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Role of Cannabis in Motor Vehicle Crashes

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INTRODUCTION

The use of cannabis is widespread throughout the world, and in many countries is increasing (1). After alcohol, the most frequently found psychoactive substance in the blood of motorists involved in traffic crashes is cannabis. The very high costs, in human and financial terms, of road traffic crashes underscores the need for a clear understanding of the contribution of cannabis use to the incidence of such crashes. If cannabis were demonstrated to be an independent risk factor for such crashes, then efforts to prevent driving after recent cannabis use could be justified.

Evidence accumulated over the last half-century or more has clearly demonstrated the relation between blood alcohol concentration (BAC) and the risk of a serious road traffic crash. Significant impairment of driving skills begins at a BAC of about 50 mg/100 ml blood and increases exponentially with increasing BAC (2). This has led to various jurisdictions imposing maximum blood alcohol concentrations for legal driving. However, the relations between driving impairment and blood concentrations of other drugs, including cannabis, have not been so well established, and the legal responses have varied.

The World Health Organization recently convened an Expert Working Group on Health Effects of Cannabis Use. This committee's report states: "There is sufficient consistency and coherence in the evidence from experimental studies and studies of cannabinoid levels among crash victims to conclude that there is an increased risk of motor vehicle crashes among persons who drive when intoxicated with cannabis" (1, p. 15). However, the references cited in support of this statement were for experimental studies and descriptive studies of cannabis prevalence in drivers. In themselves, such studies do not establish a causal association between cannabis use and motor vehicle crashes. We sought to carry out a more appropriate evaluation, using information provided by analytical epidemiologic studies. Such studies are more relevant to the question of whether cannabis, including cannabis in combination with alcohol, has a role in the causation of motor vehicle crashes.

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Abbreviations: BAC, blood alcohol concentration; CI, confidence interval; COOH-THC, 11-nor-Δ-9-carboxy tetrahydrocannabinol; 11-OH-THC, 11-hydroxy-tetrahydrocannabinol; SDLP, standard deviation of lateral position; THC, Δ-9- tetrahydrocannabinol.

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METHODS

This review primarily involves consideration of all available published analytical studies of the relation of cannabis use (with and without alcohol consumption) to driving behavior/motor vehicle crashes, with a particular emphasis on study design issues. To provide appropriate background, the following issues are summarized relatively briefly:

- the behavioral and cognitive effects of cannabis;
- the relation between cannabis biomarkers and intoxication or functional impairment;
- experimental studies of the impact of cannabis (with and without alcohol) on performance, particularly driving behavior; and
- prevalence studies of cannabis (with and without alcohol) in drivers.

Heterogeneity of odds ratios was assessed using Woolf's method (3).

RESULTS

Psychopharmacologic effects of cannabis

Cannabis, in its various forms (marijuana, hashish, and hash oil) is derived from the plant *Cannabis sativa*, and may be absorbed into the body by inhalation of smoke or by ingestion. The acute affects of cannabis on the user are well known and include mild euphoria, relaxation, increased sociability, heightened sensory perception, and increased appetite. Short-term psychomotor and cognitive effects related to the use of cannabis include impaired memory, altered perception

of the passage of time, and impaired performance in a wide variety of tasks, including handwriting and motor coordination tests (1).

Experimental studies of the combined effects on performance measures of cannabis and alcohol have indicated that generally the effects of the two substances are additive, although low doses of cannabis may be antagonistic to the effect of alcohol (4).

Biomarkers of cannabis use in relation to impairment

Although there are more than 60 cannabinoid chemicals present in cannabis products, the major psychoactive agent is Δ-9- tetrahydrocannabinol (THC). This is metabolized in the body to 11-hydroxy-tetrahydrocannabinol (11-OH-THC), which is also psychoactive. 11-OH-THC is further oxidized to 11-nor-Δ-9-carboxy-tetrahydrocannabinol (COOH-THC), which is not psychoactive and is the main urinary metabolite. Blood THC levels fall rapidly to about 10 percent of peak concentration 1 hour after smoking. One study found biphasic half-lives of 0.1 hours and 1.3 hours for THC in blood (5). COOH-THC appears in blood for several hours after smoking marijuana, and well after the psychoactive effects have worn off (6). COOH-THC can appear in urine for several days after cannabis has been smoked (7).

The finding of certain levels of THC in blood can probably be used to impute that cannabis has recently been used (8). Although there is some experimental evidence that the level of performance in certain psychomotor tasks is related to plasma THC level, no relation between blood levels of THC or its metabolites and motor vehicle driving performance has been demonstrated (5). Given the rapid decline in blood THC levels, a correlation with blood THC level would be extremely difficult to detect in a crash driver population, unless blood sampling occurred very close in time to the crashes.

Experimental studies of cannabis and driving impairment

Experimental studies have been carried out in controlled or laboratory situations to measure the psychomotor effects of cannabis use. These tests have usually taken place in driving simulators or in controlled on-road situations.

Sutton (9) carried out a study using nine male volunteers who were experienced cannabis users. The study had a randomized cross-over design in which the subjects were given alcohol/marijuana (or placebo) separately and in combination. It was found that only the combination of the two substances affected driving performance on a set course. The author suggested that the reason an effect of cannabis was not detected may have been because the course contained insufficient maneuvers that would have tested perception and attention. Also, results might have been different with subjects naïve to marijuana use.

Smiley (10) reviewed the results of seven studies of driving simulator performance and six studies (not including Sutton (9)) of on-road driving performance (almost all on closed courses) of people under the influence of cannabis and alcohol. The results of the studies were reasonably consistent and highlighted differences between the effects of alcohol and cannabis. Alcohol use generally led to an increase in speed, whereas marijuana was associated with a decrease in speed. Following cannabis use, subjects were unlikely to engage in overtaking, whereas the opposite was the case for alcohol. Following distance was also increased while under the influence of cannabis.

A number of the reviewed studies investigated the response of drivers to subsidiary task requirements in an effort to simulate the normal requirements of drivers to monitor pedestrians, other traffic, and the environment while directing the car along its course. Both alcohol and cannabis were found to increase reaction time and increase the number of initially incorrect responses. Emergency response behavior was impaired by cannabis, although when subjects on cannabis were given some warning as to when they would have to respond they were usually able to make the correct response.

Unlike alcohol, marijuana use was not associated with prolonged impairment. Other than in the initial test shortly after smoking, none of the studies showed any longer term effect of marijuana on driving performance. Effects of alcohol persisted for several hours.

Smiley concluded that, although marijuana did appear to impair driving behavior, impairment was ameliorated by drivers' awareness that they were impaired, leading to compensatory, less risky behavior such as slower driving. However, such compensation was not effective when events were unexpected or when continuous attention was required.

More recent studies have generally confirmed Smiley's conclusions. Robbe and O'Hanlon (11) found that marijuana affected maintenance of a steady position within lane boundaries. This was evaluated in terms of the standard deviation of lateral position (SDLP), which increased with marijuana intake in a dose-related fashion. As in previous studies, drivers compensated their driving performance for anticipated effects of marijuana smoking, but were unable to fully compensate for marijuana's adverse effects on SDLP. This was explained as being because SDLP is primar-

ily controlled by an information-processing function that operates outside of conscious control. By contrast, other driving performance measures, such as following distance and speed, depend more on conscious information processing, and are more accessible to compensatory mechanisms.

Robbe and O'Hanlon concluded that drivers under the influence of marijuana tend to overestimate the adverse effects of the drug on their driving ability and compensate when they can (e.g., by slowing down), whereas drivers under the influence of alcohol tend to underestimate their impairment and do not compensate.

Overall, the results of these experimental studies are consistent; they show impairment of driving ability by cannabis. However, cannabis-using drivers are aware that they are impaired and compensate their driving behavior accordingly. Compensation might not be so successful in emergency situations or during long, monotonous periods of driving.

Prevalence of cannabis use among motor vehicle drivers

Prevalence studies indicate the extent to which substances (including alcohol and cannabis) are present in the blood of drivers, including drivers involved in crashes. However, in the absence of comparable data from an appropriate driver comparison group, results of prevalence studies cannot be taken to imply anything about the role of cannabis or other drugs in causing traffic crashes.

Results of prevalence studies are shown in table 1. The list of studies summarized is not exhaustive. However, we believe it is reasonably representative of prevalence studies that have been carried out.

The studies summarized in table 1 are not directly comparable in that they report different cutoff points for defining alcohol use and have used methods with different sensitivities and specificities for THC and/or its metabolites. Also, the time periods following crashes within which blood samples were collected varied between studies. Nonetheless, consistent features have been: 1) after alcohol, cannabis use has been the psychoactive substance for which most evidence of prior use has been found among both fatally and nonfatally injured drivers, and 2) often a substantial proportion of drivers with biomarkers for cannabis use have evidence of some level of alcohol consumption.

Studies of the relation between cannabis use and motor vehicle crashes

This section summarizes and evaluates the evidence for a role of cannabis, alone and in combination with alcohol, in the causation of traffic crashes. We first consider methodological issues, particularly study design; then key results of relevant studies are summarized and we review, respectively, the evidence for a role for cannabis alone and for the combination of cannabis and alcohol in the causation of motor vehicle crashes.

Study design/methodological issues. Investigation of the relation between cannabis and traffic crashes is difficult. Commonly, epidemiologic study of the association between possible risk factors and a rare event (such as a traffic crash, injury, or fatality) would involve a case-control study approach. For example, in

TABLE 1. Summary of prevalence studies of substances in the blood of motor vehicle drivers

Study (reference no.)	Years	Country/region	Driver type	No.	Substance present (%)		
					Alcohol*	Cannabis*	Alcohol and cannabis†
Bailey (24)	1979–1980	Waikato, New Zealand	Injured	901	20	7	29
Cimbura et al. (25)	1982–1984	Ontario, Canada	Killed	1,169	57	11	84
McLean et al. (26)	1983–1984	Tasmania, Australia	Injured and killed	200	75	6	67
Soderstrom et al. (27)	1985–1986	Baltimore, MD, USA	Injured	393	35	32	51
Christophersen et al. (28)	1986–1988	Norway	Suspected drunk	270	74	29	62
Crouch et al. (19)	1987–1988	Eight US states	Killed truck drivers	168	13	13	20
Gerostamoulos and Drummer (6)	1989–1990	Victoria, Australia	Killed	193		11	
Soderstrom et al. (29)	1990–1991	Baltimore, MD, USA	Injured		37	12	
Drummer (20)	1990–1993	Three Australian states	Killed	1,045	36	11	59
Logan and Schwilke (30)	1992–1993	Washington State, USA	Killed	347	48	11	63
Hunter et al. (22)	1995–1996	South Australia, Australia	Injured	2,500	12	11	28

* All drivers with evidence of substance present, irrespective of concentration and presence of other substances. For cannabis, includes Δ-9-tetrahydrocannabinol or its metabolites.

† As a proportion of drivers with evidence of cannabis use.

a study of risk factors for drivers in fatal traffic crashes it would be appropriate to match each fatally injured driver (case) with another driver (control) who happened to be passing the crash site at about the same time of day, say, a week later. Comparable data would be collected on the characteristics of the cases and the controls, including their driving behavior. Analysis of these data, controlling for confounding factors, would identify risk factors for the crashes.

Case-control studies have successfully identified a number of factors associated with traffic crashes, including speed and alcohol consumption. Investigation of the relation between crashes and alcohol use has been facilitated by the fact that it is possible to measure alcohol levels in breath. However, a standard case-control study approach is much more problematic with regard to investigation of the relation between cannabis and traffic crashes. The principal reason is that identification of cannabis (and other drug) use status would require a blood sample from the control driver. Whereas such a sample is commonly collected from a fatally-injured driver, and frequently from a non-fatally injured driver, it cannot ethically be coerced from a driver selected as a control. Because cannabis is an illicit substance, it is probable that potential controls who are cannabis-users would be more likely than nonusers to refuse to supply a blood sample. This would bias study results in the direction of showing a stronger positive association between cannabis and crash fatalities than would really be the case. Since, generally, the proportion of non-crash drivers with cannabis in their blood is likely to be small, even a relatively small proportion of potential controls who would not supply a blood sample would throw study results into serious doubt.

A possible alternative to blood sampling for a case-control study would be saliva sampling. Sensitive methods for analyzing cannabinoids in saliva now exist (12), and sampling of saliva would be more likely to be acceptable to randomly selected control drivers than would blood sampling. Despite this, saliva sampling has its problems. 1) Control drivers would have to give consent to provide a saliva sample, and this would be likely to reduce participation rate. 2) It appears that THC is sequestered into the salivary glands during eating or smoking cannabis, and there is no significant exchange of THC between saliva and blood. Thus, there is not necessarily any relation between THC levels in saliva and the degree of cannabis intoxication. 3) Little is known about the relation of salivary THC levels and frequency or timing of cannabis use in relation to saliva sampling. It may be that THC accumulates in saliva after regular heavy use. 4) Saliva levels would not necessarily be useful for identification of the presence of other psychoactive substances (which need to be taken into account in the analysis as possible confounding factors). 5) It would be difficult to obtain comparable saliva samples from dead drivers.

Because of the nonparticipation problem, the few studies that have attempted to determine the relation between cannabis use and traffic crashes have used a different, but related, study type—the culpability (or responsibility) analysis. Epidemiologically, the culpability analysis could be described as a case-case study (13), in which one group of cases is compared with another. In a culpability analysis, drivers involved in crashes are classified in terms of their responsibility for, or culpability in, the crash, using predetermined criteria. This classification should take place without knowledge of the drug/alcohol status of the driver; such knowledge could bias the classification process, particularly for marginal cases. At its simplest level, drivers may be judged culpable or not culpable for the crash. Analysis may then take place as for a case-control study, where the drivers who are considered culpable in the crash ("cases") may be compared with the drivers who are considered not to be culpable ("controls"). This analysis generates odds ratios with their associated confidence intervals.

If it were assumed that the group of nonculpable drivers in crashes is representative of the driving population at large, then the odds ratios from a culpability analysis could be considered to be estimates of the odds ratios that would be obtained from a case-control study using non-crash drivers as controls. However, there is evidence that the odds ratios from culpability analysis studies may tend to be closer to the null than odds ratios from corresponding case-control studies using controls selected from the general driver population (14). The discrepancy between the results of the two study designs is likely to be due primarily to two interrelated factors: 1) outcome misclassification in the culpability analysis study—determination of culpability status is not exact and some misclassification can be expected; if this is nondifferential, or there is a tendency to misclassify drivers who are in fact responsible for the crash as not being responsible for it, odds ratios for culpability studies would be biased toward the null, relative to case-control studies, for which outcome misclassification is not an issue; and 2) selection bias in that selection of the comparison group of "not culpable" drivers is not under the control of the study investigators. It may be that drivers involved in crashes, whether they be judged culpable or not, tend to be similar in terms of drug or alcohol use. If so, this would bias odds ratios for culpability studies towards the null relative to case-control studies.

Some culpability analysis studies, rather than dichotomizing the outcome (i.e., "culpable" or "not

culpable"), have assumed a gradient of degree of responsibility for a crash and assumed that some drivers may be only partly culpable for the crash. If drivers judged only partially responsible for the crash are eliminated from the analysis, this can help to minimize outcome misclassification.

As well as outcome misclassification, exposure misclassification bias is also potentially a problem for studies of the relation between cannabis and traffic crash risk (although this would similarly affect both case-control studies and culpability analysis studies). As THC is metabolized rapidly, it is necessary to take the blood sample within an hour or two of the crash in order to obtain a sample that is indicative of recent cannabis use. However, even if this occurs, the relation between blood concentrations of cannabinoids and psychoactive effects or functional impairment is not understood (see previous discussion). This could lead to classification together of cannabis users who were experiencing psychoactive effects at the time of the crash with those not experiencing such effects.

In general, confounding is likely to be a lesser problem in studies of the relation between cannabis and traffic crash risk than selection and misclassification biases. It could occur if there are nonmeasured lifestyle factors associated with cannabis use that are independent risk (or protective) factors for traffic crashes. Also, since alcohol is found so commonly in association with other drugs, confounding by alcohol is a potential problem. Alcohol is such a strong determinant of road traffic crash risk that when it is in combination with other drugs the interactive or independent effect of the other drug(s) is likely to be obscured (15). This problem can be avoided by excluding subjects with alcohol present in their blood from statistical analyses of the risks associated with other substances. This leads to a further problem, limited statistical power to investigate the relation of drugs with crashes. Since psychoactive drugs are so often found in combination with alcohol, the number of drivers without alcohol and with a single other drug (including cannabis) in their blood tends to be small (15).

The impact these issues may have on interpretation of study results is discussed below in relation to the evidence for a contribution to crash risk of cannabis alone and of the cannabis-alcohol combination.

Studies that have investigated the association between cannabis and traffic crashes. There have been a number of studies that have investigated the association between cannabis use and traffic crashes. These are briefly outlined, in date order of publication.

Terhune and Fell (16) studied culpability rates in 497 drivers injured in traffic crashes and hospitalized in Rochester, New York. An analysis of the data in the report, based on calculation of odds ratios, is presented in table 2. This shows elevated odds ratios for crashes associated with both alcohol and cannabis alone. Data that would have permitted the calculation of an odds ratio for the combination of alcohol and cannabis were not presented, although the culpability rate for alcohol and cannabis together was said to differ little from that for alcohol alone.

Williams et al. (17) studied fatally-injured motor vehicle (excluding large truck) drivers in four California counties, who died within 2 hours of the crash (to minimize effects of metabolism and elimination on drug concentrations). Classification of culpability was based on a system that assigned probable culpability of a driver based on the diagram and narrative descriptions of the crash provided by the investigating officer. A total of 23 drugs or drug groups were examined. THC and COOH-THC were determined in blood samples.

There were 440 drivers eligible for inclusion for whom adequate blood samples were taken. Drugs were detected in 81 percent of drivers, two or more drugs being present in 43 percent. Alcohol was present in 70 percent of drivers, cannabinoids in 37 percent, and cocaine in 11 percent. Each of 24 other substances detected was present in less than 5 percent of drivers.

Logistic regression analysis, taking into account driver age, BAC, and THC concentration, was reported as showing that alcohol was related to crash culpability, but cannabis was not. Detailed results of the logistic regression analysis were not provided in the report.

Using data presented in the report we have calculated unadjusted odds ratios, with associated confidence intervals, for the relation between crash culpability and cannabis alone, alcohol alone, and cannabis and alcohol present together (table 3).

Results in table 3 confirm the well-established association between alcohol and crash culpability, and suggest that cannabis alone is associated with a decreased risk, although the confidence interval includes 1.0. The effect of the combination of alcohol and cannabis is

TABLE 2. Unadjusted odds ratios for nonfatally injured drivers*

Substance(s)	No. of drivers		Odds ratio†	95% confidence interval
	Culpable	Not culpable		
Drug free	94	179	1.0	
Alcohol only‡	45	16	5.4	2.8, 10.5
Cannabis only	9	8	2.1	0.7, 6.6
Total	148	203		

* Based on data reported by Terhune and Fell (16).
† Relative to drug free.
‡ Blood alcohol concentration ≥100 mg/100 ml.

TABLE 3. Unadjusted odds ratios for fatally injured drivers*

Substance(s)	No. of drivers		Odds ratio†	95% confidence interval
	Culpable	Not culpable		
Drug free	55	23	1.00	
Alcohol only	120	10	5.0	2.1, 12.2
Cannabis only	10	9	0.5	0.2, 1.5
Alcohol and cannabis	123	6	8.6 1.7‡	3.1, 26.9 0.5, 5.9
Total	308	48		

* Based on data reported by Williams et al. (17).
† Relative to drug free (unless otherwise indicated).
‡ Alcohol and cannabis together relative to alcohol only.

greater than that of alcohol alone, but not to a degree that is statistically significant. Distinguishing a difference between the alcohol-only group of drivers and the alcohol-cannabis group is made difficult by the very high culpability rate of the alcohol-only group.

Terhune et al. (18) carried out a culpability analysis study of 1,882 drivers killed in motor vehicle crashes in seven US states during 1990–1991. Alcohol was found in 51.5 percent of specimens and other drugs in 17.8 percent. Evidence of prior use of cannabis was found for 6.7 percent, two-thirds of whom were positive for alcohol also. Table 4 shows unadjusted odds ratios calculated from the data presented for this study.

The odds ratios in table 4 suggest that cannabis alone may be associated with a reduced risk of culpability for a crash fatality, and that the combination of alcohol and cannabis may be little worse than alcohol alone. However, again, the latter conclusion is clouded by the high culpability rate of the drivers with alcohol only.

A possible problem with this study is that drivers were eligible for the study if they died within 4 hours of the crash. This means that, for some subjects, considerable metabolism and elimination of drugs and alcohol could have taken place after the crash and before death and collection of postmortem blood samples. As discussed below, this could have biased the results in the direction of not detecting associations between drugs and crash culpability.

TABLE 4. Unadjusted odds ratios for fatally injured drivers*

Substance(s)	No. of drivers		Odds ratio†	95% confidence interval
	Culpable‡	Not culpable		
Drug free	541	258	1.0	
Alcohol only§	587	38	7.4	5.1, 10.7
Cannabis only¶	11	8	0.7	0.2, 1.8
Alcohol and cannabis¶	35	2	8.35 1.1#	2.1, 72.1 0.3, 10.1
Total	1,174	306		

* Based on data reported by Terhune et al. (18).
† Relative to drug free (unless otherwise indicated).
‡ Includes drivers who were judged culpable or culpable/contributory.
§ Blood alcohol > 100 mg/100 ml.
¶ Includes only drivers with Δ-9-tetrahydrocannabinol (with or without 11-nor-Δ-9-carboxytetrahydrocannabinol) present.
# Alcohol and cannabis together relative to alcohol only.

Crouch et al. (19) investigated drugs and alcohol in 168 fatally injured truck drivers. This study involved assessment of crash culpability through a detailed on-site crash investigation, specimen collecting and toxicology testing, and development of a detailed factual report of the crash. This information was supplied to a panel of pharmacologists and toxicologists who reviewed it to determine whether impairment by drugs or alcohol was likely to have contributed to the crash. In the 14 cases in which THC was found, the panel concluded that drivers were impaired by cannabis.

This study suffers from the problem that the panel made its decisions on crash culpability in full knowledge of blood THC concentrations. Although other information on the crash circumstances was also considered, it is very likely that the assignment of crash culpability was strongly influenced by beliefs of panel members concerning the effects of THC on driving ability. Although the drivers with THC detected in their blood may indeed have been responsible for crashes, the type of analysis carried out does not, in itself, establish that cannabis was contributory.

Drummer (20) carried out a culpability analysis study using data on 1,045 drivers killed in motor vehicle crashes in the Australian states of New South Wales, Victoria, and Western Australia during 1990–1993. The extent of cannabis testing varied between states: usually COOH-THC was measured in urine and, in some cases, also in blood. In a relatively few cases THC was measured in blood.

The method of culpability analysis used in this study has been described in detail (21). Briefly, it involved calculating a score for each of the drivers based on consideration of eight possible mitigating factors. A mitigating factor was a condition that was out of the control of the driver at the time of the crash. Such factors included the condition of the road, the condition of the vehicle, and the weather conditions at the time. Three categories were defined, based on arbitrary cut-off points for the calculated score: culpable, not culpable, and contributory. The latter category implied partial culpability.

Overall, the drivers ranged from 15 to 87 years (mean 34 years), and 49 percent had at least one drug (including alcohol) detected. Blood alcohol was present in 375 (36 percent) of the cases, with 97 percent of these exceeding the Australian legal limit for drinking and driving (50 mg/100 ml blood). The average blood

alcohol concentration, when alcohol was present, was 180 mg/100 ml. Evidence for the presence of cannabinoids was found for 112 (11 percent) of the cases.

Culpability analysis of the data was based on calculation of odds ratios and confidence intervals. In addition to the comparison of culpable and nonculpable drivers set out in the original study report, we have done further analysis that combines drivers judged contributory with those judged culpable, and compares this combined group with the nonculpable group. The results of these analyses are included in table 5.

Overall in table 5, it makes little difference to the results whether drivers judged 'contributory' are included in the culpable group or not. However, analysis I appears to have marginally more power to detect an association. This is probably to be expected, as it is likely that there would be some outcome misclassification when 'contributory' subjects are included in either the culpable or nonculpable group.

On the basis of these considerations, the results of analysis I only are considered below.

The largest study that has investigated this issue involved 2,500 hospitalized injured drivers in South Australia, where blood sampling is mandatory for hospitalized road crash victims (22). Culpabilty was assessed using the method of Robertson and Drummer (21). Odds ratios calculated from the presented data are shown in table 6.

This report is a valuable source of data, and it is possible to separately examine the effects of THC and of COOH-THC, including risks at different serum concentrations of these substances. The odds ratio associated with THC alone is marginally less than that with COOH-THC when there was no detected THC. Odds ratios increase with increasing serum THC concentration. The pattern with COOH-THC is less clear.

A limitation of the results in tables 2–6 is that the effects of cannabis and alcohol were not adjusted for potential confounding factors, particularly age and sex. However, a more recent publication by Drummer (23) contains odds ratios, adjusted for age and sex by logistic regression. For cannabis, the adjusted odds ratio for all drivers, comparing culpable with nonculpable, was 0.6 (95 percent confidence interval (CI): 0.3, 1.0), and for alcohol 7.6 (95 percent CI: 4.6, 12). These results, which differ little from the unadjusted values in table 5, suggest confounding by age or sex is not likely to be an explanation for the findings.

Evaluation of the relation between cannabis (alone) and traffic crashes. As discussed above, there are five studies that have presented data that can be used to address the question of whether cannabis use affects traffic crash risk. Three of these studies have been of fatally injured drivers, and two of non-fatally injured drivers. All three fatal injury studies suggest that cannabis use is associated with a reduced risk of culpability for a traffic fatality, and there is no evidence of heterogeneity of the odds ratios for cannabis alone from the three fatal injury studies ($p > 0.80$). Therefore, the odds ratios for the three studies were combined to give a Mantel-Haenszel weighted odds ratio of 0.59 (95 percent CI: 0.35, 1.00; $p = 0.05$).

Superficially, the results of the two studies of non-fatally injured drivers are contradictory. The earlier study indicated an elevated risk compared with drug-free drivers (16), whereas a reduced risk was apparent in the most recent study (22). The odds ratio in the most recent study was the more precise, with an upper confidence interval bound of 1.24. This suggests the odds ratio of 2.1 (95 percent CI: 0.7, 6.6) found in the study by Terhune and Fell (16) may have been a consequence of the small sample size of that study.

A possible interpretation for these results, consistent with the experimental evidence, is that cannabis-intoxicated drivers modify their driving behavior to compensate for their perceived impairment. This

TABLE 5. Unadjusted odds ratios for fatally injured drivers*

Substance(s)	No. of drivers			Analysis I†		Analysis II‡	
	Culpable	Contributory	Not culpable	Odds ratio§	95% confidence interval	Odds ratio§	95% confidence interval
Drug free	339	53	140	1.0		1.0	
Alcohol only	245	16	17	6.0	3.5, 10	5.5	3.2, 9.6
Cannabis only	21	8	14	0.6	0.3, 1.2	0.7	0.4, 1.5
Alcohol and cannabis	54	5	4	5.6	2.0, 1.6	5.3	1.9, 20.3
				0.9¶	0.3, 4.0	1.00¶	0.3, 4.1
Total	659	82	175				

* Using data from Drummer (20).
† Culpable versus not culpable (results from report).
‡ Culpable plus contributory versus not culpable (calculated from data in report).
§ Relative to drug free (unless otherwise indicated).
¶ Alcohol and cannabis together versus alcohol alone (calculated from data in report).

TABLE 6. Unadjusted odds ratios for hospitalized injured drivers*

Substance(s)	No. of drivers		Odds ratio†	95% confidence interval
	Culpable	Not culpable		
Drug free	944	821	1.00	
Alcohol only	173	22	6.84	4.27, 11.06
Cannabis only‡	83	81	0.89	0.64, 1.24
THC (any)	21	23	0.79	0.42, 1.50
≤1.0 ng/ml	5	2	0.35	0.03, 2.13
1.1–2.0 ng/ml	12	7	0.51	0.17, 1.41
≥2.1 ng/ml	6	12	1.74	0.60, 5.67
COOH-THC	62	58	0.93	0.63, 1.37
1–10 ng/ml	24	19	0.69	0.36, 1.32
11–20 ng/ml	15	18	1.04	0.50, 2.19
21–30 ng/ml	12	12	0.87	0.36, 2.08
≥31 ng/ml	7	13	1.62	0.60, 4.80
Alcohol and cannabis‡	66	5	11.48	4.64, 36.66
			1.68§	0.59, 5.90
Total	1,266	929		

* Based on data reported by Hunter et al. (22).
† Relative to drug free (unless otherwise indicated).
‡ Includes both Δ-9-tetrahydrocannabinol (THC) and/or 11-nor-Δ-9-carboxytetrahydrocannabinol (COOH-THC).
§ Alcohol and cannabis together relative to alcohol only.

means that they seldom take risks and tend not to drive at speeds likely to result in fatalities or serious injuries. It is still possible that, despite their slower speeds, such drivers may be sufficiently impaired that their crash rate is increased—leading to minor injuries and vehicle damage, rather than deaths and serious injuries.

Consideration needs to be given as to whether the observed reduced risk for causing fatality could be due to chance, selection bias, information bias, or confounding. That the apparent reduction in risk associated with cannabis alone could be due to chance cannot be entirely excluded, as none of the observed odds ratios were statistically significantly different from 1.0. Despite this, there is a consistency in the results which, in itself, argues in favor of a true effect. However, potentially, consistent results from epidemiologic studies can be caused by a common bias or confounding factor, and we consider this possibility below.

Selection bias could have occurred in the fatal crash studies if, for example, only some fatally injured drivers had blood samples taken (and, hence, were eligible for entry into the study). This is possible, as police are more likely to require blood samples to be taken if they have reason to suspect the involvement of drugs, or particularly alcohol (because of its smell), in the crash. It is not unlikely that this could reduce the proportions of drug-free and cannabis-only drivers, relative to the number of alcohol-consuming drivers, in the overall study samples. However, this would be unlikely to influence the relative culpability rates of the drug-free and cannabis-only groups, and, hence, should not bias the odds ratios.

There is also the possibility that the probability of blood sampling might be influenced by the attending police officer's impressions of the degree of culpability of the driver. However, again, provided that the officer's impressions were not differentially affected by the cannabis status of the driver, this should not bias the odds ratio. In South Australia the law requires a blood sample to be taken from all hospitalized injured drivers, so no such bias would be likely in the recent study of injured drivers (22).

Information bias may be a more likely possibility. This occurs when study subjects are misclassified in terms of outcome (i.e., culpable or not culpable) or in terms of exposure status (presence or absence of alcohol or a drug). Misclassification of outcome is likely in some cases. Decisions on whether drivers should be considered to be responsible for their crashes are subjective and depend on the completeness and veracity of the information available. Different criteria for deciding on culpability have been used by the different studies, and this could have led to variations between the studies in terms of the groups being compared. Similarly, there is likely to have been misclassification of cannabis exposure status. There are two main reasons for exposure misclassification: 1) In some studies there may have been delays of up to several hours between the crash and the death of the driver. Since metabolism and elimination of cannabis can be expected to continue

at least until death occurs, the postmortem blood sample may not be indicative of what was in the driver's blood at the time of the crash. This means that some of the "drug-free" drivers may, in fact, have had detectable cannabis levels at the time of the crash. 2) It is the case that COOH-THC can persist for days after smoking, long after the psychoactivity has ceased. Thus, some drivers may have been classified as under the influence of cannabis at the time of the crash, when, in fact, there could have been no cannabis impairment.

It is likely that the second of these two possibilities will be most important. Cannabis metabolites (if not THC itself) persist for some time after consumption, and anyone who was under the influence of cannabis shortly before they crashed would be likely to show evidence of this, provided death occurred within a few hours of the crash (the studies of Williams et al. (17) and Terhune et al. (18) imposed requirements of driver death within 2 and 4 hours of the crash, respectively, although the situation with the study of Drummer (20) is less clear). On the other hand, because of the persistence of metabolites, it is likely that some drivers who had consumed cannabis up to a few days before the crash would still show postmortem evidence of metabolites, even though they could not have been cannabis-impaired at the time of the crash.

On the assumption that culpability is assessed blind to cannabis use status, both outcome-misclassification and exposure-misclassification biases would probably have the effect of biasing observed odds ratios toward unity. Potentially, such biases (particularly exposure-misclassification bias) could account for a lack of observed association between cannabis use and traffic crash fatality risk. However, the biases would be expected to cause the observed odds ratios to be closer to 1.0 than the true values, and would not have the effect of reducing the odds ratios from above 1.0 (implying a causal relation) to below 1.0 (implying reduction in risk). The fact that, for all three fatal crash studies and the largest injury study, the observed odds ratios are below 1.0 suggests that the true effect of cannabis is to reduce the risk of killing or seriously injuring oneself in a traffic crash, although the studies probably underestimate the actual degree of risk reduction. In other words, the estimated odds ratios, for cannabis alone of around 0.6 for fatal crashes and 0.9 for injury crashes, may be higher than the true odds ratios.

Confounding occurs when a true risk factor for an outcome (in this case, culpability for a crash) is also correlated with the exposure of interest (in this case, cannabis use). If confounding occurred it could cause a spurious association with the exposures of interest. Potentially, this could occur if, for example, another exposure factor, correlated with cannabis use was itself protective against traffic fatalities, and thereby responsible for the observed results. This would be possible if cannabis-only users tended to have other lifestyle factors that reduced their chances of involvement in traffic crashes.

Taking into account the results of the observational studies and the experimental studies with driving simulators and controlled driving situations, it is plausible that cannabis, in the absence of other psychoactive substances, particularly alcohol, has no positive association with, and may even reduce, overall traffic crash fatality and serious injury risk. However, even if this is the case, it does not necessarily follow that the risk of less serious injury and non-injury crashes is unaffected or reduced by cannabis consumption. Cannabis users may be more likely to drive slowly than drug-free drivers. Since there is a strong relation between vehicle speed and the likelihood of fatality or degree of injury in a crash, slower driving may reduce the crash fatality and serious injury rate in cannabis consumers. However, impairment induced by cannabis may still increase the overall risk of a crash, and this possibility cannot be excluded by the studies of fatally and seriously injured drivers alone. The fact that in the studies considered above the reduction in risk for fatalities in cannabis users was less than the reduction in risk of serious injuries would be consistent with an hypothesis of cannabis use being associated with reduced consequences of traffic crashes, but not necessarily with a reduction in the risk of traffic crashes themselves.

Evaluation of the relation between combined consumption of cannabis and alcohol and traffic crashes. There have been one non-fatal injury and three fatality studies that have provided evidence on whether combined impairment by cannabis and alcohol affects traffic crash risk, relative to impairment by alcohol alone (17, 18, 20, 22). Again, there is no statistical evidence of heterogeneity of odds ratios across the three studies of fatally injured drivers ($p > 0.70$), and we have combined the results of the three studies. The Mantel-Haenszel weighted odds ratio was 1.26 (95 percent CI: 0.62, 2.83; $p = 0.61$). This compares with the odds ratio of 1.68 in the non-fatal injury study (table 6).

This provides some evidence that the effect of the combination of cannabis and alcohol may be worse than the effect of alcohol alone, at least for crash fatalities and serious injuries. Possible inference is limited for reasons to do with both statistical power and with bias or confounding.

Firstly, as discussed in an earlier section, because of the very high rate of culpability of the alcohol-only

group, the culpability analysis method has little statistical power to discriminate combined drug-alcohol effects from the effects of alcohol alone. It is possible that cannabis potentiates the risk of alcohol use, such that lower levels of alcohol, when combined with cannabis, have a risk equivalent to higher levels of alcohol use. This possibility can be investigated by stratifying culpability analysis data by blood alcohol level. Data stratified by blood alcohol level, permitting exploration of this possibility, have been presented for three of the culpability analysis studies. Using the data presented in the study reports, we have calculated odds ratios for the combined presence of cannabis and alcohol relative to the presence of alcohol only for the various strata. Results are set out in table 7.

Table 7 is equivocal in regard to whether cannabis potentiates the effect of alcohol. For the two fatal crash studies, the odds ratios decrease with increasing alcohol concentration, as would be expected if potentiation occurred. However, with the non-fatal injury study, odds ratios generally increased with increasing alcohol concentration. Caution is warranted as the number of nonculpable subjects in most exposure groups was very small, and the odds ratios are correspondingly imprecise. They would be compatible with no effect occurring.

Secondly, there is the possibility of bias or confounding influencing the results in table 7. Misclassification bias may operate in similar ways to those described in relation to cannabis only. The main effect of exposure misclassification would probably be to misclassify some drivers, who were under the influence of alcohol only at the time of the crash as being under the combined influence of alcohol and cannabis. Outcome misclassification bias would occur as previously described. The overall effect would be to bias odds ratios toward 1.0. It is unlikely that selection bias would have a significant effect on the results. An influence of confounding could occur if there are fatal injury risk factors differentially associated with alcohol use and combined alcohol-cannabis use. At this stage it is not clear what these risk factors would be.

Overall, we conclude that the weight of the evidence indicates that:

1) There is no evidence that consumption of cannabis alone increases the risk of culpability for traffic crash fatalities or injuries for which hospitalization occurs, and may reduce those risks.
2) The evidence concerning the combined effect of cannabis and alcohol on the risk of traffic fatalities and injuries, relative to the risk of alcohol alone, is unclear.
3) It is not possible to exclude the possibility that use of cannabis (with or without alcohol) leads to an increased risk of road traffic crashes causing less serious injuries and vehicle damage.

TABLE 7. Unadjusted odds ratios for the alcohol-cannabis combination, by blood alcohol concentration

Study (reference no.)	Alcohol (mg/100 ml)	Cannabis present	Culpable	Not culpable	Odd ratio	95% confidence interval
Williams et al. (17)	<100	Yes	14	1	2.55	0.22, 134
		No	22	4		
	100–140	Yes	19	1	2.45	0.18, 137
		No	23	3		
	≥150	Yes	51	2	1.02	0.11, 12.6
		No	75	3		
Terhune et al. (18)	<100	Yes	7	1	2.23	0.27, 104
		No	91	29		
	≥100	Yes	55	3	1.19	0.36, 6.2
		No	587	38		
Hunter et al. (22)	<50	Yes	5	3	0.83	0.13, 6.50
		No	20	10		
	50–79	Yes	7	1	0.93	0.04, 62.84
		No	15	2		
	80–149	Yes	24	0	NC*	
		No	58	7		
	≥150	Yes	30	1	1.13	0.09, 61.00
		No	80	3		

* NC, not able to be calculated because of zero in cell.

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