Project No. TREN-05-FP6TR-S07.61320-518404-DRUID

DRUID
Driving under the Influence of Drugs, Alcohol and Medicines

Integrated Project
1.6. Sustainable Development, Global Change and Ecosystem
1.6.2: Sustainable Surface Transport

6th Framework Programme
D 2.1.3

Working paper
Cannabis, driving and road safety: a review of the scientific literature

Date of finalisation of the working paper: 01.10.2007
Actual submission date: 21.10.2011

Start date of project: 15.10.2006
Duration: 60 months
Organisation name of lead contractor for this deliverable: INRETS
Revision 1.0

Project co-funded by the European Commission within the Sixth Framework Programme (2002-2006)		
Dissemination Level		
PU	Public	X
PP	Restricted to other programme participants (including the Commission Services)	
RE	Restricted to a group specified by the consortium (including the Commission Services)	
CO	Confidential, only for members of the consortium (including the Commission Services)	

Working paper

Cannabis, driving and road safety: a review of the scientific literature

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Project Funded by the European Commission under the Transport RTD Programme of the 6th Framework Program

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Note

This review has been last updated in 2004. Since then a number of papers have been published on the subject of driving under the influence of cannabis. Here are some of them:

Asbridge, M., Poulin, C. and Donato, A., 2005. Motor vehicle collision risk and driving under the influence of cannabis: Evidence from adolescents in Atlantic Canada. Accident Analysis & Prevention 37 (6), 1025-1034.

Bedard, M., Dubois, S. and Weaver, B., 2007. The impact of cannabis on driving. Can J Public Health 98 (1), 6-11.

Berghaus, G., Ramaekers, J. G. and Drummer, O. H., 2007. Demands on scientific studies in different fields of forensic medicine and forensic sciences: Traffic medicine--Impaired driver: Alcohol, drugs, diseases. Forensic Science International 165 (2-3), 233-237.

Bernhoft, I. M., Steentoft, A., Johansen, S. S., Klitgaard, N. A., Larsen, L. B. and Hansen, L. B., 2005. Drugs in injured drivers in Denmark. Forensic Science International 150 (2-3), 181-189.

Cheng, J., Chan, D. and Mok, V., 2005. An epidemiological study on alcohol/drugs related fatal traffic crash cases of deceased drivers in Hong Kong between 1996 and 2000. Forensic science international 153 (2-3), 196-201.

Macdonald, S., Mann, R. E., Chipman, M. and Anglin-Bodrug, K., 2004. Collisions and traffic violations of alcohol, cannabis and cocaine abuse clients before and after treatment. Accident Analysis & Prevention 36 (5), 795-800.

Smink, B. E., Ruiter, B., Lusthof, K. J., Gier, J. J. d., Uges, D. R. A. and Egberts, A. C. G., 2005. Drug use and the severity of a traffic accident. Accident Analysis & Prevention 37 (3), 427-433.

Walsh, M. J., Flegel, R., Atkins, R., Cangianelli, L. A., Cooper, C., Welsh, C. and Kerns, T. J., 2005. Drug and alcohol use among drivers admitted to a Level-1 trauma center. Accident Analysis and Prevention 37 (5), 894-901.

Also, since this review was conducted, there have been some advances in the testing of THC, in particular in saliva fluids.

1 Introduction

Based on international literature and recent data acquired in France, this paper seeks to examine how the consumption of cannabis, possibly combined with that of alcohol, affects driving behaviour and what the result is in terms of its impact on road accidents.

2 Detection and prevalence of cannabis in driver populations

In surveys of drivers, whether they are involved in accidents or not, cannabinoids regularly top the list of the illicit drugs detected. The prevalence of cannabis detected depends on the populations surveyed. Estimations are largely the result of the way in which the samples tested are selected and of the means used to detect the cannabis (see sidebar on "Detection of cannabis").

While the United States undoubtedly stands out in terms of the history of its research into this subject, with numerous papers having been published as early as the 1970s and throughout the 1980s, Europe largely made up for its late start during the 1990s.

2.1 Detection of cannabis, biological specimen and significance

Detecting cannabis is not easy because of the complex metabolism of this substance.
Remember that the major psychoactive agent is Δ^9-THC (Δ^9-transtetrahydrocannabinol or more simply **THC**), which is rapidly metabolised into 11-OH- Δ^9-THC (11-hydroxy-tetrahydrocannabino or more simply 11-OH-THC), which is also psychoactive. The blood levels of THC, as those of 11-OH-THC, diminish rapidly. The 11-OH- THC is then oxidised into Δ^9-THC-COOH (11-nor 9-carboxy-Δ^9-tetrahydrocannabinol or more simply THC-COOH), the principal metabolite found in the urine, but it is not psychoactive.

Detection in the blood: after consumption, the levels of concentration of THC in the blood rise rapidly to a peak within 10 minutes following the start of inhalation and drops rapidly. It remains detectable for about 4 hours. The 11-OH-THC is only present in the blood very briefly and in low concentrations (except for ingested cannabis). For this reason, it is rarely mentioned in road safety research. The THC-COOH is detectable in the blood in the minutes following its consumption and up to several hours after the cannabis is consumed.

Detection in the urine: The THC-COOH is detectable in the urine for 30 minutes after the consumption and can be detected for several days or weeks although the psychoactive effects have disappeared.

Detection in other biological specimen:
The advances made in toxicological analysis make it possible to propose a wide variety of screening methods, which the European Rosita (Roadside Testing Assessment) project coordinated by the toxicologist A. Verstraete[1] was set up to catalogue and evaluate. Currently, saliva appears to be interesting because of the strong THC saliva/blood relationship. THC can also be detected in sweat, but its presence is not an evidence of recent consumption. Hair analysis provides information concerning time and amount of cannabis consumption, but it is not possible to detect recent use. Hair is appropriate when it's necessary to characterise the cannabis consumption of regular users during a period of time.

In practice, detection of drivers under the influence of cannabis
It is difficult to rely solely on the THC value for classifying subjects according to whether they are "exposed to the influence of cannabis" or not. The THC level may be close to zero, yet the harmful effect may persist. Bates and Blakely (1999) stress the rapid fall in the THC level in the blood, which

1 Verstraete AG, Samyn N. Le dépistage biologique d'une conduite sous influence [Toxicological detection of driving under the influence]. Annales de Toxicologie Analytique, vol XV, n°2, 2003

makes it extremely hard to detect unless the sample is taken very soon after the accident. That justifies the use of THC-COOH. However this metabolite may be detected once its effects on behaviour have already worn off. . When they are both measured, the respective values of concentrations of THC and THC-COOH in the blood or urine can, with the help of pharmacokinetics, provide information about the status of the intoxication (time since consumption, chronic use, and so on).

In practice, one generally considers that the presence of THC in the blood is evidence of recent consumption of cannabis that could impair the driver's faculties, while the presence of THC-COOH in the blood or urine indicates consumption that could go back several days, indeed several weeks, without any connection with possible effects on driving behaviour.

2.2 Prevalence among drivers involved in accidents

In surveys of drivers who have been involved in accidents, a blood or urine sample (and sometimes both) is taken from the subjects and the cannabis is detected by looking for the presence and level of THC in the blood, or THC-COOH in the blood or urine. It is exceptional to look for 11-OH-THC because its blood concentrations are too low to be detected. The toxicological analysis process, which differs from survey to survey, may be divided into two stages – testing and confirmation – or be reduced to only one. The methodologies used entail different combinations of the choice of biological fluids for testing or confirmation and the substances looked for (THC or THC-COOH); they employ dosing techniques that have different levels of sensitivity (a test is sensitive when there are few false negatives) and different levels of specificity (a test is specific when there are few false positives). Given the rapid drop in the level of THC in the blood, the time lapse between the accident and the taking of the sample has a considerable influence on the outcome: the time lapse has to be as short as possible.

Moreover, several biases can affect the representativeness of the samples collected. In the event of an accident, a positive alcohol test generally suffices for legal action to be taken; that is why it is rare for a drug screening test to be carried out, since it is more costly and, in the event of a positive result, difficult to interpret. For that reason, the prevalence of drugs in accidents is poorly estimated. As far as fatal accidents are concerned, the data are often incomplete, to the extent that tests designed to detect the presence of drugs are not carried out on drivers that are victims of fatal accidents within the required time (or not at all). Only the systematic taking of samples from accident victims can prevent such biases.

Prevalence figures obtained from surveys of drivers involved in accidents have to be interpreted in the light of the methodological choices and precautions taken, which differ from one survey to another.

2.2.1 Europe

Tables 1 (Europe outside France) and 2 (France) in the appendix bring together data on cannabis prevalence within populations of drivers involved in accidents in different countries in Europe. The scope for making comparisons between countries remains limited: such comparisons would only have meaning if standardised methods of data collection were used, which is not the case.

Within relatively representative samples of drivers involved in accidents in Europe, the estimated proportions of positive cannabis drivers vary from 4% to 14%: from 4% to 6% in Belgium and Italy, from 10% to 12% in the United Kingdom (and the Netherlands), and from 6% to 14% in France. These differences reflect both the real phenomenon and the method used (biological fluids, compounds tested for, and thresholds).

2.2.2 France (focus on French research)

French research accurately reflects the diversity of approaches and thus does not get round the difficulty of comparing the results.

In the study of Schermann et al. (1992) carried out on a sample of about 2,500 drivers hospitalised after a road accident, between 6% and 7% of blood samples tested positive for cannabis derivatives, with 4.4% having tested positive for cannabis alone and 1.2% positive for cannabis and an illegal blood alcohol concentration. Some toxicologists now voice reservations about the results because of

the THC detection methods used in this study. According to Schermann, however, the method was appropriate given the technology of the time and the massive scale of the survey, even though this might seem inadequate within the framework of a protocol with a judicial and regulatory vocation. The studies that followed involved far more limited samples, of a few hundred drivers.

The studies of Pélissier et al. (1996) and Marquet et al. (1998) involved relatively young injured drivers and used urine as the testing and confirmation biological fluids. Pélissier et al. stress the advantages and difficulties associated with urine as the biological environment, and try to lay the foundations for a rapid, sensitive and specific testing method applicable to large populations. Marquet et al. highlighted the strong prevalence of cannabinoids in injured drivers (13.8%), with twice as many men as women found to be users of cannabis (16% as against 8.3%).

Mura and his colleagues published several studies. The first (1999) was devoted to the search for the presence and level of illicit drugs in blood samples taken from drivers involved in a serious or fatal accident and suspected of driving under the effect of drugs. For that reason, the 26% rate they arrive at for the frequency of cannabis use (presence of THC and/or THC-COOH) is an overestimate. The subsequent studies of Mura et al. involved a multi-centre sample of 900 drivers involved in an injury accident and hospitalised, with a control sample of 900 subjects hospitalised for a reason other than being involved in a road accident. The first analyses (2001) were carried out on a sample of 420 road injured drivers and a sample of 380 controls. The prevalence of cannabis (presence of THC and/or THC-COOH) was similar between the accident victims and the control group, at 11.2% and 10.8% respectively. This finding remains valid if one considers only the cases that tested positive for THC (6.9% and 5.8% respectively). On the other hand, significant differences emerge when age is taken into account: in the 18-20 age group, THC is found in 18.6% of drivers and 8% of controls. The processing of the full sample (Mura et al., 2003) confirms the role of age: one finds that 24.8% of drivers under the age of 27 test positive for cannabis (THC > 1 ng/ml), whereas the proportion for all age groups is 10%. However, the two papers do not enable us to judge the quality of sample selection methods that ought to ensure the representativeness of the samples of accident victims and controls.

Kintz et al. (2000), who participated in the European Rosita project, instituted an analytical study for evaluating the comparative merits of four biological fluids – blood, urine, saliva and sweat – in the detection of psychoactive substances on the roadside. After alcohol (present in 13.6% of cases), cannabis is the product most commonly consumed by drivers involved in accidents (9.6% of cases established by blood tests), with the concentrations of THC varying from 0.4 ng/ml to 5.4 ng/ml. The urinary metabolite is found more often in the urine (13.6%) than THC in the blood (9.6%), confirming the Belgian study's finding (6% for urine vs. 3.6% for blood). Kintz et al. (2000) point out that the prevalence of cannabis as measured by blood tests (9.6%) proves to be close to the prevalence of illegal alcohol concentrations (> 0.5g/l) in the same sample (10.6%). According to Kintz, blood samples are always available, whereas collecting urine samples is difficult even in hospitals: they were missing in 16% of cases. Samples of saliva and sweat are almost always available. Analyses of saliva and sweat have demonstrated the presence of the THC mother-substance in these two fluids, but the presence of metabolites has never been found. Nevertheless, characterising the use of psychoactive substances at the roadside with the help of alternative biological fluids must wait for tools that are adapted to these fluids.

The application of the Gayssot Act in France led to a change of scale in the size of samples. The compilation of blood samples taken by 19 expert toxicologists under the provisions of the Gayssot Act yielded 3,751 dose results (Pépin et al., 2003). This exercise revealed the presence of cannabinoids (THC or THC-COOH) in 13.8% of drivers in the sample (and 27.2% in those aged under 27).

The SAM (Stupéfiants et Accidents Mortels [illicit drugs and fatal crashes]) survey covers all the drivers involved in fatal accidents (whether killed, injured or unharmed) during the two years that the Gayssot Act was in force and does not suffer from any representativeness bias (the missing data were checked). It is now the study of reference in France (OFDT, 2005; Laumon et al., 2005). Of the approximately 10,000 drivers involved in fatal accidents with completed data on alcohol and illicit drugs testing, we counted 7% who tested positive for cannabis (THC/blood level of over 1ng/ml) and a total of 8% who tested positive for illicit drugs[2]. Recent cannabis consumption (THC/blood level over

[2] "Stupéfiants et accidents mortels de la circulation routière" (Illicit drugs and fatal road accidents) - SAM study, Conclusions, OFDT web site. The level in the blood was considered positive starting at a concentration of 1 ng/ml of THC for cannabis, 20 ng/ml for opiates, 50 ng/ml for amphetamines et 50 ng/ml for cocaine.

1ng/ml) was found in particular in fatal crash involved drivers aged under 25, since 17% of them were positive for cannabis. It should be noted that the prevalence levels reported here relate to the active ingredient of cannabis, THC, in concentrations tested positive above the legal limit, and not to cannabinoids in general. This is one of the reasons why it is not surprising to find a lower prevalence than those generally reported in other studies[2].

Another study of Mura et al. (2005) implies an increase in the prevalence of cannabis in drivers involved in accidents between 2000-2001 and 2003-2004, when it rose to 28.9% for those aged under 30 (compared with 24.8% for those aged under 27 in 2000-2001[3]). The analysis presented suffers from a lack of rigour for at least three reasons: it does not ensure comparability between the samples (injured in 2001-2002 versus killed in 2003-2004); the THC measurement thresholds are not the same (> 1 ng/ml in 2001-2002 versus > 0.2 ng/ml in 2003-2004); and the association with alcohol was not studied in 2003-2004. Their conclusion is not solidly backed up, therefore[3]. The publication in which Mura seeks to invalidate previous studies (and especially the SAM study) is hasty to say the least!

2.2.3 Outside Europe

A synthesis of prevalence studies carried out in the United States, Canada and Australia was produced by Bates and Blakely (1999). Results were reported for all three countries. The team led by Drummer (2003) recently updated the findings of these surveys. There again, the studies are not directly comparable to the extent that the thresholds for alcohol consumption are not the same, the methods used to test for the presence of THC and/or its metabolites do not have the same sensitivity and specificity levels, and the time lapse between the accident and the collection of the blood samples varies from one study to another.

The research conducted in Australia deserves particular attention. The Australian study of Longo et al. (2000a) is interesting in several respects: the size of the sample (2,500 injured drivers); the obligatory requirement for blood samples to be taken in Australia, which guarantees the representativeness of the sample; and the distinction between THC and THC-COOH (and their respective concentrations). Cannabinoids were detected in 10.8% of injured drivers: 8% tested positive for THC-COOH only and 2.8% for THC-COOH and THC. Alcohol tests were positive for 12.4% of drivers and were above 0.5g/l in 10.4% of them. The association of cannabis and alcohol (28% of those who tested positive for cannabis also tested positive for alcohol) was the most common of the cannabis-other psychoactive substance combinations, with high blood alcohol concentrations. In comparison with the group without drugs, those tested positive for THC tend to be men and young; THC alone is more frequent in two-wheelers riders; THC alone or in combination with alcohol is more frequent in car drivers involved in single-vehicle accidents. While the study of Longo et al. (2000a and b) has many advantages over previous studies, some limitations still have to be pointed out: the toxicological procedure used (radio-immuno test on blood samples) is sometimes criticized.

Drummer and his colleagues use a database covering 3,398 Australian drivers killed in road accidents between 1990 and 1999, which contains all the toxicological data concerning these drivers. The study was carried out in three Australian states (Victoria, New South Wales and Western Australia). A certified toxicology laboratory carried out tests in each state.

According to Drummer et al. (2003), cannabis (THC or THC-COOH) is present in 13.5% of all drivers killed in accidents, while alcohol (above 0.5g/l) is present in 29% of them[4]. These figures vary as a function of the category of user. Cannabis is present in 12% of car drivers, 22% of two-wheeler riders, and 6.5% of truck drivers, while alcohol is present in 30% of car drivers, 29% of two-wheeler riders and 8.6% of truck drivers.

During the decade, there was an increase in the proportion of drivers involved in accidents while under the influence of cannabis: it went up from 11% in 1990-1993 to 13.5% in 1994-1996 and 15.6% in

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[3] The publication of Mura et al (2005) only mentions as basis for comparison a figure of 15.3% which is the prevalence of *THC only* above 1 ng/ml among young adults below 27 years old

[4] In this study, among the subjects who were postive for THC-COOH, about half of them were positive to THC

1997-1999. At the same time, the proportion of drivers with illegal blood alcohol concentrations diminished, declining from 33% before 1994 to 27-28% afterwards.

Lastly, the highest prevalence is found in the 22-30 age group, both in those riding motorised two-wheelers (27%) and in those driving cars (20%), while it was negligible for the over-50s.

In the surveys carried out over the past 15 years (Table 3 in the appendix), cannabis use, as detected by the presence of cannabinoids *in the blood*, is found in a little under 10% of drivers injured or killed in an accident, and when cannabis is detected, alcohol is often found as well (in between 28% and 63% of subjects tested positive for cannabis).

As regards the risk associated with cannabis, these prevalence findings are not useful in the absence of comparable data for a control group.

2.3 Prevalence in the whole driving population

It is difficult for ethical reasons to force anyone from the driving population to give a blood or a urine sample. Surveys entailing the large-scale application of alternative methods for collecting urine or saliva from road sites are regarded as pilot studies (Germany; the Netherlands, Quebec). Their results tend to under-estimate the prevalence because cannabis users are more prone to refuse than non-drug users.

Variations in prevalence on the road, which are doubtless attributable to the different uses of cannabis in the countries concerned, are also partly attributable to the different options for surveying drivers in traffic and the different possible cannabis detection procedures. Table 4 in the appendix recapitulates the characteristics of the available surveys.

All in all, these roadside surveys conducted in the absence of an accident or of *any presumption* of driving under the influence of psychoactive substances indicate that 1% to 6% or 7% of drivers are positive for cannabis. These proportions seem lower than the 4% to 14% observed in accident situations (Tables 1 and 2 in the appendix).

Cannabis detection rates in drivers suspected of driving under the influence of drugs (*with presumption*) are, unsurprisingly, generally higher. They depend above all on the way police officers select the drivers they test, which is a source of some bias. Furthermore, they often only screen for drugs if the blood alcohol concentration is lower than the legal limit, which is another source of bias.

2.4 Alcohol and age – strongly related to cannabis

One observation which underlies the data gathered in all these surveys, both in and outside accident situations, is that the presence of cannabis is particularly frequent in young drivers aged under 25. When data for prevalence by age category are available in the literature, the highest proportions are found in the 20-24 and the under-20 age groups.

In the United Kingdom, the prevalence of cannabis consumption by drivers involved in accidents remains relatively high in the 40-60 age group. The roadside survey in Quebec showed a higher level of consumption by young drivers (18 to 35) at night: the night-time frequency for this age group was twice as high as in the day.

In France, recent cannabis consumption is particularly common among drivers involved in accidents who are aged under 25 (17% tested positive for cannabis), is still present in 25-34-year-olds (8% tested positive), but is almost non-existent over the age of 35 (1.5% in the 35-69 age group and less than 1% of the over-70s tested positive) [5].
Generally speaking, a substantial proportion of drivers tested positive for cannabis also test positive for alcohol (Table 3 in the appendix). The proportion is 40% in France, according to the SAM study [6]. It should be noted that Mura et al. (2003) estimated the proportion at 32% in drivers aged under 27.

[5] Laumon et al (2005)
[6] Among the 751 drivers who display a THC dose above 1 ng/ml, 301 of them also have a blood alcohol concentration above 0,5g/l

3 Association between cannabis consumption and accident risk

The proportion of drivers driving under the influence of cannabis and involved in accidents is sufficiently high, and the harmfulness of the product in certain situations sufficiently well established, for cannabis to be considered a major potential accident factor. But it is less easy to perform the statistical demonstration of the risk than in the case of alcohol. The first difficulty with which epidemiologists are confronted is that of putting together a control sample of crash non-involved drivers. The other major difficulty is the uncertain relationship between the presence of cannabis in the blood or urine and its effects on behaviour.

Numerous research teams have worked on the quantitative analysis of the risk linked to cannabis, and their results seem to have progressively converged. Bates and Blakely (1999) produced an excellent critical review of the available analytical epidemiological studies from the 1980s onwards in the United States and Australia. Since then, fresh studies have seen the light, especially those of Dussault et al. (2002) in Quebec, Drummer et al. (2003 and 2004) in Australia and Laumon et al. (2005) in France. After a long period of rather uncertain and sometimes contradictory results that were well highlighted by Bates and Blakely, the causal link between cannabis use and road accidents now appears to have been demonstrated (Ramaerkers et al., 2004,[7] and Laumon et al., 2005[7]).

3.1 The difficulties of the epidemiological approach

Identifying recent cannabis use involves taking a biological sample from subjects. While a biological sample is commonly taken from subjects who have been killed or injured in an accident, it is not possible for ethical reasons to force non crash-involved drivers to provide such a sample. Moreover, there are no prevalence data for the population driving on the road that can be compared with data gathered from accident victims in the majority of countries, with the exception of Quebec (Dussault et al., 2002)[8] and the Netherlands (Movig et al, 2004), where a urine sample is taken from the general driving population.

In case-control studies, the control group is sometimes chosen as patients who are hospitalised for a reason other than a road accident, for comparison with hospitalised road accident drivers (cf. Table 7 in the appendix). This method may not guarantee the representativeness of the control group compared to the general driving population.

Studies that have attempted to establish a relationship between cannabis consumption and accidents have thus for the most part used a responsibility approach. Among crash-involved drivers, the group of drivers responsible for the crash is considered as the cases group, while the group of non-responsible drivers is considered as the control group. By comparing the two groups, and in particular their cannabis prevalence, one evaluates the risk of being responsible of a crash as a function of cannabis use. The responsibility assessment must be done without knowing the drivers‘ cannabis status or other information correlated with it, especially alcohol.

Lastly, cannabis use is strongly associated with some characteristics, such as age and alcohol consumption. These are independent risk factors for road accidents. It implies that they are confusion factors in the relationship between cannabis consumption and crash risk, so that they must be taken into account when evaluating this relationship.

Each of these methodological considerations has an impact on the interpretation of the results.

[7] Ramaekers et al. (2004) provided a review focused on the dose-effect relationship, based on results from the most recent epidemiological studies, except the French SAM study which was not yet published

[8] The study of Dussault et al. (2002) combines the two approaches, the case-control study (comparing blood/breath for alcohol detection and urine/urine for cannabis detection) and the responsability approach (using the blood samples).

3.2 Studies based on responsibility for an accident

Several research studies have used the responsibility approach. Their modus operandi and their results are described in Table 5 in the appendix. The most important studies, in terms of both their scale and the rigour with which they assess responsibility, were carried out in the United States by Terhune et al. (1992) and in Australia by Longo et al. (2000) and by Drummer et al. (1994, 2004),. The Quebec study (Dussault et al., 2002), although based on a small sample, has the peculiarity of coupling an analysis of responsibility with an analysis comparing the crash-involved and killed drivers with control subjects driving on the road. Lastly, the French SAM study was conducted on the largest scale so far (Laumon et al., 2005).

In these studies, testing for cannabis is generally performed on blood samples, except in the case of those carried out by Drummer, which tends to use urine samples, and testing positive for cannabis is attested by the presence of THC-COOH or THC.

The identification of those responsible and those not responsible for the crash depends on the information available. Different criteria were used in the different studies leading to variations in the groups to be compared. Terhune et al. (1992), Robertson and Drummer (1994) and Longo et al. (2000)[9] defined three levels of responsibility – responsible, contributory, not responsible – taking account of possible attenuating factors (road condition or vehicle characteristics and general driving conditions). On the contrary, Schermann et al. (1992) used the responsible/not responsible criterion defined by the police force. The SAM group used a method adapted from Robertson and Drummer (1994). It was compared with experts assessments on a sub-sample of drivers involved in multi-vehicle crashes, and a high concordance was found between the two (kappa=0.7)

3.2.1 Cannabis-related odds ratios

Whereas these studies show a high degree of concordance of results for alcohol (all significant odds ratios are between 5 and 8), the same is not true for cannabis alone: the odds ratios do not appear significantly different from 1 in several of these studies (Terhune, 1982; Williams, 1985; Schermann, 1992; Drummer, 1994; Longo, 2000; and Dussault, 2002).

Should this absence of a significant relationship between cannabis use and responsibility for an accident be attributed to some methodological issues, to driver's compensation phenomena suggested by experimental studies, or to other social characteristics associated with cannabis use while driving but not taken into account?

Biases can appear if confusion factors are not controlled for. These may be characteristics associated with cannabis use, such as age, sex, time of the journey, and alcohol consumption. While alcohol is a factor that is often taken into account, the role of other factors is less so, or not at all. In this case, responsibility studies only identify a high risk of being responsible in accidents when one is a young man driving at the weekend, instead of a high risk associated with the recent use of cannabis.

As regards to cannabis screening:
In most research studies cannabis use is established by the presence of THC-COOH, an inactive metabolite of THC. Yet driving under the influence is identified with greater certainty by the presence of THC in the blood, which alone is evidence of a recent consumption of cannabis. Two responsibility studies explicitly used THC levels to establish driving under the influence of recent cannabis consumption, namely Drummer et al. (2004) and Laumon et al. (2005), and in these two studies, cannabis was identified as a risk factor (significant odds ratio). The adjusted odds ratio is respectively 2.7 and 1.8.

As regards to dose-response:
As Table 6 in the appendix shows, the odds ratios of responsibility increase when THC concentration rise. The data provided by Longo et al. (2000), who already considered the possibility of a more radical effect of cannabinoids at sufficiently high concentrations in the blood, are confirmed by more recent data.

[9] And also Hunter et al. (1998) report cited by Bates and Blakely (1999)

According to the more recent analysis of Drummer et al. (2004), the odds ratio calculated for drivers whose THC exceeds 5 ng/ml amounts to 6.6 (as compared to 2.7 for all positive THC levels). The constituted THC categories are of small size in these Australian studies, because of datasets of about 3,000 drivers.

The SAM study in France, which involved around 10,000 drivers, also demonstrated the existence of a higher crash risks associated with higher THC levels. The risk of being responsible for an accident rises from 1.6 for a THC below 1 ng/ml to 2.1 for a THC of more than 5 ng/ml.

This increase is less clear-cut than that displayed by Drummer et al. (2004), but his results were marred by a higher degree of uncertainty (as based on only 58 subjects).

3.2.2 The combination of cannabis and alcohol

In several studies, the odds ratios for the combination of alcohol and cannabis seem higher to the odds ratios for alcohol alone (Bates and Blakely, 1999).

The SAM study, which has a higher statistical power than the studies that preceded it, succeeded in demonstrating that the effects of cannabis and alcohol were multiplicative[10]: the risk of being responsible for a fatal accident is estimated at 14.0 in drivers tested positive for both cannabis and alcohol, which is very close to the product of the risks (15.1) associated with cannabis alone (1.8) and alcohol alone (8.5). This also implies that there is no interaction between the two.

3.2.3 Conclusion

Until the early 2000's, studies remained too uncertain to demonstrate that cannabis alone had an effect on the risk of anyone involved in a fatal or serious injury accident being responsible for that accident.

Their main limitation, apart from the often inadequate size of the sample, was their failure to distinguish between past use of cannabis (with THC-COOH as the marker) and recent use of cannabis (indicated by THC). No study shows that past use (i.e. using THC-COOH as the marker) of cannabis alone affects the risk of an accident, while increasingly accurate results show that recent use (i.e. using THC as the marker) of cannabis does increase the risk of an accident. The most recent studies highlight a significant risk of the order of 2, and in addition show a dose-response: the risk of being responsible increases with higher concentrations of THC.
The effects of THC and alcohol on driving performance and the risk of an accident combine each other, creating a very high risk, since it is the product of the alcohol risk and the cannabis risk taken separately.

3.3 Studies comparing accident victims with control subjects not involved in an accident

The epidemiological study undertaken by Dussault et al. (2002) used two data sources in parallel: blood and urine tests performed on all drivers killed in accidents in Quebec between April 1999 and November 2001 (482 drivers), and breath and urine (and saliva) tests carried out on a sample group of control drivers at 348 sites representing the population of drivers in Quebec (total sample: 11,942 drivers). The case-control analysis was conducted by comparing the urine/urine samples for cannabis, and the blood/breath samples for alcohol. In the case of cannabis, 354 deceased drivers for whom urine and blood samples were obtained were compared with 5,931 control drivers who provided urine. In addition, a responsibility analysis was performed using the Terhune method. It was then possible to compare the results obtained by these two methods.

Concerning alcohol, the case-control analysis yields an odds ratio of 39.2 and the responsibility analysis yields an odds ratio of 8.1 (both significant) for blood alcohol concentration over 0.8 g/l. Concerning cannabis, the case-control analysis gives a significant odds ratio of 2.2 whereas the responsibility analysis is not conclusive (odds ratio of 1.2, not significant). The increase for benzodiazepines (odds ratio of 2.5) according to the case-control study is confirmed by the

[10] Cf SAM study, october 2005, OFDT website

responsibility analysis. Moreover, the results confirm the particularly damaging effect of combining alcohol and cannabis (there again, the responsibility analysis is less conclusive than the case-control analysis).

The apparent divergence between the results for cannabis from the two types of studies is attenuated by the following: Dussault et al. estimated in fact two different specific risks. In their responsibility study only based on fatally injured drivers, they estimated the risk of being responsible for a fatal crash, but only among killed drivers. In their case-control study (controls in driving population), the risk they estimated is the risk of dying in a crash, among the driving population. Furthermore, the statistical power of the responsibility study is probably much lower as it is based on about 500 subjects (killed drivers) whereas the case-control study is based on about 6000 subjects.

The Movig et al. (2004) study comprises 110 cases and 816 controls. Despite its rigorous statistical methodology, the study suffers from two limitations: firstly, its small scale (resulting in wide confidence intervals for the odds ratio); and secondly, the non-homogeneous identification of positive cases: using urine and blood samples in different proportions in the two groups. In the control group, 85% of confirmed cases were established using urine (and 15% using blood), while in the group of injured drivers only 39% of confirmed cases were established using urine (and 61% using blood). In other words, controls were mainly tested for THC-COOH whereas cases were mainly tested for THC. This can be expected to result in an over-estimate of the prevalence of cannabis in the control group and thus an under-estimate of the risk associated with cannabis. The risk of being involved and injured in an accident increases significantly with benzodiazepines, with alcohol, and with the combination of alcohol and illicit drugs. But there does not appear to be a significant increase in risk with cannabis: odds ratio of 1.2 (CI of 95%; 0.55.3-2.73).

3.4 Cohort studies

Gerberich and Goodwin (2003) carried out a retrospective study on a cohort constituted from a care programme in northern California (n=64,657) to compare the frequency of hospitalisation arising from traffic accidents for illicit drug users and non-users. The members of the cohort filled out a reference questionnaire on health-related behaviour, including the use of cannabis between 1979 and 1985. Cases of hospitalisation for a road accident were identified for the period from the reference date to 1991. An increase in the risk (multiplied by 2.3) was found for drug users compared to non-users. The data from these studies clearly suggest that cannabis increases the risk of involvement in an accident, although they are sometimes disputed to the extent that there are other risk factors associated with cannabis use that need to be controlled for (such as lifestyle).

Fergusson and Horwood (2001), for example, used a cohort of 907 young New Zealanders to establish a significant statistical relationship between the frequency of self-reported cannabis use and the self-reported frequency of road accidents (1.6), but this association disappears after adjusting for other behavioural risk factors (risky behaviour). This suggests, therefore, that the crash risk for drivers using cannabis is associated with their lifestyle and their mode of driving rather than with the cannabis itself. But alternatively one could argue that cannabis use stimulates risky behaviour and/or attitudes associated with an increase in risk.

4 Conclusion

Cannabinoids are the illicit drugs that are most frequently detected in driver populations. Experimental data from the early 1980s led people to anticipate a danger on the road associated with the consumption of cannabis, but due to the absence of consistency in the results of different epidemiological studies, we had to wait until the 2000s to reach robust conclusions proving that cannabis use is a risk factor for road accidents.

Because of their low statistical power (partly due to small size of the study groups), studies based on the responsibility approach did not succeed in demonstrating that the consumption of cannabis alone increased the probability of being responsible in the event of an accident. In that respect, the situation was manifestly different from the case of alcohol.

Responsibility studies based on hospital data ignore drivers who were neither killed nor injured in an accident but who could nevertheless be responsible for it, which reduces the representative scope of the results. From this standpoint, the French SAM study is the most comprehensive, since it is exhaustive and covers all the drivers involved, even those unharmed. Furthermore, although confined to fatal accidents, its statistical power is higher then than all previous studies.

Given our current state of knowledge, it seems possible to assert today that recent cannabis (THC) use multiplies the risk of being responsible for a fatal accident by at least 2. One could add that the combined use of cannabis (THC) and alcohol greatly increases the risk of being responsible.
Over and beyond the increasingly accurate affirmation of the role of cannabis as a risk factor in accidents at the scale of a population (quantification of the risk), huge progress has been made in the detection system itself: biological fluids, thresholds and devices adapted to use on the road.

5 Main literature references

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6 Appendix

Table 1: Detection and prevalence of cannabis in drivers involved in accidents in Europe outside France

FPIA: Fluorescence polarisation immunoassay; SM/GC Mass spectrometry gaseous chromatography; EIA: Enzyme Immunoassay; EMIT: Enzyme multiplied immunoassay technique; THC: ∆9-THC
*Sample: requisitions at the request of the prosecutor

Reference country	Study group	Sample size	Detection method	Prevalence of cannabis
Belgium (1995-96) Meulemans et al., 1997; Charlier et al., 1998	Involved in injury accidents (2-wheelers and cars)	1,879 (out of 2,143)	Test: urine FPIA Confirmation: urine SM/CG (and urine/blood comparison)	(urine) 6.0% (blood) 3.6%
Spain (1994-96) Alvarez et al., 1997	Drivers killed and suspected of being under the influence.	979	Test: blood immunoassay Confirmation: blood SM/CG	1.5%
Italy (1978-1988) Ferrera, 1990	Injured drivers Tested on a Friday evening	4,350 500	Test: urine EMIT	5.5%
Norway (1993) Christophersen (1995)	Injured in non-fatal accidents	394	Test: blood immunoassay Confirmation: blood SM/CG	7.5%
UK (1996-1999) Tunbridge et al., 2000	Victims of fatal accidents (incl. 516 drivers)	1,138 516	Test: urine immunoassay Confirmation: blood SM/CG	12.0% 10.0%
Netherlands (2000-2001) Movig et al., (2004)	Injured drivers Town of Tilburg	110 (68 blood and 42 urine)	Test : urine EMIT or blood EIA Confirmation: blood or urine SM/CG	12.0%

Table 2: Detection and prevalence of cannabis in drivers involved in accidents in France.

Reference country	Study group	Sample size	Detection method	Prevalence of cannabis	
France Scherman, 1992	Drivers hospitalised after an accident (1989-1990)	2,471	Test: plasma immunoassay (without confirmation)	6.3%	
France Pélissier et al., 1996	Injured drivers aged 18 to 35 (and control group: hospitalised patients)	60 (296)	Test: urine FPIA Confirmation: urine SM/CG	10.0% (12.0%)	
France Marquet et al., 1998	Injured drivers aged 18 to 35 (and control group: hospitalised patients)	296 (278 controls)	Test: urine FPIA Confirmation: urine SM/CG	13.8% (7.6%)	
France Mura et al. (1999)	Involved in a serious or fatal injury accident (with presumption)	169	No test Confirmation: blood SM/CG	26.0%	
France Kintz et a. (2000) (Rosita project)	Involved in injury accidents	198	Test: urine FPIA Confirmation: urine and blood SM/CG, saliva and sweat tests	(urine) 13.6% (blood) 9.6%	
France Mura et al. (2001)	Injured in a injury accident (hospitalised)	420	No test Confirmation: blood SM/CG THC and/or THC-COOH	11.2%	
	Controls: hospitalised patients	381		10.8%	
France Mura et al. (2003)	Injured in a (non-fatal) accident, June 2000-Sept. 2001	900 of which: 321 <27 years	No test Confirmation: blood SM/CG THC > 1 ng/ml (only) THC (>1) + alcohol (> 0.5 g/l) THC > 1 ng/ml (only or associated)	<27 years 15.3% 9.5% 24.8%	All ages 10%
	Controls: hospitalised patients	900 of which: 310 < 27 years	No test Confirmation: blood SM/CG THC > 1 ng/ml (only) THC (>1) + alcohol (> 0.5 g/l) THC > 1 ng/ml (only or associated)	<27 years 6.7% 2.2% 8.9%	All ages 5%
France Pépin et al. (2003)	Requisitions after involvement in a fatal accident, Oct. 2001-Oct. 2002	3,851	No test Confirmation: blood SM/CG THC >1 ng/ml and/or THC-COOH	<27 years 27.2%	All ages 13.8%
France Laumon et al. (2005)	Involved in a fatal accident Oct. 2001- Sept. 2003	10,748	Confirmation: blood SM/CG THC > 1 ng/ml (only) THC (>1) + alcohol (> 0.5 g/l) THC > 1 ng/ml (only or associated)	 4.2% 2.8% 7.0%	
France Mura et al. (2005)	Killed in an injury accident and aged under 30 Jan. 2003- Dec. 2004	2,003 (all under 30)	No test Confirmation: blood SM/CG THC-COOH THC > 0.2 ng/ml	<30 years 40.0% 28.9%	

FPIA: Fluorescence polarisation immunoassay; SM/GC Mass spectrometry gaseous chromatography; EIA: Enzyme Immunoassay; EMIT: Enzyme multiplied immunoassay technique; THC: Δ^9-THC

Table 3: Detection and prevalence of cannabis outside Europe (USA, Australia and Canada) in drivers involved in accidents.

Reference country	Study group	Sample size	Alcohol	Cannabis	Alcohol if cannabis (%)
New Zealand (1979-80) Bailey, 1987	Injured	901	20%	7%	29%
Canada (1982-1984) Cimbura et al., 1990	Killed	1,169	57%	11%	84%
Australia (1983-1984) McLean et al., 1987	Injured and killed	200	75%	6%	67%
USA (1985-1986) Soderstrom et al.,1988	Injured	393	35%	32%	51%
USA, 1987-1988 Crouch et al. (1993)	Killed truck drivers	168	13%	13%	20%
Australia (1989-1990) Gerostamoulos et al. (1993)	Killed	193		11%	11%
USA (1990-1991) Soderstrom et al., 1995	Injured		37%	12%	
Australia (1990-1993) Drummer, 1994	Killed	1,045	36%	11%	59%
USA (1992-1993) Logan et Schwilke, 1996	Killed	347	48%	11%	63%
Australia (1995-1996) Hunter et al.,1998 or Longo et al. , 2000a	Injured (non-fatal accidents)	2,500	12%	11%	28%
Australia (1990-1999) Drummer et al. 2004	Killed 1990-1999	3,398	29%	13.5% (1)	
	Killed 1998-1999	Not available		8.5% (2)	43%

According to Bates and Blakely, 1999; Drummer et al., 2003
(1) Positive for THC or THC-COOH;
(2) Positive only for THC

Table 4: Detection and prevalence of cannabis in Europe and Canada: in drivers NOT involved in accidents.

Country and reference	Study group	Detection method	Sample size	Prevalence (%)
Excluding drivers with presumption of driving under the influence of psychoactive substances				
Germany (1992-94) Kruger et a ,1995	All drivers	Test: saliva FPIA Confirmation: saliva SM/CG	2,234 (out of 3,027)	0.6%
Netherlands Mathtijssen et a. 1998	Night-time and weekend drivers	Test: simultaneous saliva, sweat and urine tests	293 (out of 402)	5.0%
Italy (1994-1995) Zancaner et al., 1995	Night-time and weekend drivers	Clinical tests Clinical and toxicological verification (blood, urine)	1,237	1.5%
Canada (1999-2001) Dussault et al., 2002	Drivers on the road (representative survey, 11,952 altogether)	Urine Saliva Breathed air (alcohol)	5,931 8,177 11,574	6.7%
Netherlands (May 2000-August 2001) Movig et al. (2004)	Drivers Town of Tilburg	Confirmation: urine (85%) or blood (15%)	816	6.0%
Based on drivers with presumption of driving under the influence of psychoactive substances				
Norway (1994) Skurtveit et al., 1996	Drivers	Test: blood immunoassay Confirmation: blood SM/CG	2,529	26.0%
Denmark Worm et Steentoft, 1996	Drivers	Test: blood immunoassay Confirmation: blood SM/CG	 317 221	 10.0% 17.0%
UK, Scotland (1995-98) Seymour et Oliver,1999	Drivers	Test: blood immunoassay Confirmation: blood SM/CG	640	26.0%

Sources: Groupe Pompidou (1999), Dussault et al. (2002), Seymour and Oliver (1999), Movig et al. (2004)

Table 5: Responsibility and cannabis-related odds ratios according to the main studies: "cases = responsible / controls = not responsible", according to completed Bates and Blakely (1999).

Reference	Study group	Biological fluid and substance	Psychoactive Substance	Unadjusted Odds ratio	Confidence interval
Terhune et Fell , 1982 USA	497 injured	Blood Alcohol >1g/l THC, THC-COOH	Alcohol Cannabis Alcohol and cannabis	5.4 2.1 NA	2.8 -10.5 0.7 – 6.6
Williams et al., 1985 USA	440 killed (deceased within 2 hours)	Blood Alcohol > 0 THC, THC-COOH	Alcohol Cannabis Alcohol and cannabis	5.0 0.5 8.6	2.1 -12.2 0.2 - 1.5 3.1 - 26.9
Terhune et al., 1992 USA	1,882 killed (deceased within 4 hours)	Blood Alcohol >1g/l THC, THC-COOH	Alcohol Cannabis Alcohol and cannabis	7.4 0.7 8.4	5.1-10.7 0.2 - 1.8 2.1-72.1
Schermann, 1992 France	2,471 hospitalised casualties	Blood	Alcohol Cannabis Alcohol and cannabis	NA 1.1 6.9	
Drummer, 1994 Australia	1,045 killed (several states)	THC-COOH urine and sometimes blood (little THC) Alcohol >0	Alcohol Cannabis Alcohol and cannabis	5.5 0.7 5.3	3.2 - 9.6 0.4 - 1.5 1.9- 20.3
Longo et al., 2000 Hunter et al., 1998 Australia	2,500 injured	Blood THC, THC-COOH	Alcohol Cannabis Alcohol and cannabis	6.8 0.9 11.5	4.3 - 11.1 0.6 - 1.2 4.6 - 36.7
Dussault et al, 2002 Canada	354 killed	Blood Alcohol > 0,8 g/l THC-COOH	Alcohol Cannabis Alcohol and cannabis	2.3 1.2 NA	1.0 - 5.3 0.4 - 3.9
Drummer et al., 2004 Australia	3,998 killed	Blood Alcohol >= 0.5 THC	Alcohol Cannabis (THC) Alcohol and cannabis	6.0 2.7 NA	4.0 - 9.1 1.0 - 7.0
Laumon et al. (2005) France	10,748 involved in accidents (killed, injured or unharmed)	Blood Alcohol > 0 THC > 0	Alcohol Cannabis (THC) Alcohol and cannabis	8.5 1.8 14.0	7.1 - 10.1 1.4 - 2.2 8.0 - 24.7

Cannabis: THC or THC-COOH (unless explicitly mentioned)

Table 6: Dose-response odds-ratio.

	Reference category	THC (ng/ml)	Odds ratio	Confidence interval (95%)	Adjustment variables
Longo et al. (1998) 88 drivers THC-positive	Without THC or alcohol or any other drug	< =1 1.1-2 >=2	0.3 0.5 1.7	0.02 - 2.2 0.2 - 1.4 0.6 - 5.7	
Drummer et al (2004) 58 drivers THC-positive	Without THC or alcohol or any other drug	positive > = 5 (serum)	2.7 6.6	1.02 - 7.0 1.5 - 28.0	age, sex, type of accident, state, year , alcohol, other illicit drug
Laumon et al (2005) SAM study 759 drivers THC-positive	Without THC	<1 1-2 3-4 >=5 (whole blood)	1.6 1.5 2.1 2.1	0.8 - 3.0 1.1 - 2.2 1.2 - 3.7 1.3 - 3.2	alcohol, age, vehicle type, crash time period (day/night and weekday/week-end)

NB: 1 ng/l whole blood = 2ng/l serum

Table 7: Cannabis-related odds ratios according to the main studies "cases =injured or killed – controls =not involved in accidents".

Reference	Study group Cases/ controls	Detection environment	Substances	Odds ratio	Confidence interval
Dussault et al., 2002 Quebec, Canada	354 killed/ 11,574 controls on the road	Blood Alcohol >0,8g/l	Alcohol Cannabis Alcohol (>0,8g/l) and cannabis	9.2 2.2 80.5	6.8- 12.5 1.5 - 3.4 28.2 -230.2
Mura et al., 2003 France	injured/ 900 hospitalised controls		Alcohol Cannabis Alcohol and cannabis	2.5	
Movig et al. ,2004 Netherlands	110 injured/ 816 controls on the road		Alcohol Cannabis Alcohol and cannabis	1.2	0.5 - 2.7