate receptor system.[79]

In a sample of 10 cancer patients, it was found that high doses of THC (15–20 mg) provided superior relief for cancer pain as compared with placebo.[156] Another study with 36 cancer patients found THC and codeine to be equally effective in the reduction of cancer pain.[156]

More recently, a Canadian cross-sectional survey of chronic non-cancer pain patients found that 25 per cent of patients reported either current or past use of cannabis for pain relief.[157] Surveys of patients suffering pain following spinal cord injury have found that while small proportions report using cannabis to aid pain relief (between 2.5% and 5%), levels of perceived benefits from cannabis use were high in these groups.[158,159]

5.4.4 Cannabis in the treatment of neurological disorders

There is some evidence that cannabis may play a role in treating neurological disorders such as multiple sclerosis, spinal cord injury and some movement disorders, particularly by alleviating muscle spasticity and tremor.[160] Many reports have been anecdotal, with positive effects reported from clinical surveys and observational studies.[161] While a few small clinical trials of oral cannabis preparations have reported improvements in muscle spasticity, weakness and tics,[162–164] larger carefully controlled studies are required before clear recommendations of its efficacy can be made. Recent developments in our understanding of the effects of a variety of cannabinoids other than THC suggest these may have promise for altering the disorders' underlying disease processes, largely through their effects on the brain and spinal cord regions involved in these conditions.[165,166]

5.4.5 Cannabis in the reduction of anxiety

A small body of research has examined the role of cannabis in reducing anxiety. For instance, in a randomised controlled trial of 20 clinically anxious patients, synthetic THC produced marked improvements in anxiety measures compared to placebo, with the most common side effects being dryness of the mouth and eyes, and drowsiness.[167] Another randomised controlled trial conducted at around the same time supported these findings, indicating that synthetic THC was superior to placebo in reducing scores on measures of anxiety.[168] Among the main side effects were changes in blood pressure which resulted in light-headedness and dizziness. These effects, which increased with dose, were experienced by most patients, but were generally well tolerated.[168]

5.4.6 Cannabis in the treatment of glaucoma

Glaucoma is a common cause of blindness where increasing pressure inside of the eye progressively damages vision. The mechanism by which cannabis use may help in the treatment of glaucoma is by acting to reduce this pressure within the eye. Although evidence suggests that relatively high doses of cannabis can reduce intra-ocular pressure,[169] it is doubtful whether cannabis would be a viable ongoing treatment for glaucoma due to short-lived effects, the side effects of high doses of THC[79] and reduced effects on intra-ocular pressure with prolonged use.[170]

5.4.7 Cannabis in the treatment of asthma

Cannabis, whether smoked or ingested, typically causes bronchodilation.[171–173] This effect occurs at a faster rate when smoked. However, such a delivery method is not suited to individuals suffering from asthma because of the large array of harmful compounds in the smoke that may exacerbate the condition.[174] A considerable problem with cannabis ingestion is that effects are smaller and take considerably longer to occur. Also whether cannabis is smoked or ingested, unwanted psychoactive effects may hinder use for asthmatic symptoms.[175] Although a THC aerosol was developed to reduce the harms associated with smoke, this was found to irritate the lungs.[176]

It appears, therefore, that further research into the therapeutic applications of the large number of cannabinoids is warranted but the role of smoked herbal preparations of the plant currently has limited application.

6. What is the relationship between cannabis use and mental health disorders?

The relationship between cannabis use and mental health disorders is affected by several factors. In order to provide a framework in which to view this relationship, it is useful to briefly mention four hypotheses discussed by Hall and colleagues (2001) in a review of the relevant literature.[4]

The first possibility is that heavy cannabis use can cause mental disorders such as psychosis, commonly referred to as the causal hypothesis. Secondly, cannabis use may precipitate a mental disorder that was previously dormant. An assumption of this explanation is that some people are more prone to mental health disorders than others. Thirdly, the common cause hypothesis states that the mental illness and cannabis use may simply occur together as a result of common variables. This explanation is often the most difficult for researchers to rule out because many variables correlate with both cannabis use and mental health problems; for instance, unemployment, family difficulties and other drug use.

While findings may indicate that many cannabis users also have a mental health disorder, this is not sufficient evidence that cannabis use caused the disorder. It may be the case, for instance, that an underlying genetic predisposition leads to both cannabis use and the disorder.

A fourth explanation, the 'self-medication' hypothesis, is that people use cannabis after experiencing signs of a mental health disorder in order to alleviate symptoms.

6.1 Relationship with psychosis

Psychiatric disorders occur when certain symptoms cluster together to form a syndrome. Cannabis use may cause symptoms similar to those observed in psychotic disorders like schizophrenia where individuals experience delusional thoughts, hallucinations and impaired reality testing.[4] This is plausible because THC stimulates increased production of dopamine,[57] a neurotransmitter also implicated in psychotic disturbances. A 1996 community study in New Zealand reported that one in seven (14%) cannabis users reported 'strange, unpleasant experiences such as hearing voices' or 'becoming convinced that someone is trying to harm you' after using cannabis.[177] The 1997 National Survey of Mental Health and Wellbeing reported that, after adjusting for confounding factors, a diagnosis of cannabis dependence doubled the odds of reporting psychotic symptoms.[178]

There are several arguments for the association between cannabis and psychosis in the literature. Some believe that heavy cannabis use can lead to a temporary 'cannabis psychosis' or toxic psychosis which remits after cessation of use.[179] Others argue that cannabis use is a causal factor in the formation of schizophrenia, an often chronic psychotic disorder.[180] Research has also examined whether cannabis use exacerbates the symptoms of schizophrenia[181] or triggers the disorder in psychosis-vulnerable individuals.[182]

Evidence for a short-lived cannabis psychosis is based on case reports where heavy cannabis use has preceded the onset of an episode of psychosis, which remits upon abstinence. The largest series of case reports described 200 psychiatric patients in Calcutta who exhibited symptoms following cannabis use including sudden confusion, delusions, hallucinations and amnesia.[179] Depictions of a toxic or acute cannabis psychosis have also been reported in other countries such as New Zealand,[183] South Africa,[184] Sweden[185] and the United Kingdom.[186]

The Australian Low Prevalence Study, conducted in Perth, Melbourne, Brisbane and Canberra, found that 25 per cent of people who screened positive for a psychotic disorder also met the criteria for cannabis abuse or dependence at some point in their lives.[187] A large-scale population survey in the United States, known as the Epidemiological Catchment Area (ECA) study, found that cannabis was the second most frequently used drug (23%) besides alcohol (37%) among persons with schizophrenia. Alcohol and cannabis were the most common drug combination (31%).[188]

While cross-sectional population surveys provide evidence that cannabis use is associated with schizophrenia, this does not support the conclusion that cannabis use causes schizophrenia. Studies that follow samples of people over multiple time points are better able to disentangle the sequence of events leading to the development of psychosis.

The largest longitudinal study examining the link between cannabis and psychosis followed approximately 50,000 Swedish army conscripts for 15 years.[189] After controlling for other factors such as parental mental illness or a pre-existing psychotic illness at conscription, the study found the odds of developing schizophrenia later in life were 1.5 times higher for those who had used cannabis 1–10 times, and 2.3 times more likely for those who had used cannabis 10 times or more, compared with those who had not used cannabis. A longer-term follow-up of this cohort ruled out the argument that the use of other drugs or the existence of personality traits that pose a risk of schizophrenia may have been responsible for this association.[180]

A longitudinal study of a birth cohort in Dunedin, New Zealand, supports and extends the Swedish cohort findings.[190] After controlling for other drug use and the presence of psychiatric symptoms at age 11 years, this study found that cannabis use at age 18 was associated with significantly higher rates of schizophrenia, especially for those who initiated use of cannabis before 15 years of age.[190]

Several cross-sectional studies have examined whether cannabis use predicted later development of individual psychotic symptoms such as hallucinations or delusional beliefs.[178,182,191] In a study using ECA data, Tien and Anthony (1990) compared people who had recently experienced one or more psychotic symptoms (within the last 12 months) with those who had not had such symptoms. After controlling for demographic factors and other mental health problems, Tien and Anthony found that cannabis use doubled the risk of reporting psychotic symptoms.[191]

The most extensive longitudinal research in this area was conducted by Fergusson and colleagues (2003) in the Christchurch Health and Development Study (CHDS), which followed a New Zealand birth cohort over 21 years. A large range of possible confounding factors was considered, such as previous psychotic symptoms, other drug use, anxiety, depression, criminality and demographic variables. Cannabis dependence at

age 18 was associated with an approximate doubling of risk for developing psychotic symptoms in users at age 21, compared to those with no dependence diagnosis, after adjustment for all confounding factors measured in the study.[192]

A growing body of literature has specifically investigated whether those who are already prone to psychosis are at higher risk of developing a psychotic disorder after cannabis use. In a general population sample followed over three years, Van Os and colleagues (2002) found that, as cannabis use levels increased, so did risk for psychosis incidence. Moreover, an additive effect was evident for cannabis use and psychosis vulnerability in terms of later psychosis development. That is, cannabis use placed those with underlying psychotic tendencies at greater risk for psychosis than those without such tendencies.[181] Cannabis use was also associated with a poorer prognosis for those with an existing psychosis.

Verdoux and colleagues (2003) conducted a unique study where college students kept a personal record before and after cannabis use. After controlling for other drug use, age and gender, the study found that cannabis use posed a significant risk for experiencing psychotic symptoms in the period of hours after cannabis use. This risk was higher for individuals deemed to be prone to psychosis.[182]

Only one small study by McGuire and colleagues (1995) has directly examined the role of family history in schizophrenia and cannabis use. McGuire et al. found that schizophrenic patients with a history of cannabis use were ten times more likely to have a family history of schizophrenia compared with those who had not used the substance.[193] The authors concluded that a shared genetic predisposition to schizophrenia is associated with the disorder in the context of cannabis use.

While studies have indicated that regular cannabis use increases the likelihood of experiencing psychotic symptoms among vulnerable individuals and worsens the prognosis of schizophrenia, they are unable to provide direct evidence that cannabis use causes new cases of clinical psychoses in the population. This question was addressed by Degenhardt and colleagues using modelling techniques to assess whether rising cannabis use over the past 30 years in Australia corresponded with rising levels of schizophrenia. Their study found that, despite significant increases in cannabis use, levels of schizophrenia in the population had slightly decreased or remained stable over this time period. The authors concluded that cannabis is unlikely to cause schizophrenia, but rather may precipitate it in vulnerable people.[194] The most recent review of the question by the same group also reached this conclusion.[195] This view is supported by some evidence that cannabis users with schizophrenia have their first episode at a younger age than non-users.[196]

A recent Greek cross-sectional survey has studied subclinical positive and negative psychosis dimensions and depression.[197] The authors reported that the use of cannabis was positively associated with negative and positive dimensions of psychosis, independent of each other, and with depression. These results suggest that cannabis use may be contributing to the population level of subclinical psychosis expression.

In sum, evidence indicates that cannabis use may precipitate schizophrenia in people who are vulnerable due to a personal or family history of schizophrenia. New research also suggests that cannabis use in those who have psychosis vulnerability increases the chances of experiencing psychotic symptoms, especially when this use is regular. In addition, cannabis use appears to exacerbate the symptoms of schizophrenia.

Whether cannabis use causes additional cases of schizophrenia is undecided. Hall et al. (2000) comment that, if this were true, cannabis is likely to account for only a minority of cases. In the past 30 years, rates of schizophrenia in the Australian population have remained stationary or have decreased despite rising levels of cannabis use.[198] Cannabis may contribute, however, to subclinical levels of positive and negative psychotic symptoms.

6.2 Relationship with depression

In comparison to psychosis, there has been far less attention given to the association between cannabis use and depression. One reason may be that depressed cannabis users are less likely than those with psychosis to access treatment and, if they do, treatment providers are unlikely to enquire about depressive symptoms.[199]

Cross-sectional epidemiological evidence indicates that cannabis use and depression occur together at a frequency greater than chance. It remains unclear, however, whether this association is due to other variables that are also correlated with depression, such as age, gender and other drug use.[199] The early work of Kandel and colleagues indicated that while cannabis use in adolescence was associated with lower life satisfaction and higher frequency of hospitalisation for a psychiatric disorder in young adulthood, it failed to predict depressive symptoms.[200] More recently, Chen and colleagues (2002) re-analysed the US National Comorbidity Survey (NCS) to examine the relationship between cannabis use and a major depressive episode, and found that having been cannabis-dependent at some point in life was associated with a 3.4 times greater risk of major depression.[201] Similarly, data from the US National Longitudinal Alcohol Epidemiologic Survey indicated that a diagnosis of cannabis abuse or dependence in the past year was associated with a 6.4-fold chance of also receiving a diagnosis for major depression in that time.[202]

The Australian National Survey of Mental Health and Wellbeing also found a relationship between cannabis use and depression. However, this association reflected the use of other drugs (e.g. alcohol and tobacco) and the presence of neurotic personality traits rather than the use of cannabis per se.[31,194] Rey and colleagues conducted a survey with Australian adolescents and found a moderate association between cannabis use and depression after considering other factors including other drug use, age and gender.[203] This association was most marked in those who reported using cannabis once or more in the past month.[203]

Longitudinal research on the association between cannabis use and depression has also produced mixed results. Some studies have indicated that early cannabis use (from age 15–16 years) does not predict the later occurrence of depression after controlling for confounding factors,[204] while others suggest that cannabis use and depression are at least mildly associated.[190,205,206] The Christchurch cohort study found an association between frequency of cannabis use at age 15 years and depression at age 16–18 years.[204] After adjusting for confounding factors such as other drug use, familial, peer and socio-demographic variables, however, the cohort study found that this relationship did not reach significance. It is important to note that this study included crude measures of cannabis use frequency, only enquiring whether participants had used more or less than 10 times in the past month. Later analysis of this same cohort at age 20–21

years used more refined measures of cannabis use frequency for the past year (less than monthly, at least monthly, at least weekly). It found that at least weekly or monthly cannabis use was modestly associated with depression (increased odds of 1.7 and 1.4 respectively) after controlling for a wide range of other variables such as age, gender, other drug use and criminal behaviour.[205] By age 21 years, 30 per cent of those using cannabis at least weekly met criteria for depression, compared to 15 per cent of those who were not using cannabis at the same age.[205] The Dunedin study found that, while cannabis use by age 15 did not predict depression at age 26, having used cannabis three or more times by age 18 was a moderate predictor of depression at age 26 after controlling for variables including socioeconomic status, sex, pre-existing psychotic symptoms and other drug use.[190]

Longitudinal data from a New York cohort followed from age 13 to 22 years indicated that cannabis use was not associated with a depressive disorder, whereas other drug use (including cigarettes) was a significant predictor of anxiety and depression.[207] A re-analysis of the US ECA data found that those who abused cannabis but had no depressive symptoms at baseline in 1980 were four times more likely than non-cannabis abusers to experience individual depressive symptoms at follow-up (1994–96). This was evident after adjusting for several factors including age, gender, other drug use and antisocial behaviours.[206,208]

Patton and colleagues followed a sample of Australian secondary students (aged 14–15 years) over seven years and found that 68 per cent of daily cannabis users suffered from a mixed state of depression and anxiety. This translated to a four-fold increased risk of depression and anxiety compared to non-users after controlling for other drug use, pre-existing symptoms and antisocial behaviour (see section 6.3 for discussion on anxiety).[209] These findings, however, were evident only for females in the sample.

Research findings have not supported a self-medication hypothesis that depressed people are more likely than others to use cannabis to improve their mood.[194,200,207–210] Kandel and colleagues failed to find a relationship between depression and later cannabis use in a New York cohort.[200] Similarly, in an African American cohort, depression in 6th grade was not associated with cannabis use in 10th grade.[211] A longitudinal New Zealand study found that while cannabis use at age 15 and 18 years predicted conduct disorder and alcohol dependence, no association between early depression and subsequent cannabis use was found.[210]

Given the high rate of suicide in young Australian males and the common use of cannabis in this group, the issue of suicide risk and cannabis use is important. A small body of research has examined whether cannabis use heightens the risk of suicide or attempted suicide. Cross-sectional data from the US National Comorbidity Survey indicated that cannabis-dependent individuals were 2.4 times more likely to report a suicide attempt than non-cannabis-dependent individuals after controlling for socio-demographic factors, psychiatric disorders and other drug use.[212] Beautrais and colleagues (1999) examined 302 hospitalised cases of suicide attempts and found that 16 per cent screened positive for cannabis abuse or dependence, compared with 2 per cent of a random community sample, which translated to a ten-fold suicide attempt risk for those who had a cannabis use disorder (abuse or dependence). After controlling for depression and social disadvantage, however, the study found this was reduced to a two-fold risk.[213]

Longitudinal studies examining cannabis use and suicide risk have produced mixed results. The Christchurch study found that cannabis use by age 16 years was related to an increase in reported suicide risk.[204] This relationship, however, became non-significant after adjusting for other variables such as childhood sexual abuse, anxiety and relationship with parents.[204] Data from a Victorian secondary school study indicate that, while a relationship between suicide risk and cannabis use was not significant, cannabis use was related to higher levels of self-harm in females after controlling for alcohol use and depression.[214] The Swedish conscript study found that heavy cannabis use was associated with a four-fold mortality risk from suicide.[215] After controlling for social background factors, however, the Swedish study found this relationship failed to reach significance. A more detailed re-analysis of these data found that while drug dependence (including cannabis) was a moderate predictor of suicide risk (increased odds of 3.6), the strongest predictor was psychiatric hospitalisation by age 18 years (increased odds of 11.3).[216] Unfortunately this study did not isolate cannabis use in the overall analysis of drug dependence. It can be assumed, however, that this was the most common drug of dependence in the sample.

In sum, cross-sectional studies have generally indicated that the association between cannabis use and depression is partly explained by factors such as the use of other drugs, family structure, marital status and personality characteristics. Longitudinal research has consistently found that depression does not predict cannabis use, but that cannabis use poses a moderate risk for later depression after accounting for other influencing factors, especially for adolescent girls. Although the literature on cannabis use and suicide risk has produced mixed results, there is reason to believe that heavy cannabis use may pose a small additional risk of suicide.

6.3 Relationship with anxiety

There is little research examining the relationship between cannabis use and anxiety. While experiencing individual symptoms of anxiety is a fairly normal human experience, when several symptoms cluster together this may form an anxiety disorder. This disorder may encompass several syndromes such as panic disorder, obsessive compulsive disorder and phobias.

Like depression and schizophrenia, anxiety disorders occur at higher rates in frequent users of cannabis. However, it is unclear whether this association is due to factors such as other drug use, and personal or peer characteristics. Results from the ECA indicate that anxiety disorders (panic disorder, obsessive compulsive disorder and phobias) are roughly two to three times more common amongst those who meet criteria for cannabis abuse or dependence.[118]

Data from the Australian National Survey of Mental Health and Wellbeing indicate that cannabis dependence in the past year was associated with an approximate one-in-six chance (17%) of having an anxiety disorder, compared to one-in-twenty chance (5%) for non-cannabis users.[217] When factors such as regular tobacco smoking and alcohol use disorders were accounted for, however, the association between cannabis use and anxiety became non-significant.[217] In a survey of Australian adolescents, Rey and colleagues found that those who reported cannabis use in the past month experienced more anxiety symptoms than those who did not.[203] Unfortunately, it is unknown whether this relationship would have persisted after controlling for other factors.

Longitudinal research has generally found no relationship between cannabis use and anxiety[210] or that other factors account for this relationship.[204,218] However, there have been exceptions.[209] The Victorian longitudinal study by Patton and colleagues found, after considering other drug use, antisocial behaviour and symptoms, that females in the sample who used cannabis daily faced a four-fold increased risk of mixed anxiety and depression.[209] In contrast, the Dunedin longitudinal study found no relationship between cannabis use and anxiety at ages 15, 18 and 21.[210] In the Christchurch cohort study, Fergusson and Horwood found that those who use cannabis 10 or more times by the age of 15–16 years were more likely to have screened positively for an anxiety disorder at age 16–18: 31 per cent of those who had used 10 times or more; 19 per cent of those who had used 1–9 times; and 15 per cent of those who had never used cannabis. After controlling for individual, familial, peer and socio-demographic variables, the study found this relationship became non-significant. The most recently released findings from the cohort at 21 years indicated that substance abuse and dependence were substantially higher among those with anxiety. However, this finding could be explained by childhood and family factors, prior substance dependence, comorbid depression and peer affiliations.[218] The authors concluded that the relationship between anxiety and illicit substance use is either largely or wholly non-causal.[218] Although this study did not isolate cannabis use, the use of this substance was prevalent in the sample.

In sum, research suggests that cannabis use and anxiety disorders occur together at a rate greater than chance. However, this relationship seems to be largely mediated by other variables such as childhood and family factors, other drug use and peer affiliations, rather than cannabis use per se.

6.4 Relationship with aggression, violence and other mental health disorders

Individuals who use cannabis at an early age are at greatest risk of adverse social outcomes, including delinquency and violence (see section 7 for a detailed discussion on delinquency and crime). Young cannabis initiators are also more likely than others to engage in such behaviours before they begin to use cannabis.[100] This creates difficulty when examining the association between cannabis use and adjustment problems such as violence. The pertinent question is whether violence was a consequence of cannabis use or withdrawal, or a result of a personality that was predisposed to violence before cannabis use commenced. Further, involvement with cannabis most commonly takes place in an illegal setting, where contact with dealers and drug-using peers may lead to violent disputes.[219]

Several large longitudinal studies have examined the relationship between cannabis use and violent acts. The Christchurch cohort study assessed whether violent offences correlated with cannabis use at age 16 years.[204] Such offences included assault, fighting, use of a weapon or threats of violence against another. Findings indicated a dose–response relationship where higher cannabis use was associated with increased numbers of violent offences. This association persisted after controlling for other drug use and peer criminal behaviour, suggesting that deviant peer affiliations were not responsible for the relationship.[204] A later follow-up of this cohort revealed the same association between violent offences and cannabis use at age 21 years, with the link being most pronounced in early (14–15 years) cannabis initiators who used regularly.[205] Although these results

are suggestive of a causal relationship, the authors note that it is possible that the pre-existence of psychosocial problems may have encouraged cannabis use rather than the other way around.[205] This study would have benefited from measuring violent tendencies from a very young age to better ascertain the later role of cannabis use.

The Dunedin study used self-reporting and police records to measure violence and found that both were strongly correlated with alcohol dependence, cannabis dependence and schizophrenia. After controlling for childhood conduct disorder, in which violent outbursts are a common feature, the study found a weak relationship between cannabis dependence and violence remained. Rather than attributing this to cannabis use per se, the authors believe that this relationship was due to cannabis use in the context of an illegal drug market where violence was used to resolve disputes.[219]

A longitudinal study of African-American and Puerto Rican youth in New York measured self-reported violence towards others and found that early cannabis use doubled the risks after adjusting for a range of variables.[207] This study, however, did not account for a history of violence and delinquency before cannabis use.

The findings by Arsenault and colleagues[219] have been supported by recent twin research showing that those with a conduct disorder were more likely to use cannabis.[220] In a Welsh study of 740 identical and non-identical twin pairs, it was found that, while environment did play some part in the development of cannabis use disorder in those with conduct disorder, genetics also exerted a significant influence.[220] Put simply, the absence or presence of conduct disorder in a twin pair was a good predictor of cannabis use. This finding suggests that cannabis use and violence, at least to some extent, co-occur due to tendencies in the personality.

A Norwegian longitudinal study found that serious conduct problems, such as fighting with a weapon, breaking windows and theft, were moderate predictors of early cannabis initiation for males.[221] For females, strong predictors of early cannabis initiation were aggressive acts including violently quarrelling with a teacher, cursing openly or being summoned to the school principal.[221]

In summary, violence occurs at higher rates among regular cannabis users than occasional users or non-users. However, uncertainty remains as to whether this is because people with violent tendencies and a range of other psychosocial difficulties are more prone to using cannabis in the first place. Studies that have controlled for childhood conduct disorder have shown that this significantly weakens the association with cannabis use and violence, suggesting that childhood predisposition to violence does play a role in the association. In addition, involvement with cannabis in the context of an illegal drug market may increase the chances that violence occurs in social interactions. Also cannabis withdrawal, rather than intoxication, may lead to irritability and be associated with increased aggression.

6.5 Impact of cannabis use on mental health services

While there have been numerous reports of cannabis users with mental health problems presenting for treatment,[170,222,223] there have been no systematic reviews of the impacts of cannabis use on mental health services. This assessment would be complicated for several reasons. For instance, standardised measures would have to be implemented across services to determine whether cannabis was the main source of the mental health problem. Such an issue may arouse considerable disagreement among clinicians of varying theoretical orientations because of the wide range of variables that correlate with both cannabis use and mental health. Researchers face the same difficulty when trying to isolate the effects of cannabis use in mental health as they navigate possible explanations including other drug use, personality characteristics, pre-existing symptoms and genetic vulnerabilities.

Given that cannabis use may precipitate schizophrenia episodes/symptoms in psychosis-prone individuals[182] and that the average age of cannabis initiation is lowering,[2] one possible impact on mental health services is a higher number of younger individuals presenting with first-episode schizophrenia. There is some evidence to support this, indicating that younger cohorts of cannabis users are experiencing earlier problems with schizophrenia.[196] It is unlikely, however, that rises in cannabis use would result in a flood of new schizophrenia cases. To the contrary, there is evidence that population levels of schizophrenia have slightly decreased despite increasing rates of cannabis use.[194]

Although it is not likely that cannabis use contributes to new cases of schizophrenia, there is evidence that it may worsen the symptoms of an existing schizophrenic illness.[181] In turn, this may result in a small increase in chronic cases of the mental illness.[194] Whether or not this translates to significantly higher admissions for more individuals into mental health care services remains to be evaluated.

It is a likely assumption that levels of cannabis use have increased among people with schizophrenia in the same proportion as in the Australian population.[194] If this assumption is applied to other mental disorders, one possible implication is that mental health services will see a growing number of cases of people with a mental health disorder and a concurrent cannabis use problem.

Clearly, more research is needed to assess the impact of cannabis use on mental health services. Such an evaluation would require high levels of planning and cooperation between mental health service providers. The information yielded would provide grounds for evaluating not only the role of cannabis in mental disorders in general, but also the economic costs of cannabis use.

7. Does cannabis use impair or delay intellectual, social and emotional development in young people?

Developmental changes occur in several spheres of life during adolescence. It is a period when intellectual capacities expand and the social group becomes increasingly influential. It is also a time when young people make decisions that have ramifications for years to come. Given the widespread use of cannabis among young Australians, its possible impacts on adolescent development are an important issue.

According to the 2001 National Household Survey, approximately one in three adolescents (34.3%) reported using cannabis at least once in their life, one-quarter (24.6%) reported using the drug recently (in the past 12 months), and around one in ten (11.6%) recent users reported using daily.[4] Moreover, among the 14–19 year age group, the average age at which people are beginning to use cannabis in Australia has dropped from 14.8 years in 1995 to 14.6 years in 2001.[224] As would be expected, associations between cannabis use and developmental difficulties in young people are complex and several possible explanations are explored in the literature.

One of the debated effects of chronic cannabis use is the amotivational syndrome. This has been described as a set of characteristics including general apathy, loss of productivity, difficulty in carrying out long-range plans, lethargy, depression and inability to concentrate and sustain attention.[225] The amotivational syndrome, however, has been difficult to define. A number of authors have concluded that the symptoms of amotivational syndrome were primarily due to co-exisiting depressive symptoms.[226,227] In addition, anthropological studies of long-term daily cannabis smokers in Jamaica[228] and Costa Rica[229] failed to find evidence of the syndrome. Given the methodological complexities of studying amotivational syndrome, which require an inference to be drawn from self-reported effect and work history and controlled for the effects of chronic intoxication, a number of laboratory studies have been conducted examining the effects of cannabis use on responses to a monetary reward. These studies have consistently demonstrated that the effects of cannabis on motivational responding have been reversed when monetary reward was introduced.[225,230,231] It appears, therefore, that while clinical populations complain of the effects of cannabis use on motivation,[232] there is no compelling evidence to support the existence of an amotivational syndrome associated with cannabis use.

It has been speculated that cannabis use may affect intelligence. Tests of intelligence examine a range of abilities in order to calculate the overall 'intelligence quotient' or IQ score. For instance, the commonly used Wechsler Intelligence Test contains categories relating to general knowledge, language, memory, reasoning, spatial ability and problem solving.[232] Although some cross-sectional findings indicate that IQ may be reduced by cannabis use,[233] IQ levels prior to cannabis use were unknown. To date, there has been only one study that measured IQ before and after the onset of cannabis use. Fried and colleagues followed a group of 70 Canadian youths from birth to 17–20 years of age.[132] After controlling for a large range of variables including family income,

parental education, prenatal exposure to drugs and academic performance, the study found that current cannabis use was associated with an average 4 point decline in IQ for participants who smoked five or more joints per week. The authors mentioned that such a decrease in IQ was larger than that expected for low-level lead exposure and similar to that observed in children prenatally exposed to alcohol and cocaine.[132] Despite this, a negative effect on IQ was not found for former heavy cannabis users or for those who were current light cannabis users.

Another way to measure the impact of cannabis use on mental capacity is through the examination of cognitive processes. The term '*cognition*' refers to a broad range of abilities commonly examined in intelligence tests, such as verbal information processing, spatial judgement, memory span, attention and problem solving.[234] Studies investigating whether cannabis use leads to cognitive decrements beyond the period of intoxication have produced mixed results.[235] While most have tested adult groups, relatively few have focused on young people.

In a sample of American college students, Pope and Yurgelun-Todd compared the cognitive performance of heavy and light cannabis users after a 19-hour abstinence period. These two groups were not found to differ on tasks involving memory, auditory processing or complex reasoning.[236] Heavy cannabis users, however, scored more poorly than light users on tests of attention. More recently, Bolla and colleagues measured cognitive performance after a 28-day abstinence period in a sample of 22-year-old heavy cannabis users.[237] Findings indicated that, as the number of joints smoked per week increased, test performance decreased on tasks related to memory, complex reasoning, psychomotor speed and manual dexterity (Bolla et al., 2002). These findings are in conflict with those from well-designed studies involving adult cannabis users. For example, Pope and colleagues found that cannabis-related cognitive decrements disappeared within 28 days of use.[238]

Early cannabis initiation is associated with a variety of adverse outcomes such as dependence, criminal activity and the use of other addictive drugs.[14–16,53,239,240] Pope and colleagues examined whether early cannabis initiation (before age 17 years) confers a greater risk of developing cognitive deficits as compared to later initiation.[240] Three groups of cannabis users were compared: long-term early initiators, long-term late initiators (age 17 or above) and infrequent cannabis users. Results indicated that the only domain in which early onset users differed from controls or late-onset users was in verbal ability. As the study was cross-sectional, it was unable to ascertain whether this difference was due to cumulative neurotoxic effects of cannabis, pre-existing differences between the two cannabis-using groups, or poorer learning of verbal skills by the early cannabis initiators who rejected academic pursuits and conventional roles.[240]

There is substantial evidence that cannabis use is associated with impaired academic performance,[241–243] higher rates of absenteeism[244,245] and earlier school leaving.[246–250] A cross-sectional study of United States youth found that cannabis users reported lower grade point averages than their non-cannabis-using peers.[243] Similarly, Novins and colleagues found that cannabis use was associated with poorer school performance in

a sample of American Indian adolescents.[242] However, this effect was evident only for males. The 1999 Australian School Students' Alcohol and Drugs Survey (ASSADS) found that those who were truant on the day before the survey administration had higher levels of reported cannabis use compared with attending students.[10]

Cross-sectional findings that cannabis is associated with poorer educational outcomes have been supported by longitudinal data from the United States,[248,249,251] Columbia,[252] New Zealand[204,244,253] and Australia.[254] Perhaps the most extensive evidence comes from a 25-year longitudinal study conducted by Fergusson and colleagues in a large New Zealand birth cohort.[204,244,253] After controlling for mental health, family dysfunction, delinquent and drug-using peer affiliations and educational achievement, the study found that early initiators were 3.1 times more likely to leave school as compared to non-users.[244] A later follow-up of this cohort found that those who had started using cannabis by age 16 were at substantially higher risk of leaving school without formal qualifications.[204] By the time this cohort reached age 25 years, increasing cannabis use was associated with a higher risk of leaving school without qualifications, failure to enter university and failure to secure a university degree.[253] Consistent with the data was the finding that the association between cannabis use and poor educational outcomes was not due to cannabis impairing cognitive functioning or producing an 'amotivational syndrome', but rather due to the social context in which cannabis is used, encouraging attitudes that promote school drop-out and diminish further education opportunities.[253]

A longitudinal study of Victorian adolescents from age 15 to 21 years by Lynskey and colleagues[254] has supported the findings of Fergusson and colleagues.[204,244] After controlling for demographics, other substance use, psychiatric problems and anti-social behaviour, survey results indicated that early cannabis initiators (by age 15), who used at least weekly, were at significantly higher risk of early school leaving as compared with later initiators. The authors also attributed this to deviant peer affiliation. This is consistent with other findings that the influence of deviant peers is highest during adolescence.[255]

In addition to the association between cannabis use and adverse social outcomes such as poor educational attainment, evidence suggests that cannabis use is related to delinquency and crime. Despite this, there remains uncertainty as to how cannabis use and crime are associated. Some longitudinal evidence indicates that drug users had higher rates of criminal activity even *before* initiating substance use (including cannabis) and that subsequent drug use, with the exception of heroin, had little effect on crime.[256] This has been supported by other research in which, after controlling for demographic and psychosocial variables, studies found that adolescent drug use failed to predict crime.[249]

In contrast, a longitudinal study by Fergusson and Horwood[204] found that cannabis use predicted criminal behaviour at age 16 in a New Zealand sample after statistically adjusting for a range of factors including peer criminal behaviour and substance use. This relationship persisted at age 21, especially in early initiators. Another prospective New Zealand study found that cannabis dependence, alcohol dependence and schizophrenia were strongly associated with officially recorded violence.[219] These associations, however, were largely reduced by controlling for childhood conduct disorder. The authors suggest that the remaining association may be the result of using violence to resolve

conflicts in the illegal drug market.[219] There is also recent evidence, however, that deviant peer affiliations explain at least some of the link between drug use and crime.[255]

In addition to population-based studies linking early and/or heavy use of cannabis with increased participation in crime,[100] surveys of young people involved with the juvenile justice system report high levels of cannabis use and a relationship between frequent cannabis use and offending behaviour.[257–260] For example, young detainees in New South Wales report much higher rates of regular (at least weekly) cannabis use and a lower age of initiation than their Australian peers at a population level.[261] Eighty-three per cent of detainees in 1999[261] compared to 9 per cent of young people in the 1998 National Household Survey were at least weekly cannabis users, while the average age of initiation was 12 years compared to 15 years.[224] There was a significant increase in the proportion of detainees reporting use at this level between 1996 and 1999 (71% and 83% respectively). Almost one in three (30%) male detainees reported that they felt their cannabis use was a problem.[262]

Salmelainen's (1995) study of 247 juvenile detainees in New South Wales found that those offenders who reported higher levels of cannabis consumption were more likely to be frequent offenders, particularly those in detention for motor vehicle theft and break and enter offences.[259] There is also evidence that juveniles resort to income-generating property crime to primarily fund their consumption of cannabis, as well as of other drugs.[266] While these studies focused on young people in custodial care, a 1996 survey of New South Wales secondary schools also found cannabis use predicted criminal involvement, with the odds of participation in assault, malicious damage and acquisitive property crime between two and fives times greater among frequent cannabis users than non-users, after controlling for drug use and developmental factors.[257]

In addition to delinquency, early cannabis users are also more likely to precociously adopt adult roles before they are suitably mature to deal with such responsibilities.[249] For instance, early cannabis use predicts higher levels of leaving the family home,[248] immature sexual activity,[264] and unplanned pregnancy and abortion during adolescence.[248,264] Additionally, early cannabis users are more likely to have formed their own families by late adolescence and be divorced by young adulthood.[249] The life course of young adult cannabis users is less likely to follow a conventional path. For instance, heavy cannabis use in young adulthood is associated with decreased rates of marriage and increased chances of cohabiting with a partner.[249]

A further concern is that cannabis use may impede the emotional development of young people. While most research has focused on associations between cannabis use and mental health problems such as psychosis, depression or anxiety, a small amount of research has examined possible links between cannabis use and subjective feelings of life dissatisfaction (see section 6 for detailed discussion on cannabis and mental health).

A cross-sectional sample of young adults in the United States found that life dissatisfaction increased with levels of cannabis use.[200] More recently, it has been found that cannabis use, especially in those with an earlier age of cannabis initiation, was associated with lower life satisfaction among male and female high school students of Caucasian descent.[265] Despite this, findings for those of African-American descent were unreliable. Unfortunately, the cross-sectional design of studies examining drug use and life

satisfaction has not allowed for the nature of the association to be assessed. Future studies would benefit from a longitudinal design where levels of life satisfaction are measured before and after drug use is initiated.

Overall, there is some evidence indicating that heavy current cannabis use is associated with a moderate decrease in global IQ. These effects, however, do not appear to persist once cannabis use has ceased for some months. The lasting effects of cannabis use on cognitive processes beyond the period of intoxication also remain unclear. While some findings indicate decreases in memory, attention, psychomotor speed and manual dexterity after 28 days of abstinence, other well-designed studies have failed to replicate these results. There is evidence that those who initiate cannabis at a young age are more likely to have reduced verbal abilities. However, it is unknown whether this is due to social factors or the actions of cannabis in the brain. Nevertheless, cannabis use is associated with impaired educational outcomes, delinquency and crime. The most probable route of this association is in deviant peer affiliations and involvement in an illegal drug subculture where violence is common. In addition, the life path of young cannabis users is more likely to be unconventional due to the premature adoption of adult roles. The acute effects of cannabis intoxication may also play a role in encouraging impulsive behaviour and impairing perceptions of risk among the minority of students who are regular cannabis users.[4]

In terms of emotional development, cross-sectional studies indicate that those who use cannabis are more likely to be dissatisfied with life. These studies, however, need to be confirmed with longitudinal data.

8. What are the current best-practice treatments available for cannabis-related problems?

There is now evidence that prolonged cannabis use can produce dependence and a variety of related problems (see section 11 for a detailed discussion on cannabis dependence).[3,13,19,20,21,30,47,56,267–273] During the past decade, there has been an increase in those accessing services for problematic cannabis use.

In Australia, people seeking treatment for cannabis as the main drug of concern increased from 4 per cent in 1990 to 10 per cent in 2001.[274] Information from the 2001–02 Australian National Minimum Data Set shows that cannabis was the principal drug of concern for 21 per cent of all treatment admissions and was the most common principal drug of concern (46%) in the 10–19 year age group seeking treatment.[275]

In the United States, treatment admissions for primary cannabis users increased from 6 per cent in 1992 to 15 per cent in 2000.[276] In 2000, between 2.5 per cent and 24 per cent of treatment admissions in the European Union were also for cannabis use.[277]

Despite these increases, little research has focused on the efficacy and effectiveness of different treatment options for those who misuse cannabis.

8.1 Psychological interventions

The treatment options for cannabis dependence are far fewer than for opiate or alcohol dependence. Most include some variant of psychological intervention – commonly, cognitive behavioural therapy (CBT) or motivational interviewing (MI). While CBT examines the interplay between thoughts, behaviour and environment, the main aim of MI is to enhance the motivation of the participant to change.

The first psychological intervention study was conducted in the United States with a sample of 212 heavy cannabis users.[278] Participants were assigned to either a 10-week social support group or a 10-week relapse prevention group with a CBT focus. In the support group, discussions centred on issues including the giving and receiving of support, dealing with denial, and affiliating with friends who still used cannabis. The relapse prevention condition was more structured, including planned exercises, homework tasks and formalised quit contracts between participant and counsellor. At 12 months follow-up, there were similar rates of reduction in cannabis use for both groups – 15.2 per cent were abstinent in the CBT group compared with 18.1 per cent in the social support group. Moreover, around one in five people from both groups were judged to have improved (measured by using 50 per cent or less

than pre-treatment levels or reporting no cannabis-related problems). While these results may suggest that both treatments were effective to some degree in treating cannabis dependence, the lack of difference between both treatment conditions and the absence of a control group made interpretations difficult.

In order to overcome the problems of not having a control group to compare with the active treatment groups, Stephens and colleagues conducted a second study with a delayed treatment condition, offered four months later than in the active treatment groups, a 14-week CBT relapse prevention group and a brief two-session MI interview.[279] While the CBT condition was similar to that in the earlier experiment, the MI condition comprised two 90-minute individual sessions. Results showed that at four-month follow-up, participants in the active treatment groups had a significantly lower number of dependence symptoms and fewer cannabis-related problems compared to the delayed treatment group. They also reported using cannabis on fewer days per month and fewer times per day. Abstinence rates at four months were 37 per cent for both active groups compared to 9 per cent for the delayed treatment condition. At 16 months, abstinence rates had dropped only moderately to just below 30 per cent for both active groups. Interestingly, there was no difference between the two treatment conditions. Those who received the brief intervention were equally as likely to benefit as those in the 14-week CBT condition.[278]

An Australian study added further support for the effectiveness of brief interventions for cannabis use. A sample of 229 cannabis-dependent individuals were allocated to one of three conditions: six sessions of CBT, one session of CBT, and a delayed treatment control group.[280] This study incorporated CBT interventions with elements of MI, so rather than comparing different therapy types, as earlier studies had done,[278,279] the study compared two matching therapies, the only difference being in length. At follow-up, it was found that 15.1 per cent of participants in the six-session CBT group had achieved continuous abstinence as compared to 4.9 per cent in the one-session CBT group and 0 per cent in the delayed treatment group. Also at follow-up, those in the active treatment groups were judged to be less severely dependent than before the intervention, reporting higher levels of control over their cannabis use and fewer cannabis-related problems compared to those in the delayed treatment group.[280]

A smaller study by Budney and colleagues tested the effect of providing heavy cannabis users with vouchers as an incentive for cannabis abstinence.[281] These vouchers were exchangeable for retail items and were given only if users presented cannabinoid-free urine samples. The study rationale was based on previous research indicating that voucher incentives in conjunction with behavioural interventions improved the treatment outcome of cocaine-dependent individuals.[282] Sixty individuals seeking outpatient treatment for cannabis problems were randomly assigned to three conditions: four sessions of motivational enhancement (MET), 14 sessions of motivational enhancement plus behavioural coping skills (MET/CBT), or 14 sessions of motivational enhancement with behavioural coping skills and voucher incentives (MET/CBT/V). Findings indicated that the group receiving voucher incentives were more likely to have been abstinent during the last week of treatment – MET/CBT/V 35%, MET/CBT 10%, MET 5%. While results did indicate that the MET/CBT group performed better than MET alone, this difference was not statistically significant. At

30 days post-treatment, all groups reported using substantially less cannabis than before treatment, with a slightly higher reduction for the voucher group.

A recent study with young probation-referred cannabis abusers has strengthened findings for the utility of voucher-based incentives.[283] Participants received either three sessions of motivational enhancement therapy or this same therapy with added vouchers for attendance. Results showed that while both groups reported significantly reduced cannabis use and legal problems, more participants in the voucher group completed treatment.

One possible criticism of these studies is that participant samples have lacked diversity, being mostly male, Caucasian and drawn from single geographical locations. One way of avoiding such limitations is to conduct multi-site trials where participants are recruited from a range of geographical locations where gender and race are more varied.

In the United States a large multi-site trial was recently completed in which 450 cannabis-dependent treatment seekers were recruited from three States.[284] Participants received either two sessions of motivational enhancement therapy, nine sessions of a hybrid therapy including motivational and cognitive behavioural components, or delayed treatment. At 15-month follow-up, greater numbers of nine-session participants had been abstinent in the past 90 days (22.7%) as compared with the two-session participants (12.5%).[284] Both groups also had significantly fewer cannabis-related problems compared with the delayed treatment group. There were no gender or ethnic differences in treatment outcome.[284]

A considerable amount of literature has focused on interventions for reducing cannabis use in young people. This is because young people may be more susceptible than adults to developing cannabis dependence and a range of associated problems (see section 11 for detailed discussion).

The Cannabis Youth Treatment (CYT) Project is a multi-site study of 600 cannabis users aged 12–18 years. Participants were allocated to five treatment conditions including two mixed CBT and MI conditions of differing lengths, two family-orientated interventions and one community reinforcement intervention. This last approach was designed to enhance the rewarding aspects of abstinence by helping the adolescent to interact with their environment in a different way. The focus includes insight into the links between thought and behaviour, increased engagement in prosocial activities, decreased illegal activity and increased school attendance. At 12-months follow-up, across all treatment groups, participants had reduced their cannabis use and related problems by around one-third. Evidence indicated that the briefest intervention was most effective for those with low severity problems while the longer interventions led to more significant improvements in those with high severity problems. Besides this, there was little difference between the treatment groups.[285]

The efficacy of brief interventions for adolescent cannabis users has also been tested using multi-site methods. A study in the United Kingdom with non-treatment-seeking cannabis users was conducted in ten educational colleges in London.[286] Participants were recruited by peers and received either no treatment or a single hour of face-to-face motivational therapy. Follow-up at 12 weeks showed that the treatment group had reduced

their weekly frequency of cannabis use by an average of 66 per cent while frequency of use in the control group had increased by 27 per cent. Those who used cannabis at higher rates on entry to the study made the largest reductions in cannabis use after the intervention. Notably, substantial reductions in alcohol and tobacco use were also observed for the treatment groups.[286] This is the first published study to provide evidence for the use of brief interventions among young people who are not seeking treatment.

In addition to the interventions already discussed, a new approach is being developed for reducing cannabis use in adolescents. The Adolescent Cannabis Check-up (ACC) and the Teen Marijuana Check-up (TMC) are currently being trialled in Australia and the United States respectively.[287] Designed for young non-treatment-seeking cannabis users, this intervention may be delivered in schools (TMC) and may also include a session with a concerned other in order to strengthen the participant's involvement (ACC). The first interview focuses on patterns of substance use and the consequences of cannabis use. Using motivational enhancement techniques, the participant is re-interviewed around one week later. Preliminary results for the check-up approach are promising. At three months follow-up, 83 per cent of TMC participants reported reducing or stopping cannabis use at some point in the 90 days and 15 per cent reported complete abstinence in the past 30 days.[288] Similarly, 77 per cent of ACC participants had stopped or reduced cannabis use at some point in the past 90 days and 16.7 per cent were completely abstinent over this period.[289]

8.2 Pharmacological interventions

Research on pharmacological interventions for cannabis withdrawal and craving is in its infancy and there have been no randomised controlled trials in this area. Several small laboratory studies have examined the ways in which mood-altering substances influence cannabis withdrawal[290–292] and the impact of drugs that block the acute effects of cannabis.[290] Other research has tested whether oral THC influences decisions to continue cannabis smoking.[290]

Recently two laboratory studies have tested the efficacy of mood-altering drugs for treating symptoms of cannabis withdrawal in non-treatment-seeking individuals.[290,291] The first study involved the administration of bupropion, a substance with stimulant and antidepressant properties that has been used successfully to aid nicotine abstinence.[294,201] Among the sample of ten regular cannabis smokers undergoing abstinence, the study found that bupropion maintenance significantly exacerbated withdrawal symptoms, such as irritability, restlessness, depression and sleep difficulties. On this basis, the authors concluded that bupropion does not show potential as a pharmacological treatment for cannabis withdrawal.[291] The specific effects of bupropion on cannabis craving and relapse prevention are yet to be examined. A later study by the same research group tested the effects of nefazodone, an antidepressant with sedative elements, in a group of seven volunteer regular cannabis users.[290] Findings indicated that nefazodone maintenance during cannabis abstinence was associated

with improved ratings of muscle pain and anxiety but not irritability, miserable mood or sleep quality.[290] Such mixed findings suggest that this drug has only limited capacity in treating cannabis withdrawal symptoms.

Another agent under investigation in rodents is the mood stabiliser lithium carbonate. One study has demonstrated that injection of lithium prevented cannabis withdrawal in rats.[294] Although lithium is not yet tested on humans, two small pilot studies are currently being conducted in Canada and Australia.

There have been two small laboratory studies on the effects of oral THC maintenance for cannabis craving and withdrawal.[290,295] The first study found that the administration of oral THC had no significant effect on the frequency at which participants chose to smoke cannabis.[290] The second study tested the effects of a mood stabiliser (divalproex) and oral THC on cannabis craving and withdrawal symptoms.[295] During cannabis abstinence, it was found that divalproex decreased cannabis craving but increased ratings of other withdrawal symptoms including irritability, tiredness and anxiousness. Conversely, very low doses of oral THC were effective in decreasing all measured withdrawal symptoms in addition to craving.[295]

The use of *antagonist* pharmacotherapies is an option in the treatment of opiates, alcohol and nicotine. Antagonists are agents that block the effects of drugs by binding to receptors in the brain. Different antagonists work on different receptors and therefore inhibit the effects of different drugs. Perhaps the most well-known antagonist is naltrexone. This compound blocks the acute effects of heroin and other opiate drugs, precluding the user from achieving the drug 'high'.[296] Interestingly, some laboratory research suggests that naltrexone can prevent the development of THC dependence in rats.[297] The mechanisms behind this are complicated, but it is thought that naltrexone blocks opiate receptors that also interact with THC.[290,298] This sharing of common receptors between cannabis and opiates is supported by evidence that THC attenuates opiate withdrawal symptoms in mice.[299] However, human studies have found that naltrexone does not alter the subjective effects of low doses of oral THC[300] and may actually enhance the positive subjective effects of higher doses of oral THC.[301] Although the reason for such a counter-intuitive effect in humans remains speculative,[301] at this stage naltrexone does not appear to be a viable treatment option for cannabis dependence.

There has been some research on a specific antagonist that directly blocks the acute effects of cannabis at cannabinoid receptors. Past findings indicate that SR141716 (*Rimonabant*) inhibits signs of THC intoxication in monkeys, rats and pigeons.[302–304] In support, one human study of experienced male cannabis users found that SR141716 blocked the acute psychological and physiological effects of smoked cannabis.[292] Although no studies have used this antagonist to treat cannabis-dependent individuals over a prolonged period, SR141716 does show promise as a possible treatment for individuals who are sufficiently motivated to quit cannabis use.

8.3 Peer support and environmental approaches

There have been no formal studies on the utility of peer support treatment programs for cannabis use. However, there are self-help groups available to cannabis users which strongly endorse the therapeutic potential of peer support. For instance, Narcotics Anonymous (NA) is a self-help group where the only requirement for membership is a desire to stop using drugs.[305] Such 12-step programs view addiction as a disease and promote complete abstinence as the only option for recovery. As there are no drug rehabilitation specialists involved in 12-step meetings, the support of one former addict helping another is at the core of the program's philosophy.[305] Most people who become part of the NA program acquire a 'sponsor', or person who gives personal support and helps recovering addicts to implement the 12 steps. These include belief in a higher power and keeping a fearless moral inventory of oneself.[305]

Marijuana Anonymous, a specific program for cannabis users modelled on 12-step lines, has also been established. Evaluations of such programs have shown small beneficial effects for general drug use reduction, although no structured evaluations have been conducted on cannabis use alone.[306]

9. What are the effects of passive cannabis smoking?

Like tobacco smoke, cannabis smoke is likely to be inhaled by others in the immediate surroundings, especially when used in a social or enclosed environment. The 2001 National Household Survey found that around one in two (48.6%) recent users reported having smoked cannabis at a private party and about one in five (20.5%) reported having smoked it in a car or other vehicle.[2]

Experimental evidence indicates that passive exposure to cannabis smoke in a confined space results in the presence of THC in the blood,[309] urine[307–309] and plasma.[310] Some findings also suggest that very heavy exposure to cannabis smoke can result in slight intoxication, roughly equivalent to smoking a joint with low levels of THC.[311] However, outside experimental conditions it would be unlikely that individuals would knowingly tolerate such high level exposure.[307]

Unfortunately, there has been no formal investigation of the health effects of passive cannabis smoke exposure in the short or long term. Despite this, it is possible to develop hypotheses on the effects of passive cannabis smoking, based on the similarities between cannabis and tobacco smoke. In a review on the respiratory effects of cannabis, Taylor and Hall concluded that the risks of regular cannabis smoking are similar to those of regular cigarette smoking.[101] Tobacco and cannabis smoke produce tar deposits on the lungs, carry carbon monoxide and contain many identical carcinogens.[79,104] Passive tobacco smoking is a well-established health hazard.

A 1997 National Health and Medical Research Council report estimated that, per year, passive tobacco smoking leads to illnesses in the lower respiratory tract in 16,300 Australian children and exacerbates the symptoms of asthma in 46,000 Australian children.[312] The report also estimated that the passive inhalation of tobacco smoke causes 12 new cases of lung cancer each year in adult Australians and 77 deaths from coronary heart disease each year.[312] Due to these harmful consequences, laws banning cigarette smoking in enclosed public places have been enacted in all States and Territories of Australia.

Given the similarities between cannabis and tobacco smoke, it would appear fair to argue that the effects of passive cannabis smoking would be similar to those of passive cigarette smoking. However, in making such an assumption, it is important to consider that most cannabis use occurs in the late teens or early 20s, is intermittent, and steadily decreases with major life changes such as marriage or entry into employment.[3] As estimated by Hall and colleagues, around one in ten people who try cannabis become regular users.[4] In contrast, the use of tobacco is far more stable, generally persisting through the 20s and 30s with very little decline.[3] Taking this into account, cases where people are chronically exposed to passive cannabis smoke over a number of years are likely to be far less common compared to tobacco smoke. Furthermore, many people who smoke cannabis also smoke tobacco, especially those who are cannabis-dependent.[21,31,313–315] This creates difficulty when attempting to isolate the effects of passive cannabis smoking in children and partners of chronic cannabis smokers.

In sum, it is possible that high level exposure to cannabis smoke in a confined space can result in the presence of cannabinoid metabolites in body fluids and slight intoxication. Although there has been no research on the health effects of passive cannabis inhalation, there is reason to believe that these would be similar to tobacco. It must be considered, however, that prolonged heavy passive exposure to cannabis smoke would occur less frequently than such exposure to tobacco smoke.

10. What are the links between, and health impacts of, smoking tobacco and cannabis?

The smoking of cannabis and tobacco involves the inhalation of combustible material, exposing users to tar containing many common carcinogens.[37,79,101] This is a justified health concern because tobacco is the most widely used licit drug and cannabis is the most commonly used illicit drug. Furthermore, tobacco and cannabis are commonly used in conjunction with one another.[314,316]

Although large population surveys such as the Australian National Household Survey do not collect information regarding the *concurrent* use of tobacco and cannabis, data from community samples,[31,313] birth cohorts[316] and treatment-seeking groups[232,314] have found that a large proportion of cannabis smokers also use tobacco. For instance, in a US community sample interviewed in 1981, 41 per cent of cigarette smokers reported ever using cannabis, 27 per cent reported use in the past 30 days, and 9 per cent reported using daily for at least two weeks within the past 30 days.[317] When this sample was re-interviewed, cannabis use at baseline, especially recent or daily use, was a significant predictor of continued tobacco use 13 years later. More recently, Poulton and colleagues followed a sample of young New Zealanders from age 15 to 21 years.[316] Of the people who smoked cannabis at age 21, 69 per cent also smoked cigarettes.

Findings from the Australian National Survey of Mental Health and Wellbeing indicate that, among cannabis smokers, those who smoked cigarettes were 1.7 times more likely to be cannabis-dependent.[21] Findings of higher rates of cigarette smoking among cannabis-dependent people have been supported by studies of people seeking treatment for cannabis dependence. For instance, Moore and colleagues found that approximately 50 per cent of a cannabis-dependent outpatient sample were current tobacco smokers,[314] while 43 per cent of an Australian sample recruited for a randomised trial of brief cognitive behavioural therapy (CBT) for cannabis dependence were current cigarette smokers.[280]

A number of studies indicate that tobacco smoking among those seeking treatment for dependence on drugs such as alcohol and cocaine is associated with increased psychosocial and psychiatric problems.[318–320] Interestingly, evidence from an Australian community survey indicates that tobacco use and cannabis use were both independent predictors of psychosis.[31] Similarly, Moore and Budney found that, among cannabis-dependent outpatients, those who smoked tobacco had fewer years of education, earned less income and had increased psychiatric symptoms, legal difficulties and past alcohol problems.[314] The tobacco-smoking group did not respond as well to treatment as those who did not smoke tobacco, demonstrated by fewer cannabis-negative urine samples and fewer weeks of continuous abstinence.[314]

There is strong international evidence that the vast majority of those who try cannabis have previously used tobacco or alcohol.[13,204,321–329] For instance, in a longitudinal Australian study of Victorian secondary students, those who reported smoking tobacco and cannabis were more likely than cannabis-only smokers to continue using cannabis from mid-school

to late-school. This outcome was twice as likely for those who had ever used tobacco and 3.3 times as likely for daily tobacco smokers.[13] Re-examination of this sample at age 20–21 years found that among the risks for developing dependence on cannabis was persistent cigarette smoking.[19] The fact that tobacco use typically precedes cannabis use has aroused concerns that tobacco smoking may act as a gateway to cannabis use (for more information on the gateway theory, refer to section 12).

There is increasing evidence that the health effects of smoking cannabis and tobacco are additive.[105,330,331] In other words, smoking both of these substances confers a greater health risk than smoking each alone. For instance, Tashkin and colleagues conducted a longitudinal study with four groups: smokers of cannabis alone, smokers of cannabis and tobacco, smokers of tobacco alone, and non-smokers. At baseline, all smoking groups showed comparable levels of bronchitis symptoms. However, lung function tests revealed that cannabis smoking resulted in poorer functioning of the larger airways while tobacco smoking caused poorer functioning in the small airways. In subsequent follow-up studies of this sample, cannabis and tobacco smokers showed damage associated with both types of smoke.[331]

Fligiel and colleagues examined respiratory abnormalities in the lungs of cannabis-only smokers, tobacco-only smokers, cannabis and tobacco smokers, and non-smokers.[105] Their study found that cannabis smokers developed abnormalities at a younger age than tobacco smokers. However, the level of abnormalities was higher among cannabis and tobacco smokers.

More recently, Taylor and colleagues examined respiratory function in a New Zealand cohort followed from birth to age 21 years.[37] The authors compared the lung function and symptoms of respiratory disease among cannabis-dependent people, tobacco smokers and non-smokers of tobacco and cannabis. Findings also indicated an additive effect on impaired respiratory function in the group that used both cannabis and tobacco.

Overall, cannabis and tobacco are linked in several ways. A large proportion of cannabis smokers are also current tobacco smokers and the use of both substances may be a sign of increased psychosocial and psychiatric risk for those seeking treatment for cannabis dependence. Moreover, tobacco use typically precedes cannabis use, fuelling debate about tobacco acting as a gateway to cannabis. There is also growing evidence that the use of both of these substances has an additive adverse effect on respiratory health.

One issue that has been neglected in the literature is the common Australian practice of using a cannabis–tobacco admixture when smoking.[332] Some authors have suggested that such a ritual may lead to a reverse gateway effect where tobacco addiction is the result of cannabis use, especially in Indigenous communities where there are reports of children aged 12 or younger using cannabis.[332]

Recently, two qualitative studies in Scotland,[333] one involving semi-structured interviews and the other involving focus groups, found that participants described cigarettes as being inextricably linked to cannabis. Several participants also reported that smoking joints had been a gateway to smoking tobacco.[333] This is clearly an area that warrants further research.

11. Who is more likely to develop problems with cannabis use?

11.1 Cannabis as an addictive drug

Along with other drugs that activate reward systems in the brain, cannabis can produce dependence. Dependence is 'a syndrome manifested by a behavioural pattern in which the use of a given psychoactive drug, or class of drugs, is given higher priority than other behaviours that once had higher value'.[334]

The latest United States classification of psychiatric disorders (DSM-IV) considers seven domains when assessing substance dependence. A dependence diagnosis is made when a person experiences at least three of the following symptoms in the same 12-month period.[335] These are:

- tolerance
- withdrawal
- taking the substance over a longer period or in larger amounts than intended
- experiencing a persistent desire to take the substance or being unsuccessful in stopping or cutting down use
- a great deal of time is spent in activities necessary to obtain or use cannabis, or to recover from its effects
- giving up or reducing important activities as a result of using the substance
- using despite knowledge that the substance is causing or exacerbating physical or psychological problems.[335]

Evidence for cannabis dependence comes from a number of sources including epidemiological surveys,[3,13,19,21,30,31,56,272,273] studies of long-term users,[237,336] clinical samples of people seeking treatment,[274,276,277] controlled experiments on withdrawal and tolerance[338–340] and laboratory studies on cannabis brain mechanisms.[57]

Using standardised criteria for dependence, epidemiological studies are able to estimate population proportions of cannabis dependence and abuse. In the early 1980s the Epidemiologic Catchment Area study estimated that 4.4 per cent of the adult population in the United States had either abused cannabis or were dependent on it at some point in their life.[272]

The National Survey of Mental Health and Wellbeing estimated that approximately 300,000 people or 2.2 per cent of the adult population in Australia either abused or where dependent upon cannabis.[21] This translates to roughly one in three individuals who had used cannabis in the past 12 months.[21] The top four symptoms reported by dependent adults were: withdrawal or using cannabis as withdrawal relief (88.8%); persistent desire or unsuccessful efforts to control use (86.9%); tolerance (72.6%); and using cannabis in larger amounts or for a longer time than intended (62.8%).[341]

More recently, an Australian epidemiological survey of young adults found the most common symptoms experienced by dependent cannabis users were a persistent desire for the drug (91%), using for longer or in larger amounts than intended (84%), withdrawal (74%) and spending excessive time obtaining or using the drug (74%).[19] Around one in five cannabis-dependent young people also reported a tolerance to the drug.[19]

Young people may be more susceptible than adults to developing cannabis dependence. Adolescence is a time when the population prevalence of dependence increases steeply,

reaching up to 10 per cent in young adulthood.[19,316,321] Sudden remission of cannabis use in adolescence appears rare.[342]

Studies of long-term and regular cannabis users have found that a variety of cannabis-related problems are reported. For example, among a sample of rural Australian heavy cannabis users, around three in four people reported experiencing a persistent desire for cannabis (75%) and frequent intoxication during daily activities (73%). Just over half (54%) reported tolerance while only 5 per cent reported having withdrawal symptoms.[237] A survey of long-term Sydney cannabis users found that 78 per cent reported withdrawal and 76 per cent reported tolerance.[56] Around two in five people (39%) reported using cannabis to relieve withdrawal symptoms.[56]

Among a sample of regular cannabis users in Canada, the symptoms most frequently reported for the 12 months prior to the study were using cannabis in larger amounts or for longer than intended (32%) and a persistent desire to cut down or unsuccessful attempts to do so (24%).[343] Around one in ten people (11%) reported giving up or reducing social, recreational or work activities due to cannabis use.[343]

Clinical data from Australia, the United States and Europe indicate a growing demand for professional help with problems related to cannabis. In Australia, people seeking treatment for cannabis as the main drug problem increased from 4 per cent in 1990 to 10 per cent in 2001.[274] In the United States, treatment admissions for primary cannabis users increased from 6 per cent in 1992 to 15 per cent in 2000.[276] In 2004, around 12 per cent of all clients and 30 per cent of those new to treatment admissions in the European Union were presenting with cannabis as their primary drug problem.[277]

Both human and animal studies have demonstrated that tolerance to many of the physiological and behavioural effects of cannabis can develop with repeated exposure to the drug.[47,48] The major study of the effects of cannabis tolerance in humans was conducted by Jones and Benowitz.[47] Oral THC was administered over a 30-day period leading to a decline in the acute effects of cannabis and fewer impairments of functioning associated with cannabis intoxication.[47]

In the past, cannabis was not seen as a drug that could produce withdrawal because users did not display similar symptoms to those withdrawing from alcohol or opiates. Contrary to these beliefs, experimental research has supported the reports of users in demonstrating that heavy cannabis use can produce psychological and physical withdrawal symptoms.[267,268,338] The most convincing evidence to date for a cannabis withdrawal syndrome in humans comes from controlled experimental studies that examine the effect of cannabis abstinence over prolonged periods of time.[47,267,268,270]

Most recently, Kouri and Pope examined withdrawal symptoms over 28 days abstinence,[270] while a study by Budney looked at a time period of 45 days.[268] While the methodology and the number of symptoms measured differed between these studies, both used urinalysis to ensure participants' adherence to abstinence. The advantage of this method is that participants could go about their usual daily activities. Both studies found that abstinence caused heavy cannabis users to experience increased irritability, anxiety and depression and decreased appetite.[47,267,268,270] Most withdrawal symptoms began within 1–3 days of abstinence and lasted for about 10–14 days.[267,268,270] The withdrawal syndrome associated with cannabis use appears similar

to that for tobacco but of lesser magnitude than withdrawal from other drugs like opiates or alcohol.[268]

Importantly, experimental evidence indicates that withdrawal symptoms are alleviated when people resume using cannabis after a period of abstinence.[267] This finding is consistent with laboratory evidence that physical withdrawal symptoms can be induced in animals that have been maintained on THC. This is achieved by administering a substance that reverses the effects of THC, known as a THC antagonist.[24,293,300] Withdrawal symptoms can then be alleviated when THC is administered again.[300] To date, no study has used a THC antagonist to produce withdrawal in humans. However, one study has shown that the acute effects of THC are blocked by a THC antagonist.[293]

Recent laboratory research has focused on the role of brain chemistry in cannabis dependence. Like other drugs such as cocaine and heroin, cannabis increases the production of dopamine, a neurotransmitter associated with rewarding feelings.[57] It has been argued that the upkeep of this neurotransmitter may motivate people to use cannabis in an addictive way.[338]

Taken together, the findings support the notion that cannabis is a drug that can be addictive for some people. Some heavy users of the drug report problems including tolerance, withdrawal, craving and a variety of other social and psychological problems. Due to such problems, the numbers of people seeking treatment for cannabis use is increasing. Moreover, the ways in which cannabis acts on the brain are not dissimilar to other drugs like heroin and cocaine. However, the cannabis withdrawal syndrome is far milder than that associated with these drugs.

11.2 How many people persist with cannabis use?

Cannabis use declines from the early to mid-20s to the early 30s, with only a small proportion of users persisting beyond this point.[3,53] As with all risk-taking behaviour, life transition such as marriage, entering employment and having children plays a major role in discontinuing cannabis use.[3,53] For those with dependence, however, use patterns may remain more stable. For example, a recent follow-up of the Christchurch longitudinal study found that rates of cannabis dependence remained stable from age 21 to 26 (at just under 10 per cent).[315] It remains to be seen whether these same rates of dependence continue into the 30s and whether these findings can be replicated in other populations.

The persistence of cannabis and opiate dependence has been found to be surprisingly similar. The National Drug Strategy Household Survey reported that 60 per cent of males and 70 per cent of females who reported ever having used cannabis were not doing so in that year.[2] With regard to those with cannabis-related problems, the US Epidemiologic Catchment Area study found that 38 per cent of those who had experienced a cannabis use disorder (abuse or dependence) at some time in their lives had experienced cannabis-related problems in the past year. Sixty-seven per cent of this group reported using the drug in that period. While far fewer people in the population manifested opiate use disorders, 42 per cent of this group experienced problems in the prior month and 60 per cent used the drug in this period.[272]

11.3 Risk factors for developing problems with cannabis use

In a review of the cannabis literature, Hall and colleagues concluded that around one in ten people who ever try cannabis will become dependent at some point.[4] For those who use cannabis several times, this chance is increased from one in five to one in three. Daily users are at the greatest risk of dependence with about a one in two chance.[4]

While it is impossible to perfectly predict problematic cannabis use, researchers are able to examine some of the factors that heighten the risk of developing cannabis dependence. This is best done through longitudinal studies where people are followed up over a number of years, enabling researchers to track various aspects of social and psychological development concurrently with cannabis use.

The 2001 National Household Survey shows that of all adolescents (14–19 years) who used cannabis in the last 12 months, about one in ten used on a daily basis.[2] The chance of developing cannabis dependence and a range of associated problems is elevated by the frequency and age at which it is used, with young and frequent users being at most risk.[13,20,204,205]

Cross-sectional studies examining the association between conduct disorder and attention deficit hyperactivity disorder have reported a significant association in community[17,344,345] and in treatment populations[346] with cannabis use and dependence among adolescents.

The Christchurch longitudinal study found that the frequency of cannabis use at age 15–16 years was a strong predictor of negative outcomes by age 18.[204] More specifically, 27 per cent of those who had used cannabis ten or more times by age 15–16 screened positively for cannabis dependence by age 18 compared with 8 per cent of those who had never used by age 15–16.[204]

Although early cannabis initiation is a strong predictor of later cannabis-related problems, this relationship is complicated. The authors of the Christchurch study provide two explanations that are consistent with the study findings.[204] Firstly, those choosing to use cannabis at an early age were already a group that was at risk of later psychosocial problems, characterised by childhood adversity, social disadvantage, behavioural difficulties and adverse peer affiliations.[204] This finding is further supported by longitudinal research from the United States indicating that adolescents who frequently used cannabis were maladjusted, interpersonally alienated, had low impulse control, were emotionally distressed and had received poor parenting.[347] The second explanation was that early use of cannabis prompted relationships with deviant and drug-using peers, moving away from education and the family home, further increasing the risk for psychosocial problems at a later age.[204] These findings are similar to those indicating that regular cannabis use is associated with the adoption of a non-conventional lifestyle where adult roles are prematurely adopted.[248,249]

Findings that early cannabis initiators are a group already facing social problems have been supported by longitudinal research in Australia. A study of 2032 secondary school students in Victoria found that mid-school cannabis use was associated with factors including daily cigarette smoking, peer cannabis use and anti-social behaviour.[13] Similar to the Christchurch study, the Victorian study also found that regular use at an early age predicted persistence in use from mid- to late-school, with potentially harmful late-school use occurring in 12 per cent of mid-school initiators.[13] Transition from mid-school use into potentially harmful late-school use was more likely in males who had cannabis-using peers and ready access to the drug, and in females who had multiple extreme behaviours.[13] A recent follow-up of this group at age 20–21 years found that one in five adolescent users experienced later cannabis dependence.[20] Frequency of cannabis use was a strong predictor, with one in three individuals who used at least weekly meeting dependence criteria. Additional predictors were male gender, regular use of cigarettes at a young age and early persistent antisocial behaviour.[20]

Besides social and psychological factors that heighten the risk for cannabis dependence, a small body of research has investigated the role of genetic inheritance.[348–350] In a sample of 820 female twin pairs, a study by Kendler and Prescott indicated that while psychosocial factors were important, genetic factors were a significant predictor of cannabis dependence.[349] These findings were further supported by a later study by the same research group in a sample of male twins[348] and in a recent study by Lynskey and colleagues in a sample of young Australian twins.[350] This is consistent with research indicating a genetic role in both nicotine and alcohol dependence.[348,351]

A recent follow-up of the Christchurch longitudinal sample at age 21 years found that those who reported positive reactions to cannabis when they first used the drug were significantly more likely to become dependent later in life — 28.5 times more likely for those who reported five positive responses as compared to those who reported non-positive responses.[352] Although the underlying mechanisms that mediate this process are not known, the authors suggest that some people may be genetically predisposed to react more positively to cannabis intoxication than others. The authors also recommend that clinicians should be aware that clients reporting positive reactions to early use face higher risks for developing cannabis dependence.[352]

In sum, the following factors may be related to a heightened risk for developing problems with cannabis use: frequent use at a young age; personal maladjustment; emotional distress; poor parenting; school drop-out; affiliation with drug-using peers; moving away from home at an early age; daily cigarette smoking; and ready access to cannabis. In addition, there is emerging evidence that positive experiences to early cannabis use are a significant predictor of later dependence and that genetic predisposition plays a role in the development of problematic use.

12. What is the current evidence for cannabis as a gateway drug?

An issue of great concern is that cannabis may act as a gateway drug to the use of other illicit substances such as heroin or cocaine. The gateway hypothesis is one of the most controversial in the epidemiology of drug use.[353] Proponents of the gateway theory cite that almost all heroin users have smoked cannabis[326] and argue that cannabis use plays a causal role in the use of other illicit substances.[354]

An alternative to the gateway theory is that the use of cannabis and other drugs results from common causes. It may be the case, for example, that certain people possess personality traits or genetic vulnerabilities, or have life situations that predispose them to using a variety of illicit substances.[354–356] This is commonly referred to as the 'common cause' hypothesis.[355–357]

12.1 Evidence from cross-sectional studies

During the 1970s and 1980s Kandel and colleagues identified a sequence of drug involvement in American adolescents. Heroin or cocaine use was generally preceded by the use of cannabis, hallucinogens and tranquillisers, which in turn was preceded by the use of alcohol and tobacco.[3,325,326] Progression to the next drug in the sequence was largely influenced by the age of first use and regularity of use. For example, those who began using alcohol and tobacco regularly at a young age were at the greatest risk of using cannabis. In turn, those who began to use cannabis heavily faced the highest probability of moving to other illicit drugs.[3,325,326]

This sequence has been also been identified in other countries such as Australia,[13] New Zealand,[204,321,327] Germany[323] and Sweden.[328,329] Deviations from this sequence, however, have been found in groups where the availability of certain drugs is disproportionately high. For instance, in some African-American communities cocaine and heroin are more readily available than hallucinogens.[358]

Findings from Australian population surveys indicate that while the majority of heroin users have used cannabis, only a small percentage of cannabis users have used heroin. For example, the 1993 National Household Survey found that only 4 per cent of cannabis users had used heroin.[359] Nevertheless, this finding translated to a 30 times higher risk for using heroin in those who had used cannabis as compared to those who had not.[359] The 1998 National Household Survey found that the odds of using heroin were 78 times higher for those who had used cannabis.[28]

Results from the 1997 Australian Survey of Mental Health and Wellbeing indicate that cannabis users, particularly those meeting criteria for abuse or dependence, had an increased likelihood of using, and being dependent upon, other substances.[30] Specifically, those meeting criteria for cannabis dependence were most likely to be dependent upon sedatives, stimulants or opiates.[31] In turn, tobacco use also correlated with an increased likelihood of using cannabis.[30,31,341]

12.2 Evidence from cohort studies

Although the use of certain drugs typically precedes the use of others, this does not necessarily imply a causal connection.[359] One way of examining the causal hypothesis is to test whether cannabis use still predicts the use of other drugs once user characteristics and social variables have been accounted for statistically.

The most extensive study in this area was conducted by Fergusson and colleagues with a New Zealand cohort followed from birth to age 21 years.[194,204] A large array of social, psychological and personal variables were able to be controlled when the relationship between cannabis use and other drug use was examined. Early cannabis use (by age 16) was characterised by childhood adversity, social disadvantage, deviant peer affiliations and behavioural difficulties. After controlling for these factors, however, the study found that early cannabis use still predicted the use of other illicit drugs at age 18.[204] By age 21, around seven in ten people (70%) in the cohort had used cannabis and approximately one in four (26%) had used other illicit drugs. Of those who had used other illicit drugs, only three people had not previously used cannabis.[321] After adjusting for variables such as childhood, family and adolescent lifestyle factors, the study found cannabis use remained a strong predictor of other illicit drug use. Furthermore, the risk of other drug use increased with cannabis use in a dose–response manner. That is, as the frequency of cannabis use increased, so did the odds of trying other illicit drugs.[321] Those who used cannabis 50 times or more per year were 59 times more likely to use another illicit drug than their non-cannabis-using counterparts.[321] A later study of this group at age 21 confirmed earlier findings, with an early age of initiation and greater frequency of cannabis use increasing the risk of using other illicit drugs.[205]

These studies indicate that common causes cannot fully account for the association between the use of cannabis and other illicit drugs. Importantly, they found support for three phenomena that are essential to gateway theory. Firstly, cannabis users had a higher risk of using other drugs. Secondly, cannabis use came before the use of other drugs; and thirdly, the risk of other drug use increased with the frequency of cannabis use. Findings also suggested that cannabis use, particularly regular use at a young age, exacerbated the risk of using other drugs.[204,205,321] Although this evidence appears to be in favour of the gateway theory, the authors acknowledge the possibility that the association is non-causal and due to factors that were not adequately controlled in the statistical analysis.[321] One example would be genetic vulnerability to using a variety of drugs.[254]

The question still remains as to whether the phenomenon of sequential drug use is causal or whether common factors, not considered in previous studies, can explain the association between cannabis and other drug use. In a novel study, Morall and colleagues created a mathematical model to test the validity of the gateway theory.[357] This model incorporated the assumption that all people have differing propensities for the use of any drug. Those with a high propensity were more likely to use drugs when they were available as compared with those with a lower propensity. Another assumption of the model was that neither use of nor opportunity to use cannabis was causally associated with hard drug initiation. After running this model using estimates from a representative sample of American youths, the authors were able to mimic a gateway effect without any causal connections between drug classes. Cannabis users

were more likely to use other drugs; cannabis use came before the use of other drugs; and the higher use of cannabis conferred greater risk of using other illicit drugs.[357] This is a clever example of how three vital components of the gateway phenomenon can be satisfied without any causal linkage between the stages of drug use progression. Put simply, those with a greater generalised propensity for drug use were more likely to use cannabis and other drugs when they became available.

Although it is possible that people with a greater generalised propensity for drug use are more likely to use drugs than are others, it is important to consider other environmental factors that may contribute to drug consumption. Using economic modelling, Williams examined the effects of price and government policy on cannabis use in Australia.[360] In that study, re-analysis of National Household Survey data from 1988 to 1998 found that participation in cannabis use among youth under the age of 25 years was more price-sensitive than for those above 25 years of age. Also, while living in a State where cannabis was decriminalised did not appear to increase use among those aged 25 or younger, it was associated with higher use only among males aged 25 or older.[360] These findings shed light on influencing variables that other studies have not been able to control. In order to fully appreciate the ways in which economic and legal factors interact with drug use, more research in this area is needed.

12.3 Evidence from twin (and related) studies

Twin studies are useful in addressing questions about the influence of genes in certain behaviours. For instance, if one member of a twin pair is prone to using a range of drugs, to what extent does the other twin share this propensity? The answer to such questions may shed light on the possibility that genetic vulnerability represents a common cause for using cannabis as well as other illicit drugs.

Studies of identical and non-identical twins have found that certain people have genetic predispositions towards dependence on drugs like tobacco,[361] alcohol[351] and cannabis.[349] Only one study, however, has been conducted on whether genetic vulnerabilities mediate the likelihood of using a range of substances after cannabis. Lynskey and colleagues conducted a study with an Australian sample of 311 monozygotic and dizygotic twin pairs.[362] Findings indicated that twin members who used cannabis before age 17 were 2.1 to 5.2 times more likely to use other drugs than their co-twin who had not used cannabis by the same age. This association between early cannabis use and the use of other drugs did not differ significantly between monozygotic and dizygotic twins. Nor did the association between earlier cannabis use and use of other drugs substantially change after controlling for other environmental and psychological risk factors. The authors concluded that genetic or shared environmental factors cannot fully explain the progression from cannabis use to the use of other drugs.[362]

In their recent review, Hall and Lynskey concluded that the relationship between cannabis use and the use of other illicit drugs reflects in part, but is not wholly explained by, the selective recruitment to heavy cannabis use of those with pre-existing traits (that may be in part genetic) that predispose to the use of a variety of different drugs, and the affiliation of cannabis users with drug-using peers in settings that provide more opportunities for, and socially sanction, the use of other illicit drugs.[353]

12.4 Do people access cannabis from providers of other illegal drugs?

One potentially relevant mediating factor is exposure to other illicit drugs through dealers selling multiple substances. However, this is an issue that has remained unexplored. While the 2001 National Household Survey found that approximately one in seven (13.9%) recent cannabis users reported obtaining cannabis from a dealer,[2] it was not specified whether cannabis dealers also sold other illicit drugs.

A related issue is whether the use of cannabis increases the chances of being exposed to other illicit substances and whether cannabis users are more likely than non-cannabis users to use another drug after an exposure opportunity.[363,364] In a United States sample, Wilcox and colleagues reported that cannabis users were about 16 times more likely to be exposed to hallucinogens than non-cannabis users. Moreover, 69 per cent of cannabis users who had an opportunity to use hallucinogens progressed to hallucinogen use compared to only 16 per cent of non-cannabis users.[364]

In another American study measuring exposure opportunity over a wider range of drug classes, Wagner and Anthony found that about three in four alcohol or tobacco users had an opportunity to use cannabis by age 18 compared with only one in four who did not use alcohol or tobacco.[363] By the age of 25, three-quarters of those who had previously used cannabis, alcohol or tobacco had also been exposed to cocaine. This was in contrast to about one in ten people who had not used alcohol, tobacco or cannabis. People with a history of cannabis use were 15 times more likely to use cocaine given the opportunity as compared to those who had never used cannabis.[363]

These studies provide valuable insight into the mechanisms linking cannabis use with other drug use. Results suggest that using one drug appears to raise the risks of being exposed to a drug further up the chain and also increase the chances of using that drug. These findings, however, leave some unanswered questions. For example, drug exposure was measured by asking participants how old they were when they first had a chance to use a drug. Whether this exposure opportunity was facilitated by a dealer, friend or other entity is unknown. Another issue is how comparable these findings would be in an Australian population where cocaine is less commonly available.

Overall, it is well established that alcohol and tobacco use usually precedes cannabis use, which in turn precedes the use of drugs such as cocaine or heroin. Although the simulation study by Morall and colleagues indicates that no causal relationship is theoretically needed to explain the association between cannabis and other drug use,[357] findings from other well-structured longitudinal and twin studies

indicate that common causes such as social, lifestyle and genetic factors explain only part of the relationship between cannabis and other drug use.

In reviewing the literature, Hall and Pacula noted that the failure of common factors to wholly explain this relationship leaves open the possibility that there is a modest causal link between cannabis and other drug use.[100] They suggested that this relationship is due to a mixture of: cannabis users possessing personality and attitudinal traits that predispose them to other drug use, some of which may be genetic in origin; and cannabis users having greater opportunity to use a range of other drugs at an early age through affiliation with drug-using peers in an illicit subculture that has positive attitudes towards the use of other drugs.[100]

One hypothesis proposes that cannabis use causes chemical changes in the brain that predispose users to seek other drugs.[355] Indeed, some evidence indicates that THC acts on the same reward centres in the brain as other drugs such as amphetamines, cocaine and heroine.[57] As Hall and Pacula pointed out, however, findings of common brain pathways do not provide evidence that the use of one drug actually *primes* the use of another. At present, evidence for the pharmacological hypothesis appears weak in explaining the association between cannabis and other drug use.[100]

13. Cannabis, driving and related issues

The effects of cannabis on driving have become a public health concern.[366] As there has been no reliable method to measure cannabis intoxication analogous to random breath testing, information on the prevalence of people driving under the influence of cannabis has often relied on self-reporting[367–369] or analysis of the urine or blood of people involved in car accidents.[369]

A large review of fatal and non-fatal vehicle accident studies shows that between 1.4 per cent and 27.5 per cent (average 11.9%) of accidents involved drivers who tested positive for cannabis in their urine or blood.[370] It is important, however, to interpret these figures with caution because the presence of cannabis in urine is not proof that the person was impaired at the time of the accident. Blood samples, where active THC levels are measured, are more accurate in ascertaining whether a person was impaired at the time of an accident. However, active THC levels may be distorted by factors such as the time interval between sampling and analysis.[370]

The majority (90%) of a sample of long-term cannabis users from the north coast of New South Wales reported driving at least occasionally after using cannabis and 70 per cent reported driving sometimes while using it.[368] A recent telephone survey of 502 cannabis users aged 18–29, recruited from the general population in the same area, revealed that 11 per cent had ever driven within an hour of using cannabis, while 7 per cent had done so in the past 12 months.[371] Among regular cannabis users, 41 per cent had driven within an hour of using cannabis in the past 12 months.[371]

Evidence from a small Melbourne study also indicated that regular cannabis users drive frequently while intoxicated.[367] A large survey of American high school seniors found that 15 per cent reported having driven in the last two weeks after using cannabis.[372] Australian cannabis users generally tend to view the drug as safe for driving, emphasising that they drive with more caution when intoxicated.[267,373] There is also a common belief among users that police procedures are ill-equipped to detect cannabis intoxication.[267]

Laboratory studies have tested the effects of low doses of THC on a number of driving-related skills. Impairments occurred in areas such as attention, tracking, short-term memory, reaction time, hand–eye coordination, time and distance perception, vigilance, decision making, concentration and balance.[374] These impairments increased with dose of THC and generally lasted from two to four hours after use.

Studies using driving simulation tasks have produced smaller impairments than laboratory-based studies.[374] A review of driving simulator studies shows that earlier studies found effects for decision time, time to start and stop, and estimated time needed to overtake.[376] Despite this, no effects were found for car control.[375] Later studies that were more similar to *real* driving situations found that high THC doses did impair aspects of car control such as the ability to stay in one lane. Cannabis intoxication also increased body sway and reaction time.[375,376]

A recent simulator study conducted at Swinburne University in Victoria found that increasing levels of THC not only impaired ability to maintain correct lane position, but also slowed driver reactions to a randomly generated unexpected situation where a car would pull out in front of the vehicle, or a tree would fall in the roadway.[377] A common finding in both older and more recent simulator studies was that cannabis-impaired drivers compensated for their intoxication by driving more slowly, avoiding risky manoeuvres, and allowing larger distances from the car in front.[4,374]

While studies conducted on off-road driving courses have found modest impairments after cannabis use, those that have tested drivers in real traffic conditions have produced mixed results. For instance, a study by Klonoff found that cannabis use impaired driving on a closed circuit course, but not in traffic.[378] Some recent findings have failed to show effects from cannabis use on visual search skills.[379] When several skills are measured, however, cannabis produces small impairments in driving performance in traffic conditions.[4,380]

Research has also addressed the issue of driving after the combined use of alcohol and cannabis. According to the 2001 National Household Survey, 95 per cent of cannabis users reported having used cannabis and alcohol together.[2] There is also speculation that drunk drivers often do not report the fact that they have also been using drugs such as cannabis.[381] In a survey of 18–29 year olds in northern New South Wales, 1.8 per cent reported having driven within an hour of using both drugs within the past 12 months.

Recent findings in natural traffic environments indicate that low doses of alcohol and cannabis produce driving impairments that are greater than either drug alone, with more severe impairments evident when a range of driving skills are measured.[379,381] This is supported by experimental evidence that alcohol may strengthen the acute effects of cannabis by increasing the absorption of THC into the blood.[29]

Whether cannabis use contributes to more road accidents is still uncertain. Estimations from American household surveys suggest that cannabis users are 2 to 4 times more likely to be victims of a road accident, with the combined use of cannabis and alcohol raising the risk.[382] A New Zealand study on a cohort of young adults found that cannabis use did predict higher rates of road accidents.[383] This increased risk, however, was found to reflect the characteristics of the young people using cannabis rather than the effects of the drug itself.[383]

There have been only two controlled studies examining rates of cannabis use in drivers involved in fatal and non-fatal car accidents. The first study found that people testing positive for cannabis in their urine were no more likely to be involved in a collision than controls.[384] When only women were analysed, however, cannabis intoxication was associated with an increased accident risk.[384]

A larger study using blood sampling found that, after matching for sex and age, drivers testing positive for cannabis were 2.5 times more likely to be involved in a collision than those who were drug-free.[369] Drivers who had combined cannabis with alcohol were 4.6 times more likely to be involved in a collision than controls.[369]

Several studies have examined whether cannabis-using drivers were more culpable in fatal and non-fatal accidents than those who had not used the drug.[385–393] A recent review concluded that most culpability studies have not found that cannabis alone predicted crash culpability.[394] These studies, however, tested urine or blood for only an inactive THC metabolite. This makes it difficult to ascertain whether drivers were impaired at the time of the accident. In contrast, the few studies that have tested for active THC in the blood have found that its presence is associated with an approximate three-fold risk of accident.[394] This risk is elevated when larger quantities of cannabis are consumed or when cannabis is used with alcohol.[394]

In sum, the evidence suggests that cannabis use does produce minor impairments in driving performance. In turn, this increases the chances of being involved in, and being culpable for, traffic accidents. This is especially the case when cannabis is combined with alcohol.

Studies investigating the effects of cannabis intoxication on operating machinery other than motor vehicles have been rare. One small Canadian study of fatal occupational accidents found 3.9 per cent of victims to be positive for cannabis.[395] Although this figure is not high, examining the influence of cannabis use is difficult because of the lack of a control group.

A recent review of studies on accidental injury found that evidence for the role of cannabis was mixed.[370] Whereas one study found a significant association between cannabis use and accidental injuries, subsequent studies have found no such relationship. More rigorous studies on the topic are needed.

It would be wrong to assume that operating machinery while intoxicated by cannabis is safe merely because of the lack of evidence to the contrary. Laboratory tests have shown that cannabis use impairs attention, tracking, short-term memory, reaction time, hand–eye coordination, time and distance perception, vigilance, decision making, concentration and balance.[374] With this in mind, operating potentially dangerous machinery is not advisable while under the influence of cannabis.

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