CANNABIS 2002 REPORT

Ministry of Public Health of Belgium

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Introduction

At the end of 2000 the Health Ministers of the Netherlands (Mrs Borst), Germany (Mrs Fischer, succeeded by Mrs Schmidt), Switzerland (Mrs Dreifuss) and Belgium (Mrs Aelvoet) took the initiative to organise a scientific conference on the subject of cannabis. In the spring of 2001 the French Health Minister (Mr Kouchner) joined the initiative. The conference took place in Brussels, on February 25 2002, and was hosted by Mrs Aelvoet.

The decision to hold this conference was prompted by the ministers' observation that 'cannabis' and 'cannabis policy' are frequently the subject of debate, but it is not always clear what the scientific state of the art is. Often one argument is pitted against another, without the involved officials (as well as the press and the public) having a clear understanding of the scientific validity of the claims. One consequence of this could be that many political decisions are delayed, or are made on the basis of incomplete or incorrect arguments.

The objective of the conference was to provide the ministers concerned and all others involved in drug policy with an overview of the current state of affairs in scientific research of cannabis: what do we know, and what do we not know? On which issues do scientists agree and which issues are still under debate?
To achieve this, a Scientific Task Force, with from each participating country one co-ordinator, was assigned the task of formulating key questions with regard to cannabis, to be addressed from a variety of scientific disciplines: epidemiology, sociology, psychology, psychiatry, physiology, pharmacology and policy analysis.

During the six months before the conference authors have been busy writing documents to answer these questions. The draft documents were reviewed by more than thirty renowned scientific referees. After taking their comments into account, the revised basic documents were edited by Inge Spruit. She has added an overall summary that is also comprehensible to non-scientists.

This book incorporates the results of these activities. We believe that the authors have succeeded in reducing an enormous quantity of scientific research into comprehensible insights, although these insights make no claim to be complete. It is clear that, alongside the large amount that is known with relative certainty about cannabis, there are also numerous gaps in our knowledge. A great deal more scientific research will therefore need to be done.

The contents of this book are valuable. However, we feel that the way in which the book has been put together is equally significant. The authors' achievements are impressive and all the reviewers without exception have shown enormous conscientiousness in the comments they have made. The whole process has been characterised by exemplary co-operation and can serve as a model of international collaboration in this exceptionally complicated area. We feel privileged to have been able to play a part in creating this book.

The Scientific Task Force: Brussels, 2002

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Executive summary

Inge P. Spruit

How many people use cannabis, how often, for how long: results from epidemiological research

In the European Union (EU) the percentage of high school students who currently use cannabis has recently decreased in the UK and Ireland, explain *Rigter and Van Laar* in *chapter 1*. This percentage has stabilised in the Netherlands. The percentage of 'current users', or more properly the last month prevalence rate, is a more valid indicator of actual trends than the lifetime use or prevalence rate. It indicates how many people consumed the drug at least once in the month before the survey and includes a disproportionately lower share of people who only tried a puff once or twice in their lives. The UK and Ireland had the highest prevalence rates in the EU for current cannabis users among high school students in the mid-1990s. The recent anomaly is not explained. Because many factors influence prevalence levels, explanations offered without further study are to be mistrusted. In member states with lower prevalence rates in the same decade, and in Switzerland, the percentage of students currently using cannabis was still on the increase at the end of that period.

Cannabis (marijuana, hashish and related products) is the most widely used illicit drug in the western world. At least 45 million people in the EU have tried cannabis, once or more often, at some point in their lives. However, experience with this drug is less common in Europe than in the USA and Australia.

Most users start taking cannabis, as an experiment, in adolescence or early adulthood. In western cultures the average age of first consumption is lowest for tobacco and alcohol, followed by cannabis and then by other illicit drugs. Many people stop taking cannabis after their first experience or a brief period of use. Data about the frequency and amount of use is only available in a few countries. The characteristics of cannabis users are strikingly similar across western nations. Users of cannabis come from all social classes and demographic and educational backgrounds. Factors such as unemployment, truancy, high levels of drinking and smoking, and sometimes behavioural disorders may play a role in the case of heavy users.

Pharmacology and neurobiology

In *chapter 2*, *Streel, Verbanck and Pelc* observe that the mental effects of cannabis appear fifteen to twenty minutes after smoking and thirty to ninety minutes after oral ingestion (eating). Eating results in two to three times less THC absorption in the blood compared to smoking the same dose, but the amount administered is more difficult to adjust. Elimination from the body is slow; complete elimination of a single dose can take up to thirty days.

Cannabis acts through specific receptors. One type of cannabinoid receptor (CB_1) is located in the brain and peripheral tissues. The second type (CB_2) resides in the immune cells of the spleen. The brain contains *natural* cannabinoid-like substances (anandamide and 2-AG). The cannabinoid chemical pathway in humans is not yet fully understood.

Is cannabis a gateway drug?

In adequate epidemiological studies *Rigter and Van Laar* found no convincing proof that cannabis is a gateway drug: i.e., that the properties of the substance itself induce people to start using other illicit drugs. *Streel et al.* searched the field of neurobiology. They too concluded that no firm conclusions can be drawn, and they also assert that animal studies will not provide a conclusive answer to this question.
Epidemiological studies have reported a statistical relationship between cannabis use and the consumption of other drugs in later years, but a statistical relationship alone is never proof of causality. Most cannabis users do not progress to other drugs. Other factors may account for this relationship. A not uncommon hypothesis is that such factors may include disadvantageous personal and social characteristics, genetic and/or educational background, disorderly conduct, peer networks, greater access to illegal markets, etc. If we want to know whether the use of cannabis prompts people to take other drugs, the behaviour of people needs to be 'followed' over the years in longitudinal studies. Studies of this type have been carried out in the USA and New Zealand, but almost none in Europe.

The effects of cannabis on users' physical health and the effects of cannabis use during pregnancy

In *chapter 3*, *Bergeret, Papageorgiou, Verbanck and Pelc* point out that it is important to distinguish between casual, regular and heavy cannabis users. Occasional use of cannabis is not a major hazard to health and well-being. The way in which the drug is administered (eating, smoking) affects the duration of immediate effects such as dysphoria, heart rate changes, psychotropic symptoms, etc.

Organs that may be affected by chronic use of cannabis include the gastrointestinal, endocrine, cardiovascular, respiratory and immune systems. Many studies are carried out on animals, and extensive measurements can be made in this way, but without follow-up on human subjects the findings do not allow conclusions to be drawn about man. No animal studies were found that examined the issue of combined use of legal and illicit drugs, such as cannabis and tobacco, cannabis and alcohol, or all three. Such use is not uncommon in man.
The authors conclude from the data available that chronic cannabis use has no clinically relevant effects on any organ systems apart from the lungs. THC can also cause cardiac problems in patients suffering from a cardiovascular condition or hypertension.

THC reaches the foetus through the mother's blood and the baby through breast milk. The effects on the newborn of cannabis use by the mother have not been clearly established, nor do we know whether maternal cannabis use affects child development. Longitudinal studies are indispensable as a means of collecting this information.

Carcinogeneity of cannabis

Bergeret et al. also conclude that cannabis smoke contains about fifty per cent more carcinogens than unfiltered tobacco smoke. Other methods of consuming cannabis are not associated with the risk of developing cancer. It is the α-benzpirene in cannabis that is more carcinogenic, when burnt, than the nicotine in tobacco. However, the very few studies that have tried to find out whether the risk of developing lung cancer is higher in cannabis smokers than in tobacco smokers have failed to demonstrate such an increased risk. A question with greater relevance to actual human behaviour may be whether the hazards of regular cannabis smoking augment the hazards of the normal amount of tobacco smoking, since these substances are often used together.

In chapter 7 *Scholten* adopts the risk assessment of the prestigious British Medical Association, which takes into account the fact that even heavy cannabis smokers smoke less on average than nicotine smokers. This (among other factors) is one of the main arguments that has prompted the BMA to estimate that cannabis, when smoked, has the same carcinogenic potential as tobacco. Recently, however, the reputable French institute INSERM (1) stated that it still regards this question as open.

Mental disorders and states: certainties and continuing uncertainties about the question of cause and effect

It is clear, find *Hanak, Tecco and Pelc* in *chapter 4*, that cannabis use sometimes elicits acute psychotic reactions (delusions and/or hallucinations) in sensitive individuals. This is more likely to happen when the drug is taken orally, in high doses, and when it is used with other psychoactive substances. After abstinence the symptoms disappear.

There are still no answers to the question of whether or not cannabis can trigger the onset of schizophrenia. Another inconsistency comes from case reports, some of which state that cannabis may be harmful to people already suffering from schizophrenia while others claim that it may alleviate some symptoms. The main reasons for these persisting uncertainties are insufficient knowledge about the risk factors for schizophrenia, and the lack of adequate clinical studies and prospective (long-term) epidemiological studies.

Cannabis use is statistically related to mood disorders such as depressive, dysthemic or bipolar disorders, but the question of which comes first remains unanswered. Some authors link cannabis to an amotivational syndrome, in which apathy and a loss of drive are key features, but the existence of such a syndrome is still debated.
The role of alcohol in the statistical relationship between suicide and alcohol is complicated and not beyond debate. Chapter 4 explains that some authors also link suicide attempts to the use of cannabis. However, the indications for cannabis as a decisive factor are weak in comparison with the influence of social disadvantage, a deprived childhood, family circumstances, underlying mental disorders and other substance-related problems.

Anxiety is supposed to be a common adverse reaction to cannabis, but there is no conclusive evidence for this link. One of the main reasons for this gap in our knowledge is that studies to date have failed to distinguish adequately between the use of cannabis on its own and combined substance use.

Dependence, problems, and low demand for treatment

People may become dependent on cannabis, but it is unclear how many experience this problem, stress *Hanak et al* and *Rigter and Van Laar*. Estimates from clinical studies suggest that it is not rare among frequent and chronic users (occasional users do not appear to be at risk), but certainly less common than dependence on tobacco and possibly alcohol. In addition to the frequency and amount of use, the probability of becoming dependent appears to be related to an early onset of cannabis use and to disadvantageous personal and social factors and behavioural disorders. However, the lack of proper data, for example from research among cannabis users not in treatment, means that adequate risk assessment is difficult.
Most cannabis users keep their consumption of the drug under control. For those who become dependent, a condition classified as a pathological disorder, their drug dependence must interfere with their ability to function to such a serious extent that they pass the threshold for a clinical diagnosis (2,3). However, some types of cannabis use, or factors related to its use, may increase the

risk of developing problems that remain below this threshold. Most users experiencing problems with cannabis do not seek professional help though, which means that little information is available. The European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) in Lisbon has defined the concept of 'problematic drug use', which could well help us to understand this type of use better. However, this concept has not been extended to cannabis, as *Rigter and Van Laar* note. One reason for reconsidering this exception may be that we want to know how many people do not succeed in keeping out of drug trouble (even when using cannabis only) or cannabis-related trouble.

The question of whether the combined use of substances, both legal and illegal, bears additive risks or effects is a neglected area of study. The applied value of much research could well be enhanced by relating it to the consumption behaviour actually occurring today. Cross-cultural or cross-regional designs will also enhance the value of such studies.

Cannabis use temporarily affects cognitive functions, but gross changes are not irreversible

THC can temporarily impair cognitive functions, according to *Ramaekers, Berghaus, Van Laar and Drummer* in *chapter 5*. Doses between forty and threehundred micrograms THC per kilogram of body weight somewhat (and dose dependently) affect performance in laboratory tasks measuring memory, divided and sustained attention, and reaction time. THC impairs learning processes when the user is under the influence, but it does not affect the retrieval from memory of information learned before cannabis use.
Long-term heavy users may have memory and attention deficits, slower reaction times and an impaired ability to organise and integrate complex information. These deficits are probably related to recent cannabis use or withdrawal symptoms during the first days of abstinence. They largely disappear after prolonged abstinence. This indicates that THC does not produce any gross changes in cognitive or psychomotor functions that are permanent or irreversible.

THC, driving performance and traffic accident risks

Cannabis users who drive under the influence may actually have used not only cannabis, but also alcohol. Even at low doses, emphasise *Ramaekers et al.*, the sum of these effects is large and potentially dangerous. The combined effects of alcohol and cannabis are greater than the effects of either drug alone.

There is no simple, on-site test reliable enough to measure recent THC use when driving, comparable for example to the breath alcohol test for alcohol. Sweat and urine tests produce many 'false positive' outcomes, meaning that they indicate that drivers are under the influence when in fact they are not. Saliva tests produce many 'false negatives', that is, they often fail to identify drivers who actually are under the influence.

Laboratory studies show that THC does not affect all driving tasks equally. Performance is affected more for driving skills (tracking and speed adjustment) and less for manoeuvring skills (distance keeping and braking) and strategic performance (observation and understanding of traffic, risk assessment and planning). The performance impairments in psychomotor or cognitive tests and the variability that occurs in lateral positioning are dose related. However, these studies do not take into account actual patterns of cannabis use and actual driving in real and common traffic situations.

Because the findings of laboratory studies do not allow conclusions to be drawn about (the lower limit of) cannabis use in relation to the accident or crash risk, epidemiological research has focused on actual traffic accidents caused by cannabis use. The data from this research is not unambiguous,

but appears to indicate that recent cannabis use may increase the crash risk as compared to the risk run by drivers using neither cannabis nor alcohol.

THC quality

THC (Δ^9-tetrahydrocannabinol) quality – that is, the concentration of the active compound in cannabis – has increased in the past decade in at least the USA and the Netherlands, as *Rigter and Van Laar* report. However, recent (but still scarce) data shows that the increase is not as marked as sometimes suggested. Furthermore, it is not the quality of the THC in the cannabis product that determines the effect, but the user's internal exposure to the compound. Users may adapt their intake levels (dose, frequency), but there is little evidence about their actual behaviour. The health effects, if any, of higher THC levels in cannabis products are virtually unknown.

Is prevention of cannabis use and misuse possible?

Cuijpers concludes in *chapter 6* that education programs in schools can indeed reduce drug use, provided that they use interactive methods that foster the development of interpersonal skills. Most such programs are aimed at several substances: usually tobacco, alcohol, and often cannabis and other illegal drugs as well. The goals of these programs differ considerably. They may aim to increase knowledge about drugs, to reduce drug use or misuse, to delay the onset of first use, or to reduce the harm caused by drug use. A major problem is the dissemination of programs proven to be effective. Many programs that are widely used have not been examined at all, or have been shown to have no effect on drug use.
Mass media campaigns are apparently unable to reduce cannabis use, but they probably do increase the effects of school-based programs and community based interventions. Combining community interventions with school programs also produces a greater reduction in substance use than either of these interventions alone.
A new emerging area of drug prevention is family-based programs, which aim to reduce the likelihood of substance use in adolescents. The results of effect research in this field are encouraging.

Neglected research areas include prevention aiming at delaying the onset of hard drug use by cannabis users and prevention aiming at reducing the number of new cases of problematic drug use.

There is little European research, most evaluation or effect research is American. This is important in the field of prevention. Different approaches may 'work' in different cultures; identical programs may or may not have comparable effects. Europe is lagging behind, especially where applied research is concerned.

Cannabis as a medicine?

The question of whether cannabis can be used as a medicine is highly topical and recently prompted a series of international activities and conferences. The issues under investigation are whether cannabis preparations can alleviate pain and muscle spasms for patients with chronic diseases like asthma or neurological disorders like multiple sclerosis, or help to decrease nausea and vomiting and increase appetite in patients undergoing treatment for cancer or AIDS.

Scholten found that several widely accessible and recent state-of-the-art reviews exist on this subject, with thorough analyses. The almost unanimous conclusion of these reviews is that past research consists predominantly of case reports or clinical studies whose design is insufficient to meet the present-day criteria for providing conclusive answers. Another full state-of-the-art review would

seem to fall outside the scope of this conference book. *Chapter 7* therefore presents a brief review. It focuses on the indicators whose efficacy can probably be proven in the future and explains why a whole plant preparation should be used and not isolated substances. It also considers the requirements laid down for medicines in general. In the case of cannabis, this means that any preparation made from it must meet the requirements of quality, efficacy and safety before it can be admitted to the market as a medicine. There are also questions about the dosage form and about the strain of cannabis to be used as raw material.
An international network of participating countries is desired to follow the progress of clinical trials in different countries and promote collaboration in finding patients for international clinical trials.

The law, policy and cannabis use

Most studies find that relaxing cannabis possession laws does not increase the number of cannabis users, writes *Kilmer* in *chapter 8*. Jurisdictions with liberal possession laws do not necessarily have a higher percentage of cannabis users than those with more conservative laws. However, most of these studies do not control for the level of enforcement of cannabis possession laws. Little is known about the influence of the actual enforcement of such laws on cannabis use in Europe. The outcome of some recent analyses from the United States suggest that adults may be responsive to the enforcement of these laws, as measured by cannabis possession arrests and fines for possessing cannabis. The evidence is mixed as to whether adolescents are responsive to these fines.
According to the European Legal Database on Drugs, most Western European countries have penalties for cannabis possession, ranging from fines to incarceration. Usually an arrest leads to a fine, not to imprisonment. Data on the severity of these fines is not readily available for most countries.

The author saw clear increases in the per capita number of arrests for cannabis possession offences in the 1990s in almost all of the few countries with relevant data (six European and two non-European countries). This is remarkable in view of the tendency in many countries to reduce the severity of sanctions for infringing cannabis possession laws. Choosing one of the possible explanations seems premature at present. In four European and three non-European countries with relevant data the probability of being arrested for cannabis possession in the late 1990s appeared to be very similar, at two to three per cent of all recent cannabis users. This is remarkable too, because there are large differences between these countries in both the per capita number of cannabis users and the number of police officers.

To learn more about the possible effects of cannabis possession policies on cannabis use, models can be designed to test this relationship. Such models could include drug use history, the perceived pleasure or harm of the drug, ability to easily obtain cannabis, price, social (dis)approval, knowledge of legal aspects such as penalties and fines, the impact of having a police record, the expected sanction for a cannabis possession arrest, etc. Modelling studies using some of these variables are more common in Australia and the United States than in Europe.

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1. EPIDEMIOLOGICAL ASPECTS OF CANNABIS USE

Henk Rigter and Margriet van Laar

Summary

This chapter focuses on the member states of the European Union (EU) and Switzerland, and on Australia, New Zealand and the USA for comparison purposes. It provides information from surveys, registers and cohort studies. We will address the following questions.

How many people have used cannabis?

At least 45 million adults in the European Union have tried cannabis at some point in their lives. In a number of countries, such as Germany, the Netherlands, Switzerland and the USA, cannabis consumption in the general population has evolved in two waves. The prevalence rate of use first peaked in the seventies, then dropped, and rose again in the 1990s. Experience with cannabis among adults is less common in the EU than in the USA and Australia.
In 1999 *lifetime* use among high school students aged fifteen and sixteen was higher in the USA than in the EU, while the UK and France topped the list in the EU. France was first in terms of current use (consumption in the last month before the survey). The prevalence rate of lifetime and current cannabis consumption is no longer rising among school pupils in three EU member states: the UK, Ireland, and the Netherlands. In various other member states the prevalence rate of use in this group is still on the increase. The proportion of cannabis users among school students appears to be stabilising or falling in countries that had relatively high prevalence rates in the early 1990s, and rising in countries that formerly had low rates.

How often do people use cannabis?

Many people may try cannabis once or a few times or take the drug occasionally, such as less than once a month. Between twenty and thirty per cent of the current adolescent or young adult cannabis users in western countries for which data is available use the drug on twenty or more days a month. Daily consumption has become more prevalent in the past decade among young adults in the USA, Australia and various EU member states.
Measures of the frequency of cannabis use do not tell us the average amount of the drug consumed and even if we knew the amount consumed this would not tell us the actual dose administered, as cannabis products have varying concentrations of psychoactive ingredients.

When do people begin consuming cannabis and when do they stop?

Cannabis consumption can only be understood by considering a range of personal, social and cultural characteristics. Most users start taking cannabis in adolescence or early adulthood. In western countries the age of first consumption is usually lowest for tobacco and alcohol, followed by cannabis and then by other illicit drugs. Most people do not take cannabis for long. They use it for experimental or recreational purposes. As with other illicit drugs, many users of cannabis rapidly or eventually stop taking this drug or cut back on consumption even after years of regular use. However, some may continue the habit well into their thirties or beyond.
The strength of cannabis, i.e., the content of Δ^9-tetrahydrocannabinol (or THC), has increased in at least the USA and the Netherlands. The health effects of higher THC levels in cannabis products are not known. It is not the concentration of THC in the plant that determines the effect, but the

user's internal exposure to THC. For instance, cannabis users may adapt their dose of THC by changing the volume of smoke they inhale per puff. The evidence that they actually do so is conflicting.

How many people run into problems with their use of cannabis?

Most cannabis users keep their consumption of the drug under control. How many people do not succeed in doing so is unclear. Cannabis dependence is not rare among current users, although it is less common than dependence on tobacco and possibly alcohol. The risk of becoming dependent on cannabis is associated with conduct disorder and other disadvantageous personal and social characteristics, but also with starting to use cannabis at an early age and with the frequency and amount of consumption. Young users are more likely to become dependent on cannabis than older ones.
Most problem cannabis users seek no professional help at all. In many EU member states the proportion of people demanding treatment for problems owing to cannabis has risen recently in relation to other drugs. People seeking help for cannabis problems are mostly young men, often facing other problems with substance use or mental health.

Is cannabis a gateway drug?

The gateway theory states that using cannabis may prompt people to take other drugs later on in life. There is evidence of a *correlation* between cannabis use and later consumption of other illicit drugs, but most cannabis users do not progress to other drugs. There is no convincing proof that cannabis *in itself* is a stepping-stone towards other drug use. However, some adolescents' desire for non-conformity and perhaps genetic and educational factors may increase the probability that these young people will ultimately take other drugs besides cannabis. Other circumstances that may make cannabis users more likely to use other drugs include conduct disorder, social interaction with peers who use drugs and greater access to illegal markets.

How should cannabis use be monitored?

In view of all these data the frequency and the consequences of cannabis use is best monitored using key indicators. The EMCDDA has decided on five such indicators of drug consumption to which the member states of the EU should adhere, two of which pertain to cannabis: 1) use among the general population and school pupils, and 2) demand for treatment. There should be a set of indicators for 'problematic use of cannabis' as well, targeting questions like whether cannabis affects physical and mental health, cognitive functions, behaviour, and school and work performance.

1.1 Introduction and main questions to be addressed

Cannabis includes hashish and marijuana in various preparations. The usual way of administering the drug is to smoke it, either mixed with tobacco or on its own, but cannabis can also be eaten in baked or cooked foods. Countries have adopted varying policies to control or prevent the cultivation, sale and consumption of cannabis. To inform policy makers and the general public, we need data on the patterns and trends of cannabis use. This calls for epidemiological studies and monitoring programs.
This paper provides information from surveys, registers and cohort studies. Our intention is not to be encyclopaedic [1], but rather to highlight the similarities and differences in findings and

1 *To avoid overlap we do not address here issues that are dealt with in detail in the other chapters, such as the effects of cannabis on cognitive functions and mental states and the effects of cannabis policy on cannabis use.*

trends from a western perspective. We mainly focus here on the European Union and Switzerland, and, for comparison purposes and because of the availability of good research data, on Australia, New Zealand and the USA as well. The main questions we address are:

- How many and which people in the general population use, or have ever used cannabis, and how often?
- When and why do people start using cannabis, why do they continue and when and why do they stop? Do they use cannabis along with other substances?
- Is there any preference for a particular type of cannabis preparation and a particular strength of the product?
- How many people become dependent on cannabis and how many run into problems with their use of cannabis to such an extent that they demand treatment?
- Is cannabis a gateway to using other illicit drugs?
- How should cannabis consumption be monitored?

1.2 How many and which people use or have used cannabis?

Longitudinal studies may provide estimates of *incidence* rates. This term generally refers to the proportion of people within a group taking the drug *for the first time* within a given time frame. As data on incidence is rare, we will mainly present data on *prevalence* rates, i.e., the proportion of new plus ongoing users of cannabis in a given period of time [2].
Commonly, prevalence is measured in three ways: *lifetime (ever)*, *last year (recent)*, and *last month (current)*. A person may try cannabis only once or a few times in his or her life. These people will be included in the count of lifetime users. This practice may easily lead to misuse of statistics, with one-time and occasional users being lumped together with regular and problematic users. Data on recent and current use is far more informative than figures for lifetime use. However, data on lifetime use is more widely available for the purpose of comparisons across and between countries.

Most surveys of cannabis consumption have been retrospective, relying on the memory of the respondents. A more informative but also costly approach would be to chart people's cannabis consumption careers prospectively (longitudinally), starting even before they begin, and also applying measurements other than self-reporting. This would include the initial age at which the drug is taken, the frequency of use at any time in life, the eventual development into problematic use, and finally the age, if any, at which the user stops or reduces his/her cannabis consumption. Unfortunately, such studies have been sparse, although examples can be found in the literature (e.g. 1, 2).

1.2.1 General population

Cannabis is the most frequently used illicit drug in the western world. At least 45 million people in the European Union have tried cannabis at some time in their lives, amounting to eighteen per cent of the general population aged fifteen to 65 years [3]. This number is still growing. Table 1 presents the latest findings from EU and Swiss general population surveys [4], with the minimum age of the

2 *'Prevalence' is not the same as 'frequency'. In this chapter, 'prevalence of use' is shorthand for 'proportion of users' in a given group of people and within a given period of time. In contrast, 'frequency' does not refer to the number or proportion of users, but rather to the number of times that an event (such as cannabis use) happened.*

3 *With this notation we mean: ages fifteen to 65 years, including 64 but excluding 65. Others use the notation 'fifteen to 64' but mean the same.*

4 *Australia and the USA added for the sake of comparison. Additional data for Canada (1994, data collection by phone, sample size 12,155, age range fifteen years and over): lifetime use 29%, last year use 7% (12).*

respondents varying from twelve to eighteen years and the upper age limit generally from sixty to seventy years, apart from Belgium where it was fifty years.

- Comparisons between and across countries are hampered by differences in the quality and nature of the study designs, data collection and analysis methods, and variations in the last monitoring year and the age range of respondents.
- The truthfulness of the answers may vary depending on how respondents perceive the protection of their privacy and the risk they run by admitting that they have used drugs. However, the available evidence suggests that subjects are relatively forthcoming in surveys about their drug use (63).
- Non-response bias is another source of error. Thus, in school surveys drop-outs and absentee students, who have high rates of use, are not normally covered.

These sampling and response biases are limited and can be reduced, and then appear to be fairly stable across time. The reliability and validity of measures of self-reported cannabis use are generally good in well-designed surveys (3). With these caveats in mind, we may conclude that experience with cannabis is generally less prevalent in the EU than in Australia and the USA (4-10).

Table 1.
Prevalence rate of cannabis consumption in the general population in western nations

Country	Monitoring year	Data collection	Sample size	Age range (years)	Lifetime use	Last year use
Australia	1998	Mixed*	10,000	14 and over	39%	18%
USA	1999	Mixed**	66,706	12 and over	35%	9%
USA	2000	Mixed**	71,764	12 and over	34%	8%
England & Wales	2000	Mixed*	13,021	16 - 60	27%	9%
Denmark	2000	Face-to-face	14,228	16 - 65	24%	4%
France	1999	Phone	11,526	15 - 65	23%	8%
Belgium@	1998/1999	Phone	3,311	18 - 50	21%	?
Germany ('West')	2000	Mail	6,332	18 - 60	21%	6%
Ireland	1998	Mail	10,415	15 - 65	20%	9%
Spain	1999	Face-to-face	12,488	15 - 65	20%	7%
Netherlands	1997	Face-to-face	22,000	15 - 65	19%	6%
Switzerland	1997	Phone	13,004	15 - 60	19%	5%
Greece	1998	Face-to-face	3,752	15 - 65	13%	4%
Sweden	2000	Face-to-face	2,000	15 - 65	13%	1%
Germany ('East')	2000	Mail	1,430	18 - 60	11%	5%
Finland	1998	Mail[$]	2,568	15 - 70	10%	3%

Data collection methods included face-to-face interviews, self-completed questionnaires in a face-to-face contact, telephone interviews or mailed questionnaires. Sample size refers to the net sample. Example of age range: sixteen-sixty means from the age of sixteen through 59 years. See footnote 3.

** Face-to-face interview and self-completed.*

*** Face-to-face (computer-assisted personal interview), with sensitive questions handled by means of audio computer-assisted self-interview. Because of changes in methodology, data from surveys before 1999 is not fully comparable with that obtained from 1999 onwards.*

[@] Walloon Community. 2,112 of the respondents completed the drug section.

[$] 425 respondents were interviewed by phone.

Sources: (4-11).

Applying an upper age limit, as has been done in most of the countries listed in Table 1, will somewhat lift prevalence estimates, as prevalence of use – especially recent and current – generally decreases with age beyond early adulthood. In interpreting the data the monitoring year should be taken into account as well. The prevalence rate of cannabis consumption has risen in most western countries in the early and sometimes late 1990s (see below). Figures earlier than 1998 are therefore bound to be lower than later data, although the trend towards higher rates has since been halted or reversed in at least the USA (Table 1).

The EMCDDA publishes data for identical or similar age groups (4). For 'young adults', defined as respondents aged fifteen to 35 or forty years, England & Wales and Ireland head the EU list of recent (last year) cannabis consumption with a prevalence rate of eighteen per cent, followed by France (15%) [5], Spain (13%), the Netherlands and Denmark (both 10%), Greece (9%) and the western part of Germany (8%) [6].

In lifetime, recent or current prevalence rate of use, cannabis dominates all other illicit drugs but falls short of alcohol and nicotine.

- Two surveys, one carried out in England & Wales in 2000 and one in France in 1999, provide examples. Twenty seven per cent of the respondents aged sixteen to sixty years in England and Wales reported that they had used cannabis at some point, outranking amphetamine (11%), LSD and magic mushrooms (6% each) and ecstasy and cocaine (5% each) (8). Of the French respondents aged sixteen to 75 years, 21 per cent said they had taken cannabis at some point, three per cent inhalants, two per cent LSD, one per cent amphetamine and one per cent cocaine (14).
- Even in the USA, where rates of use of illicit drugs other than cannabis are higher than in Europe, cannabis is by far the most commonly consumed illicit drug. Thus, in the US 2000 Household Survey 59 per cent of current users of illicit drugs had solely used cannabis (marijuana [7]) in the past month. A further seventeen per cent of current users had taken marijuana and at least one other illicit drug, whereas 24 per cent had used one or more illicit drugs but not cannabis in the month before the interview (6) [8].

Cannabis is almost invariably at the top; the order of prevalence for other illicit drugs may vary between countries.

Most countries have not carried out repeated surveys with the same method of measurement. Most of the available information is therefore not fully adequate to enable trends in prevalence rates to be traced. However, we may draw the following broad conclusions:

- In a number of countries, such as Switzerland (12), the USA (15, 16), the Netherlands (17) and Germany (18), cannabis consumption in the general population has evolved in two waves [9]. Recent and current use prevalence rates first peaked between the late sixties and the early seventies, then dropped, then rose again in the 1990s, though this second wave did not rise to the level of the first wave in the USA, and possibly other countries as well. The second wave appears to be levelling off in some countries (4).
- The lifetime prevalence rate of cannabis use has increased in European nations in the past

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5 *In a more recent survey, with more respondents, the French figure was 17% (9).*

6 *Swiss respondents aged fifteen to forty: lifetime prevalence rate was 16% in 1992 and 27% in 1997; last year rate was 8% (12, 13). More recent data from Germany (2000): 13% last year rate in both the western and eastern parts (10).*

7 *In the USA cannabis use mainly relates to marijuana as hashish is difficult to obtain there.*

8 *Note that the percentages for the examples in these two bullets are not comparable. The US figures pertain to the proportion of current drug users, the figures for England & Wales and for France pertain to the proportion of all respondents.*

9 *In Western Europe the two-wave phenomenon did occur in northern countries, including the UK, Denmark, Finland and Sweden, but was absent or less marked in southern ones (Greece, Portugal, Spain) (R Hartnoll, personal communication).*

decade (4, 10, 11, 19). The rise in last year consumption of cannabis has been less marked. An upward trend in prevalence rates has been reported for the USA and Australia as well, with a particularly steep increase in the latter country (20).

1.2.2 High school students

A variety of countries regularly publish drug use figures for the full age range (twelve through eighteen or nineteen years) of high school students. The best comparative data on cannabis use, among students of fifteen and sixteen years of age, comes from ESPAD, the European School Survey Project on Alcohol and Other Drugs. A similar monitoring project – Monitoring the Future – is being carried out in the USA. Table 2 gives the latest findings [10].

Table 2.
Prevalence rate of cannabis use in 1995 and 1999 among high school students aged 15 and 16 years

Country	Lifetime use		Last month use		Six or more times in the last month	
	1995	1999	1995	1999	1995	1999
USA	34%	41%	16%	19%	7%	9%
United Kingdom	41%	35%	24%	16%	9%	6%
France	-	35%	-	22%	-	9%
Ireland	37%	32%	19%	15%	7%	5%
Netherlands*	29%	28%	15%	14%	6%	5%
Italy	19%	25%	13%	14%	5%	4%
Denmark	17%	24%	6%	8%	1%	1%
Norway	6%	12%	3%	4%	1%	1%
Finland	5%	10%	1%	2%	0%	1%
Greece	2%	9%	1%	4%	0%	2%
Portugal	7%	8%	4%	5%	1%	2%
Sweden	6%	8%	1%	2%	0%	0%

- = Not measured.
** The first set of data from the Netherlands is from 1996 rather than 1995.*
Source: (21)

10 *Results from the 1996 Australian School Students' Alcohol and Drugs Survey for twelve to seventeen-year-olds and from the 1998 National Household Survey for fourteen to nineteen-year-olds are not entirely comparable with the data in Table 2, but do suggest that lifetime and last month cannabis use rates for Australian high school students are among the highest from an international perspective (22).*

11 *Lifetime prevalence rates may be high in other European countries as well. One notable example is the Czech Republic, with 35% in 1999 (21).*

- In 1999 the USA topped the list for ever (lifetime) use among high school students. The United Kingdom and France had the highest rates in the EU [11].
- France was first in terms of last month use.
- The prevalence rate of lifetime and last month cannabis consumption has stopped rising in three EU member states for the first time in years. In the United Kingdom and Ireland the prevalence rates of both lifetime and last month cannabis use declined between 1995 and 1999 among fifteen and sixteen-year-old students. In the Netherlands the figure for ever and current cannabis use went up between 1988 and 1996, then stabilised with a tendency towards a decrease in the prevalence rate (Figure 1).
- The prevalence rate of cannabis consumption among adolescents is still growing in various other EU member states. In France, for instance, fifteen per cent of fifteen and sixteen-year-old high school boys took cannabis ten or more times in 1999, compared with six per cent in 1993. These figures were nine and three per cent respectively for girls (19, 23) [12].

Taken together, these statistics suggest that the prevalence rate of cannabis use among high school students is stabilising or decreasing in EU countries with relatively high prevalence rates in the early 1990s, and increasing in countries that formerly had low rates. Thus there is a tendency towards convergence of rates between EU member states (4) [13].

- Switzerland does not take part in the ESPAD surveys, but it does collect data from high schools. In a survey conducted in 1994 eighteen per cent of fifteen-year-old Swiss pupils said they had taken cannabis at some point and in 1998 more than thirty per cent said they had done so. The upward trend in prevalence rate was most notable for boys (12).
- Belgium does not participate in ESPAD either, but data is available for fifteen and sixteen-year-old high school students. In 1996 twenty per cent of Flemish students reported they had used cannabis at some point, while eleven per cent had done so in the last month. In 1999, in a much larger sample (over 47,000) [14], the lifetime prevalence rate was 24 per cent for Flemish students of the age concerned, and 28 per cent for Walloon students (24) [15].

Among high school students, as in the population in general, cannabis is by far the illicit drug most often tried or regularly consumed, followed at a great distance by amphetamine, ecstasy and cocaine (4, 16, 21). In the USA the trend in current (last month) consumption of cannabis among high school students has run more or less in parallel with the curve for current alcohol use from 1975 onwards, though at a level 2.5 times lower (16).

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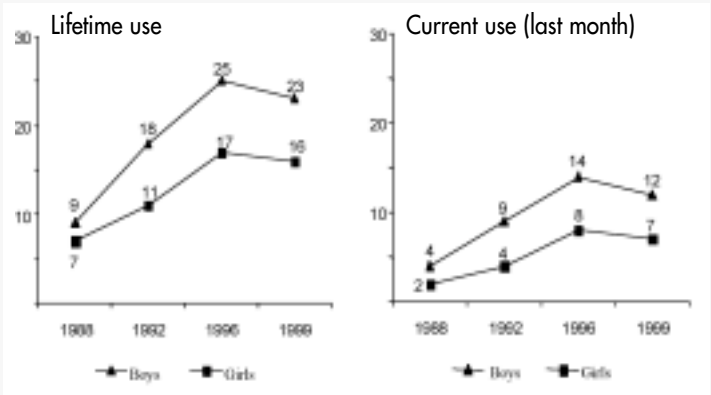
12 *Frequency of consumption depends on age and gender. At the age of eighteen, 29% of French high school boys said they had taken cannabis ten times or more in 1999, versus 14% for girls. Forty times or more: 15% of the eighteen-year-old boys and 5% of the eighteen-year-old girls (19).*

13 *However, on the measure 'six or more times of use in the last month' consumption of cannabis appears to have stabilized or fallen down in most of the countries shown in Table 2.*

14 *But with a different study protocol and without last month data.*

15 *Other EU member states that do not take part in ESPAD but have comparable data are Luxembourg (28% lifetime use for this age group in 1999) and Spain (28% lifetime use in 1998 versus 25% in 1996). Data from the EMCDDA.*

Figure 1.
Cannabis use by high school students in the Netherlands aged twelve years and over, since 1988. Percentage of lifetime (left) and current users (right)



Source: (25).

1.2.3 Groups with elevated cannabis consumption prevalence rates

Some groups contain a relatively greater proportion of people who use cannabis, often in combination with other substances, than that found in the general population. In the Netherlands the proportion of current cannabis users is a little higher among pupils who attend schools for adolescents with special educational or behavioural needs than among their peers in 'ordinary' schools (Table 3). For other groups of young people, especially the homeless, cannabis use has become the rule rather than the exception. Although school systems and institutions do differ between countries, making comparisons more difficult, the evidence available suggests that there is a widespread association between behavioural problems or disorders and high prevalence of cannabis use.

Table 3.
Rate of current (last month) cannabis use in special groups of adolescents and young adults in the Netherlands

Young people in	Survey year	Age (years)	Last month use
Ordinary schools for secondary education	1997	12 – 18	10%
Special schools for secondary education	1997	12 – 18	14%
Truancy projects	1997	12 – 18	35%
Judicial institutions for adolescents	1995	?	53%
Youth care institutions	1996	10 – 19	55%
Young drifters	1999	15 – 22	76%

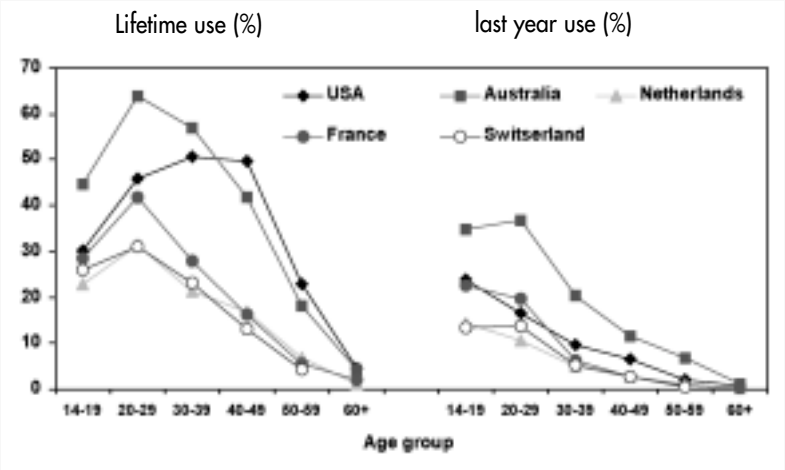
Source: (26) [16].

16 *Australian data for people aged twelve to 22 years in detention in New South Wales in 1999: prevalence rate of use ate least once a week 83%, compared with 74% in 1994 (J Copeland et al, submitted). Of a sample of 447 visitors of techno-parties in the German state of Bavaria 70% had taken cannabis in the previous year (28).*

1.2.4 Who uses cannabis?

Users of cannabis come from all social classes and demographic and educational backgrounds. In surveys conducted in western countries the majority of lifetime, recent and current users are relatively young (adolescents and young adults). In 1998, the rate of ever consumption of cannabis in the USA peaked in the age group from thirty to fifty years (Figure 2). This group included past users from the first high-prevalence wave of use [17]. More common is a peak between twenty and thirty years of age, as shown for Australia, France, the Netherlands and Switzerland. The highest prevalence rate of recent consumption of cannabis (right hand panel of Figure 2) is seen at earlier ages.

Figure 2.
Proportion of cannabis users in Australia (1999), the USA (1998), France (1999), the Netherlands (1997) and Switzerland (1997) per age group



Sources: (9, 20, 27) [18].

In general, cannabis is more popular among Caucasian whites [19] than among representatives of ethnic minorities in western countries, such as blacks, Indians and Pakistanis/Bangladeshis in England & Wales (8), and Moroccans, Turks, and people from Suriname and the Dutch Antilles in the Netherlands (29). There are exceptions to this rule. Thus, more young Maoris, for instance, have experience with cannabis than other New Zealanders in the age group from 15 to 21 (30).

A host of other determinants and correlates – factors with a statistical bearing on cannabis use – have been identified. They may vary somewhat depending on the type of prevalence of use (lifetime, recent, current) and the age group studied. Culture may have an effect, too, but more striking is the commonality of factors across western nations. In addition to being young and white, the following

17 *One reason for the relatively late peak in the USA may be that older cannabis naive Americans may still start taking the drug, perhaps more often so than in Australia and the Netherlands. From 1995 to 1998, lifetime use of cannabis increased from 38% to 49% among US respondents in their forties. Recent use among American men in this age group also went up (20).*

18 *Swiss data provided by R Müller.*

19 *In countries with non-white ethnic minorities.*

list of factors that were the best predictors of current cannabis use among US high school students (16, 64) also apply, either fully or partly, to other countries in the western hemisphere: 1) lower educational and occupational expectations, 2) living in an urban area [20], 3) not attending any religious services [21], 4) living alone, 5) having a father or a mother with advanced education, at least high school, 6) being male, and 7) living with only one parent [22].
Other factors [23] may also come into play in the case of adolescents and young adults who use cannabis more than once daily, such as (1, 2, 30-33): 1) unemployment and low socio-economic status, 2) truancy, 3) low self-esteem, 4) high levels of drinking and smoking and experimentation with other illicit drugs, 5) delinquent behaviour such as stealing, vandalism, and fare dodging, 6) (other) behavioural disorders; mental disorder, 7) having delinquent friends, and 8) hanging out on the streets in boredom. It is difficult to distinguish between cause and effect in respect of these variables.

Studies from a variety of countries have identified the main characteristics of former and regular users of cannabis with *long-term* consumption careers, often spanning more than ten years. Some of the features are familiar from the lists above (male, white, urban, drinking and smoking well above average, use of other illicit drugs). These people are less likely to live with a partner, to be married and to have children than non-users (16, 31, 34).

- In terms of experimentation with other drugs, nine per cent of the respondents from a 1993-1995 German sample of regular cannabis users reported last month use of cocaine, eight per cent stimulants, seven per cent hallucinogens, and three per cent opiates (18).
- The 'Three Cities' study carried out among regular cannabis users [24] found that the prevalence rate of co-use of other drugs was generally lower than in the aforementioned German survey (18), with peaks for cocaine (9% and 8% respectively in Amsterdam and San Francisco) and ecstasy (9% and 6% respectively, in the same two cities). The authors concluded that "although cannabis users are relatively likely to experiment with other illicit drugs, they are not so likely to continue using these drugs" and "they rarely engage in using these (other) drugs with a high frequency" (34).
- Experimentation with other illicit drugs was common in an Australian group of long-term cannabis users (31). Over nine out of ten of these respondents had tried hallucinogens and amphetamine at some point, more than six out of ten cocaine, and about half inhalants and heroin. Less than half had used these drugs regularly or in the last month. Yet almost half of this group had a history of drug problems, with twenty per cent having sought help for this problem.

In conclusion, the determinants of long-term cannabis use are quite similar across studies, although their nature and relative importance may vary somewhat between groups. There may be different types of users, whose characteristics may partly overlap (see later in this chapter) [25].

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20 *Not true of Canada (E Single, personal communication).*

21 *Or being part of particular religious groups such as Moslems and conservative Christian communities.*

22 *Another factor may be lifestyle in a broader sense: the tendency to go out to restaurants, bars, concerts and so on (34).*

23 *Similar variables related to cannabis use have been identified for adults (white, male, religion, living in urban areas). In addition, marital status is important (cannabis use is highest among those single or divorced), as is low educational attainment (but in some countries also higher educational achievement) and the lowest and highest income levels (3-11).*

24 *Amsterdam (Netherlands, 1994), Bremen (Germany, 1998) and San Francisco (USA, 1998). Regular use of cannabis: at least 25 times. Sample size: Amsterdam 216, Bremen 55, San Francisco 265. Mean length of time since first use of cannabis: fifteen to eighteen years (34, 35).*

25 *One other example of the group or situation specificity of co-use data comes from a study among visitors to techno-parties in the German state of Bavaria. More than half of these people had used cannabis in conjunction with other drugs in the previous year (28).*

1.2.5 How often do people use cannabis?

Many people consume cannabis rarely or occasionally rather than regularly. One in three of the respondents in a 1997 Dutch survey who had taken cannabis at some time in their lives had used the drug at least twenty-five times. A quarter of the current users reported daily or near daily consumption of cannabis (Table 4). This compares well with findings from other countries, including the 2000 US Household Survey: 47 per cent of American current users aged twelve and over took cannabis on less than six days in the last month, 22 per cent on six to nineteen days and thirty per cent on more than nineteen days (5)[26]. In short, twenty to thirty per cent of the mostly current adolescent or young adult users in western countries for which data is available use cannabis almost daily, if not daily.

When users move on to long-term use, their consumption intensifies in frequency and amount. Forty to sixty per cent of these consumers may take cannabis daily, especially during the peak period of their career as users (31, 34), and some people use cannabis daily for quite a while (1). The amount of cannabis taken per month at the peak of the use careers of the participants in the Three Cities survey generally did not exceed fourteen grams[27] (34).

Table 4.
Frequency of current cannabis consumption by people aged twelve years and over in the Netherlands. Survey year: 1997

Days of use in the last month	Percentage of current users
1 to 4	45%
5 to 8	14%
9 to 20	15%
More than 20 days	26%

Source: (27).

1.3 When and why do people start consuming cannabis, why do they go on and when and why do they stop?

1.3.1 Age of initiation

In western countries most users start taking cannabis in adolescence or early adulthood. Table 5 shows the average age at which twelve to seventeen-year-old American and Dutch adolescents began to use cannabis and other substances. The data comes from the 1997 US Household Survey and from the concurrent general population survey from the Netherlands (27).

- Initiation age was lowest for tobacco and alcohol and highest for hard drugs in both countries.
- Initiation age did not differ greatly between the two countries but was usually lower in the USA than in the Netherlands.
- Nevertheless, there were some notable differences between the USA and the Netherlands in the age at which cannabis was first used. The initiation age for American twelve to seventeen-

26 *Roughly similar frequency distributions have been reported for Australia (7), France (9) and Germany (10).*

27 *The corresponding number of 'units of use' depends on the manner of consumption, users' preferences, and the type, origin and perhaps strength of the cannabis. When smoked with tobacco, for instance, one gram may be processed into two to five joints.*

year-old adolescents was 13.7 years compared with 14.4 in the Netherlands. In other words, American adolescents tended to start taking cannabis at an earlier age than their Dutch peers.

Table 5.
Average starting age for alcohol, tobacco, and drug use in the USA and the Netherlands.
Self-reported age of first use by adolescents. Survey year 1997

Drug	USA	The Netherlands
Tobacco	12.4	12.9
Alcohol	13.1	13.0
Cannabis	**13.7**	**14.4**
Inhalants	12.5	13.6
Cocaine	14.6	15.7
Hallucinogens	14.4	14.6
Heroin	14.0	15.5

Sources: (27).

1.3.2 Continued and discontinued use

Most people do not use cannabis for prolonged periods of time.

- Most consumers take cannabis for experimental or recreational purposes; they try the drug once or a few times or only use it in their leisure time (3, 9-11, 18, 19, 37).
- A crude measure of the likelihood that someone who has used the drug once will become a regular user of cannabis is the conversion or continuation rate (20): this is the last year prevalence rate [28] divided by the lifetime prevalence rate times one hundred.
  - Australia has a high continuation rate – 46 per cent in 1998 – indicating that one in two Australians who have ever consumed cannabis will probably go on using the drug for a while.
  - The corresponding US continuation rate for the year 2000 was 24 per cent (29% in 1998) (6).
  - Sweden and Denmark have low continuation rates, i.e., eight and seventeen per cent respectively. The continuation rates for other EU member states and for Switzerland lie between 24 and 38 per cent (11, 27) [29].

The opposite of the continuation rate is the discontinuation rate. Both rates depend on age and gender. Table 6 presents data from the 1996 US Household Survey, showing that women tend to discontinue the use of cannabis – not necessarily the same as stopping forever – in greater numbers and at earlier ages than men. The discontinuation rate for women was 78 per cent and for men 69 per cent. In other western countries, too, many users of cannabis quickly or eventually cease taking this drug or cut back on their consumption. 77 per cent of the respondents in a New York State cohort had effectively stopped by age 34-35 (1) and seventy per cent of those in an Amsterdam cohort by the age of 32 (37). However, this tendency to stop before middle age need not be universal (see below).

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28 *Even more informative would be a continuation rate expressed as last month prevalence rate divided by lifetime prevalence rate, but we do not have enough data to compute this index for all the countries mentioned. Last month continuation rate of cannabis use is 16% in the Netherlands (age group 15-65) and 15% in the USA (age group twelve years and over). (Calculations by the present authors.)*

29 *Continuation rate for France: 29% (calculations by the present authors.) For Western Germany in 2000: 29%, and for Eastern Germany 45% (10). For Switzerland in 1997: 24% (11). No rate known for Belgium.*

Table 6.
Cannabis discontinuation rate (percentage of lifetime users who did not use in past year) in the 1996 US Household Survey

Age group (in years)	Women	Men
12 to 17	26%	20%
18 to 25	54%	39%
26 to 34	82%	74%
35 and older	91%	82%

Source: (3).

1.3.3 Careers of cannabis use for regular consumers

Several efforts have been made to devise a typology of cannabis users. The Three Cities team distinguished six career patterns for former and current regular users (34):

- A high consumption level in the beginning, then tapering off. Fewer than one in ten of the respondents followed this pattern.
- Starting low, moving to a high level of use and staying there. Again this was rather rare; it applied to fewer than one in ten of the study participants.
- Stable use for many years. Fewer than one in ten identified themselves with this pattern of consumption.
- Starting low, rising to a peak followed by decreasing use. This was the pattern most frequently reported, by 48 per cent of the Amsterdam, 44 per cent of the Bremen and fifty per cent of the San Francisco samples.
- Intermittent use, with regular starts and stops. This pattern was the most infrequent of all.
- Varying use, with ups and downs but without a clear rhythm. This pattern was second in frequency, with 24 per cent of the Amsterdam and 35 per cent of both the Bremen and the San Francisco samples reportedly matching it.

The onset and course of marijuana use have been recorded in a longitudinal study in New York State spanning a period of twenty years. Four types of marijuana users have been identified from the data, with corresponding sets of determinants (1):

- The early onset-heavy use group started experimenting with the drug earliest, at the average age of fifteen years. They all became near daily users and did so by the age of 17.5, earlier than any other group. They experienced spells of near daily consumption, lasting for a total of 131 months on average. Fortynine per cent of the people in this group were still using marijuana at the age of 34-35 years.
- The early onset-light use group started experimenting with marijuana at the age of fifteen as well, but only 44 per cent moved on to (fewer and shorter) spells of near daily use (totalling 28 months on average). They did so one year later than the early-heavy group. Only one in ten was still using the drug by the age of 34-35.
- A third group, with mid-onset but heavy use, started one year later than the early onset groups. Two thirds became near daily users (for a total of 42 months on average) and all were still consuming marijuana at the age of 34-35.
- The late onset-light use group began taking marijuana at age 19.5 and only a minority (21%) became near daily users. Virtually all of them had stopped using it by the age of 34-35.

Light users outnumbered heavy users. Heavy users had a lower level of education and were less likely to attend church. They were more delinquent in adolescence and adulthood, more likely to be part of cannabis using networks, and they changed jobs more frequently than light users. Early onset use was statistically associated with mental disorder and minor delinquency in adolescence, taking up

smoking and drinking at an early age, experimentation with other illicit drugs, and the tendency to take marijuana for positive reasons. Late onset users often took the drug for negative reasons, such as the desire to overcome feelings of depression (1) [30].

What we can learn from these findings is that *the* cannabis user does not exist. The cannabis consumption patterns of individuals and groups of people can only be understood by taking a range of personal, social and cultural characteristics into account.

1.3.4 Why do people start taking cannabis and why do they stop?

One important factor in the decision to start using cannabis is the influence of peers and especially friends [31].

- In more than seventy to eighty per cent of cases, the first cannabis was offered by friends or acquaintances (18, 21, 34).
- More than eight out of ten participants of the Three Cities study took their first cannabis in the company of one or more friends (34).
- Only about half of the participants rated their first experience with the drug as pleasant. About four out of ten said that they did not feel any effects at that time; they apparently needed more opportunities to learn to appreciate the 'high' of cannabis (34).
- The most common motives for first use are curiosity and the desire to be sociable and part of the group (31).

Adolescents may also start using cannabis to establish their independence from their parents' authority. The opposite may also be true: children from families where parents regularly consume substances such as tobacco and alcohol may feel freer to take substances like cannabis than others in their peer group (19).
Although sometimes mentioned in the literature, the role that genetic factors may perhaps play in influencing cannabis use, or at least dependence, has been largely neglected in research studies.

The majority of the regular users in the Three Cities study had their second experience with cannabis within one month of the first one. Regular consumption started 1.6 years (Bremen), 2.1 years (Amsterdam) and 2.4 years (San Francisco) after initiation. The period of heaviest use began two to three years after the start of regular consumption (34, 35).
People list a variety of reasons for continued regular use of cannabis. The top four reasons in Amsterdam, Bremen and San Francisco, though not very distinct, were 'to relax', 'to feel good', 'to enjoy music, movies, and so on' and 'to be sociable with friends' (34, 35). There is no universal set of motives for people to cease or reduce their cannabis consumption. The rank order of reasons in the Three Cities varied between Amsterdam, Bremen and San Francisco, as did that for the outcome achieved: prolonged abstinence but then starting again, cutting back on consumption, quitting totally or not wishing to resume use in the future.

- Health and financial concerns were not important motives for quitting, but they did play a part in the decision to use less.
- Negative experiences were the number one motive for quitting in San Francisco (38%), but not in Amsterdam (23%) and Bremen (27%), where loss of interest in cannabis topped the list (Amsterdam: 66%, Bremen 36%, San Francisco: 19%). The number three motive was a change of lifestyle.
- The San Francisco respondents reported lack of availability of cannabis as a reason for temporary abstinence, unlike their counterparts in the other two cities (34).

Why do non-users not consume cannabis? Most non-users cite lack of interest, or fears of adverse health effects. Fear of punishment is rarely mentioned as a reason for abstention.

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30 *Cannabis probably used as self-medication.*

31 *The perceived availability of cannabis is possibly also important.*

1.4 Preference for a particular type or strength of cannabis

Cannabis preparations differ in composition and strength of the active ingredients. The 'dose' of active ingredients determines the intended and unintended effects of consumption. Therefore, it is important to know which types of cannabis products are used.

The Amsterdam participants in the Three Cities study more often preferred marijuana to hashish than the other way around (46% versus 26%, respectively). In Bremen there was no clear preference for one or other of these cannabis preparations.
Most of the respondents in the three cities said they preferred 'moderate' or 'strong' but not 'very strong' cannabis preparations. In Amsterdam 30 per cent preferred 'mild' cannabis, which was more than in Bremen (4%) and San Francisco (16%). The Amsterdam respondents did not express a desire for stronger preparations, but almost half of their Bremen and San Francisco counterparts said that they would prefer more potent cannabis if it became available. 'Strong' in Amsterdam may not have been the same as in the two other cities. Conceivably, at the time of the study the Amsterdam cannabis market catered to the needs of users more effectively than the markets in the two other countries (34).
The content of Δ^9-tetrahydrocannabinol (THC) is a measure of the strength of cannabis. In the USA the concentration of THC in confiscated marijuana increased from less than 1.5 per cent in 1980 to 3.3 per cent in 1983 and 1984, and then more or less stabilised. Since 1992 the concentration has risen to 4.2 per cent in 1997 (38). No such increase has occurred in New Zealand, where the average THC content of non-systematically confiscated cannabis has remained within the range of two to four per cent (39).
Since 2000, the Drugs Information and Monitoring System (DIMS) has carried out annual tests on samples of domestic (Nether-weed) and foreign marijuana bought in randomly selected coffee shops in the Netherlands. The mean THC content of Nether-weed was 8.6 per cent in 2000 and 11.3 per cent in 2001 [32]. THC concentration in foreign marijuana remained stable at five per cent (40). It is hard to compare findings between countries because of differences in sampling, sampling year and analyses on the one hand, and in products on the other. With these caveats, we contrast data from the US and the Dutch analyses in Table 7.

- One reason why foreign cannabis in the Netherlands generally contains less THC than domestic products may be that domestic marijuana and hashish are fresher, as suggested by lower ratios of cannabinol to THC (40). Fresh hemp plants do not contain cannabinol, which is formed from THC.
- To some extent Nether-weed resembles Sinsemilla, literally meaning 'seedless'. Sinsemilla products are made from the non-fertilised flowers of the female hemp plant. Nether-weed is commonly grown indoors, allowing the male and female plants to be separated before they blossom.
- The average THC content of foreign marijuana in the Netherlands compares reasonably well with that for marijuana seized in the USA (5% in 2000/2002, versus 4.1% in 1997, respectively). The increase in the average THC concentration of Nether-weed in the second sampling year compared with the first one is remarkable. Time will tell whether this is a trend or a spurious result, for instance because more of the Nether-weed sampled in 2000/2001 was produced by indoor cultivation than in the preceding year (40) [33].

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32 *Marijuana seized by police and customs in France in 1999: 46% of the samples contained 0-4% THC,33% of the samples 4-8% THC, 15% of the samples 8-12% THC, 6% of the samples 12-20% THC, and 1% of the samples 20% or more THC (60). Thus, 22% of the samples contained 8% or more THC.*

33 *In September 2001 the DIMS analyzed new samples of Nether-weed in the Netherlands. The mean THC content was lower: 10%, indicating that factors as yet unknown, such as seasonal variations, may determine the level of THC (41).*

Table 7.
Comparison of the THC concentration in marijuana samples obtained in the USA and in the Netherlands. Percentage of samples containing 3% or more, 5% or more, or 9% or more THC

Year of analysis	Domestic and foreign marijuana (USA); foreign marijuana (Netherlands)			Sinsemilla (USA); Nether-weed (Netherlands)		
	≥ 3% THC	≥ 5% THC	≥ 9% THC	≥ 3% THC	≥ 5% THC	≥ 9% THC
USA, 1996	63%	25%	3%	93%	77%	49%
USA, 1997	63%	29%	6%	96%	85%	64%
Netherlands, 2000/2001	75%	48%	7%	93%	87%	35%
Netherlands, 2001/2002	80%	55%	4%	100%	99%	78%

Sources: (38, 40).

The strength of cannabis may be increasing, but does it matter? The health effects of higher THC levels in cannabis products, if any, are unknown. Ultimately, it is not the concentration of THC in the plant that determines the effect, but the user's internal exposure to THC and other cannabinoids, known as the body burden. In theory, cannabis users may adapt their dose of THC by changing the puff volume of smoke they inhale [34]. However, the evidence that they actually do so is sparse and conflicting (42).

1.5 How many people run into problems with their use of cannabis?

No drug, whether illicit or not, is without risks for those who take it. The EMCDDA applies the concept of 'problematic use' to all illicit drugs except cannabis. Our review of the literature suggests that 'problematic use' is valid for cannabis as well. We translate 'problematic cannabis use' here in terms of 1) dependence and 2) treatment demand [35], as these are variables for which data is presently available from international sources. In addition, possible effects of the drug on cognitive functions (Chapter 2, driving performance), mental states (Chapter 5), behaviour and other outcomes should be taken into account when analysing 'problematic cannabis use'.

1.5.1 Cannabis dependence

The concept of cannabis dependence – and dependence on alcohol, tobacco and any illicit drug for that matter – stems from medical diagnostic classification systems such as the DSM (Diagnostic Statistical Manual, version III-R or IV) or the ICD (International Classification of Diseases). The DSM is the most widely used in research. This system currently distinguishes seven criteria for cannabis dependence. These include: 1) the occurrence of tolerance (more of the drug needs to be

34 *This is not the only way in which users can vary the dose. For instance, people with experience can control how much cannabis they put in a joint, how many joints they smoke and how much they pass the joints that do circulate. Once again, there is little systematic evidence on this..*

35 *The EMCDDA defines treatment demand as "Any activity that targets individuals who have problems with their drug use and which aims to improve the psychological, medical or social state of those who seek help for their drug problems. Activity may take place at specialised facilities for drug users, but may also occur in the context of general services offering medical and/or psychological help".*

administered to attain the original effect), 2) the emergence of withdrawal symptoms upon cessation or interruption of consumption, 3) taking cannabis in larger amounts than intended, 4) and a persistent craving for the drug or unsuccessful efforts to cut down on use. 5) In addition, much time is spent on obtaining and using the drug or on recovering from its effects and 6) (other) important social, recreational and occupational activities are given up or reduced. 7) The user continues to take cannabis despite knowing the harm that may result from it. The diagnosis 'cannabis dependence' applies when at least three of these criteria are met at any time within one year, which may be the last year or any year before it [36].

The concept of cannabis dependence has been criticised as being too medical, fraught with circular reasoning and too fixated on the consequences of use rather than on the behaviour of users (34, 43). Admittedly, the term 'cannabis dependence' is often used too loosely. However, strictly and correctly applied DSM rules are one of the few ways of getting a comparative picture of the proportion of people facing possibly undesirable effects due to regular cannabis use. In this respect the concept of cannabis dependence is as solid and valid as 'alcohol dependence' and heroin dependence', for example.

Figures for the prevalence rate of cannabis dependence vary widely. This is because authors take either the number of users plus non-users, or the number of (ever, recent or regular) users as the denominator. Others fail to specify whether dependence was 'lifetime' or 'recent'. We mainly restrict ourselves here to dependence among ever (lifetime) and recent (last year) users of cannabis assessed with the DSM or DSM-like methods.

- *Dependence ever in life among ever users*. The most extensive set of data comes from the National Comorbidity Survey, which was carried out among US citizens aged fifteen to 55 in the early 1990s (44). Nine per cent of those who ever used this drug had a lifetime history of cannabis dependence at some time during their four or five years of heaviest consumption [37]. The prevalence rate was highest (15%) for the youngest group – those aged between fifteen and 25 – and higher for men than for women. Data collected with identical or similar methods is not available for most EU member states. One exception is the Dutch Nemesis study, which examined a random national sample of about 7,000 people aged between eighteen and 65 from the general population. Ten per cent of all ever users in this survey met the DSM criteria for ever cannabis dependence (26).
- *Dependence in the last year among ever, recent or current users*. A US survey from the early nineties found that the last year prevalence rate of cannabis dependence among recent users aged twelve and older was seven per cent on average [38], the rate being highest among adolescents and young adults (13%) (45). Even higher last year rates of cannabis dependence were found in an Australian national survey carried out among the general population aged eighteen and over. About one in five of the respondents who had used cannabis in the previous year (21%) and forty per cent of the current users met the DSM criteria for dependence on this drug. Again, the prevalence rate of cannabis dependence peaked at a young age (18 to 25 years) (46, 47).

  In a New Zealand cohort of 1,265 children who have been followed from birth into early adulthood, almost seventy per cent had used cannabis by age 21. Thirteen per cent of ever users in the cohort were or had been dependent on cannabis by that time (lifetime diagnosis) (30). Another New Zealand birth cohort study, which began with over 1,000 participants, yielded similarly high use rates (62% at age 21, 70% at 26) and cannabis dependence rates (close to 15% among ever users at age 21 and over 13% at 26) (48).

36 *We will not discuss here another cannabis related 'disorder' in the DSM, cannabis abuse.*

37 *The threshold for 'lifetime use' in DSM-IV is five consumptions of cannabis.*

38 *The corresponding figure for Germany was 8% in the 2000 national survey (10).*

Taken together, these findings highlight the fact that cannabis dependence, as defined by the DSM, is not rare, especially not among adolescents and young adults. The high rates found in Australia and New Zealand may not be typical for Europe, though. The risk of becoming dependent on cannabis increases with the quantity, the duration and most of all the frequency of use (45, 49-52). However, cannabis dependence is not just a dose-response phenomenon. A list of determinants of dependence on this drug can be derived from the studies cited, including 1) being male, 2) starting to use cannabis at an early age, 3) being unemployed, and 4) having a history of violence. In addition to demographic, social and psychological factors, biology may play a role as well. Adolescents are more likely to become dependent on cannabis than adults at the same levels of frequency and quantity of consumption of the drug. Presumably, the threshold at which adolescents become dependent is lower than that for adults (53).

Although cannabis dependence is more common than previously thought, it remains to be seen what this finding actually means for the individual, for addiction care professionals or for society as a whole. Thus, three-quarters of a group of Australians who were diagnosed as dependent on cannabis did not, in their view, experience any problems owing to this drug (31).

The user's risk of becoming dependent may be lower for cannabis than for tobacco and alcohol (44, 54). In a comparative American survey the proportion of ever users who developed dependence was 32 per cent for tobacco, 23 per cent for heroin, seventeen per cent for cocaine, fifteen per cent for alcohol, and nine per cent for cannabis (44). However, more recent findings from Australia and New Zealand challenge the long-held belief that the potential of cannabis to produce dependence is relatively low. The sequence of dependence risk for illicit drugs was quite different in an Australian survey, where cannabis came second after amphetamine in terms of the dependence rate among current users (55) [39]. In one of the New Zealand birth cohort studies the rate of cannabis dependence among users was similar to that for alcohol, but lower than that for tobacco (48).

On the other hand, dependence on cannabis usually appears to be less severe than dependence on the other substances mentioned. For instance, cannabis withdrawal symptoms are generally mild (19). Yet again, a word of caution is in place. Withdrawal was the most commonly cited symptom (89%) of cannabis dependence among those meeting sufficient criteria for the disorder in an Australian community sample (31).

1.5.2 What is the link between cannabis dependence and other substance use and dependence?

Cannabis use and other substance use often co-occur. So do cannabis dependence and dependence on other substances. This is illustrated by the findings of the Australian National Survey on Mental Health and Well-Being, which consulted a representative sample of over 10,000 adults. Cannabis dependence in the year before the survey increased the risk of being dependent on other substances even after adjustment for a variety of demographic factors and for neurosis (55). Compared with non-users of cannabis, users who were *not dependent* on this drug were three times as likely to be dependent on alcohol and four times on one or more substances from the combined group of sedatives, stimulants and opiates. However, again compared with non-users of cannabis, people *dependent* on this drug were almost five times as likely to be dependent on alcohol, and 21 times on one or more substances from the group of sedatives, stimulants and opiates. Many of the features of those dependent on cannabis also typify people dependent on other substances, such as being male and young.

1.5.3 What is the link between cannabis use and violence?

Use of a substance may be called problematic if it leads to or exaggerates violent behaviour. Cannabis, with its 'mellowing' effect, might intuitively be expected to reduce violence. The

39 *However, the cited US data relates to 'lifetime' users (here five times or more in the user's lifetime) and the Australian data to 'recent' users (five times or more in the previous year).*

available evidence suggests that it is the other way around. One of the New Zealand birth cohort studies found cannabis dependence, along with alcohol dependence and schizophrenia spectrum disorders, to be strongly related to violence at age 21 even when controlled for demographic risk factors and all other co-occurring disorders (61). In all, eleven per cent of this sample's risk of becoming violent offenders could be attributed to alcohol dependence, 28 per cent to cannabis dependence and ten per cent to schizophrenia spectrum disorders. Having two of these conditions more than doubled the risk of violence compared with single disorder study participants.
The use of cannabis in the two hours before the act did not account for the higher risk of violence among those dependent on cannabis, unlike in the case of alcohol. The violence of the cannabis dependent study participants was best explained by a history of conduct disorder. Cannabis dependent individuals with conduct disorder, possibly associated with delinquency, may become early and active participants in the illegal economy of drug markets, which may promote intimidation and violence: for instance, when transactions go awry (61). If true, this would mean that cannabis does not foster violence when the sale or trade of cannabis is not penalised. This remains to be proven.

1.5.4 Demand for treatment

Cannabis use may lead to a demand for help from the addiction care sector, although most people with cannabis-related problems seek no professional help at all. Table 8 presents the latest data for the European Union.

- In many EU member states, but also in the USA, the number of people seeking professional help for problems related to cannabis is on the increase, both overall and in comparison with other drugs. The people seeking help for cannabis problems are mostly young men. The decision to enter a drug treatment facility is not taken lightly.
- The proportion of cannabis in the total demand for treatment owing to drug related problems has been highest in Belgium, Finland and Germany in the past few years, and has most clearly increased in Germany and Ireland (4). However:
  - Treatment demand depends on the accessibility and the capacity of the addiction care institutions.
  - As the number of people seeking help with problems owing to other drugs decreases, so the cannabis figures may increase in proportion to the overall figures, and vice versa.
  - Moreover, 'demand for treatment from the (addiction) care system' is far from being interpreted alike by the different member states of the EU. The way in which the addiction care sector is organised differs from country to country.
- Treatment demand varies between countries and regions. In American cities and states, cannabis accounted for between five per cent and 31 per cent of the treatment demand for all drug-related problems in the first half of 2000. In three areas, Colorado, Minneapolis & St. Paul and Seattle, cannabis topped the list in all drug registers. This is not the case in the EU member states (62) [40].
- As we have seen, people seeking help for problems linked to cannabis may have other problems as well. One in three people who sought help from out-patient addiction care facilities in the Netherlands primarily [41] for cannabis-related problems also had difficulties with one or more other substances, such as alcohol, cocaine, and ecstasy. These are not average cannabis users.

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40 *Quite a number of people in the USA are referred to cannabis treatment facilities by a court or another judicial authority. Referral depends on policy. This also explains to some extent differences in treatment demand data between EU member states.*

41 *Whether the use of a substance is reported as a primary or secondary problem depends upon the client's perception. Figures on the number of primary cannabis clients may therefore overestimate the cannabis problem, or, conversely, underestimate problems with other substances.*

- These help-seeking individuals often suffer from mental disorders other than substance dependence, and they often primarily request treatment for these other disorders rather than for drug problems. In French clinics four to twenty per cent of the patients displaying mood disorders also met the criteria for cannabis abuse and dependence, compared with thirteen to 64 per cent of those with bipolar disorder and sixteen to 31 per cent of those with a history of suicide attempts (19).
- Similarly, people primarily seeking help for problems with other drugs often have 'secondary' problems with cannabis. According to data collected in the Netherlands in 2000, for example, more than one in three of those for whom alcohol was the main reason for seeking treatment had a problem with cannabis too. One in four cocaine and heroin clients had such a secondary problem with cannabis (26).

Table 8.
Demand for treatment for primary problems with cannabis. Overview of EU member states: outpatient and inpatient addiction care [42]

Country	Survey year	Proportion of admissions for drug-related problems
Belgium	1999	25%
Finland	1998	22%
Germany	1999	22%
Ireland	1999	17%
Denmark	1999	16%
France	1999	16%
Sweden	1998	14%
The Netherlands	1999	10%
Luxembourg	1999	10%
United Kingdom	1999	10%
Italy	1999	8%
Greece	1999	7%
Spain	1999	6%
Portugal	1999	2-3%

Source: (4, 10; R Hartnoll, JM Costes, personal communication) [43].

The prevalence of cannabis dependence in the general population is not reflected in the relatively small number of people seeking treatment (56). People may not ask for therapy "because there is a high rate of remission of symptoms in the absence of treatment, or because of a reluctance on the part of cannabis users to be treated in settings designed for heroin and cocaine users". "There may also be fewer adverse personal and social consequences of cannabis use disorder than those of alcohol and opioid dependence, with which existing treatment services are traditionally orientated to deal" (56).

42 *Inpatient admission for cannabis problems is rare in Europe.*

43 *German figure for 2000: 24% (G Bühringer, personal communication).*

1.6 Is cannabis a gateway drug?

The gateway theory states, firstly, that because of the nature of its properties cannabis may prompt people to take other drugs later on in life. Indeed, there is abundant evidence of a correlation between early cannabis use and later consumption of other illicit drugs, although a majority of lifetime cannabis users do not progress to other drug use. A second assumption derived from this theory is that use of cannabis precedes the use of those other illicit drugs. Again, this is generally true as suggested by the lower initiation age for cannabis than for most other illicit drugs in Table 5 [44]. In a 21-year longitudinal study of a birth cohort of New Zealand children, cannabis consumption preceded the eventual use of other illicit drugs in all but three cases (57).

However, statistical correlation and temporal precedence are not proof of causality. Cannabis is not a necessary physiological or pharmacological precondition for taking up the habit of heroin use, for instance, as there have been generations of opiate addicts without any experience with cannabis. Still, it may be argued that cannabis primes the user into taking other illicit drugs, either through a physiological mechanism or through personality and social factors [45]. As far as personality is concerned, cannabis users may be more novelty seeking or ready to take risks than other people of the same age. Or they may have such positive experiences with cannabis that they start to underestimate the risk of other illicit drugs (16). The data available is inadequate to test these kinds of assumptions (58).

The gateway theory can be translated into a set of quite different hypotheses. Non-conforming adolescents who have a propensity to use other drugs may be selectively recruited into cannabis use. Once this has occurred, their social interaction with drug using peers and greater access to illegal markets may increase the chance that they will use other illicit drugs (59). In a recent paper, the relationship between cannabis use and later consumption of other illicit drugs was upheld to some degree in analyses which controlled for family and lifestyle factors (57), but the researchers also concluded that the association might be non-causal. Another seminal paper, also from New Zealand, suggests that substantial early consumption of cannabis is the outcome of socio-economic disadvantage, behavioural problems in earlier life, low levels of parental attachment, and adolescent mental health disorders (2). In other words, trouble does not start with cannabis but has its roots earlier in life. The book on this issue cannot yet be closed.

1.7 How should cannabis consumption be monitored?

There is growing international consensus that drug use and its consequences can be monitored by means of indicators, to allow comparisons to be made between and within countries.

- The European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) in Lisbon has decided on five, not mutually exclusive, key indicators to which the member states of the European Union (EU) should adhere. These are: 1) use among the general population and among school pupils, 2) problematic use, 3) demand for treatment: i.e., requests for professional help, 4) drug-related deaths, and 5) occurrence of infectious diseases owing to drug use. Numbers 4 and 5 are not relevant for cannabis. People do not acutely die from taking cannabis and using this drug does not directly increase the risk of contracting an infection [46]. The EMCDDA has not yet extended the concept of 'problematic use' to cannabis.
- Usually, indicator 1 is monitored in regularly repeated general population and school surveys such as the ones referred to above.

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44 The sequence of initiation into use of different substances may vary between cultures (J Rehm, personal communication).

45 In a Swiss study (65) progression from cannabis to other illicit drug use was associated with poor communication with parents, low school performance, and not taking part in sports.

46 However, people may die from the consequences of long-term use, i.e., lung problems owing to smoking.

- As discussed one measure of 'problematic use' may be cannabis dependence, but also demand for treatment. The characteristics of users seeking professional help for problems caused by drug consumption are recorded in treatment demand registers. Measures of problematic use may also be possible effects of cannabis on cognitive functions, mental states, health [47] behaviour (driving performance, violence), and school and work performance, and progress to the use of other illicit drugs.

Structured monitoring is not limited to the EU. Similar exercises have been carried out or are being carried out in Australia and the USA, and to a lesser extent in Switzerland and other non-EU countries [48]. Some countries employ additional indicators such as criminal justice or law enforcement data, including drug-related arrests or drug use among detainees [49].

1.8 Conclusions

1.8.1 Consensus

Cannabis is the most frequently used illicit drug in the western hemisphere. The characteristics of cannabis users are well-known and do not differ much between the countries considered here. Occasional use of cannabis is not a major hazard to health and well-being. Young users are more likely to become dependent on cannabis than older users. Most people experiencing problems with their use of cannabis seek no professional help. However, the number of people seeking such help is on the increase in many countries, also in comparison with other drugs. The health effects of higher THC levels in cannabis products, if any, are not known. There is no compelling proof that cannabis *in itself* is a stepping-stone towards other drug use, i.e, causes the use of other illicit drugs.

1.8.2 Differences of opinion

Although there is consensus that consumers of cannabis are more likely to use other substances (tobacco, alcohol, other illicit drugs) than non-users, authors tend to disagree on the extent of this co-use. Recent findings suggest that co-use is sizeable among those who take cannabis regularly.
There is agreement that users may eventually develop dependence on cannabis, but to what extent this can happen is disputed. The latest data indicates that cannabis dependence is not rare.
Many believe that cannabis suppresses violence. Nevertheless, there are reports to the contrary. Juvenile conduct disorder may be a common developmental pathway to heavy cannabis use on the one hand and increased violence on the other.
Perhaps cannabis may not foster violence if the sale or trade of cannabis is depenalised. This remains to be proven.

1.8.3 Possible trends

The prevalence rate of lifetime and current cannabis consumption is no longer rising among school pupils in the UK, Ireland and the Netherlands. (A similar trend is evident in the USA.) In various other EU member states the prevalence rate of use in this group is still on the increase. Apparently, the number of cannabis users among school students is stabilising or dropping in countries with relatively high occurrence rates in the early 1990s, and going up in countries that formerly had low rates.
It is generally believed that most users of cannabis stop or reduce their intake of this drug before

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47 *An indicator used in the USA is the number of emergency visits related to drug use.*

48 *Such monitoring activities are also advocated by the World Health Organization (WHO).*

49 *The literature on these additional indicators is not reviewed here. See Chapter 8.*

their mid-thirties. In a New Zealand birth cohort study, however, use levels remained high up to the latest measurement at the age of 26, while cannabis dependence also persisted at a relatively high level. If this picture shows no change in future follow-up measurements, we may need to reconsider our ideas about the course of cannabis use and dependence.
The THC content of cannabis products may have increased or is increasing in at least some countries.

1.8.4 Gaps in our knowledge

Many of the issues raised in this chapter are not new. They can be addressed by prospectively (longitudinally) charting people's cannabis consumption careers, preferably starting even before they begin and also applying measures other than self-reporting. A few such studies have been done or are being done in Australia, New Zealand and the USA, but with few exceptions they are conspicuously lacking in Europe.
The role of biological, including genetic, factors that may influence cannabis use and dependence has been largely neglected. This line of research can be integrated into the longitudinal studies mentioned above.

To some extent we do know the differences between countries in prevalence and frequency of cannabis use. For many countries, however, the average amount of cannabis consumed by users of this drug is generally unknown, let alone the actual dose administered when the strength of the product is taken into account.

The possible health effects of higher THC levels in cannabis products are unknown and need to be examined.

More information is needed about the extent, the course and the consequences of what might be called 'problematic' cannabis use.

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2. PHARMACOLOGY AND NEUROBIOLOGY OF CANNABIS

Emmanuel Streel, Paul Verbanck and Isy Pelc

Summary

Pharmacokinetics

THC is the main psychoactive ingredient of cannabis. The course followed by its effects over time depends on the method of administration. The lowest dose of THC capable of producing behavioural effects is two milligrams when inhaled from a cannabis cigarette. Mental effects start within minutes after smoking and thirty to ninety minutes after oral ingestion. The blood concentration of THC produced by oral ingestion is two to three times lower than that produced by smoking the same dose. Complete elimination of a single dose of THC from the body can take up to thirty days. The levels of THC metabolites in the urine are not a reliable indicator on time of ingestion or on actual intoxication.

Neurobiological aspects: mechanism of action

Cannabis acts through specific receptors. Two types of cannabinoid receptors have been identified. One receptor (CB_1), or system of cannabinoid receptors, is located in various regions of the brain and in peripheral tissues. The second type (CB_2) is present in the immune cells of the spleen. The brain contains natural cannabinoid-like substances (anandamide and 2-AG). The cannabinoid chemical pathway in humans is not yet fully understood.

Neurobiological evidence for the gateway hypothesis

Several animal studies have suggested links between the opiate and cannabinoid systems. However, there is insufficient evidence at present to justify the conclusion that cannabis acts as a gateway to other, more harmful substances. Nevertheless, recent studies showed that in vulnerable individual animals (high-responder rats) a cross sensitization to amphetamine and heroin is observable.

2.1 Introduction and main questions

In 1964, Mechoulam identified and synthesized the main mind altering substance in the cannabis plant, Δ^9-tetrahydrocannabinol (referred to here as THC). It is the most abundant of about sixty related chemicals, known as cannabinoids. The psychoactive ingredients are concentrated in the flowering tops of the plant (*Cannabis sativa*), but all parts of the dried and chopped plant can be used for consumption (1). Cannabis is often taken by smoking a hand-rolled cigarette, on its own or in combination with tobacco (joint). Another way is to eat cannabis in baked or cooked foods (e.g. 'space cake'). Cannabis or THC can also be used for medical purposes in pharmaceutical preparations such as aerosols, sprays, eye-drops and suppositories (2).

The main questions addressed are:

- What is the course of THC in the body?
- How does cannabis produce its multiple pharmacological effects?
- Do animal studies provide indications for the gateway hypothesis?

2.2 Pharmacokinetics

The term pharmacokinetics refers to the factors that influence the fate and the course followed over time by a drug in the body. Information about these factors is important in order to understand how rapidly the psychoactive effects of cannabis appear, for example, and how long they last. The pharmacokinetic characteristics of cannabinoids have been reviewed several times (3,4,5,6). This paragraph gives a brief account of the main findings.

The rate of onset of the effects of cannabis and the amount of the drug absorbed are dependent on the method of administration. After smoking, *absorption* of cannabinoids from the lungs into the blood and their subsequent transport to the brain is a very rapid process, occurring within minutes. The maximum brain concentration of cannabinoids is reached after fifteen minutes, coinciding with the peak of the psychological and physiological effects. THC persists in the brain for longer than in the blood. This causes psychoactive effects to continue for some time after the level of THC in the blood has begun to decline. Most drug effects abate within three to four hours.

Doses as low as two milligrams of THC in a cannabis cigarette can bind to enough receptors to produce behavioural effects. Not all of the THC in cannabis is absorbed into the body. On average fifty per cent of the THC is available in smoke, but social smokers actually absorb no more than ten to 25 per cent of this into their blood. Thus, a one gram marijuana cigarette with a THC content of five per cent contains fifty milligrams of THC [1], of which only 0.5-13 milligrams enter the bloodstream. The amount of THC absorbed by smoking a cigarette differs widely between individuals and depends on various factors including smoking habits, such as the number of puffs, waiting time between puffs and holding time, and lung capacity. Heavy or experienced users may reach higher cannabinoid blood concentrations than light or inexperienced users after smoking the same dose, probably because they use a more efficient smoking technique (7-8). Cannabis users may also adapt their smoking behaviour according to the THC content, but the evidence for this is limited and conflicting (9,10).

THC and other cannabinoids dissolve readily in fatty tissues, but not in water. This explains why oral ingestion of cannabis results in a slow rate of cannabinoid absorption into the blood. The onset of psychoactive effects is delayed (thirty to ninety minutes), reaching a maximum after two to three hours (4,6). The effects may persist for four to eight hours. The amount of THC absorbed after eating or swallowing cannabis is two to three times lower than that absorbed after smoking the same 'dose'. This is because after absorption in the gut, a substantial amount of THC is directly metabolised in the liver before reaching the general circulation.

Once absorbed, the psychoactive ingredients of cannabis are *distributed* throughout the body, first reaching the tissues with the greatest blood supply (brain, lungs, liver, adrenals, kidneys, ovaries and testes). THC is *metabolised* or converted, mainly by enzymes of the cytochrome P450 system in the liver, to produce a by-product, 11-hydroxy-THC (or 11-OH-THC). This metabolite is biologically active. It is even more potent than THC itself and may contribute to the pharmacological effects of cannabis. 11-OH-THC is subsequently converted into 9-carboxy-THC (or THC-COOH), which has no biological effects. Many other inactive metabolites are known.

A substantial proportion of THC is not directly eliminated from the body, but accumulates in the fatty tissues. From there, it is slowly released back into other body tissues and organs, including the bloodstream and the brain (5). Elimination from the body is extremely slow and complete elimination of a single dose can take up to thirty days (11). With repeated use, high levels of

1 *See Chapter 1 for a discussion of THC concentration in cannabis products.*

cannabinoids may accumulate in fatty tissues. Most metabolites are finally *excreted* in the urine or faeces. Very little non-metabolised THC is found in the urine. This is why urine screening tests for cannabis often concentrate on identifying its metabolites, in particular THC-COOH, which is most abundant in urine. As we have said, this metabolite performs no biological activity itself. It may be detected for several days following the isolated consumption of a single dose of cannabis and for several weeks or longer with heavy daily smoking. Therefore, a urine sample that tests positive for THC-COOH does not reliably indicate whether the person is actually in an intoxicated state (see also Chapter 5).

2.3 Neurobiology

Much research has been done to try to understand how cannabis produces its multiple pharmacological effects. In the past fifteen years, major advances have been made in elucidating the cellular machinery that underlies the responses of the brain and body to cannabinoids. New research methods are being used to help to expand our knowledge (12,13).

2.3.1 Sites of action: evidence of cannabinoid receptors

In the early eighties, Howlett (14) found indirect proof of the existence of a cannabinoid receptor in neural tissue by showing that THC decreased the concentration of the second messenger molecule, cyclic adenosine monophosphate (cAMP). Howlett and Fleming (15) attributed this effect of THC to an interaction between this cannabinoid and a receptor protein in the brain that is associated with adenyl cyclase, the enzyme needed to synthesise cAMP. In 1993, Munro and co-workers (16) identified a second G-protein coupled cannabinoid receptor in the immune system. Nowadays the brain receptor is called CB_1 and the immune system receptor is CB_2. It is now certain that cannabinoids bind to these receptors, although it is not yet clear whether all the effects of these substances can be explained by this mechanism of action.

2.3.2 Progress in cannabinoid research: developing research tools

An agonist is a substance that causes a pharmacological effect by binding to a specific receptor. An antagonist blocks or inhibits the action of a receptor. Agonists and antagonists are important tools that can help neurobiologists and the pharmaceutical industry to learn more about particular brain processes and other body functions. One of the first steps in many pharmacological studies is discovering or synthesizing substances with agonistic and antagonistic properties. Agonists and antagonists are now available for both CB_1 and CB_2 (17,18). It is hoped that some of these compounds may have therapeutic value.
Another major contribution to the effort to unravel the functions of the cannabinoid system(s) is the breeding of mice deprived of CB_1 or CB_2 receptors, known as 'knockout mice' (19,20,21). Researchers compare these mice with normal mice in terms of their response to cannabinoids. If knockout animals fail to show a response to cannabinoids that is found in normal mice, this is an argument that the missing receptor is responsible for mediating that response. Thus, the common immune effects of THC were found to be absent in mice without CB_2 receptors (20), suggesting that CB_2 is involved in the regulation of immune functions.

2.3.3 Where are cannabinoid receptors found in the body?

Knowing how the cannabinoid receptors are distributed in the body is important in order to understand the effects of cannabis. According to the findings of (post-mortem) studies carried out on animals and humans, CB_1 receptors are present in various areas of the brain and also in peripheral tissues. Within the brain, these receptors are clustered the most densely in the cerebral cortex (especially the frontal cortex), the hippocampus, the basal ganglia, the cerebellum and the nucleus accumbens. These distribution patterns can help us to understand some of the behavioural

effects of cannabinoids. The presence of cannabinoid receptors in regions associated with the brain's reward system (nucleus accumbens and striatum) suggesting an influence on motivational behaviors. Indeed, THC stimulates indirectly the release of dopamine (22) although not in the same way as other illicit drugs (12). Nevertheless, the precise function of CB_1 receptors in these two brain areas remains to be determined (23).

The lower brain stem regulates basic body functions, such as respiration. The relatively low density of cannabinoid receptors in this area probably accounts for the low, virtually non-existent risk of death from overdosing among cannabis users.

CB_2 receptors have been found in the macrophages (immune cells) of the spleen. They may have a role in the body's immune functions (2).

2.3.4 Natural cannabinoids produced in the brain

The presence of cannabinoid receptors makes it likely that there are natural cannabinoid substances in the human body, also called 'endogenous substances' [or *ligands*]. The first endogenous substance discovered in the brain was archidonylethanolamide, known as *anandamide* [2]. Another one is 2-arachidonylglycerol (or 2-arachidonoylglycerol), abbreviated to 2-AG. The mammalian body may contain a whole series of anandamide-related substances (2). The concentration of anandamide and 2-AG in the brain has been compared with the distribution of CB_1 binding sites (24). Discrepancies have been found between the results for the two measures. This may be because there are as yet unidentified endogenous cannabinoids and cannabinoid receptor types. These and other discrepancies may also be artefacts of research methodology (25). This question is unresolved. More sophisticated methods for identifying the precise location and function of endogenous cannabinoids in the brain are required.

2.3.5 A specific cannabinoid pathway

Recently, Elphick and Egertova (25) described a model of cannabinoid brain function in which anandamide influences the release of neurotransmitters (substances bridging the gap between nerve cells) by acting on the terminals of the cell containing the transmitter (the pre-synaptic cell). The cell on the other side of the junction – awaiting the neurotransmitter – is called the post-synaptic cell. The main elements of the model are:

- Anandamide is made and released by the post-synaptic cell. It travels to the pre-synaptic cells, where it turns on CB_1 receptors.
- The activated receptors inhibit the release of neurotransmitters from the pre-synaptic cell.
- Anandamide frees itself from the CB_1 receptor and is taken up by the post-synaptic cell, where it is metabolized (through intracellular hydrolysis by the fatty acid amide hydrolase).

The cannabinoid-anandamide system interacts with many neurotransmitter/neuromodulator systems including cholinergic, noradrenergic, dopaminergic, serotonergic, GABA, NMDA, opioid, glucocorticoid and prostaglandin systems. However, their roles in pharmacological effects of cannabinoids are not clear (2).

The discovery of a probable cannabis signalling system in mammals has led to further studies in non-mammalian and invertebrate species. Anandamide has been detected in a variety of invertebrates (e.g. 26). However, we must be cautious about jumping to hasty conclusions about the existence of a probable cannabis pathway in humans, based solely on the presence of some components that have been associated with this pathway in mammals (25).

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2 *Also known as 'arachidonylethanolamide' and 'arachidonylethanolamine'*

2.4 Cannabis: a gateway to other drugs of abuse?

In Chapter 1 the gateway theory was discussed from the epidemiological point of view. In this paragraph, we will discuss the relevance of data from animal studies.

In some studies, a link has been found between the cannabinoid and opiate brain systems. As shown by Ledent et al. (19), CB_1 receptors may mediate some of the psychoactive properties of opiates and may also be involved in the development of physical dependence on opiates. Some studies also suggest that CB1 receptors do not appear to be involved in all responses to opiates. Pain response modulation by opiates does not seem to be affected by CB_1 suppression. (e.g. 27). Suppression of CB_1 receptors does not affect voluntary consumption of cocaine, nicotine or d-amphetamine in mice (28). The relationship therefore appears to be confined to opiates. On the other hand, another study has recently shown that cannabinoid exposure can provoke a relapse back into cocaine-seeking behaviour in rats after prolonged withdrawal periods (29). Other studies have also reported that cannabinoids can induce behavioural sensitization and cross-sensitization with other drugs such as opiates (30-31-32-33). In other words, past exposure to cannabis can influence the sensitivity to other drugs like opiates at a later date. Nevertheless, the enhanced response to amphetamine or heroin was noted in some individuals only: the high-responder rats (HR). These animals have previously been shown to be vulnerable to drug taking behaviors (33). These results are highly important, because they raise the real question: are there particular characteristics (e.g. high response to drugs) that could reflect a specific vulnerability leading to a process of gateway?

2.5 Conclusions and gaps in our knowledge

Although the psychoactive effects of cannabinoids have long been known, it was not until the eighties that the first evidence for the way in which they act on the brain became available. Cannabinoids bind to specific brain receptors, and to peripheral receptors.

Cannabinoids are not alien to the human body. Certain cannabinoids occur naturally in our brain and immune system. Their function is not yet fully understood.

Based on the data available from animal experiments, it is impossible to draw definite conclusions at present about the potential role of cannabis as a gateway drug to other substances. Nevertheless, in some vulnerable individual animals, cannabis may be associated with a cross sensitisation to other drugs. The challenge will be to identify the specific characteristics of this potential vulnerability.

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3. CANNABIS AND PHYSICAL HEALTH

Isabelle Bergeret, Constantin Papageorgiou, Paul Verbanck and Isy Pelc

Summary

Cannabis administration

It is important to distinguish between casual, regular and heavy users of cannabis, and it is also important to distinguish between the different ways of administering it. The hazards of regular cannabis smoking are different from those of occasional oral use. The effects are felt more quickly when the cannabis is smoked and they are long-lasting when it is eaten. Quick absorption of THC occurs when the drug is smoked. The THC is detectable in plasma a few seconds after the first puff of a cannabis cigarette, with peak plasma concentrations being measured three to ten minutes after the onset of smoking. With oral use, absorption is slow and erratic, usually resulting in maximal plasma concentrations after one to two hours.

Positive and negative effects on physical health

The immediate effects of psychoactive substances give people everywhere and at all times reasons for using them. Some examples of such reasons are: establishing social links, withdrawing from the world, influencing the user's mood and increasing his or her physical performance.
Many studies of the effects of this drug on physical health are animal studies which do not permit conclusions to be drawn about humans. Cannabis has no clinically relevant chronic effect on any part of the human organism, except for the lungs, but this is mainly linked with the effects of combustion rather than with cannabis itself. The tar phase of marijuana smoke contains about fifty per cent more of certain carcinogens than a comparable quantity of unfiltered tobacco.
There is no evidence for chronic effects on the gastrointestinal system, the endocrine system or the immune system. However, THC can cause cardiac problems in patients suffering from hypertension or cardiovascular disease.

Pregnancy

THC affects the foetus, but there are no clearly established consequences. Insufficient scientific data is available about the effects on children after birth or several years later.

3.1 Introduction and main questions to be addressed

Throughout history and in all civilisations, humans have consumed psychoactive substances. There are various reasons for doing so, arising from the drug's positive effects, such as: establishing social links, withdrawing from the world, influencing the user's mood, increasing physical performance, etc. After tobacco, cannabis is the most commonly smoked substance worldwide. Psychoactive substances also have negative effects on the user's physical health, but these effects differ according to the substance, the mode of administration, the frequency of consumption, and the other substances that are consumed at the same time.
It is important to distinguish between casual, regular and heavy users of cannabis. Casuals take the drug irregularly, using up to 1 g of resin at a time, with an annual total of no more than 28 g. Regulars take cannabis regularly, typically using 0.5 g of resin a day (equivalent to three or four smokes of a

joint or pipe), a total of about 3.5 g per week. Heavy users are more or less permanently stoned, using more than 3.5 g of resin per day and 28 g or more per week.

The main questions concerning the effects of cannabis on physical health are:

- Which are the immediate and chronic effects on all organs that can be affected by cannabis? These organs include the gastrointestinal, endocrine and cardiovascular systems, the respiratory system and the immune system.
- What are the effects of cannabis use during pregnancy on the foetus, the newborn child and several years after birth?

We conclude this chapter with a short paragraph on counselling and treatment.

3.2 Impact on physical health

What are the effects of cannabis on physical health? We have considered all the organ systems that can be affected by cannabis. Some of the effects on physical health are difficult to measure. Cannabis contains many psychoactive products, and their kinetics are complex. Moreover, the mode of administration of cannabis is regularly associated with tobacco and other substances. A distinction must also be drawn between immediate and chronic effects.

3.2.1 Immediate effects

The effects are faster when the cannabis is smoked and the effects are long-lasting when it is eaten. The most common side effects experienced by all users (but with less intensity by regular users) are: dysphoria, increased heart rate, conjunctival blushing, sedation, hypoglycaemia, psychotic symptoms, hypertension, increased appetite and decreased muscular tonus.
The perceptual and psychological changes occur in two phases: a euphoria phase and a somnolence phase. These two stages are coupled with changes in the user's perception of time, auditory and visual changes, and difficulty in concentrating.
These immediate effects disappear after four to six hours and are less intense in chronic users. These aspects are very thoroughly documented in the international literature (1).

3.2.2 Chronic effects

3.2.2.1 Gastrointestinal systems

It appears that there is little or no human or animal evidence that cannabinoids affect liver functioning, whether used acutely or chronically. There is reasonable evidence from animal studies that cannabinoids have a direct effect on intestinal motility via the action of the CB_1 (cannabinoid receptor 1). This effect produces a decrease in the contraction smooth muscle of the intestine. The amount of gastric delay seems to be minimal. There is little evidence of significant symptoms of constipation as a result. The most visible effects of cannabis on gastrointestinal physiology are its anti-emetic and appetite stimulant effects (2).

3.2.2.2 Endocrine system

The following effects are observed in both animals and humans. In humans, however, it seems that THC (Δ9-tetrahydrocannabinol) has no clinical relevance. The effects of THC occur on the hypothalamus-hypophysiary axis. A decrease in the following hormones is observed: Follicle Stimulating Hormone (FSH), Luteinizing Hormone (LH) Prolactin and Thyroxin Hormone. A significant increase in adrenocorticotropin (ACTH) is also found, probably due to dopamine liberation at the central level (3). A decrease in testosterone and an increase in corticosteroids are found in animals (4). This reduces the libido of male animals and probably also augments the fertility of female animals (5,6).

As far as the effects on humans are concerned, no significant hormonal changes have yet been demonstrated in women and no clinical effects on the human reproduction system have been recorded. For the moment, we have no information about the regulatory role of this receptor in the reproductive system. The effects of chronic THC use on human fertility are therefore unknown (7).

3.2.2.3 Cardiovascular system

THC taken orally has been shown to induce an immediate increase in arterial tension and in the cardiac rhythm. The heart works harder as a result, particularly the left ventricle (8). This is due to the increase in cathecholamin and the resultant increase in peripheral vascular resistance (9). These effects are transient and tolerance rapidly develops (within 24 hours). After eight to ten days of use, the inverse effects appear. This is probably due to adaptation of the parasympathetic system. Moreover, orthostatic hypotension also occurs due to the reduced effectiveness of the vascular reflex. No significant changes were observed in the electrocardiograms of the control subjects (healthy individuals) (10).
There is evidence that THC can cause cardiac problems in patients suffering from hypertension, vascular disease or coronary arteriosclerosis (as antecedents), by increasing the work that the heart has to do. However, this potential risk is much less significant than it is with amphetamines or cocaine.

3.2.2.4 Respiratory system

Early animal and human studies suggest that smoking cannabis leads to changes in the histology picture. Most of these occur in the distal airways and air spaces, including chronic inflammation, fibrosis and alveolar cell hyperplasia (11,12). Chronic heavy cannabis smoking is associated with increased symptoms of chronic bronchitis, such as coughing, sputum production, and wheezing (13).
A recent study has also provided new information about the age at which the respiratory effects of cannabis use may become apparent. In this study, all subjects were 21 years old. Only one third of the cannabis-dependent subjects were already dependent by the age of eighteen. This suggests a relatively short duration of heavy use in the cannabis-dependent groups (14).
It is still unclear whether cannabis smoking affects the respiratory function to a greater extent than tobacco smoking. THC does not directly damage the pulmonary system, but the combustion compounds do.
The tar phase of marijuana smoke contains about fifty per cent more of certain carcinogens than a comparable quantity of unfiltered tobacco. On the one hand, the mode of consumption is different: no filter is used and inhalation is deeper. On the other hand, the combustion temperature and the concentration of benzpyrene are higher. Benzpyrene plays an important role in human cancer. Moreover, THC has a broncho-dilator effect that is likely to promote tar retention in the area of the upper respiratory tract.
Conversely, when the substance is ingested there is no effect on the respiratory function.
In vitro (cell experiments) and animal studies suggest that marijuana smoking plays a role in the development of respiratory cancers. Epidemiological studies are few and difficult to conduct because cannabis and tobacco are commonly used together. A single recent epidemiological study assessing the statistical correlation between marijuana and cancer has found no significant effect of marijuana consumption on lung cancer (15).
Moreover, the function of alveolar macrophages, cells that play a key part in the lung's defences, has been shown to be impaired by cannabis smoking (16). This effect of cannabis smoking is independent of tobacco consumption (17,18,19). Many studies suggest that regular cannabis consumption reduces the respiratory system's immune response to invading organisms (15,20,21,22).

3.2.2.5 Immune system

The impact of cannabis-induced immune response modulation on health is still unclear. Few studies employing animal paradigms or human trials have been carried out to assess the effects of cannabis exposure on host resistance to bacteria, viruses and tumours. The studies that have been done in this area have used fairly high doses of cannabinoids and therefore have limited relevance to the marijuana smoking experience.
In 1993 Munro (23) discovered the specific receptors of cannabinoids on the macrophages. Several studies report modulator effects on the immune system by cannabis. In vitro studies have shown that cannabis acts on different levels of the immune system:

- The macrophages produce less cytokine and Tumour Necrosis Factor (TNF).
- Their antiviral and antibacterial activities seem to be impaired (24, 25).
- The lymphocytes' proliferation is reduced.
- The lymphocytes' antibody production decreases.
- The natural killers show decreased activity.
- The neutrophiles' anti-fungal activity is impaired (26).

These disturbances in the immune system are not clearly understood. The role of the specific receptors (CB_2 and CB_1) on the immuno-competent cells is still unclear. At present, we cannot say with certainty that the disturbances observed in the immune system are caused by the action of the THC on its CB receptors.

The cannabinoids' high degree of liposolubility could interfere with the normal functioning of the immunocompetent cells. In fact, cannabinoids can bind to different parts of the cell membrane and thus modify its permeability and other specific functions. All of this indicates that THC does have an effect on the immune system. No clinical studies have yet shown that cannabis users suffer from a larger number of infections. However, it is also clear that the immune system is relatively resistant to these drugs. Many of the effects appear to be relatively small, totally reversible after withdrawal of the cannabinoids, and produced only at concentrations higher than those required for psychoactivity (>10 μM in vitro and 5mg/kg in vivo).

3.3 Pregnancy and Cannabis

How does cannabis use during pregnancy affect the foetus and the growing child? The first studies were carried out on animals. These studies revealed a teratogene effect and demonstrated THC's toxicity for the embryo. But very high doses were needed to increase the malformation rate in these studies (27). Humans do not usually consume such doses.
As THC is highly hydrophobic, it crosses from the mother's blood system to the placenta. Following oral intake, THC plasma concentrations in the foetus seem to be much lower - about one tenth of the mother's plasma concentration - than those produced by intravenous and inhaled THC administration, at about one third of the mother's plasma concentration. THC passes into the breast milk and the THC concentration in milk was 8.4 times higher than in plasma.
The effects observed in children are associated with the quantity of cannabis consumed during pregnancy. No significant differences have been found between control groups and children whose mothers have occasionally consumed cannabis. However, several studies have suggested that foetal growth is reduced in women who regularly consume cannabis. The final reduction in the birth weight is estimated at between 80 g and 105 g. Nevertheless, this reduction is less significant than that produced by tobacco use. Cannabis also affects body length (28).
In human studies, the problem is that many factors complicate the interpretation of the results. When associations are found between cannabis use during pregnancy and adverse effects on newborns, it is difficult to interpret the findings because cannabis users are also likely to be tobacco users. The exact doses or amounts of THC used and the times at which it was used are impossible

to quantify. Other drug use and socio-economic factors cannot be controlled by random assignment to groups.
One prospective study is being carried out in the field of research into damage to foetal central nervous systems: this is the 'Ottawa prospective prenatal study' (29). This data suggests that if prenatal exposure to marijuana does have long-term consequences for the child, the effects are very subtle. There appears to be a connection between nervous system state regulation and prenatal exposure to marijuana in newborns. However, no neurobehavioral consequences have been reported in children between the ages of six months and three years. At four years, tests of verbal ability and memory discriminate between children of regular marijuana users and other children. Children between the ages of four and nine have shown deficits in sustained attention, memory and higher cognitive functioning.
THC affects the foetus. but for the time being we have insufficient scientific information to state that THC causes damage to children after birth or several years later. Long-term studies are needed to evaluate the impact of cannabis use during pregnancy on the subsequent behaviour of the children.

3.4 Counselling and treatment

A review of the literature to date reveals a relative lack of research into the effectiveness of abstinence treatment programs specifically aimed at cannabis. One of the reasons is the low level of demand for treatment. Moreover, cannabis is often used in combination with other drugs that are the main focus of treatment. The scientific experts agree that physical dependence is low, at least in common patterns of use (see the chapter on cannabis and mental health).
There is no substitution treatment. Anti-anxiety and antipsychotic drugs are occasionally needed to treat severe cannabis-induced anxiety or panic or psychosis. If the patient was using cannabis to alleviate depression, an antidepressant should be considered as substitution therapy. Moreover, the withdrawal syndrome is often discrete (e.g. irritability, insomnia). On the other hand, various psychological treatment programs are available to modulate, modify or stop cannabis use. These follow the general procedures of other drug use treatments, such as cognitive behaviour therapy, aversion therapy, or motivational therapy (30,31,32).
There is no specific program of cannabis treatment, and no agreement about the best approach to use. However, an atypical neuroleptical treatment at a low dosage level is increasingly being used to complement the psychotherapeutic program. The withdrawal symptoms are weak, but they have to be considered and treated, as they often stand in the way of abstinence. But there are no tangible results.

3.5 Conclusions

For the moment, it is difficult to evaluate the specific effects of cannabis on the user's physical health. There are various reasons for this. Many studies have been carried out on animals. In these studies, specified quantities of a specific component can be administered so that the dose-response effects can be described precisely. In addition, nearly all the developmental animal studies have focused on Δ9-tetrahydrocannabinol (THC), which is only one of more than sixty psychoactive components of cannabis. Thus, animal studies allow researchers to gain a better understanding of the effects of THC on the organism. However, extrapolating the results of these studies to humans is dangerous.
Moreover, humans often consume cannabis in conjunction with other substances, mainly tobacco.

Smoking marijuana is a potential risk factor for the development of pulmonary complications. The tar phase of marijuana smoke contains about fifty per cent more of certain carcinogens than a comparable quantity of unfiltered tobacco. It therefore seems likely that cannabis smokers will be more at risk of developing lung cancer than tobacco smokers. However, no study has clearly proved this hypothesis yet, although some cases of lung cancer have been reported in young adults.

Animal and cell experiments have demonstrated that THC also affects cellular and humoral immunity. Although the specific cannabinoid receptors affect the modulation of the immune system in some way, their precise role has not been established yet.

It has been established that when taken orally, THC immediately produces a moderate increase in arterial tension and in the cardiac rhythm. These effects are temporary and tolerance rapidly develops. Moreover, it is obvious that THC can cause cardiac problems in patients who have cardiovascular antecedents. If the effects on gastric and intestinal mobility are observed in animal and in vitro studies, these effects have no clinical relevance. There is consensus on the drug's anti-emetic and appetite stimulant effects on the gastrointestinal systems.

It is certain that the THC passes into breast milk and crosses from the mother's blood system to the placenta and affects the foetus. However, neither the short-term nor the long-term consequences have been clearly established. Long-term studies are needed to evaluate the impact of cannabis administration during pregnancy on children's health.

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4. CANNABIS, MENTAL HEALTH AND DEPENDENCE

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This chapter describes psychiatric side effects and interactions between cannabis use and mental health. It is divided into three parts. Part A focuses on cannabis use and psychotic states (including psychosis and schizophrenia). Part B focuses upon the relationship between cannabis use and mood and anxiety disorders. Part C explores the subject of cannabis dependence.

Part A. Psychosis

Summary

Cannabis-induced acute and chronic toxic psychosis

It is generally admitted that cannabis use can be responsible for triggering an acute psychotic reaction, principally consisting of delusions and/or hallucinations, in people who have previously been mentally healthy, at least apparently. The duration of this reaction seems to be limited after abstinence. Heavy doses, oral ingestion and multiple substance use seem to be contributing factors. The frequency of these reactions is unknown.
On the other hand, cannabis use is probably unable to produce a specific chronic psychosis persisting after abstinence.

Does cannabis use constitute a risk factor in the onset of schizophrenia and is it harmful to schizophrenic subjects?

We do not yet know with certainty whether cannabis use is one of the stress factors that trigger schizophrenia. The findings of a key study can be interpreted in that way, and they have opened the question up to discussion, but there is no clear conclusion as yet.
Cannabis use may be harmful to individuals already suffering from schizophrenia. According to various studies, it may provoke more acute psychotic symptoms, more relapses and more readmissions to hospital. But it may also alleviate other kinds of symptoms such as anxiety, depression, avolition and flattening of affect.

4.A.1 Introduction and main topics

The psychoactive effects of cannabis are varied and also depend on the user's expectations, his or her mental state and the environment. The most common subjective effects are: euphoria, relaxation, and a sense of well-being (often accompanied by enhanced sociability and giddy laughter). Users frequently report alterations of thought processes (feelings of enhanced insight and awareness, of a more efficient or fragmented thought, the impression that thoughts, fantasies, emotions and memories flow more freely, a sense of being able to recall distant memories and the impression that time passes more slowly). Enhanced somatosensory perceptions are quite common (seeing colours more brightly, increased appreciation of the complexity of music, heightened perception of taste and touch). At high doses, auditory and visual hallucinations are described (1-4).

The first part of this chapter explores the interaction between cannabis use and psychotic disorders. This can be divided into four subtopics:

- Cannabis-induced acute toxic psychosis.
- Cannabis-induced chronic psychosis.
- Does cannabis use constitute a risk factor in the onset of schizophrenia?
- Is cannabis use harmful to schizophrenic subjects?

The methods used are examination of the scientific literature, distinguishing between reviews, clinical studies, case reports and experimental studies.

4.A.2 Cannabis-induced acute toxic psychosis

Most reviewers agree that a toxic psychotic reaction can follow the use of cannabis, but there is still some controversy about this (1,4,5-8). The evidence is principally based on clinical studies or case reports, sometimes based on large number of cases, which are however weakened by the absence of urine testing to provide definite confirmation of a generally obvious clinical history (9-16). DSM IV recognizes this condition under the name of 'cannabis induced psychotic disorder' (17).
Several studies show that recreational users frequently experience sensory disturbances (often part of the expected effects) and paranoid ideation (2,3,18).

There is experimental evidence for a dose-response relationship between the emergence of psychotic symptoms and cannabis use. Isabel et al. (19) found that doses of Δ9-tetrahydrocannabinol (THC) in excess of 0.3 mg/kg (administered orally) or greater than 0.2 mg/kg (administered by smoking) produced visual and auditory hallucinations, depersonalisation and derealisation in volunteers (see also 20). The length of exposure also seems to be important; Georgotas and Zeidenberg (21) described how healthy subjects became paranoid after two weeks of smoking as many cigarettes containing THC daily, as they wanted. In both studies, the symptoms disappeared after cessation of cannabis ingestion or smoking.
Tien and Anthony (22) carried out an analysis of prospective data from 4,994 adults without pre-existing psychiatric conditions and found that daily cannabis users showed a relative risk of developing psychotic symptoms of 2.4 compared to non-users.

The main clinical features are the appearance of psychotic symptoms (delusions or hallucinations) shortly after or during cannabis use, no symptomatic specificity compared to acute psychosis of other origin, and the presence or absence of symptomatology evoking a state of delirium (disturbance of consciousness or cognition). Recovery generally occurs within a week of abstinence, following elimination of the substance.
Acute psychotic episodes are usually related to high doses, first use, oral ingestion or multiple substance use. A first episode can be followed by a recurrence after resumption of cannabis use.
The prevalence (proportion of subjects in the general population suffering from a disease at a given moment) is unknown. The incidence (number of new cases of subjects suffering from a disease during a specified period) is also unknown. The relationship between the causal agent and the underlying mechanisms is unexplained. Some researchers suggest a sensitisation of the dopaminergic system induced by the cannabinoid system (dopaminergic neurotransmitter cerebral pathways are activated during rewarding substance use; excessive dopaminergic transmission is also thought to be implicated in acute symptoms of schizophrenia) (23).
Heavy alcohol use and most drug use can also induce acute psychotic reactions.

4.A.3 Cannabis-induced chronic psychosis

There is currently no clear evidence that cannabis use may lead to the persistence of a specific psychotic illness after abstinence, but the topic is controversial.

Existing studies of 'cannabis psychosis' are undermined by methodological problems (imprecise characterisation of syndromes, lack of toxicological evidence and simplified models of causal associations) (1,3-6).
The various studies generally mix up cases of shorter duration psychotic episodes (patients apparently suffering from toxic psychosis) with cases of chronic psychotic states. There is no clear evidence that the latter are not schizophrenic patients using cannabis (7,9,24-30). McGuire et al (31) matched 23 psychotic patients who tested positive for cannabis in urinary screening with 46 drug-free controls, and found no difference in terms of their characteristic psychopathology and mode of onset.
There have been some case reports of individuals displaying acute psychotic states after each cannabis use. These cases are generally interpreted as the triggering of an underlying vulnerability by cannabis use. It is difficult to establish whether such cases involve a repetition of toxic episodes, a specific chronic cannabis psychosis or an atypical sub-type of schizophrenia (7,8,14).

4.A.4 Does cannabis use constitute a risk factor in the onset of schizophrenia?

This topic is extremely controversial (1,3-6,32). Drug use in general (and not especially cannabis) has been alleged to be a causative factor in the onset of schizophrenia. Some (but not all) studies show that drug abuse most often precedes or is concomitant with the onset of schizophrenia (33-34). There is uncertainty about the pre-morbid (before the actual onset of the disease) personality of drug-using schizophrenic patients, which is sometimes characterised as healthier than that of non-drug using schizophrenic patients (35). Drug-using schizophrenic patients may be younger at first onset than those who have never used drugs (30,36).
Alcohol use is not reported to constitute a risk factor in the onset of schizophrenia.

Where cannabis is concerned, the debate arises from a prospective study: Andreasson et al. (37) followed a cohort of 45,570 men for fifteen years and found a statistical correlation between the level of cannabis exposure fifteen years ago and the development of schizophrenia during the follow-up period. They concluded that cannabis use might be one of the additional stress factors that could help to precipitate the development of schizophrenia in vulnerable individuals, in interaction with other stress factors (psychosocial, chemical). The controversial points are some methodological weaknesses; a statistical correlation does not necessarily imply a causal relationship as both cannabis use and schizophrenia may be related to other underlying causes (such as anomalies in the dopaminergic system); the subjects may fail to report their use of other drugs; vulnerable individuals on the brink of psychosis may already be using cannabis as self-medication for some symptoms; and in fact cannabis use accounted for only a minority of the cases in that study.

To answer some of these questions, in 1989 Andreasson et al. analysed the medical records of a subsample of 8,483 men from the previous cohort. However, the small number of cases of cannabis use and schizophrenia (38) cautions against drawing any far-reaching conclusions, and even if cannabis was the dominant drug used, other drugs of abuse were also reported.

A recent Scottish study of people considered to be at high risk for schizophrenia (subjects aged sixteen to 25 with at least two first or second degree relatives who suffered from schizophrenia) also showed a correlation between past or present cannabis use and the presence of psychotic symptoms. A correlation was also found with other illicit drug use and with upsetting life events (39).

Conversely, there is no evidence that the incidence of schizophrenia differs in cultures with different rates of cannabis consumption (3).

4.A.5 Is cannabis use harmful to schizophrenic subjects?

This topic is also very controversial (1,3-6,40). Numerous clinical studies have found that drug use in general (and not specifically cannabis) had a negative effect on the progress of schizophrenic patients (41-44). One study found a better outcome after abstinence (45).

In experimental studies, almost all the drugs tested had the potential to exacerbate psychosis but drug response is heterogeneous. Opiates alone have not consistently been demonstrated to worsen psychosis. Alcohol use does not seem to influence the development of schizophrenia (46).

Some clinical studies found that cannabis appears to enhance the positive symptoms (e.g. delusions, hallucinations, disorganised speech) of schizophrenia (47,48). Other studies found that schizophrenic patients' resumption of cannabis use resulted in an increase in psychotic symptoms and more relapses (9,14). Linszen compared a group of cannabis using schizophrenic patients under treatment (antipsychotic medication and individual support) with a group of matched abstinent schizophrenic patients. Significantly more and earlier psychotic relapses occurred in the cannabis-abusing group (49). Caspari also found more rehospitalisations (50)
One study found a significantly lower rate of negative symptoms (for example alogia, avolition, affective flattening) in cannabis using schizophrenic patients (51). Other studies found no differences in term of symptomatology (52). Eightythree schizophrenic patients interviewed by Dixon et al (46) reported more suspiciousness and as many or more hallucinations than patients not using cannabis, but also more calmness, energy and less anxiety and depression after cannabis use.

A much-debated question is why schizophrenic patients are so frequently substance users. Maybe schizophrenic patients are seeking self-medication of some psychiatric symptoms by using drugs (especially in the case of cannabis: negative symptoms, anxiety, depressive symptoms, side effects of classical neuroleptic medications). Some think that these patients abuse drugs because doing so bears less of a social stigma than being mentally ill. Chronic psychosis presumably reduces the ability of other patients to struggle against the addictive effect of substances. Another hypothesis is that changes to the dopamine receptors caused by chronic neuroleptic medication may enhance the reinforcing effect of substances. Some researchers think that other underlying factors may increase the risk of psychosis as much as substance dependence. Scientists are just beginning to explore the interactions between dopaminergic and cannabinoid systems. A recent in vivo case study of the brain tomography of an abstinent cannabis sensitive schizophrenic patient was recently published. This patient experienced the immediate effect of cannabis as calming and pleasant. But a few hours later, there was a worsening of psychotic symptoms accompanied by an increase of brain dopamine activity (53). Finally, recent studies seem to show abnormalities in the endocannabinoid system of schizophrenic subjects (54,55). Ultimately, schizophrenic patients are probably a heterogeneous group.

4.A.6 Conclusions

The link between cannabis use and psychosis is a very controversial issue. At the moment we lack a corpus of comparable, methodologically sound studies repeatedly yielding similar conclusions. The results of existing studies are often complex or ambiguous and the personal opinions of the researchers often interfere with the interpretations. Further deepening of our scientific knowledge is still necessary.

However, there is extensive, albeit incomplete, consensus on the ability of heavy cannabis consumption or intoxication to induce an acute transitory psychotic state in healthy subjects. The frequency of this condition is unknown and the mechanisms are hypothetical.

There is no evidence that heavy cannabis use can lead to a specific chronic cannabis psychosis. Uncertainty remains about the relationship between cannabis use and schizophrenia. So far, it has not been proven that cannabis use may trigger the course of schizophrenia. However, the results of different studies show that cannabis could potentially worsen its course. How best to interpret all these results is the subject of heated debate in the psychiatric community.

4.A.6.1 Gaps in our knowledge

The etiopathogeny of toxic psychosis is not well understood. Functional imagery of the dopamine system and if possible of the cannabinoid system during intoxication at different doses in healthy volunteers should help to understand this process.

We have insufficient knowledge about the risk factors for schizophrenia. The current demand for high quality research can be satisfied by conducting prospective studies designed to identify risk factors for schizophrenia in general population cohorts, with controls for possible confounding variables (other substances used, psychosocial stress factors) and by using validated questionnaires, diagnostic classifications and toxicological measures.

Carefully designed clinical studies of the effects of cannabis on schizophrenic patients and the patterns and reasons for use (subject to the same methodological considerations) will help to establish whether cannabis is harmful to these patients. Functional imagery and measures exploring the cannabinoid and dopaminergic systems in cannabis using and non-using schizophrenic patients should also help to clarify this question.

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Part B. Mood and anxiety disorders

Summary

This part of chapter 4 focuses on the relationship between cannabis use and mood and anxiety disorders.

Is there evidence for an 'amotivational syndrome'?

The existence of this new psychiatric syndrome, characterised by loss of energy and the urge to work, could not be demonstrated in existing field studies.

Can we answer the question of which comes first, the mood disorder or cannabis use?

There is a correlation between mood disorders, such as depressive, dysthymic or bipolar disorder, and cannabis use. A higher prevalence of mood disorders was recently found among cannabis users. It has been suggested that attempted suicide behaviour may be influenced by cannabis use, social disadvantages, a disadvantageous childhood and family circumstances. Elevated rates of substance use have been found among patients in treatment for bipolar disorder. However, there is no answer to the question of 'which comes first'; the research findings support hypotheses pointing in several different directions.

Anxiety, an adverse reaction to cannabis?

In clinical settings it is assumed that anxiety is the most common type of adverse reaction to cannabis. Acute anxiety and panic attacks following cannabis use have been described in early experimental studies and case reports. However, we lack information from population studies about its prevalence and the past research does not discriminate sufficiently clearly between cannabis used as a single substance and in combination with other substances.

4.B.1 Introduction: the main questions addressed in this part of the chapter

We start by exploring the concept of the 'amotivational syndrome', followed by the relationship between cannabis use and mood disorders and cannabis use and anxiety. The main questions are:

- What is the evidence for an 'amotivational syndrome' as described in relation to cannabis use?
- What is the relationship between cannabis use and mood disorders such as depressive, dysthemic or bipolar disorders?
- Are there recent findings about the co-occurrence of present-day patterns of cannabis use and anxiety or panic attacks?

The methods used are examination of the scientific literature, separating reviews, clinical studies, case reports and experimental studies.

4.B.2 Cannabis and the 'amotivational syndrome'

It has been suggested that heavy cannabis use may lead to an 'amotivational syndrome', described as a loss of energy and the urge to work (1,2). Early descriptions have been supported only by uncontrolled studies in traditional cultures and published as monographs (3,4).

Controversy arises from methodological weaknesses and other findings showing that farm workers who smoke cannabis are as productive as their non-smoking colleagues. It has also been suggested, but is not beyond doubt, that cannabis can alleviate fatigue and can therefore have a positive effect on a worker's productivity (5).

It has not yet been possible to demonstrate the existence of a new psychiatric syndrome with these field studies. Although there is reasonable evidence that heavy cannabis use can impair motivation, an 'amotivational syndrome' has not been clearly distinguished. Other hypotheses suggest that amotivation may be linked to co-existing psychiatric or medical conditions. Although acute intoxication seems to impair motivation, the role of long-term neurotoxicity in heavy cannabis users suffering from chronic intoxication has yet to be clarified. A possible hypothesis about the amotivational symptoms observed in heavy marijuana users in treatment could be that there is a link between the lack of motivation and depression. In heavy users of marijuana, a statistical correlation has been found between depressive symptoms and low scores on the 'achievement motivation' dimension of the Thematic Apperception Test (6). However, a statistical correlation does not provide conclusive evidence about the link between cause and effect.

There is some evidence that the severity of alexithymic symptoms (assessed by the Toronto Alexithymia scale) increases with the degree of cannabis consumption (7).

4.B.3 Mood disorders

Until recently, the link between cannabis and prolonged or serious mood disorders such as depressive, dysthymic or bipolar disorder was supported by anecdotal clinical evidence only (8,9). However, recent epidemiological surveys have found a high prevalence of mood disorders among cannabis users (10). The increased rate of cannabis use among attempted suicides inferred by a recent study (11) and the possible links between mood disorders and cannabis use suggested in other studies deserve closer attention.

Cross sectional studies of adolescents show that depression is related to a variety of substance use behaviour, such as cigarette smoking, alcohol consumption and illicit substance use. Longitudinal studies have found that a depressed mood precedes the first use of marijuana and other illicit drugs by secondary school students (12).

A study involving conscripts whose urine contained cannabinoid derivatives, but who were not using other illicit drugs, reports that 55 of the 133 subjects had an axis I, DSM III-R diagnosis. The most prevalent conditions were adjustment disorders with a depressive mood, major depression, dysthymia and panic disorder. The last condition was found in only one subject (7).
The prevalence of these co-morbid psychiatric disorders and the severity of the depressive symptoms varied with the pattern of cannabis use. Of the 133 conscripts, 29 were dependent on cannabis, 58 were abusers and 46 occasional users. Furthermore, 69% (20 of the 29) of those subjects with cannabis dependence, 41% (24 of the 58) of those who were abusers and 24% (11 of the 46) of those who were occasional users were assessed as suffering from an axis I psychiatric disorder. The severity of depressive symptoms (assessed by the Beck Depression Inventory) increased with the degree of cannabis involvement.

In a study of 302 individuals who had made serious suicide attempts, 16.2 % met the criteria for cannabis dependence or abuse at the time of the attempt, compared with 1.9 % of 1,028 randomly selected control subjects (11). However, a very substantial component of the correlation came from a population of cannabis abusers or cannabis dependent subjects with a higher risk of suicide attempt behaviour as characterised by socio-demographic disadvantage (13) and disadvantageous childhood and family circumstances. When controlled for these socio-demographic factors and childhood factors, the correlation between suicide attempts and cannabis use was reduced from a

ratio of 10.3 to one of 3.2. Psychiatric co-morbidity (notably mood disorders, other substance-related problems and antisocial disorder) largely accounted for the remaining correlation. Cannabis use may also contribute to the risk of self-harm, but as we mentioned earlier, a statistical association does not necessarily imply a causal relationship.

There are three possible ways to account for the relationship between cannabis use and depression. First, both may share common risk factors, so that their relationship is not causal. Second, mood disorders may predispose people to use cannabis. Third, cannabis use may trigger or increase depressive symptoms.

As yet, there is no clear answer to this question of 'which comes first'. Mood problems at a young age slightly elevate the risk of later cannabis use (14). Deykin et al reported that sixteen to nineteen-year-olds with cannabis dependence were three times more likely to have a history of major depressive disorder (15). Participants reported that depression often preceded the substance abuse, suggesting the possibility of self-medication as a factor in the development of alcohol or substance abuse. Conversely, however, Luthar and Cushings found that cannabis use by fifteen-year-olds at the beginning of the year was associated with self-reports of depression and anxiety six months later (16).

4.B.3.1 Bipolar disorders

Most studies examining the widespread co-occurrence of substance abuse and bipolar disorder have confined themselves to reporting elevated rates of substance use among patients (18). Various hypotheses have been put forward to explain the relationship between substance use and bipolar disorder. However, these studies are based on hospital populations only, so there is no information about co-occurrence in the general population. Studies supporting these hypotheses are few, and many questions remain unanswered.
Substance use and bipolar disorders may share a common risk factor, but this has not been specifically studied.

The role played by cannabis as a DSM IV bipolar disorder criterion for manic or hypomanic episodes (excessive involvement in pleasurable activities that have a high potential for painful consequences) is ambiguous. Unlike the general population, bipolar patients are more likely to exhibit substance dependence than abuse (19). Given this finding, substance abuse seems an unlikely criterion for mania as a pleasurable activity with potential painful consequences (20). Nevertheless, bearing in mind recent data suggesting that a few days of daily cannabis use at high doses is sufficient to develop dependence, this hypothesis should be treated with circumspection (21, 22).

Clinical data suggests that many patients begin their substance abuse before the onset of their bipolar disorder. These findings support the hypothesis that substance abuse increases an existing risk of bipolar disorder. However, there is also evidence to support the hypothesis that substance abuse is an attempt at self-medication by bipolar patients (18, 23).

Substance use and bipolar disorders may share a common risk factor, but this has not been specifically studied.

4.B.4 Anxiety disorders

The co-occurrence of cannabis use and anxiety disorders within the same individual is an issue that merits closer study. This phenomenon is frequently reported, although only in clinical settings, and it is assumed that anxiety is the most common type of adverse reaction to the drug. However, standard scientific evaluation is clearly lacking. Acute anxiety and panic attacks following cannabis

use have been well described in early experimental studies and case reports (24). However, several decades have passed since then and changes in the patterns of cannabis consumption now require confirmation and further consideration. There is no information about the co-occurrence of cannabis use and severity of anxiety disorders.
Some reviews of the effects of cannabis describe these reactions as common acute adverse psychological reactions, but provide little, if any, other data to support this statement (25, 26). This is understandable, since the paucity of studies on anxiety disorders and cannabis use makes any attempt to review the situation a challenge.

Frequent anxiety/panic attacks were found in a community postal survey of adverse effects of cannabis use (27). However, conclusions must be drawn with caution from self-reported surveys, because self reported anxiety could be related to many causes.

Earlier in this chapter we mentioned a study involving 133 conscripts having cannabinoid derivatives in their urine and not using other illicit drugs. Like depression scores (Beck Depression Inventory), anxiety scores (Spielberg State-Trait Anxiety Index) increase with the degree of cannabis involvement. Interestingly, only one subject out of 133 was found to have an anxiety disorder (panic) when the structured clinical interview from DSM III-R was administered (7). If anxiety disorder is a frequent adverse reaction to cannabis, finding only one conscript suffering from an anxiety disorder out of 133 cannabis users is consistent with suggestions that individuals suffering from anxiety disorders avoid cannabis because they are more sensitive to its anxiogenic adverse effects (28).

Case reports of cannabis use and depersonalisation associated with agoraphobia (29) have yet to be confirmed.

4.B.5 Conclusions

There is not enough evidence for an 'amotivational syndrome' in relation to cannabis use as suggested in early field studies. Lack of motivation may be linked to chronic intoxication or a pre-existing medical or psychiatric disorder. Mood disorders are frequently found among cannabis users, but there is no conclusive answer to the question of 'which comes first'. The role played by cannabis in suicide attempts may be even less clear.

Anxiety is considered to be the most frequent adverse reaction to cannabis, yet few studies raise this important issue.

4.B.5.1 Gaps in our knowledge

It has been suggested that cannabis contributes directly to the risk of attempted suicide. This still controversial and sensitive issue needs to be explored further with the aid of modern study designs if we want to obtain conclusive evidence.

Our present state of knowledge about the amotivational syndrome calls for detailed studies, supplemented with clinical studies to discriminate between the effects of cannabis intoxication and symptoms associated with psychiatric syndromes.

It is assumed that anxiety is the most common type of adverse reaction to the drug, but standard scientific evaluation distinguishing clearly between cannabis use and multiple substance use is lacking.

The co-occurrence of cannabis use and other mental disorders such as bulimia and impulse control disorders is not understood at all. We have found no articles that address the issue of impulse control. With regard to eating disorders, we found one article suggesting the co-occurrence of binge eating and 'general' substance abuse.

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Part C. Dependence

This last part of chapter 4 explores the relationship between cannabis use and dependence.

Summary

Cannabis dependence does occur in human subjects, but the addictive potential of cannabis is considered to be weaker than that of many other drugs, including alcohol and tobacco. Dependence rarely seems to develop in the usual patterns of social use when doses are small or infrequent and the exposure to the drug is of limited duration.

4.C.1 Introduction: the main question addressed in this part of the chapter

For this subtopic, as for the others in this chapter, the methods used are examination of the scientific literature, separating reviews, clinical studies, case reports and experimental studies. The main question we answer here is:

- What kind of use can lead to cannabis dependence?

4.C.2 Cannabis use and dependence

Cannabis dependence occurs in man, confirming previous findings in many other species (1), but the addictive potential of cannabis is considered to be weaker than that of many other drugs, including alcohol and tobacco.

The development of physical dependence is generally associated with tolerance or/and withdrawal symptoms. The experience of withdrawal encourages continuation and it has been suggested that the development of tolerance leads to dosage escalation, although loss of control over substance use control can also be postulated. Tolerance has been demonstrated in cannabis-induced cardiovascular and autonomic changes, decreased intraocular pressure, sleep and sleep EEG patterns, and mood and behavioural changes. The rate at which tolerance develops depends on the dose and the dosage schedule (2-4).

Withdrawal syndrome has been clearly demonstrated in humans, with descriptions of aggressive behaviour, increased anxiety and restlessness, sleep disturbance, downturns in mood and loss of appetite after ceasing to use cannabis (5-8).

Some important laboratory studies confirm the existence of cannabis dependence. However, this data describes the effects of high doses of cannabis, and therefore may not reflect the effects of the usual patterns of cannabis consumption. It has been suggested that four thirty mg oral doses of THC daily or four 1.8 % THC cigarettes for four to 21 days produce a withdrawal syndrome (9-12).

Cannabis is now by far the most widely used illicit drug; ten to thirty per cent of the population in Europe report that they have used it, and there are significant reports of chronic usage in some countries (13). However, the large discrepancy between the population prevalence estimates (14) and the small number of cannabis users who actually seek treatment is a source of unease. This suggests a high rate of remission without treatment at the doses these users consume. A lack of motivation to stop cannot be ruled out as a possible reason for this (15), and the treatment available may also be unsuitable. The fact that cannabis dependence may often only impair the user's ability to function to a limited extent in comparison with other substances is also a possible factor (16).

Ultimately, dependence rarely seems to develop in the usual patterns of social use when doses are small or infrequent and the exposure to the drug is of limited duration (17).

4.C.3 Conclusions

When the usual consumption patterns are considered, cannabis dependence appears to be rare, and it also interferes less with the user's ability to function than other substances of abuse.

4.C.3.1 Gaps in our knowledge

Animal studies have shown self administration of THC. Further use can be made of this method to investigate the consequences of THC use and abuse on brain functions and neurochemical systems. It can also be employed to study the interaction between cannabis and other drugs of abuse.

Studies involving cannabis users who do not report any problems related to its use would be useful to obtain a 'natural history' of the course, patterns and attributions associated with regular cannabis use. One aspect of most studies in this area is that the definitions of heavy use, dependence and so on are specific to individual studies. This is a methodological barrier to the general applicability of drug research that needs to be addressed.

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5. PERFORMANCE IMPAIRMENT AND RISK OF MOTOR VEHICLE CRASHES AFTER CANNABIS USE

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Summary

Does THC impair driving performance?

The role of THC in driver impairment and motor vehicle crashes has traditionally been established in experimental and epidemiological studies. Experimental studies have repeatedly shown that THC impairs cognition, psychomotor function and actual driving performance in a dose related manner. The degree of performance impairment observed in experimental studies after doses of up to 300 μg/kg THC was equivalent to the impairing effect of an alcohol dose producing a blood alcohol concentration (BAC) ≥0.05 g/dl, the legal limit for driving under the influence in most European countries. Higher doses of THC, i.e. >300 μg/kg THC, have not been systematically studied but can be predicted to produce even greater impairment. The detrimental effects of THC were more prominent in certain driving tasks than others. Highly automated behaviours, such as road tracking control, were more significantly affected by THC than more complex driving tasks requiring conscious control.

Chronic cannabis use and performance

Experimental studies have also shown that cognitive deficits observed in chronic cannabis users are probably related to recent cannabis use or symptoms of withdrawal. Performance deficits in chronic cannabis users virtually disappeared over prolonged periods of abstinence, indicating that THC does not produce any gross changes in cognitive or psychomotor function that are permanent or irreversible.

Contrasts between the results of epidemiological and experimental studies

Epidemiological findings on the role of THC in vehicle crashes have sharply contrasted with findings from experimental research. Most epidemiological surveys show little evidence that crashed drivers who only used cannabis are more likely to cause accidents than drug free drivers. This apparent discrepancy between experimental and epidemiological results may be related to the use of unreliable indictors of recent cannabis use among crashed drivers in epidemiological surveys.

The role of higher doses and recent or past use of THC

Most surveys have established cannabis use among crashed drivers by determining the presence of an inactive metabolite of THC in blood or urine. Unfortunately, this metabolite can be detected in body fluids for days after smoking and can only be taken as evidence of past use of cannabis. Recent use of cannabis can only be established by directly measuring THC in the blood. The latter procedure was followed in only a few epidemiological surveys. These surveys showed that THC positives, particularly at higher doses, are two to six times more likely to be responsible for their crash than subjects who had not used drugs or alcohol. Together, this epidemiological data suggests that recent use of cannabis may increase the crash risk, whereas past use of cannabis does not.

Combined use of alcohol and THC: increased risks even at low doses

Experimental and epidemiological research yields similar findings for the combined use of THC and alcohol in traffic. Combined use of THC and alcohol produced severe impairment of cognitive, psychomotor and actual driving performance in experimental studies and sharply increased the risk of the driver's culpability for the accident in epidemiological analyses. The effects of alcohol and THC on experimental and epidemiological outcome measures appeared to be additive, but their sum was large and potentially dangerous, even at low doses.

Roadside drug testing

Currently available onsite tests of urine, saliva and sweat do not provide a full proof indication of recent cannabis use. Saliva tests revealed many 'false negatives' and correctly identified only 18-25% of the THC positives in reference blood. Sweat and urine tests produced many 'false positives' in the presence of inactive THC metabolites. Results from roadside drug tests may well provide good grounds for suspecting cannabis use in drivers, but need further confirmation by demonstrating the presence of THC in blood.

5.1 Introduction and main questions addressed

The effects of Δ9-tetrahydrocannabinol (THC) on the ability of drivers to operate safely have traditionally been determined in epidemiological surveys of THC users' involvement in traffic accidents and in experimental studies to measure the drug's influence on skills related to driving (1-5). The purpose of epidemiological studies is to determine both the severity of THC impairment and the prevalence of THC use among the driving population by measuring the frequency of cannabis use among drivers who do and do not become involved in crashes. Essentially they aim to determine whether cannabis use is over represented among drivers who were involved in accidents. Experimental studies are designed to predict the effects of cannabis on driving ability by measuring cannabis users' performance in laboratory tests of isolated psychological functions, driving simulators and on-the-road driving tests. In the context of well-designed experiments, drugs that produce large performance impairments in many different tests can be considered potentially hazardous to drivers, whereas drugs that fail to produce any impairment can be considered safe. Experimental studies often provide the earliest evidence of a drug's hazard potential for driving.

The present review attempts to summarise and integrate what is known about the effect of cannabis on performance and driving ability in particular. Particular attention will be also be given to the short and long term effects of THC on cognitive functioning, since these may be relevant to the driving task and other performance domains as well. A summary of the literature relevant to the following research questions will be given, along with a number of gaps in the available research literature:

- Does cannabis impair psychomotor, cognitive and actual driving performance and increase the risk of becoming involved in traffic accidents?
- Is there a relationship between performance impairment and cannabis dose or its concentration in plasma?
- Do the combined effects of cannabis and alcohol on driving performance differ from those of either drug alone?
- Does cannabis affect all aspects of the driving task alike?
- Does long-term use of cannabis produce residual cognitive deficits?
- Do roadside drug tests of urine, saliva and sweat serve as reliable predictors of THC concentrations in blood?

5.2 Prevalence of THC use among drivers involved in road accidents

Surveys conducted in widely separated locations have generally revealed the presence of THC in between four and twelve per cent of drivers who sustained injury or death in traffic accidents (6-13). Higher values have occasionally been reported for groups of (predominantly) young males operating in various large American cities (14-16). However, this data cannot be accepted as evidence that THC was responsible for the crashes, even though the prevalence of THC in the general driving population is assumed to be lower. The reason is that alcohol was also found in fifty to eighty per cent of the same drivers. It is highly likely that the combination of THC and alcohol poses a bigger risk potential than that of either drug alone.
A limitation of these surveys is their lack of an appropriate control group. Prevalence studies indicate the extent to which substances such as THC and alcohol are present in the blood of (fatally) injured drivers. In the absence of comparable data from an appropriate control group drawn from the general driving population, the results of prevalence studies can never be taken to indicate the role of THC or other drugs in causing traffic accidents.

5.3 Culpability studies on the relationship between THC use and traffic accidents

Epidemiologists have tried to overcome the lack of normative data from the general driving population by analysing the culpability index of drivers involved in traffic accidents. Basically, they distinguished between drivers who were responsible for their crash and those who were not. The former are taken as the cases and the latter as controls, to determine the odds ratio for responsibility for traffic accidents under the influence of cannabis. Classification of culpability should of course be carried out without knowledge of the drugs/alcohol status of drivers to avoid bias in the classification process.

In general, the use of cannabis has been determined by measuring THC or its inactive metabolite THC-COOH in the urine or blood of drivers. Several culpability studies have investigated the association between cannabis, alcohol and traffic crashes. A summary of these studies and their measure of association is given in Table 1. The odds ratios and 95% confidence intervals (CI) presented in Table 1 are taken from the original study reports or adapted from Bates & Blakely's (4) re-analyses of this data. It is important to note that in this type of analysis the crash culpability rates among drivers positive for THC are compared to crash culpability rates in drug (including alcohol) free drivers. The odds ratio of drug free drivers becoming involved in traffic accidents is equal to 1.0, and serves as the point of reference to determine the statistical significance of changes in odds ratios for drivers under the influence. If this reference value of 1.0 falls outside the 95% CI associated with the odds ratios for a certain drug, we can safely conclude with 95% certainty that this drug significantly affected crash culpability. However, if the 95% CI includes the reference mean, we must conclude that the crash culpability rates of drugged drivers are comparable to crash culpability rates in drug-free drivers. A summary of the studies listed in Table 1 is given below.

Terhune and Fell (7) tested 497 injured drivers for the presence of a wide range of drugs during treatment at Rochester General Hospital in New York. THC was detected in the blood of 9.5% of the drivers, but more than half of them also tested positive for alcohol. Bates and Blakely (4) reanalysed their data and showed elevated odds ratios for crash culpability associated with THC and alcohol alone. Data enabling the odds ratios for the combination of THC and alcohol to be calculated was unavailable.

Table 1
Culpability studies indicating odds ratio (OR) of becoming involved in fatal or injurious traffic accidents under the influence of cannabis, alcohol or their combination.
The significance of changes in OR is indicated as follows:*<. 05).

Authors	Substances	Odds ratio	95% CI	N of drivers culpable / not culpable
Terhune & Fell	Drug free cases	1.0		94/179
(1982)	Alcohol	5.4 *	2.8-10.5	45/16
	THC	2.1	0.7-6.6	9/8
	Alcohol / THC	-	-	-
Williams et al.	Drug free cases	1.0		55/23
(1985)	Alcohol	5.0	2.1-12.2	120/10
	THC or THC-COOH	0.2	0.2-1.5	10/9
	Alcohol / THC or THC-COOH	8.6 *	3.1-26.9	123/6
Terhune et al.	Drug free cases	1.0		541/258
(1992)	Alcohol	7.4 *	5.1-10.7	587/38
	THC	0.7	0.2-1.8	11/8
	Alcohol / THC	8.4 *	2.1-72.1	35/2
Drummer (1994)	Drug free cases	1.0		392/140
	Alcohol	5.5 *	3.2-9.6	261/17
	THC-COOH	0.7	0.4-1.5	29/14
	Alcohol / THC-COOH	5.3 *	1.9-20.3	59/9
Hunter et al.	Drug free cases	1.0		944/821
(1998)	Alcohol	6.8 *	4.3-11.1	173/22
	THC			
	≤1.0 ng/ml	0.35	0.03-2.1	2/5
	1.1-2.0 ng/ml	0.51	0.2-1.4	7/12
	>2 ng/ml	1.74	0.6-5.7	12/6
	THC-COOH			
	1-10 ng/ml	0.69	0.5-2.2	19/24
	11-20 ng/ml	1.04	0.4-2.1	18/15
	21-30 ng/ml	0.87	0.6-4.8	12/12
	> 30 ng/ml	1.62	0.6-4.8	13/7
	Alcohol / THC	11.5 *	4.6-36.7	66/6
Lowenstein &	Drug free cases	1.0		114/126
Koziol-McLain	Alcohol	3.2	1.1-9.4	17/6
(2001)	THC-COOH	1.1	0.5-2.4	17/17
	Alcohol / THC-COOH	3.5 *	1.2-11.4	16/5
Drummer et al.	Drug free cases	1.0		1209/372
(2001) and	Alcohol	5.7 *	4.1-8.2	720/39
Swann (2000) [1]	THC	3.0 *	1.2-7.6	49/5
	THC > 5 ng/ml [1]	6.4 *	1.3-115.7	24/0
	THC-COOH	0.8	0-1.3	68/26
	Alcohol / THC	19 *	2.6-136.1	65/62

Williams et al. (14) studied fatally injured motor vehicle drivers in California who died within 2 hours of the crash. THC or THC-COOH were found in 37% of the 440 driving fatalities, whereas alcohol was found in 70% of the cases. They concluded that crash culpability was related to alcohol but not THC, but details of their analysis were not presented. Additional analyses carried out by Bates and Blakely (1999) on data presented in the original report confirmed these findings. In addition, they reported that the effect of the combination of alcohol and THC was greater than that of alcohol alone, although this difference was not statistically significant.
Terhune et al. (8) performed a large post mortem survey. This involved a sample of 1882 fatally injured drivers from seven American states during 1990-1991 who died within 4 hours of the crash. Drug-free drivers comprised 42.1% of the sample, while drivers showing the presence of alcohol comprised 51.1%. THC was found in only 6.7 %, and two thirds of these drivers tested positive for alcohol as well. Drug-free drivers were held responsible for 67.7% of their cases. The responsibility rate for drivers showing only the presence of alcohol depended on their blood alcohol concentrations (BAC). For those with BACs below 0.10 g/dl this rate was 75.8% and for those at or above that level, 93.9%. 57.9% of drivers showing only the presence of THC were held responsible, i.e., fewer than the drug-free drivers, but the difference was not statistically significant. However, the group showing the combined presence of THC and alcohol in any concentration at all was held responsible in 94.6% of its crashes. This rate differed significantly from that of the drug-free drivers, though not from that of the subgroup with the highest BAC. Odds ratios similarly suggested that, relative to drug-free drivers, THC alone was not associated with elevated crash culpability, and that alcohol or the combination of alcohol and THC severely increased the drivers' relative risk.

Drummer (17) performed a culpability analysis of 1,045 drivers killed in motor vehicle accidents in three Australian states during 1990-1993. Alcohol was detected in 37% of the cases, and THC-COOH in 11%. In about two-thirds of the latter cases alcohol was detected as well. The odds ratios for crash culpability were elevated for alcohol and for THC and alcohol combined, but not for THC-COOH alone.

Hunter et al. (18) conducted a survey among drivers involved in non-fatal crashes. This involved 2,500 hospitalised injured drivers in Australia. Bates and Blakely (1999) calculated the associated odds ratios for crash culpability of drivers using THC, alcohol or the combination. In addition, they also calculated the separate effects of THC and its metabolite THC-COOH at different serum concentrations. The results showed that the odds ratio associated with THC was about the same as with THC-COOH when THC was not present in plasma. Furthermore, the odds ratios increased with increasing concentrations of THC and, though less markedly, THC-COOH.
Lowenstein and Koziol-McLain (19) studied 414 injured drivers in Colorado who arrived at an urban emergency room within 1 hour of their crash. Thirty-two percent of the urine samples were positive for at least one potentially impairing drug. THC-COOH was detected most frequently (17%), surpassing alcohol (14%). Compared with drug and alcohol free drivers, the odds of crash responsibility were higher in drivers testing positive for alcohol and for alcohol in combination with THC or other drugs.

Drummer et al. (20) carried out a responsibility analysis on 3,400 Australian cases recorded in their database between 1990 and 1999. THC was present in 57 cases in which no other psychoactive drug or alcohol was found. The median THC concentration was 8 ng/ml, with a range from 1-228 ng/ml. THC positive cases showed an odds ratio of 3.0 compared to drug free drivers, suggesting an increased crash risk. The confidence limits were not supplied by the authors, but were calculated from the information provided in the manuscript. The range of the confidence interval strongly suggested significance of the OR value as it did not include the reference value 1.0. When alcohol was combined with THC the risk increased to 19. Additional logistic regression analysis conducted by the present authors confirmed the statistical significance of these findings, even when

interactions for age, gender, crash type, jurisdiction and year of collection were taken into account (i.e., adjusted OR for drivers using THC alone: 2.68, 95% CI: 1.02-7.04). Analyses of a subset of cases collected in the Australian state of New South Wales between 1995-1998 revealed an culpability ratio of 6.4 in THC driver fatalities as compared to drug free cases (21). THC concentrations in blood were relatively high in the former group and ranged from 5 to 100 ng/ml.

In summary, most culpability studies seem to indicate that cannabis does not increase crash culpability. However, most culpability studies have also identified cannabis use among drivers by measuring THC-COOH, an inactive carboxy metabolite of THC, in blood or in urine. Following the use of cannabis, THC-COOH may be present in the blood or urine for days. The presence of THC-COOH thus does not necessarily imply recent use of cannabis or impairment. Recent exposure to cannabis can only be safely assumed in the minority of culpability studies that determined cannabis use by the presence of THC in the blood. Those studies generally show elevated risk ratios for THC positive cases as compared to drug free drivers, suggesting an increased crash risk with recent cannabis use. Crash culpability also increased with rising concentrations of THC in plasma, indicating that THC significantly increases crash responsibility rates at higher doses. Alcohol and the combination of alcohol with cannabis significantly and seriously elevated crash culpability rates in all studies. In most studies the combined effects of cannabis and alcohol on crash culpability appeared to be additive, although a weak suggestion of a synergistic effect was also apparent in some.

5.4 Experimental studies of the effects of THC on performance

The effect of THC on performance has mostly been determined on the basis of information provided by the field of psychopharmacology. Psychopharmacologists have devised a large number of experimental performance tasks for measuring the behavioural effects of drugs. The earliest tests were developed to diagnose neurological, ophthalmological and vestibular disorders. Later, 'psychomotor' tests, characterised by contingent motor responses to an imposed discrete or continuous signal, were used (e.g. reaction time, attention, tracking and critical flicker/fusion frequency tests). 'Cognitive' tests were also added: primarily to measure various mnemonic functions, but also deductive reasoning. Finally, tests were developed to measure some aspects of 'real life' performance such as driving in a simulator, through staged manoeuvres on a course closed to other traffic, or on public roads in actual traffic. All of these tests have generally been used in single dose studies of recreational users of THC. They have employed both parallel group and crossover designs, most with both placebo and alcohol controls. The great advantage of the experimental studies that have been conducted is their ability to determine the intrinsic pharmacological effects of THC on performance without the confounding factors that always obscure or exaggerate these effects in the natural environment. Until now, however, the experimental approach has mainly been limited to studies assessing the acute effects of THC on performance: i.e., the effects of THC on performance after a single dose. Experimental data on performance effects after repeated doses of THC is generally lacking. As a consequence it is currently not known whether THC users adapt to acute effects of this drug as a result of tolerance. Nor have the effects of THC on novel users versus experienced users been studied systematically to establish differences in sensitivity between subgroups of users. These issues will certainly gain importance with the possible introduction of cannabis as a medicinal drug for the (sub)chronic treatment of pain or inflammation. It is for this reason that the Institute of Medicine recommends that the patient's cognitive and psychomotor functioning should be assessed before and regularly during the course of a chronic regime of cannabis treatment to determine the extent to which tolerance to the impairing effects of cannabis develops and whether new problems emerge (22).

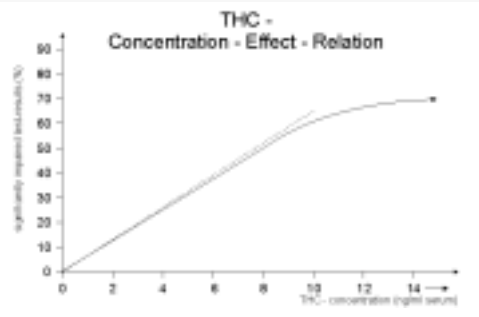
Table 2.
Frequency of performance impairments (%) observed in the total number of psychomotor tests applied in 87 experimental studies as a function of dose, time after dosing and route of administration of THC.
Performance decrements associated with fewer than twenty psychomotor assessments are shown in brackets because of their limited predictive validity. (Adapted from: Berghaus et al., 1998a (2)).

	Time after smoking (hrs)									
THC dose	<1		1-2		2- 3		3-4		4-5	
	Impaired	Tests	Impaired	Tests	Impaired	Tests	Impaired	Tests	Impaired	Tests
Route of THC administration: smoking										
< 9 mg	61%	271	36%	33	(30%)	10	(0%)	10	(0%)	11
9 - 18 mg	53%	193	38%	48	(38%)	8	(0%)	6	(0%)	2
≥ 18 mg	64%	64	36%	28	(40%)	10	(53%)	15	(67%)	3
Overall	**58%**	**528**	**37%**	**109**	**36%**	**28**	**26%**	**31**	**(13%)**	**16**
Route of THC administration: oral										
< 9 mg	(33%)	3	14%	49	27%	37	(8%)	13	-	-
9 - 18 mg	(0%)	3	39%	41	42%	45	(18%)	17	-	-
≥ 18 mg	(0%)	3	60%	45	(40%)	15	(33%)	15	(45%)	11
Overall	**(11%)**	**9**	**37%**	**135**	**36%**	**97**	**20%**	**45**	**(45%)**	**11**

5.4.1 Psychomotor performance and cognition

Numerous experimental studies have been conducted to investigate the effects of THC on isolated cognitive functions and psychomotor skills related to driving performance. These have generally shown that THC in doses between forty and 300 μg/kg causes a dose dependant reduction in performance on laboratory tasks measuring memory function, divided and sustained attention, reaction time, tracking or motor control (reviews: 1,2,5,23). One of the most consistently reported behavioural effects of THC is a disruption in the free recall of previously learned information. Recall of items learned before cannabis use is generally not affected, suggesting that THC impairs learning and the acquisition of information but not its retrieval from memory. THC may interfere with attention focusing by increasing the tendency to be distracted by irrelevant information, and this may contribute to deficits in information acquisition and information transfer from short to long-term memory. Short-term or working memory is generally impaired in complex tasks, but also in simple tasks at high doses.

Figure 1
Frequency of performance decrements (%) observed in the total number of psychomotor tests conducted in 87 experimental studies as a function of THC concentration in plasma after eating (---) and smoking (—) cannabis. (Adapted from Berghaus et al., 1998a (2))



The magnitude of the effects of THC on performance also varied with the method of administration, i.e. smoking or oral intake, and the length of time after THC use. Berghaus et al. (2,3) conducted a meta-analysis of 87 published placebo controlled studies on the effects of THC on laboratory based psychomotor tasks related to driving, including tracking, reaction time, perception, hand-eye coordination, body sway, signal detection, and divided or sustained attention tasks. Their analysis demonstrated that the percentage of psychomotor tasks showing significant performance impairment after THC administration was highest during the first hour after smoking or between one and two hours after oral intake. Peak impairment after THC was comparable to the alcohol induced performance impairment seen at blood alcohol concentrations (BACs) of >0.05 g/dl. The number of significant performance effects sharply declined to about zero over three to four hours after THC use. Only higher doses of THC produced prolonged performance impairment. The meta-analysis also indicated that plasma concentrations of THC are strongly related to the magnitude of performance impairment. In general, performance declined in about thirty per cent of all tests applied at plasma concentrations of <5 ng/ml THC, when compared to a placebo. Impairment increased with higher plasma levels of THC. The greatest performance decrement, i.e. impairment in seventy to eighty per cent of all psychomotor tests, was seen at concentrations between fourteen ng/ml and sixty ng/ml of THC. A summary of the major findings from Berghaus et al.'s meta-analysis is given in Table 2 and Figure 1.

5.4.2 Driving simulators and on-the-road driving tests

A major drawback of experimental laboratory studies is that it is doubtful whether tests of skills related to driving serve as a good model for the driving task as a whole. Many tests are short and relatively simple and do not necessary reflect performance in the real world. Driving is probably one of the most complex psychomotor tasks. It is difficult to conceive, much less simulate, every situation that confronts drivers. Tests designed to measure the effects of drugs in driving simulators, over closed-course driving terrain or on real roads in normal traffic are the most likely to approach reality. Yet these tests too can often measure only parts of a driver's total driving behaviour. However, it is generally accepted that the closer a test approaches reality, the better the chance of measuring the effects that cause crashes.

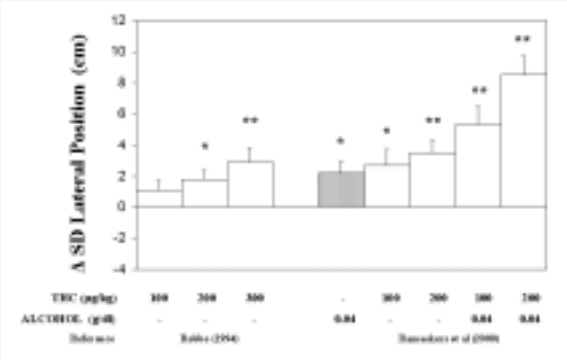
Smiley et al. (24) conducted the first study of THC and alcohol in a driving simulator. The simulated tasks contained a 45 minute scenario that included following curves, reacting to gusts of wind, following cars, selecting a route from signs, avoiding an obstacle that appeared in front of the simulated vehicle and overtaking. A visual choice reaction time task was also superimposed on the driving task. Three groups of cannabis users smoked cigarettes containing 0, 100 and 200 μg/kg, with and without alcohol. The quantity of alcohol consumed varied between groups in order to reach the intended BACs of 0.00, 0.05 and 0.08 g/dl respectively. The test began fifteen minutes after smoking. Both THC doses increased variability of lateral positioning and headway and caused the subjects to ignore navigational information. The highest dose increased speed variability and caused the subjects to hit obstacles in the road more often and to react more slowly in the subsidiary task than the placebo subjects. Yet both THC doses also caused the subjects to drive in a more conservative way. They maintained a longer headway, refused more opportunities to overtake, and when they did, began this manoeuvre at a greater distance from the approaching vehicle. The effects of alcohol were generally insignificant in this study. There were also no significant interactions between the combined effects of alcohol and THC on performance.
Stein et al. (25) conducted two studies on the effects of alcohol and cannabis on performance using a driving simulator and a fifteen minute scenario that were very similar to those employed by Smiley et al. (1981). Alcohol placebo and alcohol sufficient to produce a BAC of 0.10 g/dl were given in both studies. THC doses of 0, 50 and 100 μg/kg were given in the first, and 0, 100 and 200 μg/kg in the second study. This time, alcohol had the expected impairing effects on all performance parameters. Also in contrast to the study by Smiley et al. (24), THC had almost no significant

effects except that subjects drove at lower speeds after the higher THC dose. The combination of THC with alcohol caused more 'accidents' than alcohol did alone.
Four studies tested the effects of cannabis and alcohol on vehicle handling performance during staged manoeuvres on courses closed to normal traffic (26-29). With the exception of the study by Peck et al. (29), these studies seem of minor importance. Their tests varied making comparisons very difficult, and the THC doses and numbers of subjects were generally too low to achieve sufficient statistical power to detect any drug effects on performance. Peck et al.'s study (29) was a positive exception. These researchers assigned 84 subjects in equal proportions to four treatment conditions: placebo, alcohol (0.08 g/dl BAC), 270 μg/kg THC and both drugs combined. The subjects were tested four times in complete replications of a driving test battery. Ratings of the subjects' driving proficiency were obtained from licensed driving instructors and from California Highway Patrol officers who followed the subjects' vehicle in a police car. A risk acceptance test was included to measure the subjects' willingness and ability to drive through pylons in a chicane. Finally, a standard police field sobriety test and two standard laboratory tests (tracking and time estimation) were administered to the subjects. Several hundreds of measures were obtained. No dramatic performance effects were reported after THC alone or in combination with alcohol.

A series of driving tests in actual traffic was conducted by a group of researchers at Maastricht University in the Netherlands. Robbe (1) investigated the effects of THC doses of 0, 100, 200 and 300 μg/kg on performance in a 1-hour Road Tracking Test and a 30-minute Car-Following Test conducted on a primary highway, as well as the effect of alcohol and THC 100 μg/kg on performance in a City Driving Test. The combined effects of THC and alcohol were investigated further in two subsequent studies. The first assessed the effects of THC 0, 100 and 200 μg/kg with and without a low dose of alcohol on road tracking and car-following performance (30). In the second study (31), a licensed driving instructor rated the effects of THC 0 and 100 μg/kg with and without a low dose of alcohol (BAC <0.05 g/dl) on general driving proficiency during a City Driving Test, using a standardised questionnaire. In addition, the subjects' visual search for traffic approaching intersections was recorded by means of head-mounted cameras which registered the subjects' eye movements and direction of gaze in the visual field. All subjects were recreational users of cannabis. In these studies, THC produced a dose related increment in the Standard Deviation of Lateral Position (SDLP), a measure of lateral position variability or 'weaving', during the Road Tracking Test. Reaction time to accelerations/decelerations in the speed of a leading vehicle and general driving proficiency were not affected by THC in the Car-Following Test and the City Driving Test respectively. The effects of THC on lateral position variability were moderate and comparable to those of an alcohol dose producing a BAC of about 0.05 g/dl, the legal limit for driving under the influence in most European countries. However, the combination of THC with a low dose of alcohol produced severe performance impairment in the Road Tracking Test, and to a lesser extent also in the Car-Following and City Driving Test. There was no significant interaction between alcohol and THC, indicating that the effects were additive. When compared to a previously established alcohol calibration curve (32), the combination of THC 100 and 200 μg/kg with alcohol produced a rise in mean SDLP equivalent to that associated with BACs of 0.09 g/dl and 0.14 g/dl respectively. A summary of the effects of THC and alcohol on lateral position variability is given in Figure 2. Values on the Y-axis indicate change scores from placebo.

Figure 2

Mean Δ SDLP (+SE) in the Road Tracking Test after incremental doses of THC alone and after THC combined with alcohol as measured in studies by Robbe (1) and Ramaekers et al. (30) respectively. Alcohol concentrations reflect the subjects' mean BACs while conducting the driving test.
The significance of changes in SDLP is indicated as follows: * p<.05; **, p<.01. Mean (range) plasma THC concentrations after 100, 200 and 200 _g/kg were 7.9 (0.8-17.2), 12.0 (1.5-27.1) and 16.1 (4.7-30.9) ng/ml (1).



5.4.3 Cognitive effects of chronic cannabis use

Chronic or long-term effects refer to residual changes in central nervous functions resulting from prolonged exposure to cannabis, which are not caused by acute pharmacological effects and persist beyond the elimination phase of THC from the body. The effects of chronic cannabis use on psychomotor and cognitive functions have been inadequately studied. Several investigations have reported deficits in memory and attention, slower reaction times and a reduced ability to organise and integrate complex information in long-term heavy users of cannabis (5,33,34). However, most studies of the long-term effects of THC have measured cognitive functions in heavy users after only twelve and 72 hours of abstinence. It is therefore difficult to determine whether such deficits are temporary, i.e., due to residual THC in the brain, or the result of acute withdrawal, or long-term. A recent study (35) strongly suggests that cognitive deficits in long-term heavy users are reversible and related to recent cannabis exposure rather than to cumulative lifetime use of THC. The investigators administered a battery of neuropsychological tests to groups of current heavy users, former heavy users and normal controls before and after one, seven and 28 days of abstinence from cannabis use. The test battery included tests for measuring intellectual functioning, verbal fluency, sustained attention and memory. Current heavy users scored significantly below control subjects on memory tasks before and after one and seven days of abstinence. By day 28, however, there were virtually no significant differences between the three groups' performance on any of the tasks.

A series of studies using sensitive and direct measures of information processing by the brain (event-related potentials) suggests that chronic cannabis use is nonetheless associated with subtle but consistent deficits in cognitive functioning, i.e., in selective attention. In one study, Solowij (5) compared 32 users with different durations and frequencies of cannabis exposure with sixteen controls on performance in a selective attention task. Brain activity was measured concurrently. The users were abstinent for at least 24 hours (range 24 hours-30 days). The levels of THC-COOH in urine samples were zero on the day of testing for 60% of this group. The results showed that information processing (as indexed by the latency of a large positive brain potential, the P300) was slower in heavy users than in light users and controls. Based on the frequency of use and THC levels, this delay was apparently related to recent cannabis exposure. However, another type of brain activity (processing negativity), which indexes the ability to focus attention and reject complex

irrelevant information, deteriorated progressively with the numbers of years of cannabis use, regardless of frequency of use or time since last use. According to the authors, this increased distractibility pointed at long-term changes in brain functioning.
In a subsequent study, Solowij (5) investigated the reversibility of these deficits among 28 ex-users who were abstinent for a mean period of two years (range: six months to six years). Sixteen controls, sixteen current long-term cannabis users (mean ten years) and sixteen current short-term users (mean three years) were also included for comparison purposes. The results showed that the size of the deficit in selective attention (processing negativity) fell between that of the controls and the current long-term users. Moreover, there was some evidence that ex-users with a high IQ could somehow compensate for the impairing effects of cannabis. These findings indicated that changes in information processing might (only) be partially reversible with prolonged abstinence and that there are individual differences in vulnerability.
The studies of Pope et al. (35) and Solowij (5) show that cognitive deficits in long-term cannabis users seem to be related to recent cannabis exposure and may largely disappear after a prolonged period of abstinence. However, limited evidence suggests that subtle changes in brain functioning may be more persistent, although the practical significance of these findings is not clear. In any case, the degree of impairment in chronic cannabis users is by no means comparable with the gross deficits seen in heavy alcohol users (34).

In summary, experimental studies indicate that THC impairs psychomotor, cognitive and actual driving performance in a dose related fashion. The degree of driving impairment seen after THC doses of up to 300 μg/kg are comparable to an alcohol dose producing a BAC of 0.05 g/dl or more. The effects of THC seem more prominent in tests measuring road-tracking precision as compared to tests measuring more complex driving tasks. However, the combined effects of THC and alcohol produced severe driving impairment in most studies, even at low doses. Cognitive deficits observed in long-term cannabis users seem to be related to recent cannabis exposure and virtually disappear after a prolonged period of abstinence.

5.5 Roadside drug testing: biological indicators of cannabis use

Blood is generally considered to be the most useful sample for identifying drugs for quantitative analyses. However, being an invasive procedure, the collection of blood requires trained medical personnel which effectively rules out routine blood sampling during road side drug testing by traffic police. Alternative matrices, such as urine, saliva and sweat, have been explored for their functionality and predictive validity in roadside drug testing. In countries with 'impairment' legislation, roadside analysis can confirm a police officer's suspicions and focus their attention on drugs. In countries with 'per se' legislation, screening devices are crucial to detect driving under the influence of cannabis, before subsequent measures can be taken: i.e., blood sampling. Non-invasive collection of saliva and sweat is easy to perform and cost effective because this can be carried out by untrained personnel. Moreover, the presence of cannabinoids in saliva offers a better indication of recent use of THC than when the drug is measured in urine. The biological picture provided in urine is complex in the case of cannabis. The drug may only be present as a metabolite, i.e. THC-COOH, even though the parent drug is no longer present in the blood. Traces of THC-COOH can be detected in urine up to three or four days after smoking a single joint, or up to weeks after repeated smoking. Saliva is the only fluid that could be used as a substitute biological indicator for blood, since drug concentrations in saliva may appear in almost the same concentration as unbound drug in plasma (36). However, the correlation between salivary and plasma drug concentration (S/P ratio) has not been determined for most psychoactive compounds, including THC. In general, once drugs have been eliminated from the buccal cavity there is thought to be a high correlation between salivary and blood concentrations for many compounds (37). It should be noted however that cannabis produces elevated salivary concentrations for several hours after smoking due to contamination of the oral cavity. In addition, THC does not readily pass from blood into saliva

because it is highly protein bound and cannabis itself inhibits salivary secretion. Sample collection time thus may cause variability of S/P ratios in cannabis users (36).

A European union project on roadside drug testing (ROSITA) recently evaluated currently available onsite drug tests in urine (eight products), saliva (two products) and sweat (one product) in 2968 subjects. The consortium consisted of contractors from 8 European countries, including national toxicology institutes, university departments of legal medicine and manufacturers of onsite drug tests (38). A comparison between urine, saliva and sweat samples by means of a reference laboratory GC-MS analysis revealed a high predictive accuracy, i.e. 91%, of THC in saliva samples as compared to blood. The correspondence between blood and sweat or urine was not as good as for saliva, i.e. 78% and 83%. Both sweat and urine analyses produce many 'false positives': i.e., the presence of THC in sweat or urine is not confirmed in blood. Unfortunately, the commercially available on-site devices for detecting THC in saliva were poorer predictors than GC-MS techniques. They produced many 'false negatives' and correctly identified only 18-25% of the THC positives in reference blood (38-40). A possible explanation for the lack of sensitivity of on-site saliva drug tests is their inability to detect THC in low concentrations. Commercial on-site urine tests demonstrated better accuracy than on-site sweat and saliva tests, i.e. 90%, but also produced many 'false positives' when THC-COOH was present in urine (38). In conclusion, none of the currently available on-site drug tests for urine, saliva and sweat possesses sufficient predictive validity to replace blood sampling as a means of demonstrating recent THC use or impairment. They may however provide sufficient grounds for suspecting cannabis use in drivers to justify imposing a further corroborative measurement of THC in blood.

5.6 Conclusions

The epidemiological and experimental literature has provided conflicting information on the role of THC in performance impairment and motor vehicle crashes. Most epidemiological studies show little evidence that drivers who only used cannabis are more likely to cause accidents than drug free drivers. In contrast, experimental studies have convincingly and repeatedly demonstrated that THC in doses up to 300 μg/kg causes impairment of various cognitive and psychomotor functions and of driving performance as measured in driving simulators or on-the-road tests. The magnitude of this performance impairment was comparable to that of the alcohol induced performance impairment seen at BAC ≥0.05 g/dl, and should be regarded as practically relevant. The reason for the apparent discrepancy between experimental and epidemiological results is largely unknown, but may be related to inadequate attribution of cannabis use to crashed drivers in epidemiological surveys. These frequently relied on the detection of an inactive metabolite of THC in drivers' urine to establish the use of cannabis. However, this metabolite, THC-COOH, can be detected in body fluids for hours or days and is not a reliable indication of recent cannabis use or impairment. Recent exposure to cannabis can only be safely assumed in the minority of culpability studies that determined cannabis use by the presence of THC in the blood. This latter procedure was only followed in four surveys. In two of these studies, the culpability odds ratios for THC positives were generally higher than those for THC-COOH positives. Moreover, the culpability odds ratios for THC positives were two t six times higher than those for drug free drivers, depending on the concentration of the drug detected in blood. Together, these data indicate that recent cannabis use may increase the crash risk, whereas past use of cannabis as determined by the presence of THC-COOH in drivers does not.

There are more general limitations to culpability studies that should be considered as well. The analysis assumes that drug free drivers involved in crashes are representative of the driving population at large. If so, culpability odds ratios may well provide reliable estimates of the odds ratios that would be obtained in case-control studies using non-crash drivers from the general driving population as controls. However, this may not always be the case. Bates & Blakely (4) pointed out

that outcome misclassification may introduce bias. Determination of culpability status is not an exact process, and there may be a tendency to misclassify drivers who are in fact responsible for the accident as non-culpable, or vice versa. It is remarkable in this respect that the ratio of culpable to non-culpable drivers in the survey by Drummer et al. (20) was about five to ten times higher than the same ratio in other surveys. This difference could be due to larger THC concentrations found in crash victims in Drummer's survey, but may also reflect a structural difference in outcome classification.

Bias may also occur if the control group of drug free cases is not controlled for confounding factors. Confounding could occur if there are lifestyle factors associated with cannabis use that are also independent risk factors for traffic crashes, such as age, sex, time of accident or the use of alcohol. Confounding by alcohol is always avoided in culpability studies by excluding cases with alcohol present in their blood from statistical analyses of risk associated with cannabis. However, the potential role of other confounding factors is generally not taken into consideration. For example, Drummer et al. (20) do not mention whether their cases and controls were matched for differences in lifestyle, other than alcohol. The possibility therefore exists that they identified an elevated risk of dying in road accidents for drivers who are young, male and driving at the weekend, instead of an elevated crash risk after recent use of THC as suggested. To further explore this possibility, we conducted a logistic regression analysis on Drummer et al.'s data, taking into account potential confounding factors such as age, sex, crash type, jurisdiction and year of collection. The analysis confirmed Drummer et al.'s earlier results and provided extra support for their view that the rise in culpability ratio was caused by cannabis and not by some other factor.

Experimental and epidemiological research converges on the fact that the association between THC and driver impairment is dose related. The odds ratios for accident culpability were shown to increase with increasing concentrations of THC in the blood of injured drivers. Likewise, performance impairments in psychomotor or cognitive tests and lateral position variability in experimental driving tests were shown to gradually increase with increasing doses of THC. This may prove relevant, since it has been argued that most of the THC doses used in experimental research have been smaller than those used for recreational purposes in real life. In a dose finding study by Robbe (1), 23 subjects who were all recreational users of THC indicated that they had achieved their desired psychological effect after smoking a mean dose of 300 μg/kg THC[2]. The range of this preferred dose varied between 194 and 524 μg/kg THC, indicating considerable inter-individual variation. It is thus likely that drivers in the general population will at times use doses that are higher than the ones used in experimental studies or associated with the average concentrations detected in epidemiological surveys. It can be predicted from the currently available experimental data that the use of higher doses (i.e. >300 μg/kg THC) will be associated with severe driving impairment, equivalent to BACs >0.08 g/dl.

The clear dose/concentration-effect relationship between cannabis and driver impairment or crash risk raises the question of whether a 'per se' limit above which drivers are always at risk can be identified. Meta-analyses of experimental performance data provide some good indications that maximal performance impairment will be achieved at THC concentrations ≥ 14 ng/ml. However, it has not yet been established whether the performance impairment observed at such concentrations also coincides with an elevated crash risk. The elevated culpability ratios observed in Drummer et al.'s [20] analyses applied to a large group of THC positives with widely varying plasma concentrations, i.e. between 1 and 228 ng/ml THC. It is impossible to tell which part of the distribution was actually responsible for the elevated OR observed in this sample. The elevated mean OR pertains to the whole distribution range and may be much less in cases with low THC concentrations and much higher in cases at the opposite end of the distribution. The same argument pertains to the analysis conducted by Swann [21]. What is needed is a detailed analysis of the culpability ratios for THC positives as a function of THC concentration. Hunter et al. [18] provided

a first indication of a dose related effect of cannabis on culpability ratios, but their findings mainly applied to THC concentration ranges below 2 ng/ml. Their approach should now also be extended to cases with higher THC concentrations in order to confirm and support current ideas about per se limits from experimental performance data.

It is also absolutely clear from epidemiological and experimental studies that the combination of alcohol and THC plays a major role in performance impairment and motor vehicle crashes. The epidemiological evidence shows that the combination of alcohol and THC is over-represented in injured and dead drivers, and particular in those responsible for causing the accident. Experimental studies have shown that alcohol and THC combined can produce severe performance impairment even when given at low doses. The combined effect of alcohol and cannabis on performance and crash risk appeared to be additive in nature: i.e., the effects of alcohol and cannabis combined were always comparable to the sum of the effects of alcohol and THC when given alone.

Experimental studies also indicate that not all driving tasks are equally sensitive to the detrimental effects of THC. Performance was always worst in tests measuring driving skills at the operational level, i.e., tracking and speed adjustment, as compared to performance in tests measuring driving performance at the manoeuvring level, i.e., distance keeping and braking, and the strategic level, i.e., observation and understanding of traffic, risk assessment and planning. Strategic and manoeuvring levels are particularly demanding on resources, in that they require effortful processing and attention. Thus processing is relatively slow and flexible. In contrast, the operational level is considered to be an automatic, routine process, which is fast and relatively inflexible. Drivers may be particularly vulnerable to the detrimental effects of THC in traffic situations where they specifically employ driving skills that operate at lower levels of automation, such as during highway driving. The implication may be that drivers under the influence of THC may be more likely to be involved in specific types of traffic accidents, such as single vehicle crashes. By definition, culpability studies have neglected this possibility, since drivers involved in this type of accident are practically always responsible, irrespective of drug use.

Some experimental studies have indicated persistent cognitive and psychomotor deficits as a result of chronic use of cannabis. However, most of the research on chronic cannabis users which supports this idea is somewhat flawed by the lack of experimental control over confounding variables such as recent use of cannabis and or withdrawal symptoms. The results from these studies were confirmed by studies that were sufficiently well designed to assess the long-term effects of cannabis use on cognition. They clearly showed that the cognitive deficits that are present in chronic users of cannabis during the first days of abstinence largely disappear during a prolonged period of abstinence. These results strongly indicate that THC does not produce any gross changes in cognitive or psychomotor functions that are permanent or irreversible.

A final comment should be made concerning the value of roadside tests of urine, saliva or sweat for detecting recent cannabis use. None of the commercial test devices currently available demonstrated high levels of accuracy or selectivity as compared to blood tests. Moreover, roadside drug tests only determine the presence/absence of cannabis and do not offer a quantitative analysis of the drug's concentration. These would have limited value in countries attempting to introduce per se legislation with analytical limits for THC concentrations analogous to BAC limits. More sophisticated techniques are needed to provide a quantitative measure of THC concentrations in saliva as well. In the ROSITA project, laboratory GC-MS analyses of saliva samples demonstrated relatively high levels of accuracy. This suggests that oral fluids such as saliva are promising specimens for detecting cannabis, and that more accurate and more sensitive commercial onsite tests may be developed in the near future. At present blood testing remains the most effective procedure for detecting and quantifying recent cannabis use in drivers. However, there is international consensus that blood samples should only be taken if there is reasonable suspicion that

a driver is under the influence of a substance. On-site drug tests, particularly of urine, are certainly suitable for providing an early indication of cannabis use in drivers and could support drug law enforcement by providing the legal justification for subjecting a driver to blood sampling.

5.6.1 In brief

THC has been shown to impair cognition, psychomotor functions and actual driving performance in a dose related manner.

The degrees of impairment observed in laboratory or actual driving tests after doses of up to 300 μg/kg THC were comparable to the impairing effects of a dose of alcohol producing a BAC ≥0.05 g/dl, the legal limit for driving under the influence in most European countries.

There is no indication that past use of THC alone affects crash risks, but there is growing evidence that recent use of THC increases the risk of culpability for motor vehicle accidents compared to drug free drivers, particularly at higher concentrations.

The detrimental effects of THC appear more prominently in highly automated driving behaviour, as compared to more complex driving tasks that require conscious control.

The effects of THC and alcohol on driving performance and the risk of motor vehicle crashes appear to be additive, but the sum can be large and potentially dangerous. Combined use of THC and alcohol produces severe driving impairment and sharply increases the risk of drivers' culpability for accidents as compared to drug free drivers, even at low doses.

Cognitive deficits observed in chronic THC users are probably related to recent cannabis use or withdrawal symptoms, and were shown to virtually disappear after a prolonged period of abstinence.

Commercially available on-site drug tests of urine, saliva and sweat offer no full proof indication of recent cannabis use. They may however arouse reasonable suspicion of cannabis use in drivers sufficient to justify imposing a further corroborating measurement of blood THC.

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6. PREVENTION OF CANNABIS USE AND MISUSE

Pim Cuijpers

Summary

Traditional goals and target groups of prevention, and the results of evaluation research

Dozens of drug prevention programs have been developed and examined in the past few decades. Most drug prevention interventions are aimed at tobacco, alcohol, illegal drugs, or any combination of substances. No research examining or describing preventive interventions aimed only at cannabis use or misuse was found. Most research is American, scarcely any European studies have been published in the international literature.
Drug prevention programs have different goals, including: increasing our knowledge about drugs; reducing the use of drugs; delaying the onset of first use; reducing misuse of drugs; and minimising the harm caused by the use of drugs. Most research has been conducted on school-based drug prevention programs. School-based drug prevention programs can reduce the use of drugs, including cannabis, provided that they use interactive methods that foster the development of interpersonal skills. All school-based drug prevention programs (interactive and non-interactive) can increase our knowledge about drugs. Although effective school-based prevention programs are available, their dissemination in schools has not been successful for most programs.

Family-based drug prevention: a new emerging area

Family-based drug prevention programs are a promising new area of drug prevention. The results of effect research in this area are encouraging.

Mass media campaigns or community intervention?

Most research examining the effects of mass media campaigns about drugs is flawed by major methodological problems. Research suggests that these campaigns cannot reduce the use of cannabis, but they may increase the effects of community based interventions on substance use. No negative effects have been found for mass media campaigns. Community interventions (a combined set of activities organised in a specific region or town, with the participation of the residents) are probably more effective than each of the interventions alone.

Cannabis prevention : a separate issue?

Specific education programs focusing on cannabis use are not acceptable for most schools, as they would have to present separate programs for several substances, with many common elements. Furthermore, there is no evidence that targeting one substance only is more effective than targeting substance use in general.
Separate prevention programs could be developed in so-called 'coffeeshops' in the Netherlands, where many cannabis users can be found. Pilot projects could examine these new possibilities.

1 *The author thanks Mr. Richard Muller from the 'Schweizerische Fachstelle für Alkohol- und andere Drogenprobleme' for his valuable contribution to the conception of this paper.*

Neglected areas of prevention research

Most prevention research is American and we cannot be sure that the results of these studies are also valid in European countries. No research has examined interventions aimed at preventing the onset of schizophrenia or other mental disorders caused by the use of cannabis, nor interventions aimed at preventing hard drug use by cannabis users.

6.1 Introduction and main issues

In the last three decades, dozens of interventions have been developed in Western countries to prevent the use and the misuse of cannabis and other drugs. Most of these interventions are conducted in schools, but there are also interventions aimed at the parents of adolescents, interventions aimed at professionals working with drug users, and interventions consisting of activities aimed at schools, parents, and the larger community as well. Furthermore, mass media campaigns aimed at the use and misuse of drugs are conducted regularly in many Western countries.

In this chapter we present:
- an overview of the goals, target groups and general contents of these interventions,
- and an overview of the scientific research examining the effects of the interventions.

Most drug abuse prevention interventions are aimed at tobacco, alcohol, illegal drugs, or any combination of substances. We found no research in the international literature that examined or described preventive interventions aimed at cannabis use or misuse only. In this paper we will therefore describe drug abuse prevention programs in general, focusing where possible on cannabis use.

Most research examining the effects of drug prevention programs has been conducted in the United States. In a recent systematic review of the international scientific literature, we found many studies on this topic but scarcely any about European interventions (1). Because the results of these international studies are not automatically valid in European countries, the paragraphs describing this research should be interpreted with caution.

6.2 Classification of preventive interventions

Traditionally, preventive interventions have been classified into the categories of primary, secondary, and tertiary prevention. Primary prevention is aimed at preventing the use of drugs altogether, or at preventing abuse and dependence disorders as defined by diagnostic criteria. Secondary prevention is defined as the early identification and treatment of people who use or misuse drugs. Tertiary prevention is defined as the treatment of identified cases to reduce the damage caused by the drug use or misuse. Tertiary prevention is now in fact generally considered to be treatment, and not prevention. Tertiary prevention will not be discussed in this chapter.

In recent years, a new more specific framework for defining preventive interventions has been spreading rapidly among scientists working in the area of addiction and mental disorder prevention (2,3). Three categories of preventive interventions are distinguished:
- *Universal* preventive interventions are aimed at the general population or a part of it that is not identified on the basis of individual risk factors (e.g., mass media campaigns and school-based programs aimed at all students).
- *Selective* interventions are aimed at individuals or groups of people who have an increased risk of drug use problems (e.g., programs aimed at children of alcoholics or high-risk inner city youth).
- *Indicated* prevention is aimed at subjects who do not have addiction problems according to

diagnostic criteria, but who have some early characteristics of problematic use (e.g., interventions aimed at young people experimenting with drugs).
- Early intervention is aimed at subjects who do have addiction problems according to diagnostic criteria, but who have not yet considered seeking help. In practice, it is often not possible to differentiate between indicated prevention and early intervention. In this paper, we will consider them as one category of interventions.

6.3 Goals and settings of preventive interventions

- Preventive interventions in the three categories described above may have different goals, including:
- Increasing our knowledge about drug use by adolescents;
- Reducing the use of drugs;
- Delaying the onset of first use;
- Reducing misuse and abuse of drugs;
- Minimising the harm caused by the use of drugs.

The interventions that have been developed are conducted in several settings. Most interventions are developed for schools, but there are also several interventions aimed at the families of (potential) drug users. Other interventions are aimed at the broader community, and may include mass media interventions, community mobilising committees, educational activities in bars, cafes, discos, and house parties, and training of general practitioners, teachers, and other professionals who work with adolescents. Most interventions are aimed at children and adolescents between the ages of ten and sixteen. It is during this age span that most people start using substances, and preventive interventions try to intervene just before the adolescents start using drugs. Table 1 presents an overview of universal, selective, and indicated preventive interventions in school, family, and community settings.

Table 1.
Examples of universal, selective and indicated preventive interventions in school, family, and community settings

	School	Parents/family	In the community
Universal	- lessons about drugs for all students in high schools	- parent training about parenting and drug use, for all interested parents - homework assignments for parents and child, taken home from school	- mass media campaigns (all residents) - 'community' interventions - prevention at the workplace - community mobilising committees - educational activities in bars, discos
Selective	- support groups for children of alcoholics - training programs for high risk youths	- parent training for addicted parents - support groups for parents of high-risk youths (inner city, minority, etc.)	- mass media campaigns (high- risk groups) - prevention at the workplace (high-risk groups)
Indicated[a]	- mentor programs for first offenders - screening and early intervention programs - counselling programs	- parent training for youths with beginning or early drug problems	- training health professionals (GPs, social workers) and teachers in screening for addiction problems - training of 'coffeeshop' owners (Netherlands)

[a] *including early intervention*

Prevention interventions are ideally based on scientific knowledge about the prevalence of drug use in the target population, the age of first use, determinants of drug use, patterns of drug use, mental health problems in the specific population, and a theoretical view of the intervention components that may change behaviour. However, preventive interventions are often not developed systematically in daily drug prevention practice. In recent years various manuals, guidelines and overviews have been published to assist with the systematic development of complex interventions, such as drug abuse prevention programs (e.g., the framework for developing and evaluating randomized controlled trials for complex interventions to improve health, from the British Medical Research Council) (4).
In the following paragraphs we will focus on the main categories of preventive interventions, school-based interventions, family based interventions, mass media campaigns and interventions in the community, and describe the research that has been conducted in these areas.

6.4 Interventions

6.4.1 School-based interventions

Three phases can be distinguished in the development of school-based drug prevention programs over the past thirty years (5-7). In the first phase (early 1960s to early 1970s), programs largely focused on providing information about drugs and the risks of drug use. During the second phase (early 1970s to early 1980s), so-called affective programs predominated. Most of these programs were not drug-specific but concentrated on broader issues of personal development, such as decision making, clarification of values and stress management (5). In the third phase (early 1980s to date), the social influence model has dominated school-based drug prevention programs. Resistance skills are developed in this model, sometimes in combination with broader personal and social skills (including components of stress reduction and decision making) (8).
During these three phases of program development, several hundred studies have investigated the effects of drug prevention programs and several dozen have been found to be methodologically well-designed (9). In the last two decades several meta-analyses have been conducted; their aim has been to integrate the results of individual studies statistically in order to get a better estimate of the real effects of prevention programs than individual studies can provide. The most recent and comprehensive meta-analysis found that drug prevention programs have large and significant effects on students' knowledge about drugs (9). Several of these programs are aimed at illegal drugs, including cannabis, and it is well established that prevention programs lead to increased knowledge about cannabis use.
This meta-analysis also found that interactive drug prevention programs that foster the development of interpersonal skills result in significant reductions of drug use, while non-interactive programs do not. In interactive programs the lessons are less structured and the focus is not on didactic presentations but on discussions, role-playing, and interaction between students. Non-interactive programs are structured, they focus on oral presentations by the teacher, and do not stimulate interaction between students. No separate results are presented for cannabis use in this meta-analysis. An earlier, comparable meta-analysis found that there were only minor differences between the effects of drug prevention programs on separate substances (10).
The conclusions from these meta-analyses should be interpreted with caution, as the interventions that are examined vary greatly from study to study, they are based mainly on self-report measures, and studies differ widely their in design, evaluation methods and measurements of substance use. Despite these limitations, however, the conclusion that interactive programs focussing on the development of interpersonal skills are superior to other programs is the best summary of research results available to date.

Most school-based prevention programs are universal interventions, aimed at all students regardless of their risk status. Several studies have also examined the effects of selective and indicated

prevention programs on drug use. However, the number of these studies is considerably smaller than the number of studies of universal programs. The results of the studies examining selective and indicated prevention programs are not conclusive. Some studies find no effects on substance use (11,12), others do indicate some positive effects (13-17). Therefore the conclusion must be that there is no convincing evidence that selective or indicated school-based prevention programs can reduce substance use or misuse.

6.4.2 Family based interventions

There is no doubt that parents have an important influence on the use of substances by their children, through both genetic factors (18) and social factors such as parental neglect or abuse (19). Protective parental characteristics, such as a close relationship between parents and children and involvement of the parents in adolescent activities outside the family (20), reduce the chance of substance use in adolescents. It is assumed that the influence of parents decreases when children become adolescents while the influence of peers increases strongly at this age (21). But there are also indications that the parents continue to have a strong influence: for example in the selection of peers (22), or as models for a lifestyle that their children have internalised earlier. The parents can also function as role models for their children, and their peers and their substance use may increase the availability of drugs to their children.

Several interventions have been developed for parents and families to prevent or reduce substance use and misuse in their children. A recent systematic review of the literature found seven family based drug prevention programs whose effects were examined in eight controlled studies (1). The goals, target populations and contents of the interventions were diverse, and the studies were of varying quality.
There is some evidence that universal family based prevention programs may reduce drug abuse. An example of a universal family based program is the 'Preparing for the drug free years' program, a five session training program in which any parent who is interested can learn to identify risk factors for drugs use, parenting skills, and conflict management skills. In a well-designed randomised study of 667 families, it was found that adolescents whose parents participated in the program used less drugs than adolescents whose parents received only a minimal intervention (23-25). In another universal intervention children take a number of homework assignments home from school. They are supposed to work on these assignments together with their parents (the 'Keep A Clear Mind' project). In a randomised trial in which 511 students participated, no difference in drug use was found between adolescents participating in the project and students on a waiting list (26).
There is also some evidence that selective and indicated family based interventions may reduce drug abuse and risk factors for drug use. For example, the 'Strengthening Families' program is a training program for addicted parents, aimed at reducing drug use and other problem behaviour in their children. In this program, two parallel fourteen-session training courses are delivered to parents (parenting skills, communication skills) and to their adolescent children. A randomised trial in which 118 families participated found positive and significant effects on drug use in adolescents and their parents who participated in the program, compared to families who did not participate (27,28). Another study found that the 'Stars for Families program' had positive and significant effects on substance use (29,30). In this program, high-risk families receive individual health advice and skills training for parents. Unfortunately, only the effects of the intervention on alcohol use were examined, but not the effects on cannabis use. Another program, 'Dare to be You', is aimed at very young high-risk children (two to five years), and effect research did indicate positive effects on the children and good results on the style of upbringing, but the children were too young for effects on drug use to be found (31).

Overall, we have to conclude that although family based interventions are an interesting new way of preventing cannabis and other drug use in children, there is insufficient evidence for their effectiveness to warrant dissemination of these programs on a large scale. Recruitment of families

who are expected to benefit most constitutes an important problem in most family interventions. It is important, however, to encourage pilot projects and research in this promising area.

6.4.3 Mass media interventions

Mass media campaigns on substance use are conducted regularly in most Western countries. However, only a few studies have examined the effects of mass media campaigns on drug use, and the studies that have been conducted are hampered by several methodological shortcomings.

A recent systematic literature review found only five studies (published after 1990) examining the effects of mass media campaigns aimed at drug or substance use in the international literature (32). Three of these did not include a control group (33-35). Because it is often not feasible to use proper control groups in studies examining the effects of mass media campaigns (as the total population is exposed to the intervention), it may be acceptable not to use a traditional pre-post randomised intervention-control group design, but rather a time series design in which several measurements are conducted before and after the intervention. The three uncontrolled studies did not use such a design either. In one of the remaining two studies that did use a control group, the effects on drug use were not measured (36). The other study examined the effects of the 'Midwest Prevention Project' and was relatively well-designed, but this project was in fact a large community intervention consisting of several diverse components, such as school interventions, community mobilisation, and mass media campaigns (37-39). The effect study of this project did not make it possible to determine which component of the set of interventions was responsible for the effects. We must therefore conclude that there are no recent well-designed studies giving information about the effectiveness of mass media campaigns on drug use. A much-cited review of older studies (40) also concludes that the quality of most studies in the area of mass media campaigns on drugs use is inadequate.

There is a broad consensus within the field of health education that mass media campaigns are not capable of changing risky behaviour in general (32). This is also supposed to be true of mass media campaigns on substance use. However, there are indications that mass media campaigns can increase knowledge and may strengthen the effects of local or community interventions (37).

6.4.4 Community interventions

In recent years, researchers, practitioners and policy makers have become increasingly interested in 'community interventions'. In these interventions, a combined set of activities is organised in a specific region or town and aimed at adolescents, as well as parents and other people and organisations. An important characteristic of such community interventions is that people living in the community play an important role in deciding which interventions are developed for whom (41). The increasing popularity of community interventions is the result of the growing consensus among scientists and practitioners that the combination of several interventions at different levels is more effective than individual interventions.

Within the field of community interventions aimed at substance use, several well-designed studies have been conducted on the prevention of alcohol problems (42-45). These studies have shown that it is possible to significantly reduce alcohol use, alcohol related violence, alcohol related admissions to hospital, and drink-driving.

Very few studies have been conducted in the area of community projects aimed at drug use, the most important exception being the studies examining the effects of the 'Midwestern Prevention Project'. The interventions in this project include school programs designed to develop skills in resisting peer pressure to use drugs and knowledge about drugs (eighteen lessons), along with mass media campaigns, several activities to stimulate the involvement of parents in drug prevention, and a co-

ordinating committee in the local community. Two studies have examined the effects of the Midwestern Prevention Project. In the first quasi-experimental study, 42 schools were assigned to an experimental (community intervention) or control (mass media campaign only) condition. Significant effects of the community intervention were found on substance use, including cannabis use, one year after the intervention, with 7% of the experimental group and 10% of the control group using cannabis. In a second, randomised trial, 57 schools were included (39). The results of this study were comparable, but because more follow-up measurements were taken it was able to show that the effects of the intervention decreased over time, until no effects were found any longer three and a half years after the intervention.

In summary, there is not enough evidence to conclude that community prevention interventions can reduce cannabis use in the community. Because of the research in other areas of community interventions aimed at substance use, especially alcohol, it seems reasonable to assume that combined sets of interventions in a specified community may be more effective than each of the interventions alone.

6.4.4.1 Other preventive interventions in the community

Apart from 'community interventions', in the sense of a combined set of interventions in a specified region, several other preventive interventions have been developed that can be conducted in communities. Examples are training of general practitioners or teachers in recognising drug problems and early interventions; educational activities at dance parties; specific interventions for high risk groups or minority groups; and interventions at the workplace. Most of these interventions are not specifically aimed at cannabis, but at substance use and misuse in general. In the Netherlands, where cannabis is sold in 'coffeeshops', interventions in these coffeeshops are feasible, such as providing cannabis information programs or training coffeeshop owners to recognise problematic use and refer users to treatment services. Unfortunately, hardly any research examining the effects of these interventions on cannabis use or misuse has been conducted and it is not clear if these interventions can prevent the use or misuse of cannabis (46).

6.5 Research into the cost-benefit and cost-effectiveness of drug abuse prevention

In the past decades, only a handful of studies examining the cost-benefit and cost-effectiveness of drug abuse prevention have been conducted and the results have found to be elusive. A recent review of these studies has only resulted in some evidence suggesting that exposure to drug abuse prevention programs could be justified on the basis of the data derived from these studies (47). There is no research available that has examined the cost-benefit and cost-effectiveness of drug abuse prevention specifically aimed at cannabis use.

6.6 Dissemination

Dissemination of effective interventions is an important issue in drug prevention. There is sufficient evidence that drug prevention at school is potentially effective in reducing drug use. However, many of the more effective prevention programs have been developed in research settings and do not fit into the school system easily, because of the large number of sessions and the requirements of scientific research. Other programs are disseminated widely in schools, but are not effective in reducing substance abuse. The most well-known example in the international literature is the DARE program. This is the most widely used drug prevention program in the United States, but many well designed studies have shown that it has no significant effects on substance abuse (48-50). Although the DARE program has proven to be ineffective, the program is now being implemented on a large scale in several European countries, including the UK and the Netherlands. This clearly

illustrates the fact that successful dissemination is possible even though the program has no effect on drug use.

One of the next major steps in drug abuse prevention must be the dissemination of effective prevention programs and the results of the scientific knowledge base that has been built up in recent decades. That it is possible to disseminate widely drug prevention programs which have been proven to be effective is shown by the Dutch 'Healthy School and Drugs' project. This is now used in 64% to 73% of Dutch secondary schools (51).

6.7 What determines the effectiveness of school-based drug prevention programs

It is not clear which characteristics make prevention programs effective. It is known, as was indicated earlier, that school-based drug prevention is effective when it is interactive. There are some indications that community interventions consisting of several activities in different settings are more effective than each of the components separately. It is also plausible that long-term interventions are more effective than short-term interventions, as several studies have shown that the effects of short-term interventions slowly fade away. There is, however, consensus among experts that several other components are essential for interventions to be successful (52-54). In general, drug prevention programs should (53):

- aim to reduce risk factors and to improve protective factors;
- be long-term;
- be of low intensity for low-risk groups and of high intensity for high risk groups;
- consist of several interventions aimed at several settings in a community;
- take the cultural background of the targeted population into account;
- consider the developmental phase of the targeted age group.

Furthermore, experts agree that school-based programs should:

- be based on a solid theoretical base and scientific knowledge;
- teach skills to resist peer pressure for drug use;
- present accurate information about drugs to young people, depending on their developmental stage;
- teach general coping and social skills;
- consist of at least 10 lessons in the first year, and five in the following years;
- be culturally sensitive.

Unfortunately, although most of these characteristics seem logical there is no solid research base confirming that these are the critical components of drug prevention programs. More research is clearly needed in this area.

6.8 Conclusions

In this chapter we found that many universal, selective, and indicated interventions have been developed for use in schools, in the family and in the community to prevent substance use and misuse. Most effect research has been conducted in the area of school-based drug prevention, and this research indicates that school programs are effective in reducing substance use, including cannabis, if they use interactive methods. Other drug prevention programs in the family or in the community have not been subjected to sufficient research to enable us to conclude that they reduce substance use or misuse. However, several of these interventions, such as parent training programs and community interventions, are promising and may indeed reduce substance use and misuse.

An important question is whether preventive interventions aimed specifically at cannabis should be developed, or interventions aimed only at substance use in general or at multiple substances.

Evidence from school-based drug abuse preventive interventions shows that aiming at one substance is no more effective than aiming at substance use in general (9). From the viewpoint of people working in the field, it is more efficient to focus on multiple substances in most settings. For example, schools are often very interested in drug prevention programs, but they do not have enough time to devote separate series of lessons to tobacco, alcohol, and each of the most widely used illegal drugs. At this point, therefore, it is not advisable to develop separate preventive interventions for cannabis use. One exception in the Netherlands could be the 'coffeeshops' where cannabis is sold. This setting offers new possibilities for prevention and early interventions, because many cannabis users can be reached through this channel. Examples of such programs are training of coffeeshop owners and educational activities in these outlets.

The majority of drug prevention programs are aimed at children and adolescents aged ten to twenty years. Very few preventive interventions have been developed for other age groups. It is known that in most cases drug problems disappear spontaneously when young people grow up. Only a very small proportion of people continues to have drug problems after the age of about twenty-four. It is very useful to examine the characteristics of those with continuing problems, and develop more intense prevention programs for subjects with a high risk of ongoing problems.

Several goals of drug prevention programs were presented at the beginning of this chapter, such as increasing our knowledge about drug use by adolescents, delaying the onset of first use, reducing drug use and misuse, and minimising the harm caused by drug use. Most research has concentrated on the effects of prevention programs on knowledge and the use of drugs. Some studies have also examined the effectiveness of prevention programs in delaying the onset of drug use. Few studies, however, have examined whether it is possible to reduce the number of new cases of problematic drug use. Accordingly, it is not known whether the number of subjects with serious drug problems (according to the DSM-IV diagnostic criteria) is significantly reduced by drug prevention programs, although this is in fact one of the most important issues from a public health perspective.
It has been suggested that the use of cannabis may cause schizophrenia in certain cases, but there is insufficient evidence to confirm this hypothesis (55). It is plausible, however, that cannabis use may provoke the first episode of schizophrenia in individuals with a predisposition for this disorder (56-58). We found no studies in the international literature that examined interventions aimed at preventing the onset of schizophrenia or other mental disorders allegedly caused by the use of cannabis. We also found no interventions aimed at preventing hard drug abuse in cannabis users.

In the last few decades, major advances have been made in the prevention of abuse of cannabis and other substances. This includes the development of school-based programs which are capable of reducing the use of cannabis and other drugs. It also includes the development of many new interventions, such as parent training, mass media campaigns, and community interventions that have promising effects. But many questions still remain unanswered. Can we reduce major drug problems with prevention programs? Can we prevent drug problems of a chronic nature? And how should effective programs be disseminated? These and other questions are the ones that must be addressed in the decades ahead.

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7. MEDICINAL CANNABIS: A QUICK SCAN ON THE THERAPEUTIC USE OF CANNABIS

Willem K. Scholten

Summary

Cannabis and cannabis derived preparations have been used as a medication in many cases and for many physical diseases. Various thorough state of the art reviews show that there is an abundance of case reports on this subject and small-scale clinical studies have also been carried out in recent decades. However, none of the studies and reports published can give sufficient or conclusive scientific evidence about its alleviating effects. This is mainly due to the poor overall quality of the study designs and lack of statistical power. However, some provide promising indications of the efficacy of cannabis as a medicine; in conditions causing chronic pain and slight spasticity, for instance, and in cases of asthma or treatment conditions causing nausea and vomiting.

The world-wide standard requirements for acceptance of any preparation as a medicine relate to its quality, efficacy and safety. If cannabis is to be used as a medicine it must satisfy these requirements.

To enhance further studies a network to share information is desirable, as well as international co-operation in finding enough patients for international clinical studies.

7.1 Introduction and main issues

Cannabis has been used for years by individual patients suffering from a variety of somatic diseases to alleviate symptoms such as pain, nausea and a general feeling of ill-being. Based on their experiences and small-scale studies, much has been written about the possibility of using cannabis as a medicine. Various thorough state of the art reviews have also recently been published on this subject. Although there are sufficient indications to justify taking the subject of cannabis as a medication seriously, a prominent and unanimous conclusion from all the reviews appears to be that almost none of this abundance of publications allow satisfactory answers to be given to the question of whether this drug really can be a valid and reliable medicine in certain states of ill health. If we wish to pursue this question further, we now need to design and carry out new studies that can actually meet the requirements with which preparations must comply in order to be acknowledged as medicines.

It does not seem efficient to produce another state of the art review here. Instead I have chosen to present a quick scan of the state of the art, followed by an overview of the most important questions that must be answered before decisions can be made about cannabis as a medicine.

7.2 State of the art

Numerous *pharmacological* studies have been carried out on animals with cannabis and dronabinol. However, very few *clinical* studies have been carried out, probably due to the administrative restrictions which have made it very difficult to undertake studies of this kind.

In the last few years several well analysed state of the art reviews have been published by various institutions and researchers, presenting an overview of past experience and research. One review by Williamson et al. was published in the reputable journal Drugs (1). In 1997 the British Medical Association published a review entitled 'Therapeutic Uses of Cannabis' (2). This also gives an overview of the situation and many suggestions for further research. The British House of Lords and the American Institute of Medicine have also published on the state of the art in the last few years (3,4). Three reviews have appeared in the Journal of Cannabis Therapeutics (5-7).

A study of the literature carried out by the Dutch Health Council in 1996 (8) highlights four applications for which cannabis and cannabinoids in particular are alleged to be effective:

- Chemotherapy-induced nausea and vomiting
- As an appetite stimulant in AIDS patients and cancer patients
- As a muscle relaxant and tremor suppressor in multiple sclerosis (MS)
- To lower intraocular pressure in glaucoma.

To assess the efficacy of cannabis and cannabinoids for these indications, a committee of the Health Council studied the literature published in the years 1970-1995. Based on this literature survey, the committee concluded that there is insufficient evidence to justify the medical use of cannabis. Furthermore, with regard to cannabis, the committee believes that physicians cannot accept responsibility for a product of unknown composition that has not been subjected to quality control. This does not only apply to smoking, but also to other forms in which the drug can be consumed, such as tea. The committee was unable to respond to the Minister's request for a comparison between the use of marijuana, or any other preparations of the hemp plant, and the active ingredient dronabinol (this is the International Nomenclature Name (INN) for Δ9-tetrahydrocannabinol as generally used in medicine and pharmacy), or other components, since there are no published reports on systematic research on this topic.

More recently two meta-analytical studies were published in the British Medical Journal.

- Systematic review of randomised controlled trials in patients with acute, chronic non-malignant, or cancer pain (9). Nine trials were included in a meta-analysis (222 patients). All the active substances tested were cannabinoids; no cannabis was tested. The conclusion of the authors was that cannabinoids are no more effective than codeine in controlling pain and have depressant effects on the central nervous system that limit their use. However, this conclusion can be criticised, because the study comprised only dronabinol and two synthetic cannabinoids, all taken orally. It did not extend to cannabis or other cannabinoids, or to other dosage forms.
- Systematic review of randomised controlled trials for controlling chemotherapy-related sickness (10). Thirty randomised comparisons were included in a meta-analysis (1,366 patients). Oral nabilone, oral dronabinol and intramuscular levonantradol were tested. The conclusion was that cannabinoids may be useful as mood-enhancing adjuvants for controlling chemotherapy-related sickness. (Exactly the same criticisms can also be levelled at this study). Many letters to the editor were published in the journal itself, most of them criticising both articles (11-15).

There are numerous case reports in which patients suffering from a variety of diseases said that they benefited from the use of cannabis, but case reports do not say anything from a scientific point of view. The medicine used in studies is often not clearly defined in medical literature. Furthermore, many studies were not carried out with cannabis, but with dronabinol, but were nonetheless presented as cannabis studies. Many patients say that this makes a difference. This difference can be explained by the fact that cannabis contains up to seventy cannabinoids in addition to dronabinol, as well as other classes of constituents. This means that the results of studies with dronabinol cannot automatically be extrapolated to cannabis or cannabis extracts.

What is noticeable from the literature is that, until a short time ago, hardly any good clinical studies had been carried out with cannabis. As the Dutch Health Council has already concluded, a major weakness of many studies is that the cannabis used is of unknown composition. Cannabis can show great variations, both in the strength of the cannabinoids and in their profile (the relative composition of the cannabinoids).

A large number of indications (tens, or even hundreds) for which cannabis could be used as a medicine are evident from the literature mentioned above and from patients' experiences, though there only seems to be a good chance of proving the effectiveness of cannabis scientifically for a few of them. Of these, the following conditions are the most promising:
- controlling nausea and vomiting (as with chemotherapy, radiotherapy and HIV therapy), and
- stimulating appetite, for instance in cases of cancer.

Other relatively promising conditions are:
- a combination of slight spasticity with pain, as in the case of multiple sclerosis,
- (chronic) pain,
- some extra-pyramidal symptoms (a group of neurological disorders), and
- asthma.

There also seems to be a relatively good chance of proving the efficacy of a cannabis-based medicine for Tourette's syndrome (16) and therapy resistant glaucoma, but there is a problem with local (ocular) administration in the case of glaucoma.

Cannabis use for medicinal reasons by patients with a somatic disease is relatively safe, on condition that it is not smoked; when smoked it has the same carcinogenic potential as tobacco (2). The alternatives are oral administration or inhalation using a vaporiser.
The acute toxicity of cannabis is very low; it is almost impossible to die of an overdose (users would have to eat or smoke their own weight in fresh cannabis, or 7,500 grams of dried cannabis, to achieve this). The principal side effects in therapeutic use are psychosis and euphoria. Little is known about this drug's addictive effect in medical use, though experience with the use of morphine for pain relief has shown that the risk of psychological addiction is low – much lower than when used as a stimulant. As the addictive effect of cannabis is also quite low when used as a stimulant, it may be assumed that this will always be very low in a medical setting.

When estimating the chronic toxicity of cannabis, it should be borne in mind that the doses used in therapeutic applications will probably be lower than those used for 'recreational' purposes, decreasing the risk of side effects. However, this does not imply that no research should be carried out into this question.

7.3 Requirements for the acceptance of medicines and questions still to be answered about the medical use of cannabis

The standard requirements that are laid down world-wide for acceptance of any preparation as a medicine relate to its quality, efficacy and safety. When cannabis is used as a medicine it must satisfy these requirements.

Quality requires the development of a dosage form of constant and known composition that is easy to administer by or to the patient. Clinical trials cannot be carried out without such a dosage form, as it is then not known what is being investigated, and it is also impossible to manufacture the product again if a positive result is obtained. (This reproducibility requirement is an important reason for not carrying out studies using confiscated cannabis).

Efficacy requires that high-quality clinical trials should demonstrate convincingly that the medicine is effective. This calls for a study that is at least controlled (against a placebo or therapeutic standard) and randomised and has sufficient statistical power. The studies must also be compared with existing therapies.

Safety requires that the side effects should be in reasonable proportion to the desired therapeutic effect.

Hardly any of the studies reviewed in all the state of the art reviews were designed to answer the questions that make it possible to satisfy these standard requirements. Such designs, allowing conclusive evidence to be collected, are essential if cannabis is to be considered seriously as a medication. Besides the need to develop a specific registered dosage form, the following questions must also be answered in order to develop good, optimally effective medicines:

- Is there any difference in action between (synthetic) dronabinol and cannabis? What is the role of other cannabinoids?
- Which cannabis profile is optimal in which condition?
- Is there any difference between oral and other dosage forms?
- Which dosage form is the most effective (can it be different for each condition)?

A number of recent studies can clarify these questions to some extent. However, most of these studies were primarily designed to answer questions about the efficacy and safety of the preparations under study. They cannot yet provide satisfactory answers to the more fundamental questions in this paragraph.

In some cases it may be useful to investigate the use of cannabis in conditions where the treatment with cannabis is not promising, but that are said by laymen to be useful. The results obtained in such cases, either negative or positive, can be useful for political decision-making, because they will show the public the reasons for refusing or permitting the use of cannabis for these purposes.

7.4 Recent efforts

In recent years greater efforts are gradually being made to assess the efficacy of cannabis and cannabis based medicines. The UK based company GW Pharmaceuticals has developed a preparation from cannabis on which Phase III studies (this is the phase in which the medicine is tested on a larger scale) are now being conducted. The Berlin-based Institute for Oncology and Immunology has also developed a preparation which is being tested in cases of multiple sclerosis and as an appetite stimulant in cachectic conditions.
Both these studies are being conducted with several hundreds of patients and are expected to yield findings from which statistically valid conclusions can be drawn. Depending on the outcome, these studies may lead to the registration of the preparations under study as medicines.

In November 2001 an international conference of policy advisors involved in medicinal cannabis was held to discuss policies in the participating countries. The report and reader of this conference give an overview of the situation in the participating countries (17). The delegates agreed that it may be useful to create a network to follow the process of clinical trials in the participating countries and to enhance collaboration for finding patients in international clinical trials.

7.5 Conclusions

Although numerous pharmacological studies have been carried out on animals with cannabis and dronabinol, very few clinical studies have been carried out. The quality of past clinical studies has generally been poor.

A large number of indications are evident from the literature mentioned above and from patients' experiences, though there only seems to be a good chance of proving the effectiveness of cannabis scientifically for a few of them. Of these, the following conditions are promising (starting with the most promising):

- controlling nausea and vomiting (as with chemotherapy, radiotherapy and HIV therapy);
- stimulating appetite, for instance with cancer;
- a combination of slight spasticity with pain, as in cases of multiple sclerosis;
- (chronic) pain;
- some extra-pyramidal symptoms (a group of neurological disorders);
- asthma;
- Tourette's syndrome, and;
- therapy resistant glaucoma.

Cannabis use for medicinal reasons by patients with a somatic disease is relatively safe, on condition that it is not smoked. Its acute toxicity is very low. The principal side effects in therapeutic use are psychosis and euphoria. Little is known about the addictive effect in medical use, though experience with the use of morphine for pain relief has shown that the risk of psychological addiction is low – much lower than when used as a stimulant. As the addictive effect of cannabis is also quite low when used as a stimulant, it may be assumed that this will always be very low in a medical setting.

When estimating the chronic toxicity of cannabis, it should be borne in mind that the doses used in therapeutic applications will probably be lower than those used for 'recreational' purposes. However, this does not imply that no research should be carried out into this question.

To enhance further studies a network for sharing information is desirable, as well as international co-operation in finding enough patients for international clinical studies.

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8. DO CANNABIS POSSESSION LAWS INFLUENCE CANNABIS USE?[1]

Beau Kilmer

Summary

What can we conclude from studies of the relationship between cannabis use and cannabis possession laws?

Most studies find that relaxing cannabis possession laws does not increase cannabis use and that jurisdictions with more liberal possession laws do not necessarily have higher prevalence rates; however, most of these studies do not control for the level of enforcement of cannabis possession laws. Little is known about the influence of the actual enforcement of such laws on cannabis use in Europe. Advanced analyses from the United States suggest that cannabis possession arrests and fines may decrease cannabis use, but not much and not for everyone.

What happened to per capita cannabis possession arrests in the 1990s?

Almost all countries with arrest data saw clear increases in the per capita number of arrests for cannabis possession offences in the 1990s. Despite national differences in the number of cannabis users and crime-to-officer ratios, the probability of being arrested for cannabis possession in the late 1990s was fairly similar for most countries at two to three per cent.

What is the most common punishment for possessing cannabis?

According to the European Legal Database on Drugs, most countries have penalties for cannabis possession ranging from a fine to incarceration. Reports from national and international sources suggest that most arrests only lead to a fine, not imprisonment. Few data are available on the levels of these fines in Europe and what happens when they are not paid.

How can we learn more about the effects of cannabis possession laws on cannabis use?

Models testing this relationship could include data on individuals' demographic characteristics, drug use history, perceived pleasure or harmfulness of using cannabis, ability to easily obtain cannabis, and knowledge of cannabis possession laws and sanctions. It would also be helpful to include data on the social (dis)approval of cannabis, the price of cannabis and other substances, the impact of having a police record for a cannabis possession offence, and the number of cannabis possession arrests. Until these data are readily available, focusing on the expected sanction of a cannabis possession arrest may be the best approach for cross-national and intra-national comparisons involving European countries.

1 *I wish to thank Lorenz Boellinger, Pierre Kopp, Margriet van Laar, Sarah Lawrence, Erin Neel, Peter Reuter, Henk Rigter, and Eric Single for their comments. The views presented here are mine and do not necessarily reflect the opinions of the reviewers or the Trimbos Institute.*

8.1 Introduction: main question to be addressed

A variety of interrelated factors may influence someone's decision to use cannabis. These include the perceived pleasure or harmfulness of consumption, social (dis)approval of cannabis, availability and price of cannabis, price of alcohol and other substances, likelihood of being arrested for possession or use, severity of punishment, and the legal status of cannabis. Many of these factors are part of or affected by 'cannabis policy': the laws, guidelines, and government-sponsored initiatives that are intended to influence cannabis use.

A jurisdiction's cannabis policy is multifaceted and complex. It includes prevention and treatment programs as well as criminal justice interventions[2]. It can be as obvious as destroying cannabis crops or as subtle as augmenting alcohol and tobacco taxes[3]. Many analyses of cannabis policy have focused on the criminal justice aspects, especially laws sanctioning possession of cannabis[4]. There is much debate about whether cannabis possession laws produce more benefits than harm. These laws are intended to reduce cannabis use, but they may have unintended and counterproductive effects (3). Further, there are many consequences associated with enforcing these laws that have not been adequately documented. The available data are not sufficient to carry out a cross-national cost-benefit or cost-effectiveness analysis of cannabis possession laws. I refer to the broader set of data needed for such analyses, but the main question I pose is of a more limited scope: Do cannabis possession laws influence cannabis use?

The chapter consists of two parts. First, there is a literature review on the effects of cannabis possession laws on cannabis use. The review makes it clear that there are few studies that have adequately addressed this question. Second, requirements for a comparative study on the effects of cannabis possession laws are discussed. This chapter explains how this can be done with limited information and provides data on police capacity, cannabis possession arrests, and cannabis possession sanctions for Australia, North America, and Western Europe[5].

8.2 What does the literature suggest about the effects of cannabis possession laws on cannabis use?

Most of the research on the relationship between possession laws and cannabis use focuses on depenalisation[6]. Investigations of the effect of possession laws either compare jurisdictions with 'liberal' and 'conservative' policies or examine jurisdictions before and after cannabis possession laws were depenalised. I first review the cross-national research from Reuband, the Nordic Drug Study, the University of Amsterdam, and the Council of Europe and then continue with a review of intra-national studies of Australia, the Netherlands, the United States, and Switzerland.

A problem for all such studies is that countries and sub-national jurisdictions differ from each other in many respects, not only with regard to drug laws. Moreover, the law may say one thing but law enforcement activities may tell another story. Few investigations of the relationship between cannabis consumption and cannabis possession laws have included measures of enforcement such as the probability of being arrested for use. The 'bark' of a country's cannabis laws may not match the 'bite' of the actual enforcement of these laws in the streets (5).

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2 *Prevention is addressed in Chapter 6.*

3 *The available evidence suggests that tobacco and cannabis are economic complements; the evidence is mixed for alcohol and cannabis (1, 2).*

4 *This chapter does not consider possession laws and use laws separately. The term 'possession laws' refers to laws prohibiting possession and use.*

5 *The data for all calculations are reported in Appendix A.*

6 *There is a difference between decriminalization (removing any sanction) and depenalization (reducing sentences to fines and/or administrative sanctions; incarceration is not an option). This chapter does not address legalization: the elimination of cannabis possession laws and the regulation of cannabis distribution. For a detailed discussion of these regimes see (4).*

8.2.1 Cross-national comparison of cannabis use and cannabis possession laws

Reuband. After evaluating Western European cannabis laws, Reuband (5) concluded that countries with liberal policies have neither higher nor lower prevalence rates than countries with more repressive policies[7]. At the time, he classified the Netherlands, Spain, Denmark and Italy as liberal, and Germany, the United Kingdom, France, Norway and Sweden as repressive with regard to cannabis.

- Most national prevalence rates of lifetime users of cannabis ranged from five to ten per cent in these countries in the 1980s irrespective of the classification, well below the corresponding US rate of 33 per cent for 1988[8].
- As Reuband acknowledged, the official legal systems may not have reflected the actual law enforcement activities[9]. This limits the internal validity of the conclusion.

Nordic Drug Study. The Nordic Drug Study surveyed almost 10,000 people in Scandinavian countries from 1993 to 1995 (8).

- The share of the general population with lifetime experience with cannabis was thirty per cent in Denmark, eleven per cent in Sweden, eight per cent in Norway, and seven per cent in Finland. Attitudes towards hashish users and sentencing practices for using hashish were more liberal in Denmark than in the other three countries (9)[10], but data on cannabis possession arrests were not reported.

University of Amsterdam. Cohen and Kaal (10) recently published the survey results of a random sample of cannabis users who used cannabis more than 25 times in Amsterdam, San Francisco, and Bremen.

- The survey of experienced cannabis users revealed that the percentage of lifetime, past-year, and past–month use in the household population was highest for San Francisco (62%, 29%, 15%, respectively), second highest for Amsterdam (35%, 12%, 8%), and lowest for Bremen (15%, 5%, 2%).
- These figures along with a host of other statistics on cannabis use lead the authors to argue that "policy is not a key determining factor when it comes to the usage patterns of experienced users." The laws of Bremen and San Francisco (and how they are enforced) are not discussed in detail; thus, it is difficult to assess this hypothesis.

Council of Europe. The Council of Europe's Pompidou Group reports trends in drug use, drug related health indicators, drug prices, and drug arrests for cities and countries.

- In most cities or nations for which trend data were available, the prevalence of cannabis use by young people was relatively stable or declining over the 1980s, and generally lower than in the early 1970s (11).
- The number of arrests for cannabis was stable in Hamburg, Paris, and Portugal in the 1980s and increased in the late 1980s in Dublin, London, Rome, and Spain.

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7 *In a more recent report on cannabis use and laws, Reuband (7) upheld his earlier conclusion: "Banning something does not necessarily mean that people will practice the banned activity less often."*

8 *See Chapter 1 for a thorough discussion of cross-national prevalence rates.*

9 *Reuband's footnote 5 reads: "In some of the countries it might well be that the discrepancy between proclaimed liberal enforcement policy and reality is due less to the specialized narcotics departments than to the ordinary police: the latter might still engage in the traditional practices or they might use the cannabis offense label in order to deal with suspects whom they cannot deal with on the grounds of other, proven offenses."*

10 *The general survey asked respondents if a sentence of imprisonment should be imposed for smoking hashish. The share of respondents supporting such a penal sanction was 27% in Finland, 25% in Norway, 29% in Sweden, and only 10% in Denmark.*

- It was argued that "cannabis arrests appear to reflect policy differences between cities to an even greater extent than those for other drugs." Such differences are hard to measure and thus the interpretation offered cannot be accepted uncritically. Also, it is only possible to separate cannabis possession and trafficking arrests for Hamburg.

The most recent multi-city study by the Pompidou Group assessed trends in arrests and prevalence of use in the 1990s with a special focus on comparisons between Western and Eastern Europe (12). The only cannabis prevalence data that allowed for cross-national comparisons were for students in ten cities in circa 1998.

- Cities in the West tended to have higher prevalence rates of current (past month) cannabis use than in the East [11].
- However, the comment that "Western Europe shows more arrests for cannabis-related offences, which indicates a less widespread use of cannabis in Eastern Europe" may be erroneous because cannabis arrests are not a good proxy for use (13) [12].

The Pompidou Group is not the only body of the Council of Europe to examine the relationship between drug use and drug policy. In February 2001, the Social, Health and Family Affairs Committee published a report on the social consequences of and responses to drug use in four Western European countries (14). The report compared the Netherlands, Sweden, Switzerland, and the UK, mainly because Sweden and the UK continue to emphasise the prohibition of illicit drugs while the other two countries focus more on harm reduction and on differentiating between hard and soft drugs.

- The report found that "there is far less use of cannabis in the Netherlands, where there are no legal penalties for possession and transportation of 'user amounts', than in the United Kingdom, where legal penalties are relatively heavy."
- The author concluded: "Existing data imply that the prevalence of drug use in a particular state does not appear to vary in relation to the severity of the legal sanctions attached to drug possession and use in that state. To express this conclusion slightly differently, there is no evidence that measures designed to deter drug use have any effect whatsoever on the prevalence of drug use."
- It was acknowledged that there are other factors that can influence use besides policy and that the paucity of comparable data makes policy analyses difficult.

8.2.2 Intra-national comparisons of cannabis use and cannabis possession laws

Australia. In 1987 the state of South Australia reduced the penalties for cannabis possession to a fine, ranging from 50 to 150 dollars ($AU) for up to hundred grams of cannabis or twenty grams of cannabis resin. The Australian Capital Territory (ACT) followed the depenalisation in 1992 by setting a fine of up to hundred dollars ($AU) for possession of 25 grams of cannabis or less. The Northern Territory, Victoria, and Western Australia have recently relaxed penalties, too (15).

- Using data from five household surveys carried out from 1985 to 1995, adjusted for age and sex by state, Donnelly and colleagues (16) concluded that South Australia's depenalisation regime did not lead to higher weekly prevalence rates of cannabis use. The lifetime use rate in South Australia went up from 1985 to 1995 but this was not attributed to the legal change because 1) there were increases in other states, 2) the increase in South Australia was not greater than the increase in other states, and 3) there was no increase in the weekly prevalence rate in South Australia.

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11 The East is quickly catching up to the West. See Chapter 1.

12 Aggregate data for the Western cities suggest that cannabis related arrests per 100,000 were about 100 in 1992, 200 in 1995, and close to 100 in 1998. In the East, the cannabis related arrest rate was fairly constant at less than 50 per 100,000 for 1994 to 1998 except for a peak in 1997 at approximately 75 offenses per 100,000 inhabitants.

- McGeorge and Aitken (17) assessed the policy change in the Australian Capital Territory by surveying 221 university students in the ACT and 246 university students in another state without a depenalisation scheme. The prevalence rate for lifetime use of cannabis was similar for the two groups (about 53%) and a lack of difference in cannabis use patterns (once a day, once a week, and so on) for the groups in 1992 and 1994 convinced the authors that depenalisation had no effect on use.
- A recent econometric study[13] by Cameron and Williams (2) included data from household surveys; price data for cannabis, alcohol, and tobacco; and a depenalisation variable. They found that the "liberalisation of cannabis laws in South Australia may have led to a temporary increase in cannabis use among the over-30 age group."
- Most of the data reported for Australia suggest that possession laws do not influence cannabis use (15, 18). Lenton's (18) review of the literature concluded "[I]t is now beyond a reasonable doubt that applying criminal sanctions for minor cannabis offences does not deter cannabis use but results in significant social costs for those who run afoul of it, and therefore, that is not in the best interests of the community."

The Netherlands. Best remembered from the 1976 cannabis policy changes in the Netherlands are the coffee shops. Little attention has been given to the 1976 to 1984 period when there were no penalties for possession of small amounts of cannabis (less than 30 grams) and relatively few coffee shops.

ß Korf (19) found no evidence that any real change occurred in cannabis use for several years after the statutory depenalisation in 1976. *De facto* decriminalisation of possession already occurred in some Dutch cities in the early 1970s when authorities tolerated house dealers of cannabis and focused on users and dealers of other illicit drugs (20, 21).

ß In 1998, Reuband (22) published another study on the relationship between drug policy and drug use prevalence rates. This paper included a discussion on supply and demand factors as well as a section on the effect of changes in drug policy, with emphasis on the Netherlands. Reuband argued that the initial decrease in youth cannabis use after liberalisation of cannabis policy in the Netherlands proves that the removal of prohibitions does not necessarily lead to an explosion of drug taking and he concluded, "neither liberal nor repressive policies promote or reduce drug use."

ß According to MacCoun and Reuter (23)[14], the prevalence rate of lifetime cannabis use by Dutch adolescents was slightly declining before the policy change in 1976 and did not change much until the mid-1980s, hovering between fifteen and twenty per cent from 1970 to 1984. They suggested that "there is no evidence that the depenalisation component of the 1976 policy, per se, increased levels of cannabis use."[15]

United States. From 1973 to 1978 eleven states lessened the penalties for cannabis possession to about a 100 dollar fine ($US) for one ounce (28.7 grams) or less.[16][17] While the federal government still prohibited cannabis, users in those states were almost completely immune from arrest and trial (27).

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13 *These econometric studies are discussed in detail later in this chapter.*

14 *Using modeled data from Driessen and colleagues (24).*

15 *MacCoun and Reuter note that the Driessen data (24) do not form a coherent time series and there are no useful enforcement data for the years immediately preceding the change in policy in the Netherlands. They report that the trend line from 1970-1976 is smooth and slightly declining, suggesting not only that there may have been a reduction in enforcement before 1976, but that it did not have a detectable effect on use. MacCoun (25) adds: "Ceteris paribus; we can't rule out the possibility that some other factor drove use down enough to offset an enforcement-reduction increase in use. But that's implausible; the demographics, economy, and social norms were all, if anything, moving in the direction of promoting use, not discouraging it."*

16 *Four of the eleven states that depenalized cannabis possession still consider it a misdemeanor, thus a criminal offense (26). This complicates comparisons of depenalized and non-depenalized states.*

17 *Alaska's decriminalization regime is not considered in this chapter.*

- Single (28)[18] reviewed depenalisation studies in the United States and concluded: "The available evidence indicates that the 'decriminalisation' of marijuana possession had little or no impact on rates of use." He noticed that immediately following the change in laws the number of arrests for cannabis possession decreased in at least four depenalised states, leading to a reduction in spending on cannabis law enforcement and an increased use of fines. Comparable arrest figures for other states were not reported; thus, it is not known how much of this reduction in arrests was actually attributable to depenalisation.
- Model (30) took a different approach and assessed the impact of depenalisation for those who visited a hospital emergency room (ER) from 1975 to 1978. The depenalisation of cannabis was accompanied by both an increase in the number of cannabis-related ER episodes and a decrease in the number of mentions of other drugs. There is no way to separate the effect of policy change, if any, from trends in crisis occurrence, ER visitation, and changes in reporting[19]. Unfortunately, there was no information on the actual enforcement of these policy changes.
- Theis and Register (32) examined past month cannabis use and its frequency among 14 to 21 year-old males in 1984 and 1988, with a sample of about 4,000 for each year. They used depenalisation status, a measure of arrests for 'common crimes,'[20] and a host of demographic variables, including church attendance and urbanisation. There was no relationship between depenalisation and cannabis use in any of the models.
- Researchers affiliated with the National Bureau of Economic Research in the US have carried out most of the econometric studies addressing questions about cannabis possession laws, sanctions, enforcement, and use. Table 1 summarises their findings. Each model controlled for demographic factors and often included the prices of alcohol, tobacco, and other illicit drugs. Based on these econometric studies, there does not seem to be a clear relationship between use and depenalisation.
- Farrelly and colleagues (33) found a statistically significant negative relationship between cannabis possession arrests and use, but the effect was small for adults and non-existent for youth: If the ratio of marijuana possession arrests to total arrests increased by ten per cent, one would expect the probability of past-thirty day marijuana use to decrease by 1.57 per cent for adults age twenty-one to thirty.
- The studies summarised in Table 1 suggest that adults are responsive to fines for cannabis possession, but the evidence is mixed for adolescents[21].

Switzerland. A cross-canton analysis by Schmid (34) examined the relationship between cannabis use and cannabis denouncements while controlling for friends' drug use and urbanization. The dependent variable was lifetime cannabis use for fifteen-year-old students and the denouncements concerning cannabis included any incidents when a police officer wrote a report or notice for consumption, trafficking, or smuggling of cannabis.

- There was a tremendous difference in the rates of denouncements for the 26 cantons ranging from 0.6 per 1,000 inhabitants in Uri to 9.23 per 1,000 inhabitants in Valais.
- No relationship was found between lifetime cannabis use and the per capita number of denouncements at the canton level.
- This finding should be interpreted with caution since the number of denouncements for a particular year (1998) is used to explain lifetime cannabis use (which could have occurred in a

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18 *Single reviewed a host of studies, from the often cited Johnston, O'Malley and Bachman publication (29) to obscure analyses by the depenalization states.*

19 *MacCoun and Reuter (31) note that this finding "may indicate increased consumption by current users or increased willingness to acknowledge marijuana use" in depenalized states.*

20 *Total arrests relative to arrests for violent crimes.*

21 *This observation was made by Pacula and her colleagues (1).*

year other than 1998). Per capita denouncement rates for a particular canton may be different for 1996, 1997, and 1998; thus, the denouncement rate in 1998 for a canton may be a poor indicator (as the findings suggest) of cannabis use in that canton in 1996 or 1997. It is likely, however, that many of these lifetime users did use in 1998 since the study only looks at fifteen-year-olds.

Table 1.
Selected studies and findings on the relationship between possession laws and cannabis use from National Bureau of Economic Research in the US

Author(s)	Findings about cannabis possession laws and penalties
Dinardo & Lemieux (35)	Depenalisation had no effect on marijuana use among high school seniors.
Pacula (36)	No relationship between cannabis depenalisation and the demand for marijuana by young adults.
Pacula (37)	Higher common crimes per officer (an indicator for the enforcement risk of using marijuana) were associated with increased use of marijuana by young adults [22].
Saffer & Chaloupka (38)	Cannabis depenalisation increased the probability that someone consumed marijuana by four to six per cent.
Chaloupka et al. (39)	Students were more likely to use marijuana and more frequently if they lived in a state that had depenalised the possession of small amounts of marijuana. More marijuana was consumed by current users if median fines for marijuana possession were lower.
Chaloupka, Grossman, & Taurus (40)	High school seniors living in depenalised states were more likely to be marijuana users in the past year, but not in the past month. They also found that "doubling the fines which can be imposed for marijuana possession would reduce the probability that a youth uses marijuana by less than one per cent, while reducing overall youth marijuana use by about one and one-half per cent".
Farrelly et al (33)	Adult use of marijuana (age 21 to 30) decreased as cannabis possession arrests (divided by total drug arrests) increased. They also found that "a doubling of the current median fines would decrease the probability of marijuana use by 0.8 per cent". However, measures targeted at reducing marijuana use did not appear to influence use among youths.

8.2.3 Summary of the literature review

According to most studies, relaxing cannabis possession laws does not affect cannabis use very much and jurisdictions with more liberal possession laws do not necessarily have higher prevalence rates.

22 *Pacula argued that "A decrease in the number of crimes (burglary plus robbery) per officer increases the risk of getting caught selling marijuana, which increases the price of marijuana, and decreases the quantity of marijuana involved."*

However, most of the investigations did not control for the level of enforcement of cannabis possession laws. In part this is because of a paucity of criminal justice data on cannabis possession. Advanced analyses from the United States suggest that cannabis possession arrests and fines may decrease cannabis use, but not much and not for everyone.
To learn more about the relationship between the law and drug use in Europe, it is imperative that more attention be given to measuring enforcement rather than to labelling regimes as 'liberal' or 'decriminalised' or 'depenalised' and then comparing their prevalence rates to other regimes.

Fortunately, the quality, collection, and dissemination of relevant European data have vastly improved since the mid-1990s [23]. The following section outlines the data requirements for a European comparative study on the effects of cannabis possession laws.

8.3 How can the effect of cannabis possession laws on cannabis use be measured?

Models testing this relationship could include data on individuals' demographic characteristics, drug use history, perceived pleasure or harmfulness of using cannabis, ability to easily obtain cannabis, and knowledge of cannabis possession laws and sanctions. It would also be helpful to include data on the social (dis)approval of cannabis, the price of cannabis and other substances, the impact of having a police record for a cannabis possession offence, and the number of cannabis possession arrests. Extensive analyses using these variables have not yet been carried out for Europe.
Until these data can be collected and merged, the expected sanction of a cannabis possession arrest will be useful for cross-national and intra-national comparisons. In addition to explaining how to calculate the expected sanction, this section provides data on police capacity, cannabis possession arrests, and cannabis possession sanctions for Australia, North America, and Western Europe.

8.3.1 Police capacity

Cross-national comparisons of the effects of cannabis possession laws should consider differences between countries in per capita police officers and their workloads. These data are available from the United Nations World Survey on Crime Trends and Criminal Justice Systems (UN Crime Survey) that has been carried out since the 1970s (41) [24]. These data are reported in Appendix A.

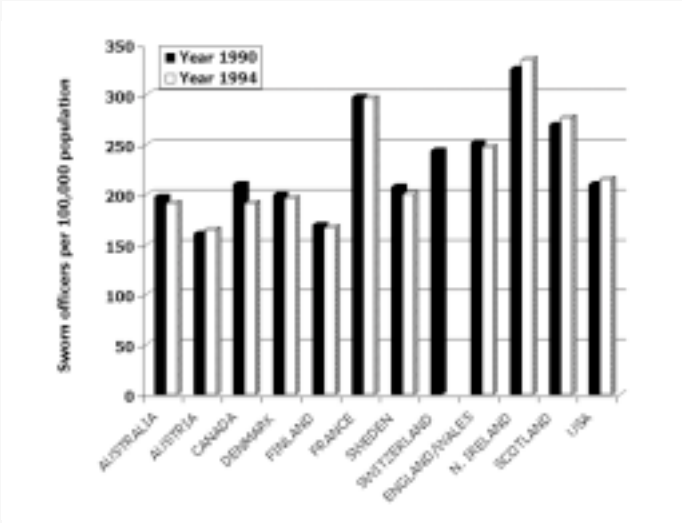
- Figure 1 shows the per capita number of sworn police officers for Western Europe, North America, and Australia. Most countries had 150 to 250 sworn officers per 100,000 people, with France reporting almost 300. These officer figures were fairly stable going from 1990 to 1994 and there was no pattern of increase or decrease.
- There was much more between-country variation in the number of crimes per officer. The 1994 rates ranged from about 20,000 crimes recorded per 1,000 police officers in France to over 60,000 in Sweden [25].

23 *Mostly because of the EMCDDA, Pompidou Group, and the proliferation of the Internet.*

24 *Questions about total sworn police personnel were only asked in 1990 and 1994 in the most recent wave. The UN Crime Survey does ask questions about drug possession offenses (not by drug) and their disposition, but these questions are rarely responded to, especially for the 1990 to 1994 period.*

25 *The US rate was approximately 25,000 crimes per 1,000 police officers. Austria, England and Wales, and Scotland were close to 40,000 crimes per 1,000 police officers while Finland, Canada, and Denmark were close to 50,000.*

Figure 1.
Per capita sworn police officers



Sources: See Appendix A

8.3.2 Enforcement of cannabis possession laws

Very important for cross-national comparisons is the number of arrests for infringing possession laws. These data are available from national sources for some countries, but 'arrest' has different meanings in different places (see Appendix A). The lowest common denominator is that either the offender's name or the incident of a confiscation was recorded by a police officer.

The per capita number of cannabis possession arrests increased for most countries in the 1990s. Figure 2 captures the trend from 1990 to 1999[26][27]. Although Switzerland had the highest per capita rate each year, it experienced the lowest overall change from 1991 to 1998 (82 per cent)[28]. France, the US, the UK and Germany had fairly similar growth rates over this period (156 per cent, 147 per

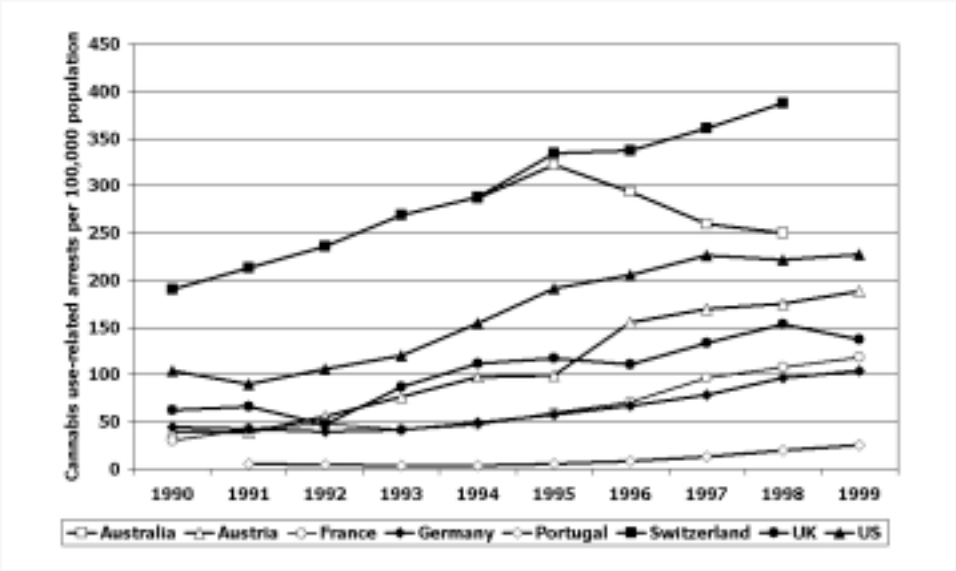
26 *French drug officials (42) offer two explanations for the increase in France: "There is no simple explanation for the rise in arrests over recent years, though broadly speaking there are two main causes. The first is possible changes in the behaviour of the police and gendarmerie. For example, according to the review of the implementation of the 1995 Justice Ministry circular on therapeutic injunction, nearly all public prosecutors' offices instructed the police and gendarmerie to use standard descriptions for users. The implementation of these instructions may have led to a rise in the number of recorded arrests. Internal reorganizations within the police services may have also have helped increase the number of arrests, and particularly the tendency to grant the public security services greater autonomy in relation to narcotics. The second main factor concerns the increasingly common nature of cannabis consumption and major changes in the context in which it is used. Given the state of current knowledge, it would be presumptuous to say that one or other of these explanations is the more likely."*

27 *The arrest trends in Figure 2 differ strikingly from those published by the Council of Europe's Pompidou Group (12). The Pompidou Group reported aggregate cannabis related arrests per 100,000 population of about 100 in 1992, 200 in 1995, and close to 100 in 1998 for four Western European cities. I cannot explain this apparent discrepancy. There were differences in the arrest categories (cannabis possession arrests in Figure 2 versus cannabis related arrests in the Pompidou Group reports) and populations (entire countries versus cities), but neither seems to be so great as to account for the opposite findings.*

28 *This is especially interesting considering that one study classified Switzerland as a country with relatively liberal drug laws (14).*

cent, 131 per cent, 127 per cent, respectively). The largest relative increase occurred in Austria (351 per cent). The decrease in Australian rates from 1995 to 1998, which included expiation notices, runs counter to the picture for all other countries shown [29].

Figure 2.
Per capita cannabis possession arrests



Sources: See Appendix A

Note: Australian data in this figure are only reported from 1994 to 1998.

The rise in number of arrests is remarkable given the tendency in many countries to lessen the severity of sanctions for infringing cannabis possession laws. The similar growth rate for many of these countries also merits further consideration.

It is also useful to relate the number of possession arrests to the number of police officers. Figure 3 shows a rise in the number of cannabis possession arrests per sworn officer from 1990 to 1994 for Austria, France, the UK, and the US [30]. This increase raises questions about why it occurred (Did the police become more efficient? Were there simply more users to arrest?), but it also begs the question: At what (and at whose) expense did the cannabis arrest- per-officer ratio increase? This is an important question for those interested in performing cost-benefit analyses of cannabis possession laws.

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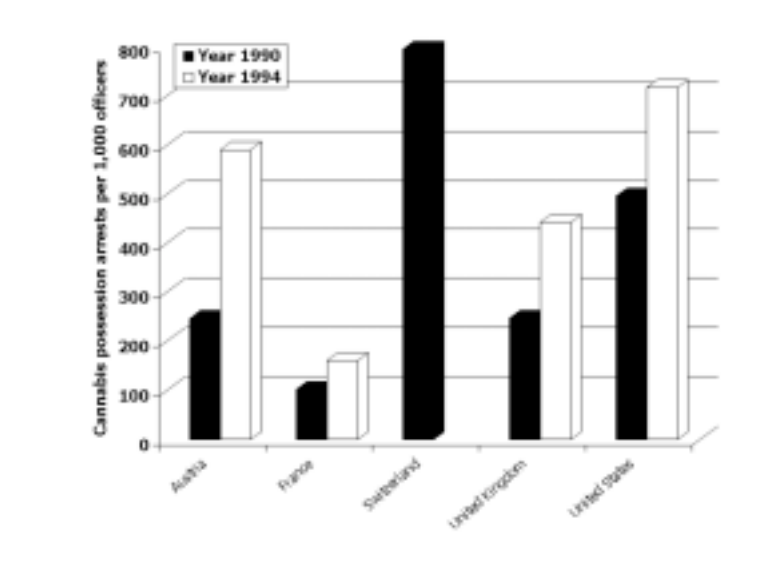
29 *I did not find figures that included expiations and arrests for all of Australia pre-1994; however, 1987-1999 data for expiation notices in South Australia are available (43). One reviewer noted (44): "The anomalous decrease in arrest rates after the mid-1990s may reflect a return to normal following a period of expanded enforcement following the introduction of the CEN scheme. Indeed, the so-called 'net-widening' that occurred following decriminalisation of cannabis in South Australia (45) raises the issue that decreases in penalties can in some situations lead to increased enforcement because the police may be reluctant to vigorously enforce laws which they and/or the public consider to be too severe." See (15) for a more detailed discussion.*

30 *Combining the UN Survey with national data on arrests severely limits the number of countries and the years for which this ratio can be calculated.*

Figure 3.
Cannabis possession arrests per 1,000 sworn police officers



Sources: See Appendix A

To really learn more about the significance of the increase in the per capita number of cannabis possession arrests, one should consider the annual probability of being arrested for a cannabis possession offence. This conditional probability statistic was reported for Canada in the early 1970s (46), the US in the early 1990s (47), the US in the mid-1990s (48), and for Western Australia in the mid-1990s (18); with rates of between one and three per cent. To calculate this figure one divides the number of people in a country who were arrested for a cannabis possession offence in Year X by the number of people who used cannabis in the same year. Since the denominator requires an estimate of all recent (past year) users of cannabis in a nation, which often is unknown, this ratio cannot be calculated for many countries [31].

Table 2 presents the annual probability of being arrested for a cannabis possession offence. For the countries shown there was roughly a two to three per cent chance that someone possessing cannabis was arrested. There are several reasons why this table should be interpreted with caution:

- As mentioned before, 'arrest' may mean different things in different places.
- The prevalence studies used for the denominator differed in content and method (see Appendix A).
- For the ratios to be truly comparable, one must assume that the frequency of cannabis use by past-year users and the share of people arrested more than once in a year were the same for each country. Data from France suggest that multiple arrests for a cannabis user in a single year are rare (42) and a recent cross-national survey of regular cannabis users found that "the timing, length, and patterns of cannabis use careers are very similar in the three cities studied" (10). Still, caution should be exerted.

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31 *A reviewer noted that this calculation would be more precise if the numerator included the total number of times cannabis was used (use incidents) in a year instead of the number of users (44). I agree. Unfortunately, these incident data are not readily available for most countries. MacCoun and Reuter (48) reported that, "Each year an average user [in the US] faces a 1 in 40 chance of being arrested; [for] per use episode, the risk is only about 1 in 4,000."*

Table 2.
Probability of being arrested for cannabis possession

	1995	1996	1997	1998	1999
Australia	3.7%			2.1%	
Canada	1.8%				
France	1.6%				2.0%
Germany			2.7%		
Sweden			2.4%		
United Kingdom		2.1%		2.9%	
United States	2.8%	3.0%	3.1%	3.2%	3.2%

Sources: See Appendix A

8.3.3 Punishments for cannabis possession laws

Future studies of cannabis laws must also focus on the most common sanctions for cannabis possession arrests.

- Some argue that the international conventions on drugs do not state what the punishments for cannabis possession should be and a lot of flexibility is given to signatories, explaining variations among European countries (49, 50).
- According to the European Legal Database on Drugs (51), most Western European countries have penalties for cannabis possession ranging from a fine to incarceration. As Table 3 shows, using a variety of national and international sources, most arrests in practice only lead to a fine. Few data are available on the levels of these fines in Europe and what happens when they are not paid[32].

There are other costs associated with being arrested for a cannabis possession offence.

- Findings from Australia suggest that those who receive a criminal conviction for a minor cannabis offence are more likely to experience negative employment consequences of their offence than those who just receive an expiation notice (61).
- In the United States, students convicted of a drug offence, including cannabis possession, are ineligible for federal student aid for university for a designated period of time. Of the 9.8 million applicants for aid for the 2001-2002 school year, 43,436 were rejected or risked automatic denial for not answering the question about drug arrests (62).

It would be helpful if these and similar consequences of being arrested and convicted for a cannabis possession offence were published for European countries. This would permit more accurate cross-national comparisons with regard to the effects of cannabis possession laws.

32 *Here are three examples, all from outside the EU. In South Australia, only half of the fines are paid in the allotted time (43). Failure to pay the fine in time can lead to a prosecution and a recorded conviction, but it is unclear how often a more severe sentence is imposed, especially for those who did not pay because of financial hardship. In Canada, there "are still a significant number of users imprisoned for simple possession (and significant associated costs) due to failure to pay fines" (44). In Swiss cantons where a fine is the normal sentence for consumption of cannabis, fines frequently go unpaid but are not converted into prison sentences: they go unpunished (52).*

Table 3.
Cannabis possession results in a fine in most Western European countries

Country	Penalties according to ELDD (51)	What usually happens after arrest and conviction?
Austria	Up to 6 months	"Persons convicted of misdemeanours [which includes possession of small amounts] are often sentenced to pay fines and rarely punished with unsuspended prison sentences" (53).
Belgium	Fine to 5 years	Punishments for possession are not separated by drug. However, a 1998 directive created a distinction between cannabis possession and other offences and the former are given 'the lowest prosecution priority' (54).
Denmark	Fine to 2 years	"In Denmark, possession of small quantities typically results in a warning" (55).
Finland	Fine to 2 years	For those convicted of a drug offence in 1999, 71 per cent were fined, 19 per cent received prison offences, and 8 per cent were given suspended sentences. "Incarceration apparently concerns persons who have allegedly committed aggravated drug offences. It seems that the prosecutor decides not to press charges if the amount used (or possessed) is small." (56).
France	Fine to 1 year	"Apart from receiving treatment orders, arrested users may either be released without charge, cautioned (this is the most common), or prosecuted" (42).
Germany	Fine to 5 years	"In the practice of courts and public prosecutors nation-wide more than 90 per cent of all criminal procedures with a maximum of 10 g are suspended" (57)[33].
Greece	Counselling to 5 years	"Non-addicted users who are arrested for the first time are obliged to follow a counselling program." There have been cases where cannabis possession is punished more strictly than heroin because the latter causes addiction and those arrested were in need (58).
Ireland	Fine to 3 years	"Ireland does not penalise consumption and possession is penalised with a fine." Offenders can be incarcerated for third offence (51).
Italy	Administrative sanctions	"Offences involving cannabis use and small-scale dealing attract only an administrative fine" (52).

33 *Just before publication it was brought to my attention by Joe Wein of the Association for Drug Policy (Verein für Drogenpolitik e.V.) via electronic mail that this quotation is misleading : "The source quoted by the German Annual Report in fact states something very different: In ninety per cent of simple possession cases dismissed without penalty, the amount involved was no greater than ten grammes of cannabis. This is not the same as the above [quote in Table 3]. The Aulinger study only analyzed dismissed cases by quantity, but not cases that led to a trial and conviction. Hence it could not make any reliable statement about dismissal rates based on quantity, even though this claim has often been attributed to it. The Aulinger study did however provide some data that suggests that in 1995 number of cases dismissed as a percentage of the total number of simple possession cases varied from 10% to 92% on a state-by-state basis." I did not have time to explore this further and find a new source for Table 3.*

Table 3 continued.
Cannabis possession results in a fine in most Western European countries

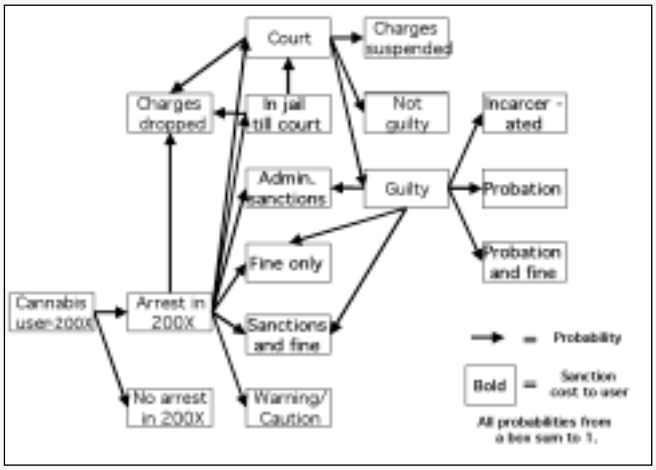
Country	Penalties according to ELDD (51)	What usually happens after arrest and conviction?
Luxembourg	Fine	However, "using cannabis in front of a minor, a school, or in the workplace can lead to a prison sentence (eight days to six months)" (51).
Netherlands	Fine to 1month	There is no arrest for possessing less than five grams (59).
Portugal	Cannabis offences are decriminalised	"It is the recreational drug users who are most likely to be fined. Addicts will be sent to detoxification or other health programs" (60).
Spain	Administrative sanctions	"Administrative fines have been levied since 1991 against anyone found consuming any form of illegal substance in a public place or possessing illegal substances" (52).
Sweden	Fine to 6 months	Users are usually fined, which may be exchanged for treatment (51).
Switzerland		From 1991 to 1994, "the majority of those convicted for mere consumption received a fine, but custodial sentences are also imposed, not all of them suspended" (52).
United Kingdom	Caution to 5 years	"Where only small amounts are involved for personal use, the offence is often met by a fine" (51).

8.3.4 Estimating the effects of cannabis possession laws on cannabis use with limited data

The data needed to assess the impact of cannabis possession laws on cannabis use are mentioned throughout this chapter. Multivariate regressions that include administrative and individual-level data (especially individual-level data on perceived certainty and perceived severity of being sanctioned) would be ideal, but these data are not available for most jurisdictions. There are, however, better ways to study the effects of drug laws than simply comparing regimes that are assumed to be different.

For the time being, focusing on the *expected sanction of a cannabis possession arrest* may be the best approach for cross-national and intra-national comparisons. I offer a conceptual model in Figure 4. The expected sanction cost can be used to compare the effects of cannabis possession laws between countries and to assess the impact before and after a national policy change. In theory, policies intended to increase the risk of being arrested for cannabis possession or increase the severity of punishment should increase the expected sanction. The figure could be related to measures of (dis)approval of cannabis, frequency of use, and other findings from prevalence surveys – preferably broken down by age, sex, and race/ethnicity.

Figure 4.
A conceptual model for calculating the expected sanction of a cannabis possession arrest



To compute the expected sanction of being arrested for possession of cannabis, one multiplies the probabilities leading to a **bolded** box by the monetary value for that box. The costs for the seven bolded boxes are then summed to estimate the total expected sanction cost for a cannabis user for a given year[34]. Some of the data required for this model are available for Western European countries but other data may be difficult to collect for most countries in the near future. Therefore, one may wish to settle for less elaborate models, such as the one presented in Appendix B.
Detailed as these models may be, they may not reflect the full reality. Users of cannabis may not be influenced by the expected sanction cost, even if it includes future social costs. The cost may simply be too low to have an effect or the risk of getting caught may be underestimated[35] [36]. Not only may users be unaware of the legal risk, there is also the possibility that the risk may attract users – the 'forbidden fruit effect' (3). This calls for even more careful and detailed cross-national comparisons.

8.4 Conclusions

I am unaware of any studies in the literature that strongly challenge Single's 1989 finding that "the available evidence indicates that the 'decriminalisation' of marijuana possession had little or no impact on rates of use" (28). In the econometrics literature there is disagreement about the effects of depenalisation, but none of the studies suggest that relaxations will have a tremendous impact on use. As for penalties, one study found that adults are responsive to fines for cannabis possession and the evidence is mixed for adolescents.

34 *This model should be changed once more is learned about the social costs associated with being arrested and/or convicted for a cannabis possession offense.*

35 *Canadian high school students believed that the likeliest outcome of a cannabis encounter with the police was confiscation of the drug and not arrest (63).*

36 *According to a review of the deterrence literature (64) "perceptions of the certainty and severity of punishment do not seem to deter the trivial and infrequent behaviors [including marijuana use] of high school and university students."*

Many studies focus on 'labelling and comparing' cannabis regimes rather than actually examining cannabis law enforcement activities. The most rigorous study on the subject (33) did find a statistically significant relationship between cannabis possession arrests and use of the drug (the more arrests, the lower the prevalence), but the effect was small for adults and was absent for adolescents.

Many authors agree that there are not enough data to permit definitive cross-national comparisons with regard to the effects of cannabis possession laws.

8.4.1 Possible trends

Most Western European countries have reduced, or are considering reducing, penalties for cannabis possession. Almost all countries with arrest data saw clear increases in the per capita number of arrests for cannabis possession offences in the 1990s. Despite differences in the per capita number of cannabis users and police officers, the annual probability of being arrested for cannabis possession in the late 1990s was fairly similar for most countries at two to three per cent.

8.4.2 Gaps in our knowledge

In Europe, many of the data needed to test the relationship between cannabis possession laws and actual use of this drug are unavailable. For instance, data on the severity of fines imposed for possession of cannabis are lacking for most European countries, or at least they are not included in the national reports for the EMCDDA. Future studies should give more attention to the social costs of cannabis possession laws and their penalties. Priority, however, should be given to collecting cannabis possession arrest data for as many national and sub-national units as possible.

It should not be long before European countries together can carry out the kind of modelling that is done in the US and Australia. Europe is an interesting resource for this sort of investigation because of the rich diversity of policies between and within counties. For example, some cantons in Switzerland do not enforce fines for possession, Laenders in Germany have different definitions of 'small amounts' for prosecution, and one London Borough is only confiscating cannabis instead of prosecuting offenders. Add to this Belgium's 1998 directive to give cannabis possession 'the lowest prosecution priority' and Portugal's 2001 policy change for all drug possession offences and one finds a vast playing field for examining the effects of cannabis laws and how they are enforced.

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Appendix A (of chapter 8)

Data for Figure 1 and Figure 3 (41)

Country	Population		Sworn Officers		Recorded Crimes	
	1990	1994	1990	1994	1990	1994
Australia	17,170,000	17,931,000	33,971	34,306		
Austria	7,718,000	8,031,000	12,418	13,256	457,623	504,568
Canada	26,584,000	29,248,000	56,034	55,946	2,946,730	2,919,557
Denmark	5,140,000	5,205,000	10,272	10,212	527,416	546,928
Finland	4,986,000	5,095,000	8,467	8,496	437,700	389,287
France	56,735,000	57,747,000	168,772	171,078	3,492,712	3,919,008
Sweden	8,559,000	8,780,000	17,800	17,632	1,218,812	1,112,505
Switzerland	6,712,000	6,995,000	16,358		354,037	357,794
England & Wales	50,562,447	51,439,203	127,090	127,358	4,543,611	5,249,478
United States of America	249,911,000	260,651,000	525,075	561,543	14,475,600	13,989,500
Northern Ireland	1,589,400	1,631,822	5,175	5,470	57,198	67,886
Scotland	5,102,400	5,132,400	13,777	14,219	535,864	527,064

Data for Figure 2

	Australia	Austria	France	Germany	Portugal	Switzer-land	United Kingdom	United States
Total arrests								
1990		3,056	17,214	35,000		13,000	36,086	260,391
1991		3,036	24,101	34,000	610	14,750	38,457	226,240
1992		4,443	27,575	32,000	488	16,500	27,444	271,932
1993		6,134	23,950	34,000	418	19,000	50,687	310,859
1994	51,393	7,821	27,547	40,000	370	20,500	65,099	402,717
1995	58,359	7,980	34,876	47,500	556	24,000	68,598	503,350
1996	53,832	12,502	41,396	55,000	865	24,250	65,099	546,751
1997	48,122	13,656	56,693	64,456	1,365	26,000	78,943	606,519
1998	46,933	14,192	63,560	79,495	2,033	28,000	90,858	598,694
1999		15,258	69,767	85,668	2,604		81,381	620,541
Population								
1990		7,718,106	56,735,103	79,380,394		6,838,380	57,620,937	249,947,792
1991		7,812,971	57,055,392	79,984,244	9,918,984	6,922,535	57,807,900	252,638,753
1992		7,909,501	57,374,125	80,594,946	9,914,824	7,001,168	58,015,103	255,374,482
1993		7,983,117	57,658,233	81,126,711	9,930,759	7,064,069	58,207,959	258,082,867
1994	17,892,557	8,022,047	57,906,791	81,408,696	9,954,549	7,119,599	58,408,622	260,599,089
1995	18,116,171	8,041,935	58,149,674	81,648,399	9,968,849	7,166,492	58,613,976	263,043,646
1996	18,348,078	8,055,908	58,390,513	81,885,179	9,979,834	7,197,655	58,814,763	265,462,901
1997	18,565,243	8,072,113	58,627,229	82,096,931	9,994,921	7,212,605	59,006,721	268,008,430
1998	18,768,789	8,091,582	58,864,801	82,327,716	10,012,197	7,225,466	59,187,127	270,560,981
1999		8,111,238	59,100,912	82,561,399	10,030,143		59,355,419	273,131,194

Sources for Figure 2

Total population divided by 100,000 is the denominator. These figures come from the U.S. Census Bureau's International Database (65).

Australia. The numerator is the number of arrests for cannabis use/possession and includes expiation notices, drug infringement notices, and simple cannabis offence notices (66). These figures do include expiation notices for paraphernalia. The 1995 numerator includes the arrests for the fiscal year 1995/1996. The 1996 figure is the average of the 95-96 and 96-97 figures. Similar calculations are performed for 1997 and 1998.

Austria. Since the drug-specific data do not distinguish between possession and trafficking, the number of reports to the police for cannabis violations is multiplied by the percentage of all drug offences that are misdemeanours (usually for use and small-scale dealing) for the numerator (53). The number of arrests is likely to be inflated because it includes some sales offences and those arrested for multiple drugs were reported in multiple categories.

France. Cannabis use arrests are combined with the cannabis use/dealing arrests (different from trafficking) in the official statistics; however, total drug use arrests are reported separately from total drug use/dealing arrests (42). The per cent of total use and use/dealing arrests that are just for drug use is multiplied by the figure for cannabis use and use/dealing arrests to generate the numerator.

Germany. The German cannabis use offence statistics are mainly for possession and purchase (57). They do not include arrests where other substances were found. Years 1990-1996 were approximated from a bar chart.

Portugal. These figures had to be interpreted from a figure titled "Haxixe apreendido, numero de appreensoes e de presumiveis infractores, segundo o ano, por situacao face a droga" (67) which roughly translates to Hashish confiscated, number of arrests and those suspected of infraction, by year, for each type of drug offence. The arrests are for all cannabis offences while the 'suspects' category is broken down by trafficking, consumption, trafficking/consumption, and another small category. The number of arrests is very similar to the number of suspects for consumption only and the latter is used in Figure 1. Even if the arrest and suspects were summed, Portugal would still have the lowest arrest rates and almost the same relative changes throughout the decade.

Switzerland. Charges for consumption of marijuana, hashish, hemp plants, or hash oil (52). These numbers are derived from a bar chart on page 50.

United Kingdom. The number of individuals who were found guilty, cautioned, given a fiscal fine, or dealt with by compounding for unlawful possession of cannabis (68).

United States. The numerator is the total arrests for cannabis possession (69). It does not include arrests where other drugs were found or a more serious offence took place.

Data for Table 2

	Australia	Canada*	France	Germany	Sweden	United Kingdom	United States
1995							
Rate	13%	7.4%					8.4%
Sample size	na	na					~18,000
Sample age	14+	15+					12+
Methodology	na	na					Face
Past year users	1,564,674	1,773,390					17,755,000
1996							
Rate						9%	8.6%
Sample size						~10,000	~18,000
Sample age						16-59	12+
Methodology						Face	Face
Past year users						3,131,694	18,398,000
1997							
Rate				3.8%-4.8%	1%		9.0%
Sample size				3,000-7,000	1,500		12+
Sample age				12-59	15-69		~25,000
Methodology				Face/Mail	Face		Face
Past year users				2,414,000	60,873		19,446,000
1998							
Rate	18%					9%	8.6%
Sample size	~10,000					~10,000	~26,000
Sample age	14+					16-59	12+
Methodology	Face/Mail					Face	Face
Past year users	2,255,467					3,151,521	18,710,000
1999							
Rate			7.6%				8.9%
Sample size			na				~67,000
Sample age			12-75				12+
Methodology			Tel				Face
Past year users			3,529,508				19,573,000**

na = Not available. Many of these statistics came from secondary sources.

* *Canadian 1994 prevalence rate multiplied by 1995 population*

** *A revised estimate puts this figure at 19,102,000. This would put the conditional probability at 3.3%*
http://www.samhsa.gov/oas/nhsda/2kdetailedtabs/Preface.htm#TopOfPage

Sources for Table 2

Most numerators are described in the notes for Figure 2.

Australia. The denominator is the product of the annual cannabis prevalence for those fourteen years and older and the number of Australians aged 15-64 (70,71). Population aged 15-64 in 1995=12,035,952; 1997=12,530,370.

Canada. The numerator is the number of cannabis possession offences in 1995 (72). The denominator is the 1994 past-year prevalence estimate for those over 14 (72) multiplied by the number of Canadians over fourteen in 1995. The number of those over 14 was calculated by multiplying the total population in 1995 by the per cent of the total population that was over fourteen in 2000. Population over the age of fourteen in 1995=23,964,735.

France. The numerator is generated in two steps: 1) Dividing the total number of drug use arrests by the sum of the arrests for drug use and drug use/dealing; 2) Multiplying this quotient by the number of cannabis use and cannabis use/dealing arrests. For 1995, a figure of 2.2 million annual users was reported in (42). The 1999 denominator is the product of the annual cannabis prevalence for those 12-75 years and older (42) multiplied by the number of individuals aged 12-75 in 1999. Population aged 12-75 in 1999=46,440,897.

Germany. The denominator includes the number of 12-59 year olds (in East and West Germany) who used cannabis in the past year (57). The number of past-year users in 1997 was 2,151,000 for West Germany and 263,000 in East Germany.

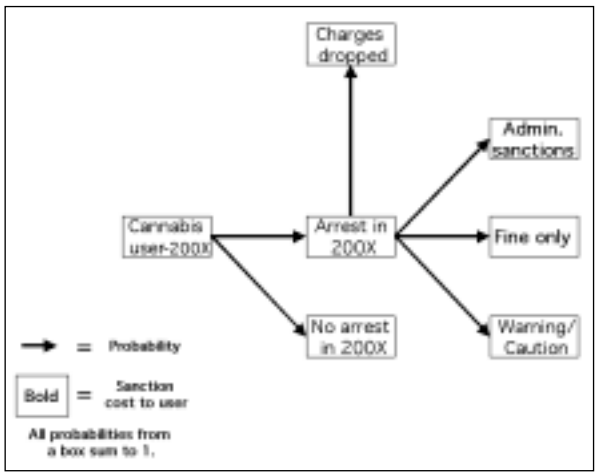
Sweden. The numerator is the number of people arrested for possession/abuse in 1997 (73). The denominator is the annual cannabis prevalence rate for those aged 15-69. Since national estimates put this at 1 per cent for 1996 and 2000, I estimate the prevalence to be 1 per cent for 1997. The number of 15-69 year olds was calculated by multiplying the total population in 1997 by the percentage of the total population in 2000 aged 15-69. Population aged 15-69 in 1997=6,087,265.

United Kingdom. The denominator is the product of the annual cannabis prevalence rate for 16-59 year olds in England and Wales (74) multiplied by the total UK population aged 16-59. To compute the denominator for 1996 it is assumed that the percentage of the UK population aged 16-59 is the same as it was reported for 1998. UK population aged 16-59 in 1996=34,796,598; 1998=35,016,900.

United States. The denominator includes the annual estimates of cannabis users aged 12 and older (75).

Appendix B (of chapter 8)

A practical model for calculating the expected sanction of a cannabis possession arrest



RECOMMENDATIONS BY THE SCIENTIFIC TASK FORCE

Right from the outset, the Task Force's understanding was that its job was to describe the current state of play in scientific research into cannabis, and to do so within a relatively short time.
That meant two things: firstly, that by definition we would not be able to tackle every topic, so we would have to make a choice; and secondly, that our task did not include giving our opinion on present or proposed cannabis policy. Cannabis policy is a subject that, by definition, is much wider than merely formulating and answering questions on the basis of science. However, we do see it as our role, based on the knowledge that we have collected, to make a number of recommendations about the way in which science can make a contribution to the development of this policy.

About the main findings

We do not want to repeat here the chapters of this book and the excellent summary by Inge Spruit. That would not do justice to their thoroughness and comprehensiveness. In a nutshell these findings are that:

- There is little relationship between different forms of legal policy and cannabis use.
- The cannabis pathway in the human body is not well enough understood.
- The gateway theory focusing on neurobiological processes is not proven today.
- Cannabis can affect physical health; THC affects the foetus.
- Cannabis may affect (often temporarily) mental health.
- Dependence on cannabis exists, and this can be treated.
- THC may affect cognitive functions and therefore driving capacities.
- Well-designed prevention can influence the behaviour of potential consumers.

In our view, none of these insights that have emerged have made us feel: "this is so new and surprising that it forces us to radically revise our views on cannabis." This is hardly surprising, of course, since a great deal was already known about cannabis. This is confirmed by the fact that – in all but a few areas – the excellent report on cannabis produced by INSERM in France some time ago corresponds very closely with the findings of our report.

The main conclusion is that cannabis is not a harmless substance.

About the follow up

Numerous follow-up questions have been formulated for some topics; without attempting to be exhaustive or using scientific language, we want to draw your attention to the following recommendations.

- *Epidemiology*: the report argues in favour of better and more systematic epidemiological data collection. In particular, it highlights the importance of striving to achieve quality and co-ordination. A good example of the latter is the problem of comparability between the Swiss figures and those for the EU countries. Policy can only be compared effectively if the statistics are comparable.
- Follow-up questions need to be answered in the area of *pharmacology and neurobiology*, to gain a better understanding of the effects of cannabis on the human body.
- Turning to the *gateway theory*, longitudinal human studies are recommended to find out whether cannabis use encourages people to use other drugs, and in which specific conditions this occurs more frequently.

- There are also follow-up questions in the area of *physical health*, especially concerning cannabis use in combination with other drugs and alcohol and tobacco.
- *Mental health*: follow-up research is recommended into co-morbidity issues and into the consequences of combined use of cannabis, other drugs and alcohol and tobacco.
- *Dependence*: there are also recommendations for follow-up research and activities in this area, such as to start experiments with forms of treatment, improving case finding and carrying out long-term research into the careers of cannabis users, paying particular attention to the combined use of substances and to other risk factors. We have to promote the study to know much more about the thresholds of consumption (quantity and frequency) leading to harmful use and dependence.
- Follow-up questions in the area of *cannabis and traffic*: research into the threshold values for acceptable driving behaviour and measurement techniques to determine whether a driver is under the influence to such an extent that driving is reckless.
- Concerning the relationship between the THC *quality and quantity* and its influence on use and health: research into the dose-response relationship and the dose-frequency-effect relationship is needed.
- *Prevention*: we recommend more research into the effectiveness of programmes designed to prevent cannabis users from moving on to hard drugs, or at preventing problematic cannabis use.
- Concerning the question of "*cannabis as a medicine*", the report states that a lot of research is under way, but that attention needs to be paid to developing a network to disseminate this knowledge more effectively.
- Finally, concerning the relationship between *policy and use*: here the report argues in favour of more systematic collection of statistics on cannabis policy in practice, including figures on police and legal action, data on the views and expectations of the users, social factors, etc. It is recommended that models should be developed based on these statistics, so that the relationship between policy and cannabis use can be established.

The Task Force recommends that the ministers study these follow-up questions more closely and see whether they can be incorporated into research. If so, that research should preferably be capable of being carried out under a joint schedule. It is conceivable that the more complicated and expensive studies in particular could be set up and funded jointly. We believe that research can be planned and carried out much more efficiently through co-operation and co-ordination. In fact, that does not only apply to cannabis policy.

About research and policy

Finally, we want to make a recommendation about the relationship between research and policy. It will be clear to you from the report that a great deal of knowledge already exists about cannabis. This gives us an understanding of three of the key elements of cannabis policy: policy, substance use and health, and the interaction between these elements. Based on this understanding, we argue that the contribution that science can make should be used more extensively and systematically when developing cannabis policy, without setting science up in place of the policymakers responsible for this. Monitoring, evaluation and follow-up research can all help to improve the effectiveness of policy. Science can also make a proactive contribution to policy development, by thinking through the consequences of future forms of policy. Based on the knowledge that we have now and that we will develop in the future, we can gain an understanding of the consequences to be expected from a more restrictive policy, from different forms of regulation or from legalisation of cannabis policy.

We sincerely believe that science can help to ensure that cannabis policy gradually develops into an evidence-based policy.

The members of the Scientific Task Force

GLOSSARY AND MAIN CONCEPTS

Adrenocorticotropin

Cerebral hormone stimulating secretions of substances from the suprarenal cortex.

Agonist

Drug that binds to a receptor site and thus produces a response; it may mimic or strengthen the effects of an endogenous transmitter.

Annual probability of being arrested for cannabis possession

The likelihood that a cannabis user will be arrested for violating a cannabis possession law in a given year.

Antagonist

Drug that binds to a receptor site and does not produce a response; it blocks the action of an agonist or endogenous transmitter.

Anti-emetic

Effect of a drug that stops vomiting.

Anxiety disorder

A pathological state characterised by a feeling of dread accompanied by somatic signs indicative of hyperactive autonomic nervous system. Differentiated from fear, which is a response to a known cause. Panic disorder refers to massive anxiety with sudden onset, usually with no precipitating factor.

BAC

Blood Alcohol Concentration

Bipolar disorder

The designation of bipolar I disorder is a syndrome with a complete set of symptoms for mania during the course of the disorder. DSM IV has also formalised the criteria, for a disorder known as bipolar II disorder characterised by the presence during the course of the disorder of depressive episodes and hypomanic episodes – that is, episodes of manic symptoms that do not quite meet the criteria for a full manic syndrome.

Cannabinoids

Class of chemical compounds that occur in the cannabis plant, or are produced within the body after consumption and metabolism of cannabis. Artificial cannabinoids have also been synthesised. More than sixty cannabinoids are known, some of which have an effect on the brain. The most important psychoactive cannabinoid is Δ^9-tetrahydrocannabinol (synonym dronabinol or Δ^9-THC). See also: Endogenous cannabinoids.

Cannabis

Hashish and marijuana and related products, originating from plants of the genus Cannabis.

Cannabis-induced psychotic disorders

Diagnostic criteria from DSM IV:

A. Prominent hallucinations or delusions.
B. Evidence from the patient's history, physical examination or laboratory findings that the symptoms in Criterion A developed during, or within a month of, substance intoxication.
C. The disturbance is not better accounted for by non-substance-induced Psychotic Disorder. Evidence that the symptoms are better accounted for by a non-substance-induced Psychotic Disorder might include the following: the symptoms precede the onset of the substance use, the symptoms persist for a substantial period of time (e.g., about a month) after the cessation of severe intoxication, or substantially exceed what would be expected given the type or amount of the substance used or the duration of use, or there is other evidence that suggests the presence of an independent non-substance-induced Psychotic Disorder (e.g., a history of recurrent non-substance-related episodes).
D. The disturbance does not occur exclusively during the course of a delirium.

This diagnosis should be made instead of a diagnosis of cannabis intoxication only when the symptoms are in excess of those usually associated with the intoxication syndrome and when the symptoms are sufficiently severe to warrant independent clinical attention.

Cannabis possession laws

The actual laws on the books that make possession and use of cannabis illegal and codify the range of penalties.

Carcinogens

Substances that may induce cancer.

Catecholamines

Substances secreted by the suprarenal glands and affecting the sympathetic nervous system: i.e., adrenaline, dopamine.

Cognitive functions

Executive mental/psychological functions such as memory, planning, reasoning, attention and decision making.

Community prevention interventions

A combined set of prevention activities, in a specific region or town, aimed at adolescents, as well as parents and other people and organisations. An important characteristic of such community interventions is that people living in the community play an important role in deciding which interventions are developed for whom.

Comorbidity

Proportion of a population with dual diagnosis. Dual diagnosis means the presence of an additional disease diagnosis in a person who already has a diagnosed disease.

Continuation (or conversion) rate

Here: the last year prevalence rate of users of cannabis divided by the corresponding lifetime prevalence rate times one hundred.

Culpability index

Rate of crash involved drivers reponsible for their accidents versus those not responsible.

Current use; last month prevalence of cannabis use

Consumption of cannabis at least once in the past month, usually expressed as a proportion of the population who used cannabis at least once in a given month.

Cytokine

Factor produced by some cells of the immune system in order to assume regulation of the proliferation in the others cells in the same system.

Decriminalisation

The removal of all penalties for using cannabis or possessing a small amount for personal use.

Depenalisation

The reduction of penalties for violating a cannabis possession law. Some argue that this definition should refer to the removal of incarceration as a sentencing option.

Dependence

People are considered to be dependent on cannabis according to the DSM classification system if they meet at least three out of seven criteria, including the occurrence of tolerance and withdrawal, craving, and the continuation of use despite a wish to stop or despite knowing the harm that may result from consumption.

Depressive episode (major)

Clinical criteria from DSM IV

A. Five (or more) of the following symptoms have been present during the same two-week period and represent a change form the previous functioning; at least one of the symptoms is either (1) depressed mood or (2) loss of interest or pleasure. Note; do not include symptoms that are clearly due to a general medical condition, or mood-incongruent delusions or hallucinations.

(1) Depressed mood most of the day, nearly every day, as indicated by either subjective report (e.g., feels sad or empty) or observation made by others (e.g. appears tearful) Note: In children and adolescents, it can be irritable mood.

(2) Markedly diminished interest or pleasure in all, or almost all, activities of the day, nearly every day (as indicated by either subjective account or observation made by others).

(3) Significant weight loss when not dieting or weight gain (e.g., a change of more than 5% of body weight in a month), or decrease or increase in appetite nearly every day. Note: In children, consider failure to make expected weight gains.

(4) Insomnia or hypersomnia nearly every day.

(5) Psychomotor agitation or retardation nearly every day (observable by others, not merely subjective feelings of restlessness or being slowed down).

(6) Fatigue or loss of energy nearly every day.
(7) Feelings of worthlessness or excessive or inappropriate guilt (which may be delusional) nearly every day (not merely self-reproach or guilt about being sick).
(8) Diminished ability to think or concentrate, or indecisiveness, nearly every day (either subjective account or as observed by others).
(9) Recurrent thoughts of death (not just fear of dying), recurrent suicidal ideation without a specific plan, or a suicide attempt or a specific plan for committing suicide.

B. The symptoms do not meet criteria for a mixed episode.
C. The symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.
D. The symptoms are not due to the direct psychological effects of a substance (e.g. a drug of abuse, a medication) or general medical condition (e.g. hypothyroidism).
E. The symptoms are not better accounted for by Bereavement, i.e., after the loss of a loved one, the symptoms persist longer than two months or are characterised by marked functional impairment, morbid preoccupation with worthlessness, suicidal ideation, psychotic symptoms, or psychomotor retardation.

Discontinuation rate

100 per cent minus the continuation rate (%).

Dopamine

Neurotransmitter produced by the suprarenal glands that induce vasodilatation,

Dopaminergic system

Cerebral pathways mediated by the neurotransmitter dopamine are thought to be implicated in reward mechanisms including drug effects or addiction and maybe in acute symptoms of schizophrenia.

Drug prevention

Interventions aimed at

- increasing knowledge about drug use by adolescents;
- reducing the use of drugs;
- delaying the onset of first use;
- reducing misuse and abuse of drugs; and/or minimising the harm caused by the use of drugs.

Dysphoria

Opposite to euphoria

Dysthymic disorder

Clinical criteria from DSM IV. The diagnostic criteria require the presence of a depressed mood most of the time for at least two years (one year for children and adolescents). To meet the diagnostic criteria, the patient should not have symptoms that are better accounted for as major depressive disorder. The patient should never have had a manic or hypomanic episode.

Diagnostic criteria:

A. Depressed mood for most of the day, for more days than not, as indicated either by subjective account or observation by others for at least two years. (In children and adolescents, mood can be irritable and duration must be at least one year.)
B. Presence, while depressed, of two (or more) of the following:
(1) poor appetite or overeating
(2) insomnia or hypersomnia
(3) low energy or fatigue
(4) low self esteem
(5) poor concentration or difficulty making decisions
(6) feelings of hopelessness
C. During the two-year period (one for children and adolescents) of the disturbance the person has never been without symptoms in criteria A and B for more than two months at the time.
D. No major depressive episode has been present during the first two years of the disturbance (one for children and adolescents); i.e.: the disturbance is not better accounted for by chronic major depressive disorder, or major depressive disorder in partial remission.
Note; there may have been a previous major depressive episode provided there was a full remission (no significant signs of symptoms for two months) before the development of the dysthymic disorder. In addition, after the initial two years (one for children and adolescents) of the dysthymic disorder, there may be superimposed episodes of major depressive disorder, in which case both diagnosis may be given with the criteria are met for a major depressive episode.
E. There has never been a manic episode, a mixed episode or a hypomanic episode, and the criteria have never been met for cyclothymic disorder.
F. The disturbance does not occur exclusively during the course of a chronic psychotic disorder, such as schizophrenia or delusional disorder.
G. Symptoms are not due to direct physiological effects (e.g., a drug of abuse, a medication) or a general medical condition (e.g. hypothyroidism).
H. The symptoms cause clinically significant distress or impairment in social occupational or other important areas of functioning.

Specify if: early onset: before the age of 21, late onset: at the age of 21 or later.
Specify (for most recent two years of dysthymic disorder) with atypical features.

Economic complements

Two goods are considered economic complements if an increase in the price of good A leads to a decrease in the demand for good B.

Economic substitutes

Two goods are considered economic substitutes if an increase in the price of good A leads to an increase in the demand for good B.

Endocrine system

Concerns intern glandular secretion.

Endogenous cannabinoids

Substances naturally produced in the body that acts on a cannabinoid receptor and whose effects are mimicked by THC or other cannabinoids. Examples: anandamide or 2-AG.

Expected sanction of a cannabis possession

If we transform the sentences for cannabis possession into monetary values, the expected sanction is the theoretical amount of money that a cannabis user will lose due to sentences for violating possession laws each year.

Follicle Stimulating Hormone

Cerebral hormone affecting male and female sexual glands.

Gateway substance

A drug or other substance with properties inducing the user to take other substances later in life.

Glaucoma

Increased pressure of the liquid in the eye ball with blindness as result if untreated. In some patients existing registered medicines do not work, or not enough. This is called "therapy resistant glaucoma". There are cases known that cannabis could lower the eye pressure sufficiently in patients with such a therapy resistant glaucoma.

Hydrophobic

Substance that will not dissolve in water.

Hyperplasia

Abnormal growing of a histological tissue characterised by a multiplication of the cells.

Hypoglycaemia

Low level of glucose in the blood.

Hypothalamus-hypophysiary

Cerebral system controlling, among other actions, all the hormonal regulation.

Immunocompetent

Cells that act in the immunity system.

Incidence

The proportion of new cases in a given period of time, e.g. the percentage of adolescents gaining experience with cannabis for the first time, in the past year.

Indicated prevention

Preventive interventions aimed at subjects who do not have addiction problems according to diagnostic criteria, but who have some early characteristics of problematic use (e.g. interventions aimed at young people experimenting with drugs).

Initiation age of use

Age of first use of the substance concerned.

Legalisation

The elimination of cannabis possession laws and the regulation of cannabis distribution. This regime is similar to alcohol and tobacco regimes in most countries.

Lifetime use; lifetime prevalence of cannabis use

Consumption of cannabis at least once ever in life, usually expressed as a proportion of the populations who used cannabis at least once ever in life.

Liposolubility

Substances which can be dissolved in fats.

Luteinizing Hormone

Cerebral hormone commending the secretion of progesterone.

Lymphocytes

Type of white blood cells influencing the immunity system.

Macrophages

Blood cells able to include and destroy macroscopic exogenous bodies.

Manic episode

Clinical criteria from DSM IV

A. A distinct period of abnormal and persistent elevated, expansive, or irritable mood lasting at least one week (or any duration if hospitalisation is necessary).
B. During the period of mood disturbance, three (or more) of the following symptoms have persisted (four if the mood is only irritable) and have been present to a significant degree:

(1) Inflated self esteem or grandiosity.
(2) Decreased need for sleep (e.g., feels rested after only three hours of sleep).
(3) More talkative than usual or pleasure to keep talking.
(4) Flight of ideas or subjective experience that thoughts are racing.
(5) Distractibility (i.e., attention too easily drawn to unimportant or irrelevant external stimuli).
(6) Increase in goal-directed activity (either socially, at work or school, or sexually) or psychomotor agitation.
(7) Excessive involvement in pleasurable activities that have a high potential for painful consequences(e.g. engaging in unrestrained buying sprees, sexual indiscretions, or foolish business investments).

C. The symptoms do not meet criteria for a mixed episode.
D. The mood disturbance is sufficiently severe to cause marked impairment in occupational functioning or in usual social activities or relationships with others, or to necessitate hospitalisation to prevent harm to self or others, or there are psychotic features.
E. The symptoms are not due to the direct psychological effects of a substance (e.g. a drug of abuse, a medication) or general medical condition (e.g. hypothyroidism).
Note: manic episodes that are clearly caused by somatic antidepressant treatment (e.g. medication, electroconvulsive therapy, light therapy) should not count towards a diagnosis of bipolar I disorder.

Meta-analysis

A statistical method to integrate the results of several studies on the same issue (e.g., of clinical trials, of preventive interventions) into one outcome measure.

Motility

All the movements of an organ.

Multiple sclerosis

Chronic neurological disease in which the myeline shaft of the neuronal axis of the nerve cell is affected in the brain and the spinal cord. One of the symptoms is spasticity in combination with pain. Cannabis is said to be of help to this disease, and especially to this symptom.

Neurotransmitter

Chemical substance in the brain for the transmission of signals between nerve cells.

Neutrophiles

Type of white blood cells.

Orthostatic hypotension

Low blood pressure induced by a standing position.

Parasympathetic system

Global reaction of relaxing of the body induced by the sympathetic nervous system.

Pharmacokinetics

Study of the factors that influence the absorption, distribution, metabolism, and excretion of a licit or illicit drug.

Pre-morbid

Before the actual onset of the disease.

Prevalence

The proportion (usually per cent or per mil) of existing cases (e.g. cannabis users or cannabis dependents) in a given period of time (e.g. a year).

Prolactin

Cerebral hormone commanding the lactation.

Recent use; last year prevalence of cannabis use

Consumption of cannabis at least once in the past year, usually expressed as a proportion of the populations who used cannabis at least once in a given year.

Receptors

A location in the nervous system (usually a protein on the surface of a cell) at which a neurotransmitter or drug binds to exert its effects.

Requirements for market admission (to a medicine)

Before market admission of a medicine is granted (i.e. called "registering" in the EU, and "licensing" in the USA) it should be shown that the product applied for meets three requirements: quality, efficacy and safety.

Quality. Especially the concept of quality is not what is understood by "quality" in daily language: in registration practice it is defining clearly what is to be registered. This comprises defining the composition and other properties of the product and the methods to examine the composition (content and the purity of the constituents) and other properties.

Efficacy is providing the evidence that the product is different from a placebo treatment.

Safety in registration practice is a relative matter. The side effects should be proportional to the beneficial action of the product (in the case of a more serious illness more serious side effects are taken for granted) and also should be taken into account the availability of other safe treatment.

Schizophrenia

Clinical criteria from DSM IV.

A. Characteristic symptoms: two (or more) of the following, each present for a significant portion of time during a one-month period (or less if successfully treated):
(1) Delusions;
(2) Hallucinations;
(3) disorganised speech (e.g., frequent derailment or incoherence);
(4) grossly disorganised or catatonic behaviour;
(5) negative symptoms, i.e., affective flattening, alogia, or avolition.
Note: only one criterion A symptom is required if delusions are bizarre or hallucinations consist of a voice keeping up a running commentary on the person's behaviour or thoughts, or two or more voices conversing with each other.

B. Social/occupational dysfunction: for a significant portion of the time since the onset of the disturbance, one or more major areas of functioning such as work, interpersonal relations, or self-care are markedly below the level achieved prior to the onset (or when the onset is in childhood or adolescence, failure to achieve expected level of interpersonal, academic, or occupational achievement).

C. Duration: continuous signs of the disturbance persist for at least six months. This six-month period must include at least one month of symptoms (or less if successfully treated) that meet Criterion A (i.e., active-phase symptoms), and may include periods of prodromal symptoms, or signs of the disturbance may be manifested by negative symptoms only, or two or more of the symptoms listed in Criterion A may be present in an attenuated form (e.g., odd beliefs, unusual perceptual experiences).

D. Schizoaffective and mood disorder exclusion: Schizoaffective Disorder and Mood Disorder with Psychotic Features have been ruled out because either (1) no Major Depressive, Manic, or Mixed Episodes have occurred concurrently with the active-phase symptoms; or (2) if mood episodes have occurred during active-phase symptoms, their total duration has been brief relative to the duration of the active and residual periods.

E. Substance/general medical condition exclusion: the disturbance is not due to the direct physiological effects of a substance (e.g., a drug of abuse, a medication) or a general medical condition.

F. Relationship to a Pervasive Developmental Disorder: If there is a history of Autistic Disorder or another Pervasive Developmental Disorder, the additional diagnosis of Schizophrenia is made only if prominent delusions of hallucinations are also present for at least a month (or less if successfully treated).

SDLP

Standard deviation of lateral position.

Selective prevention

Preventive interventions aimed at individuals or groups of people who have an increased risk of drug use problems (e.g., programs aimed at children of alcoholics or high-risk inner city youth).

Statistical power (in clinical trials)

A clinical trial has more statistical power if it can discriminate more convincingly between the effects of the intervened group and the control group.

Substance Abuse

Clinical criteria from DSM IV

A. A maladaptive pattern of substance use leading to clinically significant impairment or distress, as manifested by one or more of the following occurring within a twelve-month period:

(1) Recurrent substance use resulting in a failure to fulfil major role obligations at work, school, or home (e.g. repeated absences or poor work performance related to substance use, substance related absences, suspensions, or expulsions from school; neglect of children or household).

(2) Recurrent substance use in situations in which it is physically hazardous (e.g. driving an automobile or operating a machine when impaired by substance use).

(3) Recurrent substance related legal problems (e.g. arrests for substance related disorder conduct).

(4) Continued substance use despite having persistent or recurrent social or interpersonal problems caused or exacerbated by effects of substance (e.g. arguments with spouse about consequences of intoxication, physical fights).

B. Symptoms have never met the criteria for substance dependence for this class of substance.

THC

Tetrahydrocannabinol.

THC-COOH

11-nor-Δ^9-tetrahydrocannabinol-9-carboxylic-acid.

Thyroxin Hormone

Thyroid hormone containing iodine.

Universal prevention

Preventive interventions aimed at the general population or a part of it that is not identified on the basis of individual risk factors (e.g., mass media campaigns and school-based programs aimed at all students).

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